Prescribing Outlook

New Medicines

September 2015

A resource for the NHS to help with budget setting, prescribing planning and medicines management.

UKMi
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NHS

Contents

Foreword

Managing new medicines

Underpinning the strategic direction for managing new medicines is the Department of Health's (DH) report Innovation Health and Wealth, Accelerating Adoption and Diffusion in the NHS. It sets out government support for the NHS to embrace innovation to meet current and future healthcare challenges, and outlines the importance of early adoption and uptake of clinically and cost effective innovative practices, including medicines. Horizon scanning is essential for this process at many organisational levels so new medicines that have been shown to improve patient outcomes can be planned for and adopted. Increasing financial pressure facing the NHS means it is even more important that the introduction of new medicines is actively managed.

Funding of medicines in the NHS is inextricably linked to the national tariff payment system. Monitor, in conjunction with NHS England, is responsible for the National Tariff of NHS prices which includes producing the 'High Cost Drugs' (HCD) list for drugs that are not funded within Tariff. This year (2015-16) two national tariff systems are operating; the Enhanced Tariff Option (ETO) and the Default Tariff Rollover (DTR) option for trusts who opted out of the ETO. This has implications for funding drugs as financial flow could differ depending on which Tariff a particular Trust is operating to; in particular, the HCD list will differ slightly. Throughout this document when it is stated a drug is a 'Specified high cost drug' it is the ETO HCD list 2015-16 used as reference. Those Trusts on the DTR option should refer to the 2014-15 HCD list. Many drugs on these lists are not yet available in the UK but are included so that commissioners and providers can start a dialogue about funding in advance of launch. In *Prescribing Outlook,* for medicines not listed on the ETO HCD list, an 'educated guess' regarding potential tariff positioning has been made.

NHS England has a strategic medicines management role and is responsible for commissioning most high cost drugs as well as all cancer chemotherapy. An updated list has recently been published (March 2015) of medicines not reimbursed through national prices that are used in the delivery of services directly commissioned by NHS England. The list outlines mechanisms for funding, highlights which drugs have been appraised by NICE, which are formally commissioned via policies and those which require an Individual Funding Request (IFR). In addition, it highlights which drugs are managed by specialist centres and which may be suitable for shared care between the specialist centre and secondary care. There is a move for CCGs to take on more commissioning of specialised services and therefore associate drug costs so the latest available list should be used.

Funding for most cancer drugs differs and involves use of the Cancer Drugs Fund (CDF) for drugs that have yet to be appraised by NICE. The CDF has undergone significant review this year and is likely to undergo further significant change following recent publication of an independent cancer taskforce report which proposes it becomes a 'managed access' fund that could support data collection in advance of NICE appraisal. In *Prescribing Outlook* the current CDF status is highlighted.

Inevitably, more expensive medicines will receive most attention but a comparatively cheaper drug could still have a big financial impact in the NHS if used in a large number of patients. *Prescribing Outlook* includes such drugs but quantifying their impact is difficult. However, there are other mechanisms in place at a national level to mitigate the financial impact of such drugs.

The mechanism agreed between the government and the pharmaceutical industry for setting the NHS cost of new drugs is known as the Pharmaceutical Price Regulation Scheme (PPRS). This scheme is negotiated every five years. The latest scheme PPRS 2014 is very different to previous schemes. A question and answer document outlines how it operates. Pharmaceutical companies decide whether to join the PPRS scheme. If they decide not to join they are subject to the alternative statutory scheme which imposes a price cut on individual medicines of 15% of their NHS list price. If they join the scheme they are subject to an overall aim of limiting growth of NHS spending on branded medicines. Growth in the branded medicines bill above the agreed level will result in a 'PPRS Payment' being made by pharmaceutical companies back to the DH with payments based on the difference between the agreed forecast and the allowed growth level. The overall allowed growth rate in the NHS branded medicines bill is 0% for the first two years and then only a small growth rate (less than 2% per year) for the remaining three years of the current scheme. Future payments will be adjusted if actual growth is above or below the agreed forecast. There are exclusions to this; further detail is in the question and answer document. The scheme has been in operation for over a year now and, up to end of March 2015, a total of £517 million has been paid back to the DH.[1] The rebate is divided across the home countries according to primary care spend on licensed branded medicines. In Scotland, the money will go into a New Medicines Fund, set up last year to support funding for orphan, ultra-orphan and end-of-life drugs for patients. In England, a proportion of the rebate has been allocated to NHS England.

A further mechanism for reducing the cost of new medicines to the NHS is use of a Patient Access Scheme (PAS) for those undergoing a NICE technology appraisal. This allows NICE to recommend treatments that it might otherwise not find cost effective. PAS are either cost (discounts, free stock, etc.) or outcome (price variation linked to patient outcomes) based but the finer details are confidential. A list of NICE technologies with an approved PAS can be viewed on the NICE website. In *Prescribing Outlook* current PAS schemes are highlighted if they are relevant to a new medicine in the same therapeutic area, and, although this will not give an indication of the likely cost of the new medicine, it suggests that subsequent treatment options will have to be competitive.

In addition to producing technology appraisals, NICE supports uptake of guidance and implementation of appraisal outcomes with a number of tools. In *Prescribing Outlook* there are links to a therapeutic area overview page on NICE Evidence from which all relevant tools and details of guidance and appraisals in progress can be accessed. Anticipated publication dates of NICE technology appraisals are subject to change but up-to-date information can be accessed from the overview page.

There have also been changes in regulatory processes impacting on availability of new drugs in the UK following launch of the early access to medicines scheme (EAMS). This scheme is operated by the MHRA and aims to give patients with life threatening or seriously debilitating conditions access to medicines that do not yet have a licence when there is a clear unmet medical need. It does not replace the normal licensing systems but will mean that a small number of medicines will be available to patients earlier than normally anticipated. A few drugs have already been awarded promising innovative medicine (PIM) designation; the first stage of the

EAMS process. Whether a PIM designation has been awarded or not is only known if the company chooses to publicise it.

At the other end of the lifecycle of a drug, biosimilar and generic medicines introduce competition into the market resulting in lower costs to the NHS. Biosimilars are also driving development of new formulations from the originator manufacturer but, unlike traditional generic drugs, they are more costly to develop and take longer to license. It is estimated about 50% of the current UK market for biological medicines spend may be subject to biosimilar competition by 2019 and is a significant growth area.[2] Unlike chemical generic drugs, biosimilars are not exactly interchangeable with the originator product and therefore need to be more actively managed into the NHS. *Prescribing Outlook* highlights which biosimilars are in development and when the originator patent expires so that managed entry can be planned.

About Prescribing Outlook publications

The aim of the annually published *Prescribing Outlook* series, produced by UK Medicines Information (UKMi), is to assist NHS organisations plan, implement and budget for new medicines or licence extensions and national guidance. It provides support to commissioners and providers by highlighting new medicines and service developments that may have financial and operational resource implications. The *Prescribing Outlook* series is produced for primary and secondary care NHS organisations and has a national perspective. The content and presentation of the series has evolved over the years following consultation with users.

This document is the first in the annually published series that comprises *Prescribing Outlook - New Medicines* and *Prescribing Outlook - National Developments,* and is supported by an electronic *Cost Calculator.* These are all available at www.ukmi.nhs.uk. The component documents of the *Prescribing Outlook* series are published each autumn in line with annual budget planning timeframes and key outputs from NICE. Updates on progress of individual medicines at other times throughout the year can be found in the UKMi *New Drugs Online* (NDO) database.

Further specialist medicines information not included in the series can also be obtained from local and regional medicines information centres. See www.ukmi.nhs.uk.

Prescribing Outlook – New Medicines.

This publication primarily aims to provide advance information about new medicines (and new licensed indications or formulations) with anticipated market launches in the next 18 to 24 months (2015, 2016 or 2017).

The content is not comprehensive but focuses on medicines with the potential for significant clinical or financial impact on the NHS. Estimates of potential uptake, patient, service and financial implications are included where possible. Reference is made to relevant national guidance and links to in-depth independent reviews are included, where available.

How is the content for pipeline drugs decided?

Various criteria are applied to prioritise those medicines in the pipeline likely to have the largest impact. These include considering whether:

- *the medicine is expected to provide a significant improvement in disease management,*
- *the medicine is first-in-class or has a major new indication,*
- *there are limited alternatives,*
- *the medicine cost will be high,*
- *the target population is large,*
- *there is likely to be a significant effect on service implications e.g. route/ formulation/ method of delivery,*
- *the medicine or disease area is an NHS priority,*
- *the medicine has significant additional indications in the advanced pipeline stage,*
- *the medicine is in the EU licensing process,*
- *there is likely to be significant media interest.*

There will be additional, unquantifiable, factors that have implications for the NHS such as local demographics and prescribing preferences which cannot be accommodated in a national document.

How is the content for pipeline drugs (Table 1) presented?

Monographs are organised by BNF category. Within each BNF category, monographs are further subdivided by commissioning route in England and then collated by indication to highlight developments for a particular condition. This enables readers to more easily focus on which drugs are a priority for managed entry into the NHS.

For individual drugs there are three types of monograph:

Detailed monograph – for launches anticipated in 2015 or 2016 (except chemotherapy drugs).
Abbreviated monograph – for launches anticipated in 2017 and for all chemotherapy drugs.
Biosimilar monograph – for all biosimilar drugs in development with potential to launch on the UK market between 2015 and 2017. Many biosimilars in world-wide development could obtain a licence within this timeframe but if the originator product patent is still in force in the UK then launch is not possible so they have not been included. The fields in these monographs have been tailored to the nature of information needed for managed entry of biosimilar products into the NHS.

All entries are linked to *New Drugs Online* (NDO) monographs for more detailed information that is updated more frequently.

The layout of each monograph in *Prescribing Outlook – New Medicines* facilitates conversion to an Excel spreadsheet to be published shortly after publication of *Prescribing Outlook – New Medicines*.

What other information is in Prescribing Outlook – New Medicines?

As drugs move from clinical trials through the licensing process inevitably some don't make it to market. Some will have been highlighted in previous editions of *Prescribing Outlook* so are included in a table (Table 2) just for information. In addition, brief details of drugs launched in the last 12 months are included (Table 3) as this is often useful for local planning purposes.

As in previous editions of *Prescribing Outlook*, drugs with patents due to expire in the near future are highlighted. It is important that generic options are considered as part of the wider medicines management agenda. This document includes an 'educated guess' as to which drugs have potential for generic competition and an indication as to whether generic product licence applications are currently in progress in the EU.

More detailed information on the medicines listed can be obtained from the UKMi *New Drugs Online* (NDO) database which can be accessed directly from the generic name hyperlink in this document.

Please direct comments on *Prescribing Outlook – New Medicines* to the editor: Helen Davis, North West Medicines Information Centre, Pharmacy Practice Unit. helen.davis@lrippu.nhs.uk.

Other UKMi horizon scanning resources

Prescribing Outlook – New Medicines (Excel spreadsheet) content based on this document. Access is via www.ukmi.nhs.uk.

Prescribing Outlook – National Developments estimates the impact on clinical practice and prescribing budgets of national guidance, mainly that issued by NICE. It is intended to inform discussions between commissioners and providers, and highlight issues around implementating guidance. Access is via www.ukmi.nhs.uk.

Prescribing Outlook – Cost Calculator is an Excel spreadsheet tool to facilitate estimates of potential prescribing changes for a local population. Access is via www.ukmi.nhs.uk.

Please direct comments on *Prescribing Outlook – National Developments* and the *Cost Calculator* to: Devika Sennik or David Erskine, London and South East Medicines Information Centre, Guy's and St. Thomas' NHS Foundation Trust. devika.sennik@gstt.nhs.uk, david.erskine@gstt.nhs.uk

New Drugs Online (NDO) database includes information on medicines in clinical development from late phase II trials to product launch and includes links to evidence-based reviews up to one year post launch. This database is maintained by UKMi and forms the basis of the content of *Prescribing Outlook – New Medicines*. It is updated daily and can be used to produce reports based on a number of criteria including possible launch date, stage of clinical development or pharmaceutical company. Access is free to all with an NHS email address via www.ukmi.nhs.uk but requires individual registration. Limited access is freely available to non-registered users via Evidence Search (www.evidence.nhs.uk).

Please direct comments and enquiries on *New Drugs Online* (NDO) to: nwmedinfo@nhs.net.

1. DH June 2015. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/433013/PPRS_Q1_2015.pdf
2. Anon. What are biosimilars and are they important? Drug and Therapeutics Bulletin 2013; 51(5): 57-60.

The information in these resources is the best available at the time of publication but is subject to significant change with time.

If you have any comments about any aspect of the Prescribing Outlook series please let us know at:
https://www.surveymonkey.com/r/NCNQW3M

Abbreviations

AWMSG	All Wales Medicines Strategy Group
BNF	British National Formulary
CCG	Clinical Commissioning Group
CCP	Clinical commissioning policy
CDF	Cancer Drug Fund
DH	Department of Health
EMA	European Medicines Agency
EU	European Union
HRG	Healthcare Resource Group (definition)
i.m.	Intramuscular
i.v.	Intravenous
L(C)NDG	London (Cancer) New Drugs Group
LMEN	London Medicines and Evaluation Network
MHRA	Medicines and Healthcare products Regulatory agency
MTRAC	Midland Therapeutics Review & Advisory Committee
NDO	New Drugs Online
NHSE	NHS England
NIHR HSRIC	National Institute for Health Research-Horizon Scanning Research and Intelligence Centre
NICE	National Institute for Health and Care Excellence
NICE-ES	NICE Evidence Summary
NNH	Number needed to harm
NNT	Number needed to treat
ns	Not significant
NTAG	Northern Treatment Advisory Group
PAS	Patient Access Scheme
RDTC	Regional Drug & Therapeutics Centre, Newcastle
s.c.	Subcutaneous
SIGN	Scottish Intercollegiate Guidelines Network.
SMC	Scottish Medicines Consortium
SmPC	Summary of Product Characteristics
TBC	To be confirmed
UKMi	United Kingdom Medicines Information
US	United States

Key

Generic name and formulation *[Brand name];* Company *Medicines* are listed by BNF category and linked to relevant publicly available pages of the NDO database. The *company* that holds marketing rights in the EU is listed together with a co-promoter company if relevant.	
Pharmacology:	Therapeutic class and/or mode of action and administration details.
Indication:	Indication for the product. The closer the drug is to launch, the more specific this can be.
Current status:	*PII/III* – in phase two/three trials. *Filed* – licence application has been submitted. *Recommended for approval* – opinion of the advisory committee of the licensing authority is that the medicine should be licensed. In the EU a full licence is likely within three months. *Licensed* – the product has been granted a marketing licence. The company determines launch date. *Launched* – the medicine is marketed in the UK. If launched elsewhere in the world, but not the UK, there are links to prescribing data. Some drugs are assigned a special status by regulatory authorities which can affect speed of progress to market and accessibility prior to full licensing. *Promising innovative medicine (PIM)* designation and Early Access to Medicines Scheme (EAMS) opinion are only relevant to the UK (see page 1 for more detail). *Orphan status – EU and US,* see definition. US expedited programmes: *Breakthough therapy* status – evidence indicates substantial improvement over existing therapies on clinically significant outcomes; *Fast-track status* – potential to address unmet needs; *Priority review* – significant improvement in safety or effectiveness. EU authorities grant similar expedited review status but less often and with less publicity than in the US. US data are included to highlight significance.
UK availability:	Authors' informed estimate based on public domain information and knowledge of regulatory processes and timescales. This is easier to predict when a product enters the licensing process as known time frames apply. After a licence is granted the company decides when and where to launch; if it is a licence extension, the product is available immediately for prescribing. In terms of biosimilar products, this date is linked to the patent expiry of the originator product (see below).
Reference product & company:	Only relevant for biosimilar drugs.
Patent expiry of reference product	Only relevant for biosimilar drugs. Although a biosimilar product can undergo clinical study and obtain a licence at any time, it can only be launched on the UK market when the UK or EU patent (including any supplementary patent protection) has expired. Therefore this date is pivotal to estimating UK availability of the competitor biosimilar product.
Population:	Data on prevalence (number with the disease) and incidence (number of new cases each year) are reported for a 100,000 population, if possible.
Sector:	An indication of which sector in the NHS the medicine is likely to impact, at least initially.
Implications:	Factors highlighted include patient options, monitoring or testing requirements and service implications related to medicine delivery.
Financial:	In assessing cost implications assumptions are made about place in therapy and whether it will displace, compete with or be added to existing therapy. In addition, it is difficult to quantify likely uptake of the medicine. For launched products, costs are taken from latest published NHS costs. Where a patient access scheme (PAS) may apply, this is indicated.
Tariff:	Actual or anticipated tariff position based on historical assumptions. For drugs not yet launched this becomes an educated guess. Drugs previously referred to as 'PbR exclusions' are now known as 'Specified high cost drugs'. If a drug is not likely to be specified as a high cost drug it is therefore, by default, likely to be included within tariff and will be listed as 'HRG included'. Where a drug already appears in the High Cost Drugs list this applies to the 2015-16 version applicable to the Enhanced Tariff Option (ETO); those Trusts not on the ETO should refer to the 2014-15 High Cost Drugs list.
CDF:	Only for chemotherapy drugs, an indication of its listing in the Cancer Drugs Fund list.
Efficacy:	Key studies with a link to trial details, especially when relevant for licence application. Primary outcome data and patient, rather than disease, orientated outcomes are preferentially included where available.
Safety:	For medicines already marketed for other indications, a link to product information is included. For new medicines, information is included where it is thought adverse effects reported to date may influence licensing requirements e.g. increased monitoring, or where they differ significantly from those associated with current treatments.
Guidance:	*England*: **NICE** - National Institute for Health and Care Excellence: www.nice.org.uk, **NHSE** - NHS England: www.england.nhs.uk. Links to relevant Clinical Commissioning Policies (CCP) included. *Scotland*: **SMC** - Scottish Medicines Consortium: www.scottishmedicines.org.uk, SIGN - Scottish Intercollegiate Guidelines Network: www.sign.ac.uk *Wales*: **AWMSG** - All Wales Medicines Strategy Group: www.wales.nhs.uk/awmsg
Reviews:	***Reviews:*** Independent national and regional reviews published between 2013 and 2015. L(C)NDG - London (Cancer) New Drugs Group LMEN - London Medicines Evaluation Network MTRAC - Midlands Therapeutics Review & Advisory Committee: mtrac.co.uk NICE-ES - NICE Evidence Summaries produced by NICE Medicines and Prescribing Centre. A critical review of evidence but it is not NICE guidance. NIHR-HSRIC NIHR Horizon Scanning Research & Intelligence Centre: hsric.nihr.ac.uk RDTC - Regional Drug & Therapeutics Centre, Newcastle: rdtc.nhs.uk NTAG - Northern Treatment Advisory Group: ntag.nhs.uk

Summary of predicted launch dates

This list summarises the ***earliest*** predicted UK launch date for pipeline drugs listed in **Table 1 – Pipeline drugs and biosimilars.** Refer to the index for a full list of generic and proprietary names. The timeframe for inclusion of drugs in this document is likely launch 2015 to 2017.

*Indicates which drugs have been assigned orphan status in the EU (see definition page 7).

BNF	Drug	Indication	Comm iss-ioner?	Page
2015				
2	clevidipine	Hypertension	CCG	11
2	propranolol	Haemangioma	CCG	11
2	alirocumab	Hyper-cholesterolemia	CCG	14
3	mepolizumab	Asthma	NHSE	17
3	lumacaftor/ ivacaftor	Cystic fibrosis (CF)	NHSE	19
4	guanfacine	Attention-deficit hyperactivity disorder	CCG	21
4	tasimelteon *	Insomnia, blind adults	CCG	21
4	capsaicin patch	Diabetic neuropathy	CCG	22
4	safinamide	Parkinson's disease	CCG	24
4	dextro-methorphan / quinidine	Pseudobulbar affect	CCG	26
4	naltrexone/ bupropion	Obesity	CCG	26
5	levofloxacin *	Pseudomonas infection in CF	NHSE	31
6	empagliflozin/ metformin	Type 2 diabetes	CCG	35
6	bazedoxifene/ conjugated estrogens	Menopausal symptoms	CCG	39
8	dinutuximab *	Neuroblastoma	NHSE	41
8	ceritinib	Non-small cell lung cancer (NSCLC)	NHSE	42
8	crizotinib	NSCLC	NHSE	42
8	sonidegib	Basal cell carcinoma	NHSE	48
8	trametinib	Malignant melanoma	NHSE	48
8	cobimetinib	Malignant melanoma	NHSE	49
8	talimogene laherparepvec	Malignant melanoma	NHSE	49
8	blinatumo-mab *	Acute lymphoblastic leukaemia	NHSE	50
8	carfilzomib *	Multiple myeloma	NHSE	50
8	panobino-stat *	Multiple myeloma	NHSE	50
8	bendamustine hydrochloride	Non-Hodgkin's lymphoma	NHSE	52
9	sebelipase alfa	Lysosomal acid lipase deficiency	NHSE	54
9	alipogene tiparvovec	Lipoprotein lipase deficiency	NHSE	55
10	ataluren *	Duchenne muscular dystrophy (DMD)	NHSE	61
11	aflibercept	Myopic retinal choroidal neovascularisation	CCG	64
13	afamelano-tide *	Erythropoietic protoporphyria	CCG	66
2016				
1	eluxadoline	Irritable bowel syndrome	CCG	8
1	ustekinumab	Crohn's disease	CCG	8
1	obeticholic acid *	Primary biliary cirrhosis	CCG	9
2	sacubitril/ valsartan	Heart failure	CCG	10
2	ticagrelor	Cardiovascular disease prevention	CCG	12
2	andexanet alfa	Anticoagulation reversal	CCG	13
2	idarucizumab	Anticoagulation reversal	CCG	13
3	house dust mite allergy vaccine	Allergic ashma and rhinitis	CCG	16
3	reslizumab	Asthma	NHSE	17
3	ataluren *	CF	NHSE	19
4	lurasidone	Bipolar depression	CCG	20
4	nabiximols	Cancer pain	CCG	22
4	botulinum A toxin [Dysport]	Limb spasticity post stroke	CCG	23
4	botulinum A toxin	Limb spasticity in cerebral palsy	CCG	23
4	opicapone	Parkinson's disease	CCG	24
5	actoxumab + bezlotoxumab	Clostridium difficile infection - prevention	CCG	28
5	amikacin liposomal *	Mycobacterial lung infection	CCG	29
5	amikacin liposomal *	Pseudomonas infection in CF	NHSE	30
5	tobramycin	Pseudomonas infection in CF	NHSE	30
5	isavucona-zole *	Mucormycosis	NHSE	31
5	isavucona-zole *	Aspergillosis	NHSE	32
5	tenofovir/ elvitegravir/ cobicistat/ emtricitabine	HIV infection	NHSE	32
5	sofosbuvir/ velpatasvir	Hepatitis C infection	NHSE	33
5	grazoprevir/ elbasvir	Hepatitis C infection	NHSE	33
6	dapagliflozin/ saxagliptin	Type 2 diabetes	CCG	34

6	empagliflozin/ linagliptin	Type 2 diabetes	CCG	35
6	omarigliptin	Type 2 diabetes	CCG	36
6	exenatide	Type 2 diabetes	CCG	37
6	anamorelin	Cancer cachexia	CCG	38
6	odanacatib	Postmenopausal osteoporosis	CCG	40
8	brain cancer vaccine *	Glioblastoma	NHSE	41
8	afatinib	NSCLC	NHSE	42
8	mereletinib	NSCLC	NHSE	43
8	necitumumab	NSCLC	NHSE	43
8	nivolumab	NSCLC	NHSE	43
8	pembrolizu-mab	NSCLC	NHSE	44
8	buparlisib	Breast cancer	NHSE	44
8	everolimus	Neuroendocrine tumours	NHSE	45
8	palbociclib	Breast cancer - second line	NHSE	45
8	palbociclib	Breast cancer - first line	NHSE	45
8	tipiracil/ trifluridine	Colorectal cancer	NHSE	46
8	cediranib *	Ovarian cancer	NHSE	46
8	apaziquone	Bladder cancer	NHSE	47
8	eribulin	Soft tissue sarcoma	NHSE	47
8	ipilimumab	Malignant melanoma	NHSE	49
8	nivolumab	Malignant melanoma	NHSE	49
8	vosaroxin *	Acute myeloid leukaemia	NHSE	50
8	daratumu-mab *	Multiple myeloma	NHSE	51
8	ixazomib *	Multiple myeloma	NHSE	51
8	elotuzumab *	Multiple myeloma	NHSE	51
8	chlor-methine *	Cutaneous T-cell lymphoma	NHSE	52
8	daclizumab	Multiple sclerosis	NHSE	52
9	mercaptamine bitartrate *	Huntington's disease	NHSE	55
10	certolizumab pegol	Rheumatoid arthritis (RA)	CCG	56
10	ixekizumab	Psoriatic arthritis	CCG	58
10	secukinumab	Psoriatic arthritis	CCG	58
10	apremilast	Psoriatic arthritis	CCG	59
10	secukinumab	Ankylosing spondylitis	CCG	59
10	lesinurad	Gout	CCG	60
10	drisapersen *	DMD	NHSE	61
10	idebenone *	DMD	NHSE	62
10	epratuzumab	Systemic lupus erythematosus (SLE)	NHSE	63
11	sirolimus *	Uveitis	CCG	64
11	autologous corneal cells *	Ocular burns	NHSE	65
13	ixekizumab	Psoriasis	CCG	67

2017

1	allogenic stem cells *	Perianal fistulas	CCG	9
1	tofacitinib	Ulcerative colitis	CCG	9
1	lubiprostone	Constipation in children	CCG	10
2	ticagrelor	Stroke prevention	CCG	12
2	bococizumab	Hyper-cholesterolaemia/ hyperlipidaemia	CCG	14
2	evacetrapib	Cardiovascular disease prevention and hyperlipidaemia	CCG	14
2	autologous stem cells	Heart failure	NHSE	15
2	ciclosporin	Myocardial reperfusion injury prevention	NHSE	15
3	beclo-metasone/ formoterol/ glycopyrrolate	Chronic obstructive pulmonary disease (COPD)	CCG	15
3	interferon beta 1a *	Respiratory distress syndrome	CCG	16
3	mepolizumab	COPD	CCG	16
3	benralizumab	Asthma	NHSE	18
3	lebrikizumab	Asthma	NHSE	18
3	masitinib	Asthma	NHSE	18
3	mepolizu-mab *	Eosinophilic granulomatosis	NHSE	18
3	VX-661/ ivacaftor	CF	NHSE	20
4	botulinum A toxin {Xeomin]	Limb spasticity post stroke	CCG	23
4	botulinum A toxin	Sialorrhoea	CCG	25
4	idalopirdine	Alzheimer's disease	CCG	25
4	leuco-methyl-thioninium	Alzheimer's disease	CCG	25
4	leuco-methyl-thioninium	Dementia	CCG	25
5	cadazolid	Clostridium difficile infection	CCG	28
5	eravacycline	Intra-abdominal infection	CCG	28
5	eravacycline	Urinary tract infection	CCG	29
5	omadacycline	Pneumonia	CCG	29
5	daclatasvir/ asunaprevir/ beclabuvir	Hepatitis C infection	NHSE	34
6	exenatide implant	Type 2 diabetes	CCG	37
6	elagolix	Endometriosis	CCG	39
6	odanacatib	Osteoporosis in men	NHSE	40
6	metreleptin *	Lipodystrophy	NHSE	40
7	ICES13	Urinary stress incontinence	CCG	41
8	nivolumab	Head and neck cancers	NHSE	42
8	atezolizumab	NSCLC	NHSE	43

8	defactinib *	Mesothelioma	NHSE	44
8	ganetespib	NSCLC	NHSE	44
8	regorafenib	Hepatocellular carcinoma	NHSE	45
8	nivolumab	Renal cell carcinoma	NHSE	46
8	atezolizumab	Bladder cancer	NHSE	47
8	custirsen	Prostate cancer - treatment	NHSE	47
8	evofosf-amide *	Soft tissue sarcoma	NHSE	48
8	inolimomab *	Graft versus host disease	NHSE	53
8	masitinib	Multiple sclerosis	NHSE	53
8	ocrelizumab	Multiple sclerosis	NHSE	53
9	CM-4612	Autism	CCG	53
9	eculizumab	Myasthenia gravis	CCG	54
9	biotin	Multiple sclerosis, primary progressive	NHSE	56
9	biotin	Multiple sclerosis, secondary progressive	NHSE	56
10	tofacitinib	RA, second-line	CCG	57
10	baricitinib	RA, second-line	CCG	57
10	tofacitinib	RA, methotrexate naïve	CCG	57
10	tofacitinib	Psoriatic arthritis	CCG	58
10	apremilast	Ankylosing spondylitis	CCG	60
10	canakinumab	TNF-Receptor Associated Periodic Syndrome	NHSE	62
10	eteplirsen *	DMD	NHSE	62
10	belimumab	SLE	NHSE	63
10	rigerimod	SLE	NHSE	63
11	pegpleranib	Age-related macular degeneration	CCG	65
12	esketamine	Tinnitus	CCG	66
13	dimethyl fumarate	Psoriasis	CCG	67

Uncertain

1	amoxicillin/ omeprazole/ rifabutin	Helicobacter pylori infection	CCG	10
2	vorapaxar	Cardiovascular disease prevention	CCG	12
3	tiotropium	Asthma (aged under 17 years)	CCG	15
5	dalbavancin	Skin infection	CCG	27
5	oritavancin	Skin infection	CCG	27
6	alogliptin/ pioglitazone	Type 2 diabetes	CCG	36
6	albiglutide	Type 2 diabetes	CCG	37
6	insulin inhaled	Type 1 and 2 diabetes	CCG	38
8	paclitaxel *	Ovarian cancer	NHSE	46

*Indicates which drugs have been assigned orphan status in the EU.

To qualify for orphan designation, a medicine must meet one of these criteria:

- It is intended for a life-threatening or chronically debilitating condition affecting no more than 5 in 10,000 (50 in 100,000) people in the EU;
- It is intended for a life-threatening, seriously debilitating or serious and chronic condition and without incentives it is unlikely that the revenue after marketing would cover the investment in its development.

The US definition of an orphan drug is different. It is defined as a rare disease occurring in less than 200,000 individuals. Assuming a US population of about 311 million this translates to a prevalence of about 65 in 100,000.

The definition of an ultra orphan condition used by NICE is a UK prevalence of less than 1 in 50,000.

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Table 1. Pipeline drugs

BNF 1. Gastrointestinal system

Likely CCG commissioned

Eluxadoline **oral** *[Viberzi];* Allergan	
Pharmacology:	Mu-opioid receptor agonist and delta opioid receptor antagonist, first-in-class.
Indication:	Irritable bowel syndrome (IBS), diarrhoea-predominant.
Current status:	Filed in EU June 2015. Licensed in the US May 2015 – see prescribing data.
UK availability:	2016
Population:	According to strict diagnostic criteria (Rome III), 5-11% of people suffer from IBS, although other estimates suggest 10-20% may be sufferers. Only about a third of those affected will seek help from their GP. About one third of patients have diarrhoea-predominant IBS.
Sector:	Primary care.
Implications:	IBS is a relatively common disease with limited treatment options. As first in a new class, eluxadoline could be useful, especially for patients with a poor response to loperamide.
Financial:	Eluxadoline will cost more than loperamide and be either added to, or used instead of, loperamide.
Tariff:	Likely HRG included.
Efficacy:	In PIII trials (IBS3001 and IBS3002, n=2,428) the primary outcome was a composite response based on abdominal pain and stool consistency. In study 3001, responder rates (weeks 1-26) were 29.3% for 100mg eluxadoline vs. 19.0% for placebo. In study 3002, responder rates were 32.6% and 20.2%, respectively (p=0.001 for both, NNT=8). In a published PII trial (n=807) more patients on 25mg (12.0%) or 200mg (13.8%) eluxadoline met the primary outcome of clinical response (mean reduction in daily pain score from baseline of ≥ 30%, and of at least 2 points on 0-10 scale, as well as a stool consistency score of 3 or 4 on the Bristol Stool Scale (1-7) for at least 66% of daily diary entries during that week) than patients on placebo (5.7%; p<0.05).
Safety:	Potential for clinically relevant drugs interactions including drugs metabolised by the CYP pathway.
Guidance	**NICE**: Irritable-bowel-syndrome.
Reviews:	NIHR HSRIC October 2014.

Ustekinumab **injection** *[Stelara];* Janssen	
Pharmacology:	Monoclonal antibody, interleukin antagonist, given i.v. (induction), then s.c. injection every 8 or 12 weeks.
Indication:	Crohn's disease, moderate to severe, treatment-refractory, in adults (license extension).
Current status:	PIII in EU.
UK availability:	2016
Population:	Estimates of UK prevalence of Crohn's disease are 50-100 per 100,000 people; 20% may have severe disease and up to 50% may be resistant to, or intolerant of, existing therapy, including TNF inhibitors.
Sector:	Secondary care.
Implications:	Likely to compete with i.v. vedolizumab as an option for patients with inadequate response to or intolerant of alternatives, including TNF inhibitors, administration by s.c. injection could be an advantage.
Financial:	As a further treatment option it will be additional to current costs. The annual cost of a maintenance dose of 90 mg every 8 or 12 weeks is about £17,200–£25,800.
Tariff:	Specified high cost drug.
Efficacy:	In the published PII CERTIFI study (n=526), 39.7% of patients receiving ustekinumab (6mg/kg, expected licensed induction dose) achieved clinical response at week 6 vs. 23.5% on placebo (p=0.005, NNT=6). The PIII UNITI-1 trial (n=769) in patients resistant to, or intolerant of, TNF inhibitors completed in July 2013, and the UNITI-2 (n=642) in patients resistant to, or intolerant of, conventional therapy or dependent on steroids completed in August 2014. Patients completing these can enter IM-UNITI maintenance trial.
Safety:	See medicines.org.uk.
Guidance	**NICE**: Inflammatory bowel disease.
Reviews:	NIHR HSRIC September 2014.

Allogenic stem cells injection *[Alofisel];TiGenix*	
Pharmacology:	Allogenic stem cells, expanded adipose-derived mesenchymal, first-in-class. Given by intralesional injection.
Indication:	Perianal fistula, complex and refractory to conventional and/or biologic agents in adults with Crohn's disease.
Current status:	PIII in EU with orphan status.
UK availability:	2017
Sector:	Secondary care.
Tariff:	Likely specified high cost drug.
Guidance:	**NICE**: Inflammatory bowel disease.
Reviews:	NIHR HSRIC March 2015.

Tofacitinib oral *[Xeljanz];* Pfizer	
Pharmacology:	Janus kinase inhibitor.
Indication:	Ulcerative colitis, moderate-to-severe active disease.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care.
Tariff:	Specified high cost drug.
Guidance:	**NICE**: Inflammatory bowel disease.
Reviews:	NIHR HSRIC April 2014.

Obeticholic acid oral*;* Intercept	
Pharmacology:	Modified bile acid, farnesoid X receptor agonist, first-in-class.
Indication:	Primary biliary cirrhosis (PBC), second-line.
Current status:	Filed in EU and US June 2015, with orphan status. Has fast track status in US.
UK availability:	2016
Population:	The estimated prevalence of PBC is 12,000 -15,000 in the UK. Most people with PBC are aged between 50 and 60 years; and around 90% of people with the condition are women.
Sector:	Secondary care initiated.
Implications:	Ursodeoxycholic acid (UDCA) is currently the only licensed therapy for PBC, but around 40% of patients have an inadequate response. Obeticholic acid (OCA) is intended for use in combination with UDCA in patients with an inadequate response (persistent elevation of alkaline phosphatase [ALP]) to UDCA alone, or as monotherapy in adults unable to tolerate UDCA.
Financial:	As a further treatment option this will be additional to current costs, but may reduce the need for liver transplantation.
Tariff:	Likely HRG included.
Efficacy:	In the PIII POISE study (n=217), OCA, met the primary composite outcome of a reduction in ALP <1.67x upper limit of normal and total bilirubin within normal limits at 12 months. The primary outcome was achieved in 47% and 46% in the OCA groups, respectively vs. 10% on placebo (both p<0.001 vs. placebo; NNT=3). Mean decrease in ALP from baseline was 39% and 33% vs. 5%, respectively (both p<0.001).
Safety:	Frequently reported adverse reactions include dose-dependent pruritus.
Guidance:	**NICE**: Liver conditions: general and other.
Reviews:	NIHR HSRIC December 2013.

Lubiprostone **oral** *[Amitiza]*; Sucampo Pharma	
Pharmacology:	Chloride channel activator.
Indication:	Chronic idiopathic constipation in children (licence extension).
Current status:	PIII
UK availability:	2017
Sector:	Secondary care initially.
Tariff:	HRG included.
Guidance:	**NICE:** Constipation.
Reviews:	None.

Amoxicillin/ omeprazole/ rifabutin **oral**; RedHill Biopharma	
Pharmacology:	Fixed-dose combination of two antibiotics and a proton pump inhibitor in a single capsule.
Indication:	*Helicobacter pylori* infection.
Current status:	EU status uncertain. PIII in US with Qualified Infectious Disease Product (QIDP) and fast-track status.
UK availability:	Uncertain.
Sector:	Primary care.
Tariff:	Likely HRG included.
Guidance:	**NICE**: Digestive tract conditions.
Reviews:	None.

BNF 2. Cardiovascular system

Likely CCG commissioned

Sacubitril/ valsartan **oral** *[Entresto];* Novartis	
Pharmacology:	Neprilysin inhibitor with an angiotensin receptor antagonist, first-in-class. Available as sacubitril/valsartan 24/26 mg, 49/51 mg, and 97/103 mg strengths.
Indication:	Chronic heart failure (HF), NYHA class II-IV and left ventricular ejection fraction <40%.
Current status:	Filed in EU February 2015 with promising innovative medicine status. Licensed in US July 2015 – see prescribing data.
UK availability:	2016
Population:	Around 800,000 people in the UK have HF and in England in 2013/14 about 65,000 people were admitted to hospital with HF. Up to 40% of patients diagnosed with HF die within the first year.
Sector:	Secondary care initiated, primary care continued.
Implications:	Established first-line options include ACE inhibitors, angiotensin receptor and beta-blockers. If the observed beneficial effects on mortality and hospitalisation can be achieved in clinical practice, this fixed dose combination has the potential to displace current options.
Financial:	Likely to be considerably more costly than generically available first-line options.
Tariff:	Likely HRG included.
Efficacy:	In the published PIII PARDIGM-HF study (n=8,442), sacubitril/valsartan (200mg twice daily) was compared to enalapril (10mg twice daily). The primary outcome was a composite of death from cardiovascular causes or first hospitalisation for worsening HF. The trial was stopped early as the boundary for an overwhelming benefit with sacubitril/valsartan had been crossed. At study closure, median follow-up 27 months, the primary outcome had occurred in 21.8% of patients receiving sacubitril/valsartan vs. 26.5% on enalapril (p<0.001, NNT=21). Death due to cardiovascular causes was 13.3% vs. 16.5% (NNT=32), and hospitalisation for heart failure 12.8% vs. 15.6%, respectively (NNT=36).
Safety:	The most common adverse events were hypotension, hyperkalemia, and renal impairment.
Guidance:	**NICE**: Heart failure. **SIGN**: Heart disease.
Reviews:	NIHR HSRIC July 2013.

Clevidipine injection *[Cleviprex];* The Medicines Company	
Pharmacology:	Ultra short-acting dihydropyridine calcium channel antagonist, given by i.v. infusion.
Indication:	Hypertension, perioperative.
Current status:	Licensed in UK November 2011- see prescribing data.
UK availability:	2015
Population:	At least 25% of patients undergoing noncardiac surgery have hypertension prior to their procedure. Perioperative hypertension occurs in 25% of hypertensive patients that undergo surgery.
Sector:	Secondary care.
Implications:	Clevidipine is one of only two drugs (the other being esmolol) licensed for the management of perioperative hypertension. Other unlicensed options include glyceryltrinitrate, nicardipine and sodium nitroprusside. Clevidipine may be of use in situations where stringent blood pressure control is required.
Financial:	Likely to be more expensive than available generic but unlicensed options.
Tariff:	Likely HRG included.
Efficacy:	Published results from 3 open-label PIII studies (ECLIPSE 1, 2 & 3), in 1,512 patients undergoing cardiac surgery suggest there was no difference in primary outcome events (death, MI, stroke or renal dysfunction at 30 days) between the clevidipine and the pooled comparator group (glyceryl trinitrate, sodium nitroprusside or nicardipine). Clevidipine was more effective than glyceryl trinitrate (p=0.0006) or sodium nitroprusside (p=0.003) in maintaining blood pressure within the prespecified range (secondary outcome).
Safety:	See medicines.org.uk.
Guidance:	**NICE**: Hypertension.
Reviews:	None recent.

Propranolol oral *[Hemangiol]*; Pierre Fabre	
Pharmacology:	Beta blocker.
Indication:	Infantile haemangioma (IH), proliferating, requiring systemic therapy.
Current status:	Licensed in EU May 2014 – see prescribing data.
UK availability:	2015
Population:	Around 3-5% of infants may be affected by IH; however, there are no reliable recent data. Older data may overestimate incidence due to differences in vascular birthmark stratification. Most cases do not require treatment, except where it is large, ulcerating, or interferes with important functions or development.
Sector:	Secondary care.
Implications:	This is the first drug licensed for this indication which may lead to more infants being treated. Current options included corticosteroids and propranolol products.
Financial:	Likely to cost considerably more than currently used unlicensed alternatives.
Tariff:	Likely HRG included.
Efficacy:	A published PII trial compared propranolol (2mg/kg/day) with placebo in 40 children aged between 9 weeks and 5 years. At week 24 the reduction in IH volume was 60% vs. 14%, respectively (p=0.01). A published PII/III study (n=456) compared four regimens (1 or 3 mg/kg/day for 3 or 6 months) to placebo. The primary outcome of complete or nearly complete resolution of IH at week 24 was 60% for propranolol 3mg/kg/day for 6 months vs. 4% for placebo (p<0.001, NNT=2). A systematic review of uncontrolled trials found a response rate of over 90%.
Safety:	See prescribing data. Blood pressure and heart rate is monitored after first dose and any dose increase.
Guidance:	None.
Reviews:	None.

Vorapaxar oral *[Zontivity]; MSD*	
Pharmacology:	Antiplatelet, thrombin receptor (PAR-1) antagonist, first-in-class.
Indication:	Reduction of atherothrombotic events in adult patients with a history of myocardial infarction (MI).
Current status:	Licensed in EU January 2015 – see prescribing data. Launched in US March 2015.
UK availability:	Uncertain.
Population:	About 103,000 people have an MI every year in the UK, and around 1.5 million people have had an MI.
Sector:	Secondary care initiated, continued in primary care.
Implications:	Likely to be added to existing therapies but bleeding risk could affect uptake.
Financial:	Likely to be considerably more expensive than current options.
Tariff:	Likely HRG included.
Efficacy:	In a published PIII study 26,449 patients with prior MI, stroke or peripheral artery disease received vorapaxar or placebo plus standard therapy. 3- year Kaplan Meier estimates for the primary outcome (cardiovascular death, MI or stroke) were 9.3% vs.10.5%, respectively (p<0.001, NNT=83). Equivalent figures for the licensed population (history of MI only, n=16,897) were 7.4% vs. 9.0% (p<0.001, NNT=63).
Safety:	3-year Kaplan Meier estimates for moderate/severe bleeding in the overall study population were 4.2% for vorapaxar vs. 2.5% for placebo (p<0.001, NNH=59). In the licensed subgroup, 3-year estimates were 3.1% vs. 2.2% (p<0.001, NNH=111).
Guidance:	**NICE**: Acute coronary syndromes. **SIGN**: Prevention of CV disease.
Reviews:	None recent.

Ticagrelor oral *[Brilique]*; AstraZeneca	
Pharmacology:	A reversible P2Y12 antagonist inhibiting adenosine diphosphate-mediated platelet aggregation.
Indication:	Secondary prevention post-myocardial infarction (MI), extended use (licence extension).
Current status:	Filed in EU early 2015.
UK availability:	2016
Population:	About 103,000 people have an MI every year in the UK, and around 1.5 million people have had an MI.
Sector:	Secondary care initiated, continued in primary care.
Implications:	Extended ticagrelor use is associated with an increased bleeding risk.
Financial:	This is recommended by NICE for 12 months post MI, extending use will be an additional cost.
Tariff:	HRG included.
Efficacy:	In a published PIII study, 21,162 patients with a history of MI 1-3 years previously received ticagrelor 90mg twice daily, 60mg twice daily or placebo, plus aspirin. After a median follow up of 33 months, the primary outcome (cardiovascular death, MI and stroke) occurred in 7.85%, 7.77% and 9.04%, respectively (p≤0.008 for both vs. placebo; NNT=84 and 79).
Safety:	See medicines.org.uk. In the published study major bleeding occurred in 1.06% on placebo vs. 2.3-2.6% on ticagrelor 60mg and 90mg, respectively (p<0.001 vs. placebo for both, NNH= 81 and 65).
Guidance:	**NICE**: Acute coronary syndromes. **SIGN**: Prevention of cardiovascular disease.
Reviews:	NIHR HSRIC April 2013.

Ticagrelor oral *[Brilique]*; AstraZeneca	
Pharmacology:	A reversible P2Y12 antagonist inhibiting adenosine diphosphate-mediated platelet aggregation.
Indication:	Stroke or transient ischaemic attack, secondary prevention of vascular events (licence extension).
Current status:	PIII
UK availability:	2017
Sector:	Secondary care initiated, primary care continued.
Tariff:	HRG included.
Guidance:	**NICE**: Stroke and TIA. **SIGN**: Stroke and TIA.
Reviews:	NIHR HSRIC April 2015.

Andexanet alfa **injection**; Portola Pharmaceuticals	
Pharmacology:	Factor Xa inhibitor antidote.
Indication:	Anticoagulation reversal.
Current status:	PIII
UK availability:	2016
Population:	Annually, around 1-4% of patients treated with Factor Xa inhibitors may experience major bleeding and 1% may require emergency surgery.
Sector:	Secondary care.
Implications:	An important option for patients receiving factor Xa inhibitors who experience a major bleeding event or require emergency surgery. There are currently no licensed reversal agents for any factor Xa inhibitor.
Financial:	Likely to be expensive.
Tariff:	Likely HRG included.
Efficacy:	In the PIII ANNEXA-A study (n=33), 2-5 minutes after an i.v. bolus of andexanet alpha, the anticoagulant activity of apixaban was reversed by about 94% vs. placebo (p<0.0001), as measured by anti-Factor Xa activity. An i.v. bolus followed by a 2-hour infusion maintained reversal of the anticoagulant effect (92.7%; p<0.0001 vs. placebo). In the PIII ANNEXA-R study (n=41) an i.v. bolus of andexanet alfa reversed the activity of rivaroxaban by >90% vs. placebo (p<0.0001). The PIII ANNEXA-E study evaluating the effect on reversal of edoxaban activity is due to begin in 2015.
Safety:	No safety concerns to date.
Guidance:	None.
Reviews:	None.

Idarucizumab **injection**; Boehringer Ingelheim	
Pharmacology:	Fully humanised monoclonal antibody fragment with a highly specific binding affinity with dabigatran.
Indication:	Anticoagulation reversal in patients taking dabigatran.
Current status:	Filed in EU and US March 2015. Granted priority review and breakthrough therapy status in US.
UK availability:	2016
Population:	Across trials evaluating dabigatran for various indications, up to 3.4% of patients experienced major bleeding events.
Sector:	Secondary care.
Implications:	A treatment for patients on dabigatran who experience life-threatening or uncontrolled bleeding, or who require emergency surgery.
Financial:	Likely to be expensive.
Tariff:	Likely HRG included.
Efficacy:	A published interim analysis of the PIII RE-VERSE AD study in 90 patients on dabigatran with either serious bleeding (group A), or the need for urgent surgery or intervention (group B) showed that, the median maximum percentage reversal of anticoagulation within 4 hours after administration of i.v. idarucizumab was 100%, based on dilute thrombin and ecarin clotting time. In those who underwent a procedure, normal haemostasis was reported in 92% and mild to-moderate impairment in 8%.
Safety:	No serious adverse events related to idarucizumab were reported in the RE-VERSE AD study.
Guidance:	None.
Reviews:	NIHR HSRIC February 2015.

Alirocumab injection *[Praluent];* Sanofi-Aventis	
Pharmacology:	Monoclonal antibody, PCSK9 inhibitor, given by s.c. injection available as pre-filled syringes and pens.
Indication:	Hypercholesterolaemia (primary), heterozygous familial and non-familial, as adjunct to diet in patients not at goal with standard cholesterol lowering therapy.
Current status:	Recommended for approval in EU July 2015.
UK availability:	2015
Population:	Two thirds of the UK population have a serum cholesterol level greater than 5.2 mmol/L.
Sector:	Secondary care initiated with potential for continuation in primary care.
Implications:	Alirocumab will be an additional option as a monotherapy or in combination with a statin or other lipid lowering therapies. Use may be limited by s.c. administration but this is suitable for self administration.
Financial:	Likely to be more expensive than oral lipid lowering options and costs will be additive to current treatments. It will compete with evolocumab.
Tariff:	Likely specified high cost drug.
Efficacy:	Ten PIII studies (n=5,296), demonstrate efficacy vs. placebo or ezetimibe in addition to standard therapy. Studies using an up-titration regimen found a mean reduction in LDLc from baseline of 45.6 to 48.9%, whilst those studying 150mg fortnightly dosing found reductions of 60.4%. Patients on placebo had a 0.5-4.2% increase in LDLc, whilst those using ezetimibe showed reductions of 19.3 to 22.3%.
Safety:	Injection site reactions and pruritis are common. Allergic events occurred rarely.
Guidance:	**NICE**: Lipid disorders. Alirocumab due June 2016. **SIGN**: Prevention of cardiovascular disease.
Reviews:	None recent.

Bococizumab injection; Pfizer	
Pharmacology:	PCSK9 inhibitor.
Indication:	Hyperlipidaemia, primary hyperlipidaemia or mixed dyslipidaemia and heterozygous familial hypercholesterolaemia.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care initiated, with potential for continuation in primary care.
Tariff:	Likely specified high cost drug.
Guidance:	**NICE**: Lipid disorders **SIGN:** Prevention of cardiovascular disease.
Reviews:	None.

Evacetrapib oral; Lilly	
Pharmacology:	Cholesteryl ester transfer protein (CETP) inhibitor.
Indication:	Cardiovascular disease, prevention and hyperlidaemia.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care initiated, continued in primary care.
Tariff:	Likely HRG included.
Guidance:	**NICE**: Lipid disorders. **SIGN:** Prevention of cardiovascular disease
Reviews:	None.

Likely NHSE commissioned

Ciclosporin injection *[CicloMulsion];* NeuroVive	
Pharmacology:	Cremophor-free lipid emulsion formulation of ciclosporin, given by single i.v. injection.
Indication:	Prevention of myocardial reperfusion injury, prior to stenting post-MI.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care
Tariff:	Likely HRG included.
Guidance:	**NICE**: Acute coronary syndromes. **SIGN**: Antithrombotics.
Reviews:	NIHR HSRIC June 2014.

Autologous stem cells injection *[C-Cure];* Celyad	
Pharmacology:	Autologous stem cells, bone marrow-derived, given by intramyocardial injection, first-in-class.
Indication:	Heart failure, chronic, advanced.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care.
Tariff:	Likely specified high cost drug.
Guidance:	**NICE**: Heart failure. **SIGN**: Heart failure.
Reviews:	None.

BNF 3. Respiratory system

Likely CCG commissioned

Beclometasone/ formoterol/ glycopyrrolate inhaler; Chiesi	
Pharmacology:	Fixed-dose combination of a corticosteroid (beclometasone dipropionate 100microgram), long-acting beta agonist (LABA, formoterol fumarate 6microgram) plus long-acting muscarinic antagonist (LAMA, glycopyrrolate bromide 12.5microgram) in a metered dose inhaler.
Indication:	Chronic obstructive pulmonary disease, severe.
Current status:	PIII
UK availability:	2017
Sector:	Primary care.
Tariff:	HRG included.
Guidance:	**NICE**: COPD. **Global Strategy for Diagnosis, Management and Prevention of COPD (GOLD)**: COPD.
Reviews:	None.

Tiotropium bromide inhalation *[Spiriva Respimat];* Boehringer Ingelheim	
Pharmacology:	Long-acting muscarinic receptor antagonist (LAMA).
Indication:	Asthma, persistent, moderate-to-severe, in children aged 6-11 years and adolescents aged 12-17 years (licence extension). Licensed for use in adults.
Current status:	PIII
UK availability:	Uncertain.
Sector:	Primary and secondary care.
Tariff:	HRG included.
Guidance:	**NICE**: Asthma. **British Thoracic Society/SIGN**: Asthma. **Global Initiative for Asthma**: Asthma.
Reviews:	None.

Interferon beta-1a injection *[Traumakine];* Faron	
Pharmacology:	Upregulates CD73 increasing adenosine levels to reduce lung capillary leakage, given by i.v. injection.
Indication:	Acute respiratory distress syndrome in adults.
Current status:	PII in EU with orphan status.
UK availability:	2017
Sector:	Secondary care.
Tariff:	Specified high cost drug.
Guidance:	**NICE**: Acute and critical care.
Reviews:	NIHR HSRIC June 2014.

House dust mite allergen immunotherapy sublingual *[Mitizax];* ALK-Abello	
Pharmacology:	A rapidly-dissolving sublingual tablet containing allergen extracts from *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*, given in doses of 6 or 12 development units (DU) daily.
Indication:	Allergic asthma, allergic rhinitis and rhinoconjunctivitis, third-line.
Current status:	Filed in EU November 2014.
UK availability:	2016
Population:	Allergic rhinitis affects over 20% of the UK population, with about 20% uncontrolled on currently available pharmacotherapy (4,000 per 100,000). Around 90% of people with allergic rhinitis experience at least one day of ocular symptoms per week. About 1 in 2 adults with asthma have an allergic component to their disease, and 80% of children with asthma show skin hypersensitivity to house dust mite.
Sector:	Highly specialist allergy centres.
Implications:	House dust mite allergen immunotherapy (HDM-AIT) would be used in selected patients in whom rigorous allergen avoidance and standard pharmacotherapy fail to control symptoms. Sublingual immunotherapy (SLIT) may be an attractive alternative to s.c. immunotherapy, which is time-consuming and commonly associated with local adverse events, although treatment duration may be longer.
Financial:	May reduce use of highly specialist allergy centres and expenditure on s.c immunotherapy.
Tariff:	Likely HRG included.
Efficacy:	In the 12-month PIII MERIT study (n=922), median combined rhinitis symptom and medication score was reduced by 22% for HDM-AIT dose vs. placebo ($p<0.01$). In the placebo-controlled PIII MITRA study in 834 patients with allergic asthma, those who received HDM-AIT had a 34% reduction in risk of suffering a moderate-to-severe exacerbation during withdrawal of inhaled corticosteroids ($p<0.05$).
Safety:	HDM AIT was well tolerated in the MERIT and MITRA studies.
Guidance:	**NICE**: Asthma. **British Thoracic Society/SIGN**: Asthma. **British Society for Allergy & Clinical Immunology**: Immunotherapy for allergic rhinitis.
Reviews:	NIHR HSRIC December 2013.

Mepolizumab injection; GSK	
Pharmacology:	Monoclonal antibody specific for interleukin 5 (IL-5), given by monthly s.c. injection.
Indication:	Chronic obstructive pulmonary disease (COPD), severe, in patients with at least 1 severe or 2 moderate exacerbations in the past 12 months and a blood eosinophil count of at least 150cells/microlitre.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care.
Tariff:	Specified high cost drug.
Guidance:	**NICE**: COPD. **Global Strategy for Diagnosis, Management and Prevention of COPD (GOLD)**: COPD.
Reviews:	None.

Likely NHSE commissioned

Mepolizumab injection; GSK	
Pharmacology:	Monoclonal antibody specific for interleukin 5 (IL-5), given by monthly s.c. injection.
Indication:	Severe asthma in adults with raised blood eosinophil levels, and a history of recurrent exacerbations or who are oral corticosteroid-dependent (step 5 of BTS/SIGN guidelines).
Current status:	Filed in EU November 2014. Recommended for approval in US June 2015.
UK availability:	2015
Population:	5.4 million people in the UK are currently receiving treatment for asthma. About 5% (341 per 100,000 people) have severe therapy resistant asthma. High expression of cytokines, interleukin-5 and -13 occurs in eosinophilic asthma and inflammation may persist despite high-dose inhaled corticosteroids.
Sector:	Highly specialist respiratory centres.
Implications:	There are no specific therapies licensed for severe eosinophilic asthma.
Financial:	Mepolizumab will be additive to current therapy but will compete with other monoclonal antibodies. Cost of omalizumab 600mg every 4 weeks is £1,025 (PAS available – simple discount).
Tariff:	Specified high cost drug.
Efficacy:	In the published 32-week PIII MENSA study (n=576), mean rates of clinically significant exacerbations/ patient/ year were 0.93 for 75mg i.v. mepolizumab, 0.83 for 100mg s.c. mepolizumab, and 1.74 for placebo; relative reductions 47% and 53%, respectively (p<0.001 vs. placebo for both). 6% of patients on s.c. mepolizumab vs. 13% on placebo had an exacerbation requiring an emergency department visit or hospitalisation (relative reduction 61%, respectively; p=0.02; NNT 14). In the published SIRIUS study (n=135), median reduction from baseline to 20 weeks in glucocorticoid dose was 50% vs. 0% for 100mg s.c. mepolizumab and placebo groups, respectively (p=0.007). Despite a reduced glucocorticoid dose, those on mepolizumab had a relative reduction of 32% in annualised rate of exacerbations vs. placebo (1.44 vs. 2.12; p=0.04).
Safety:	Adverse events include nasopharyngitis, headache and injection-site reactions.
Guidance:	**NICE**: Asthma. Mepolizumab due July 2016. **BTS/SIGN**: Asthma. **Global Initiative for Asthma**: Asthma.
Reviews:	NIHR HSRIC June 2014.

Reslizumab injection *[Cinquil];* Teva UK	
Pharmacology:	Monoclonal antibody specific for interleukin 5 (IL-5), given by monthly i.v. infusion. A s.c. formulation is also in development.
Indication:	Asthma in patients aged ≥12 years with raised blood eosinophil levels who are not controlled on high-dose inhaled corticosteroids (step 4 of BTS/SIGN guidelines).
Current status:	Filed in EU July 2015.
UK availability:	2016
Population:	5.4 million people in the UK are currently receiving treatment for asthma. About 5% (341 per 100,000 people) have severe therapy resistant asthma. High expression of cytokines, interleukin-5 and -13 occurs in eosinophilic asthma and inflammation may persist despite high-dose inhaled corticosteroids.
Sector:	Highly specialist respiratory centres.
Implications:	There are no specific therapies licensed for eosinophilic asthma. An alternative to s.c. mepolizumab in adults.
Financial:	Reslizumab will be additive to current therapy but will compete with other monoclonal antibodies. Cost of omalizumab 600mg every 4 weeks is £1,025 (PAS available – simple discount).
Tariff:	Specified high cost drug.
Efficacy:	Pooled data from two jointly-published, 12-month PIII studies, involving 953 patients with blood eosinophils of ≥400cells/μL and ≥1 exacerbations in the previous year, showed 32% of patients on reslizumab had one or more exacerbations vs. 50% on placebo (0.84 vs. 1.81 events/patient/year, rate ratio 0.46; p<0.0001; NNT=6).
Safety:	Common adverse events with reslizumab were similar to placebo and included worsening asthma symptoms, upper respiratory tract infections and nasopharyngitis.
Guidance:	**NICE**: Asthma. **BTS/SIGN**: Asthma. **Global Initiative for Asthma**: Asthma.
Reviews:	NIHR HSRIC April 2015.

Benralizumab injection; AstraZeneca	
Pharmacology:	Interleukin-5 receptor (IL-5R) monoclonal antibody that depletes eosinophils and neutralises IL-5, given by monthly s.c. injection.
Indication:	Asthma in adults and adolescents with persistent poor control on high-dose inhaled corticosteroid and at least one other controller therapy (step 4 of BTS/SIGN guidelines).
Current status:	PIII
UK availability:	2017
Sector:	Highly specialist respiratory centres.
Tariff:	Likely specified high cost drug.
Guidance:	**NICE**: Asthma. **BTS/SIGN**: Asthma. **Global Initiative for Asthma**: Asthma.
Reviews:	None.

Lebrikizumab injection; Roche	
Pharmacology:	Anti-interleukin-13 (IL-13) monoclonal antibody, given by monthly s.c. injection.
Indication:	Asthma in adults and adolescents with persistent poor control on high-dose inhaled corticosteroid and at least one other controller therapy (step 4 of BTS/SIGN guidelines).
Current status:	PIII
UK availability:	2017
Sector:	Highly specialist respiratory centres.
Tariff:	Likely specified high cost drug.
Guidance:	**NICE**: Asthma. **BTS/SIGN**: Asthma. **Global Initiative for Asthma**: Asthma.
Reviews:	None.

Masitinib oral; AB Science	
Pharmacology:	Protein tyrosine kinase inhibitor that targets mast cells and macrophages.
Indication:	Asthma, severe, persistent, oral corticosteroid-dependent in adults (step 5 of BTS/SIGN guidelines).
Current status:	PIII
UK availability:	2017
Sector:	Highly specialist respiratory centres.
Tariff:	Specified high cost drug.
Guidance:	**NICE**: Asthma. **BTS/SIGN**: Asthma. **Global Initiative for Asthma**: Asthma.
Reviews:	None recent.

Mepolizumab injection; GSK	
Pharmacology:	Monoclonal antibody specific for interleukin 5 (IL-5), given by monthly s.c. injection.
Indication:	Eosinophilic granulomatosis with polyangitis (formerly Churg-Strauss syndrome), relapsing or refractory.
Current status:	PIII in EU and US, with orphan status in US.
UK availability:	2017
Sector:	Secondary care.
Tariff:	Specified high cost drug.
Guidance:	**NICE**: Peripheral circulatory conditions.
Reviews:	None.

Lumacaftor/ ivacaftor **oral** *[Orkambi];* Vertex	
Pharmacology:	Fixed-dose combination containing cystic fibrosis transmembrane conductance regulator (CFTR) corrector (lumacaftor 200mg) and CTFR potentiator (ivacaftor 125mg).
Indication:	Cystic fibrosis (CF), in patients aged ≥12 years and homozygous for Phe508del-CFTR (formerly F508del) mutation.
Current status:	Filed in EU November 2014, with accelerated assessment and orphan status. Licensed in US July 2015, with breakthrough therapy, orphan and priority review status – see prescribing data.
UK availability:	2015
Population:	CF affects 1 in every 2,500 newborn. Around 10,000 people in the UK have CF (14 per 100,000 people); about 75% have the Phe508del-CFTR mutation and about 50% are homozygous for this mutation.
Sector:	Highly specialist cystic fibrosis service.
Implications:	The first combination therapy targeting Phe508del-CFTR mutation.
Financial:	A further treatment option that will be additional to current costs. Improved symptoms and fewer exacerbations could reduce cost of existing treatments and services. Ivacaftor (*Kalydeco*) is available for patients aged ≥6 years and G551D mutation (monthly cost £14,000, NHS England discount available).
Tariff:	Specified high cost drug. Excluded from CF mandatory national 'Year of Care' tariff.
Efficacy:	Pooled data from identical, jointly published PIII TRAFFIC and TRANSPORT studies (n=1,108), show lumacaftor/ ivacaftor increased mean percent predicted FEV_1 from baseline to week 24 by 2.5% vs. a decrease of 0.32% with placebo ($p<0.001$). A relative increase in predicted FEV_1 of at least 5% was seen in 39% on lumacaftor/ivacaftor vs. 22% on placebo ($p<0.001$). There were 152 pulmonary exacerbations in 369 patients on lumacaftor/ivacaftor group vs. 251 in 371 patients on placebo group (rate ratio 0.61; $p<0.001$; NNT 4), plus 61% and 56% relative reductions in exacerbations leading to hospitalisation or i.v antibiotics, respectively (both $p<0.001$).
Safety:	Most frequently reported adverse events include infective pulmonary exacerbation, cough, headache and increased sputum. Liver function needs monitoring. Lumacaftor is a strong inducer of CYP3A liver enzymes and has the potential to affect other liver enzymes.
Guidance:	**NICE**: Cystic fibrosis. **NHSE**: CCP-Ivacaftor.
Reviews:	NIHR HSRIC February 2014.

Ataluren **oral** *[Translarna];* PTC Therapeutics	
Pharmacology:	Cystic fibrosis transmembrane conductance regulator (CFTR) stimulant that suppresses nonsense mutations, first-in-class.
Indication:	Cystic fibrosis (CF), nonsense-mutation mediated, in patients aged ≥6 years (licence extension).
Current status:	PIII with orphan status in EU and US, plus fast track status in US.
UK availability:	2016
Population:	CF affects 1 in every 2,500 newborn. Around 10,000 people in the UK have CF (prevalence 14 per 100,000 people). About 10% have a nonsense mutation.
Sector:	Highly specialist cystic fibrosis service.
Implications:	Ataluren is the first drug for nonsense-mutation CF.
Financial:	Likely to be expensive and as a further treatment this will be additional to current costs.
Tariff:	Likely specified high cost drug (already listed for non-CF indications). Likely excluded from CF mandatory national 'Year of Care' tariff.
Efficacy:	In a published PIII study (n=238), mean relative change from baseline to week 48 in the primary outcome of percentage predicted FEV_1 was -2.5% for ataluren vs. -5.5% for placebo (p=ns). However, post-hoc analysis of patients not using chronic inhaled tobramycin showed a significant change of -0.7% vs. -6.4%, respectively (p=0.008). There were fewer pulmonary exacerbations in the ataluren group (1.42 events vs. 2.18 events; rate ratio 0.60; p=0.006). The PIII ACT CF study is ongoing and due to complete November 2016. Patients with recent (within 4 months) use of inhaled aminoglycosides are excluded.
Safety:	Increased creatinine concentration occurred in 15% of those on ataluren vs. <1% on placebo.
Guidance:	**NICE**: Cystic fibrosis. **NHSE**: CCP-Ivacaftor
Reviews:	None.

VX-661/ ivacaftor **oral**; Vertex	
Pharmacology:	Fixed-dose combination of cystic fibrosis transmembrane conductance regulator (CFTR) corrector (VX-661) and CTFR potentiator (ivacaftor).
Indication:	Cystic fibrosis (CF), heterozygous or homozygous for the Phe508del-CFTR mutation.
Current status:	PIII in EU. PIII in US, with orphan status, and breakthrough therapy status for homozygous CF.
UK availability:	2017
Sector:	Highly specialist cystic fibrosis service.
Tariff:	Likely specified high cost drug.
Guidance:	**NICE**: Cystic fibrosis. **NHSE**: CCP-Ivacaftor.
Reviews:	None.

BNF 4. Central nervous system

Likely CCG commissioned

Lurasidone **oral** *[Latuda];* Sunovion	
Pharmacology:	Dopamine D2 receptor and serotonin 5HT2A/7 receptor antagonist.
Indication:	Bipolar depression, as monotherapy and adjunct treatment (licence extension).
Current status:	PIII in EU. Launched in US - see prescribing data.
UK availability:	2016
Population:	The lifetime prevalence of bipolar I disorder (mania and depression) is about 1000 per 100,000 adults and bipolar II disorder (hypomania and depression) affects about 400 per 100,000 adults.
Sector:	Secondary care initiated.
Implications:	A second-line option when NICE recommended first-line treatments are ineffective or not tolerated.
Financial:	Olanzapine, fluoxetine, quetiapine and lamotrigine are available as generics and considerably cheaper. Based on current prices lurasidone costs about £90/ month.
Tariff:	HRG included.
Efficacy:	In the published PIII placebo-controlled PREVAIL-1 (n=348) study lurasidone was added to lithium or valproate in patients with insufficient response to monotherapy. The primary outcome was change from baseline on the Montgomery-Åsberg Depression Rating Scale (MADRS). Lurasidone reduced mean MADRS total score at week 6 vs. placebo (17.1 vs. 13.5; p=0.005). PREVAIL-2 (n=505) compared lurasidone 20-60mg/day or 80-120mg/day monotherapy with placebo. Mean MADRS total scores were reduced in both lurasidone groups (15.4; p< 0.001 vs. placebo). PREVAIL-3 (n=342) is a placebo-controlled, flexible-dose (20-120mg/daily) study of lurasidone added to lithium or valproate. Luraidone reduced mean change from baseline in MADRS total score at week 6 by 11.8 vs. 10.4 in the placebo group. PERSIST is an on-going placebo-controlled study (n=1,060) of lurasidone added to lithium or valproate for prevention of recurrence.
Safety:	See medicines.org.uk.
Guidance:	**NICE**: Bipolar disorder. **SIGN**: Bipolar affective disorder.
Reviews:	None.

Tasimelteon **oral** *[Hetlioz];* Vanda	
Pharmacology:	Melatonin MT1 and MT2 receptor agonist, first-in-class.
Indication:	Insomnia, non-24-hour sleep wake disorder (N24HSWD) in totally blind adults.
Current status:	Licensed in EU July 2015 with orphan status - see prescribing data. Launched in US April 2014.
UK availability:	2015
Population:	A rare condition which occurs in the totally blind. The prevalence of N24HSWD is estimated to be no more than 33 per 100,000 people.
Sector:	Secondary care.
Implications:	This is the first licensed treatment for this indication; off-label and unlicensed melatonin formulations are currently used in adults and children.
Financial:	Likely to be expensive, cost in US is about $10,000/month. Melatonin (*Circadin*) costs about £15/month.
Tariff:	Likely HRG included.
Efficacy:	In two placebo-controlled PIII studies, SETS (n=84) and RESET (n=20), the primary outcome of entrainment of the melatonin (aMT6s) rhythm was achieved. In the SETS study entrainment was obtained in 20% and 2.6% of tasimelteon and placebo recipients, respectively (p<0.05, NNT=6). In the RESET withdrawal study, entrainment was obtained in 90% and 20%, respectively (p<0.005).
Safety:	Adverse effects are headache, somnolence, nightmares or unusual dreams and raised liver enzymes.
Guidance:	None.
Reviews:	None.

Guanfacine **oral** *[Intuniv];* Shire	
Pharmacology:	Selective alpha 2 adrenoreceptor agonist, first-in-class. Once daily modified release tablet.
Indication:	Attention deficit hyperactivity disorder (ADHD) in children ≥ 6 years and adolescents, for whom stimulants are not suitable, not tolerated or have been shown to be ineffective
Current status:	Recommended for approval in the EU July 2015. Launched in US – see prescribing data.
UK availability:	2015
Population:	UK prevalence of ADHD is around 2.4% of children in the UK.
Sector:	Secondary care initiated, possibly primary care continued.
Implications:	An additional option when first-line treatments are not effective or not tolerated.
Financial:	As a further treatment option it will be additional to current costs. US cost is about $30/ month.
Tariff:	Likely HRG included.
Efficacy:	In a published PIII study (n=345), least squares mean reduction in ADHD-RS IV for guanfacine monotherapy (2-4mg daily) at 5 weeks was 16.7 vs. 8.9 for placebo (p<0.001). In a similar published study (n=324), mean reduction at 6 weeks was 19.6 for guanfacine (1 to 4mg daily) vs. 12.2 for placebo (p<0.02). In another published study (n=333), mean reduction at week 8 was 20.0 for guanfacine vs. 11.0 for placebo (p<0.001). In another published study (n=461) guanfacine or placebo was added to usual therapy. The mean reduction in ADHD RS-IV at week 8 was 4.5 for morning guanfacine dosing (p<0.01 vs. placebo) and 5.3 for evening guanfacine dosing (p<0.001 vs. placebo).
Safety:	Adverse effects include somnolence, fatigue, nausea and hypotension. Postmarketing, hallucinations have been added to US prescribing data.
Guidance:	**NICE**: Attention deficit disorder. **SIGN**: Attention deficit and hyperkinetic disorders.
Reviews:	None.

Capsaicin patch *[Qutenza];* Astellas	
Pharmacology:	Transient receptor potential vanilloid 1 receptor (TRPV1) agonist.
Indication:	Peripheral neuropathic pain (PNP) in adults with diabetes (licence extension).
Current status:	Recommended for approval in EU July 2015.
UK availability:	2015
Population:	Diabetes, the most common cause of peripheral neuropathy, can affect 60-70% of people with diabetes. Estimated UK prevalence of diagnosed diabetes mellitus was 3.3 million people in 2014.
Sector:	Secondary care.
Implications:	An additional treatment option for PNP, for initiation by specialists in patients when first-line oral treatments or capsaicin cream are ineffective or not tolerated.
Financial:	An alternative treatment option in diabetic PNP. Based on current prices cost will be £210-£840 every three months.
Tariff:	HRG included.
Efficacy:	In PIII, placebo-controlled STEP study (n=369), pain in the last 24 hours was assessed using the Brief Pain Inventory- Diabetic Neuropathy (BPI-DN). Mean reduction in average daily pain score from baseline to between weeks 2 - 8 in the capsaicin group was 27.44 vs. 20.85 (p=0.025) for placebo. The PIII PACE study (n=468) compared change in health-related quality of life score in patients receiving capsaicin patch plus standard-of-care (SOC) vs. SOC alone. The study has completed but results not published.
Safety:	See medicines.org.uk.
Guidance:	**NICE**: Neuropathic pain, Diabetes. **SIGN**: Chronic pain, Diabetes.
Reviews:	None recent.

Nabiximols oromucosal *[Sativex];* Bayer	
Pharmacology:	Cannabinoid receptor agonist.
Indication:	Cancer pain, adjunct to optimum chronic opioid therapy (licence extension).
Current status:	PIII in EU and US with accelerated status in US. Launched in Canada.
UK availability:	2016
Population:	About 396 per 100,000 people are diagnosed with cancer; 30-50% have some sort of pain. At least 30% receive inadequate pain relief with strong opiates and more experience dose limiting adverse events.
Sector:	Secondary and primary care.
Implications:	This will provide an additional non-opioid pain relief option for those on optimal opioid therapy and delay use of parenteral opioid therapy.
Financial:	As a further treatment option it will be additional to current costs. Based on a maximum dose of 10 sprays per day, mean monthly cost per patient is about £400.
Tariff:	HRG included.
Efficacy:	In 3 PIII trials the primary outcome is patient assessment of pain using a 0-10 Numeric Rating Scale (NRS), and the primary analysis percent improvement in pain. The first trial (n=380) did not meet its primary outcome. The second trial (n=399) is completed but no results yet available. The third trial (n=540) is ongoing and is due to complete in September 2015.
Safety:	See medicines.org.uk.
Guidance:	**NICE**: Cancer. **SIGN**: Cancer pain.
Reviews:	NTAG November 2014.

Botulinum A toxin injection *[Dysport];* Ipsen	
Pharmacology:	Neuromuscular blocking agent that inhibits acetylcholine release, given as i.m. injection.
Indication:	Lower limb spasticity (LLS), in adults post stroke or traumatic brain injury (TBI) (licence extension).
Current status:	PIII
UK availability:	2016
Population:	Between 30-500 per 100,000 people have had a stroke and a third might have LLS. 100-230 per 100,000 people per year experience TBI; about 12% might have LLS.
Sector:	Secondary care initiation, primary care continuation.
Implications:	This will be an additional option to skeletal muscle relaxants.
Financial:	As a further option it will add to current costs. 500 –1,500units botulinum A toxin costs £154- £462.
Tariff:	Specified high cost drug.
Efficacy:	In a PIII study (n=348), improvement of muscle tone in the treated limb was measured ≥ 1 point improvement on the Modified Ashworth Scale (MAS) at week 4. MAS scores range from 0 (no increase in tone) to 4 (affected limb rigid in flexion or extension). 1,500 units significantly improved muscle tone (p values not stated). In another PIII study in 243 hemiparetic patients with LLS due to stroke or TBI, improved muscle tone was seen in 73.8% on 500units, 78.5% on 1,000 units vs. 22.8% on placebo, respectively (p<0.0001; NNT=2).
Safety:	See medicines.org.uk.
Guidance:	**NICE**: Stroke. Botulinium toxin A due TBC. **SIGN**: Stroke. Brain injury rehabilitation
Reviews:	None.

Botulinum A toxin injection *[Xeomin];* Merz	
Pharmacology:	Neuromuscular blocking agent that inhibits acetylcholine release, given as i.m. injection.
Indication:	Lower limb spasticity**,** post stroke (licence extension).
Current status:	PIII in EU.
UK availability:	2017
Sector:	Secondary care initiation, primary care continuation.
Tariff:	Specified high cost drug.
Guidance:	**NICE**: Stroke. Botulinium toxin A due TBC. **SIGN**: Stroke.
Reviews:	None.

Botulinum A toxin injection *[Dysport];* Ipsen	
Pharmacology:	Neuromuscular blocking agent that inhibits acetylcholine release. Given as i.m. injection.
Indication:	Limb spasticity, in children and adolescents with cerebral palsy (licence extension).
Current status:	PIII
UK availability:	2016
Population:	The prevalence of cerebral palsy is about 250 per 100,000 children; about 80% might have lower limb spasticity (LLS).
Sector:	Secondary care initiation, primary care continuation.
Implications:	This will be an additional treatment option to skeletal muscle relaxants.
Financial:	As a further option it will be additional to current costs. Maximum cost of £308/ leg/ treatment cycle.
Tariff:	Specified high cost drug.
Efficacy:	In a PIII placebo-controlled study (n=235), at week 4, doses of 10U/kg/leg and 15U/kg/leg improved muscle tone (p values not available). A PIII study (n=210) to evaluate multiple doses in the treatment of upper limb spasticity in children with cerebral palsy is due to complete in 2016.
Safety:	See medicines.org.uk
Guidance:	**NICE**: Cerebral palsy. **SIGN**: None.
Reviews:	None.

Safinamide oral *[Xadago];* Zambon	
Pharmacology:	Alpha-aminoamide, MAO-B inhibitor (selective and reversible)/ sodium and calcium channel antagonist/ dopamine uptake inhibitor/ glutamate release inhibitor, first-in-class, taken once daily.
Indication:	Parkinson's disease (PD), mid-late stage fluctuating, add-on to levodopa (alone or in combination with other PD drugs).
Current status:	Licensed in EU February 2015 – see prescribing data.
UK availability:	2015
Population:	100-200 per 100,000 people have PD. About 50-90% of people who have received levodopa for 5-10 years have long term problems which include motor fluctuations, axial problems and PD dementia.
Sector:	Secondary care initiation, primary care continuation.
Implications:	As first in a new class this could be attractive for patients poorly controlled on standard therapy.
Financial:	As a further treatment option it will be additional to current costs.
Tariff:	Likely HRG included.
Efficacy:	In the PIII 24-week SETTLE study (n=549) safinamide 100mg daily improved the primary outcome of change in 'ON' time by 0.96 hours/day vs. placebo (p<0.001) in patients on stabilised standard therapy. In another PIII study (n=669), the change in 'ON' time was 0.51 (p=0.023) in the 50mg group and 0.55 (p=0.013) in the 100mg group vs. placebo. A published extension study (n=544) did not meet its primary outcome of mean change in Dyskinesia Rating Scale score at 24 months.
Safety:	In studies adverse events were low compared to placebo. Transient dyskinesia occurred more frequently with safinamide and retinal degeneration may occur.
Guidance:	**NICE**: PD. **SIGN**: PD.
Reviews:	None recent.

Opicapone oral; Bial	
Pharmacology:	Catechol-O-methyl transferase (COMT) inhibitor, given once daily.
Indication:	Parkinson's Disease (PD), with end-of-dose motor fluctuation (in combination with levodopa plus a dopa decarboxylase inhibitor).
Current status:	Filed in the EU January 2015.
UK availability:	2016
Population:	100-200 per 100,000 people have PD. About 50-90% of people who have received levodopa for 5-10 years have long term problems which include motor fluctuations, axial problems and PD dementia.
Sector:	Secondary care initiated, continued in primary care.
Implications:	Once daily opicapone provides another option in patients who do not respond to, or cannot tolerate other COMT inhibitors. Entacapone is given with each dose of levodopa, tolcapone is given three times a day (but does not have to be taken at the same time as levodopa) and use is restricted because of unpredictable serious hepatic reactions.
Financial:	Likely to be competitively priced with other COMT inhibitors. Entacapone costs about £48 -£161/ month and tolcapone costs £80 -£160/month, depending on dose.
Tariff:	Likely HRG included.
Efficacy:	Results from two PIII studies, BIPARK-I (n=600) and BIPARK-II (n=286) with a 1-year extension open-label phase are available. The first study compared opicapone (5, 25 and 50 mg) given once daily vs. entacapone (200 mg) or placebo administered with each dose of levodopa. Opicapone 50mg and entacapone reduced the absolute OFF-time to 1.95 hours (p<0.01) and 1.61 hours (p<0.05), respectively vs. placebo (0.93 hours). The second study also compared the change in absolute OFF-time of opicapone 25mg and 50mg vs. placebo, with changes of 1.71 hours, 2.07 hours and 1.07 hours, respectively (significance not stated).
Safety:	In a pooled analysis of studies, no serious adverse effects including hepatic effects were reported.
Guidance:	**NICE**: PD. **SIGN**: PD.
Reviews:	None.

Botulinum A toxin injection *[Xeomin];* Merz	
Pharmacology:	Neuromuscular blocking agent that inhibits acetylcholine release, given as i.m. injection.
Indication:	Sialorrhoea, in Parkinson's disease and paediatric cerebral palsy (licence extension).
Current status:	PIII
UK availability:	2017
Sector:	Secondary care.
Tariff:	Specified high cost drug.
Guidance:	**NICE:** Parkinson's disease, Cerebral palsy. **SIGN**: Parkinson's disease.
Reviews:	NIHR HSRIC March 2015.

Idalopirdine oral; Lundbeck	
Pharmacology:	Selective 5-HT6 antagonist, first-in-class.
Indication:	Alzheimer's disease, mild-to-moderate, adjunct to other acetylcholinesterase inhibitor donepezil.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care initiation, primary care continuation.
Tariff:	Likely HRG included.
Guidance:	**NICE**: Dementia. **SIGN**: Dementia.
Reviews:	NIHR HSRIC October 2014.

Leuco-methylthioninium oral; TauRx	
Pharmacology:	Tau protein aggregation inhibitor, first-in-class.
Indication:	Alzheimer's disease, mild and moderate.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care initiation, primary care continuation.
Tariff:	Likely HRG included.
Guidance:	**NICE**: Dementia. **SIGN**: Dementia.
Reviews:	NIHR HSRIC August 2013.

Leuco-methylthioninium oral; TauRx	
Pharmacology:	Tau protein aggregation inhibitor, first-in-class.
Indication:	Dementia, behavioural variant frontotemporal.
Current status:	PIII with orphan status.
UK availability:	2017
Sector:	Secondary care initiation, primary care continuation.
Tariff:	Likely HRG included.
Guidance:	**NICE**: Dementia. **SIGN**: Dementia.
Reviews:	NIHR HSRIC October 2013.

Naltrexone/ bupropion **oral** *[Mysimba];* Orexigen	
Pharmacology:	Modified release combination of an opioid receptor antagonist (naltrexone 8mg) and dopamine/ noradrenaline reuptake inhibitor (bupropion 90mg) taken twice daily. The maximum daily dose is 32mg naltrexone hydrochloride and 360 mg bupropion.
Indication:	Obese or overweight adults (body mass index ≥ 27kg/m^2), in combination with lifestyle modification. Treatment should be stopped after 16 weeks if patients have not lost at least 5% of their initial weight.
Current status:	Licensed in EU March 2015 – see prescribing data.
UK availability:	2015
Population:	In 2012 in England, 24% of men and 25% of women (aged >16 years) were classed obese and a further 42% of men and 32% of women were overweight.
Sector:	Primary care.
Implications:	Another option before surgery in patients who have tried existing weight management programmes. The licence is almost identical to that for orlistat, but can be used at BMI ≥27kg/m^2 vs. >28 kg/m^2 for orlistat.
Financial:	As a further treatment option it will be additional to current costs.
Tariff:	HRG included.
Efficacy:	In published PIII studies, COR-I (n=1,742), COR-II (n=1,496) and COR-Diabetes (n=505), the co-primary outcomes were change in body weight and ≥5% weight loss. At week 56 across the 3 studies, *Mysimba* was associated with a reduction in body weight of 5- 6.5% vs. 1.3-1.9% with placebo (p<0.001). 44.5-55.6% vs. 16.4-19.8%, respectively, achieved a ≥5% weight loss. In another published PIII study COR-BMOD (n=793), change in body weight was 9.3% for *Mysimba* vs. 5.1% for placebo (p<0.001) and 66.4% vs. 42.5%, respectively achieved ≥5% weight loss (p<0.001; NNT=4) at 56 weeks.
Safety:	Common adverse effects are nausea and vomiting, constipation, headache, dizziness and dry mouth. Risks in this group of patients with other co-morbidities are currently unknown.
Guidance:	**NICE**: Obesity. Naltrexone/bupropion due TBC. **SIGN**: Obesity.
Reviews:	LMEN June 2015, NIHR HSRIC December 2013.

Dextromethorphan/ quinidine **oral** *[Nuedexta];* Jenson	
Pharmacology:	Dextromethorphan is a sigma-1 receptor agonist and NMDA antagonist. Quinidine, a CYP2D6 inhibitor, increases plasma levels of dextromethorphan.
Indication:	Pseudobulbar affect (PBA) - sudden outbursts of uncontrolled laughing/crying.
Current status:	Licensed in EU June 2013 – see prescribing data.
UK availability:	2015
Population:	PBA may occur following stroke or traumatic brain injury (TBI) and a range of other neurological conditions, including dementia/ Alzheimer's disease (AD), multiple sclerosis (MS), Parkinson's disease (PD) and amyotrophic lateral sclerosis (ALS), The estimated overall prevalence of this under recognised condition is about 10,000 per 100,000 across the range of people with these neurological conditions.
Sector:	Secondary or specialist care.
Implications:	First drug licensed for this indication which may increase referrals to specialist neurosciences.
Financial:	Likely to be considerably more expensive than unlicensed alternatives (SSRIs, TCAs, levodopa, amantadine and thyrotropin-releasing hormone).
Tariff:	Likely HRG included.
Efficacy:	A published 12-week PIII study (n=326) compared dextromethorphan plus quinidine (30/10mg (DMq-30) or 20/10mg (DMq-20) twice daily) with placebo in patients with ALS and MS with clinically significant PBA. The primary outcome of PBA-episode daily rate was 46.9% lower for DMq-30 and 49.0% lower for DMq-20 vs. placebo (p<0.01 for both). An open-label study (PRISM II) is evaluating efficacy in patients with dementia, AD, stroke and TBI (n=367). The primary outcome is mean change in Centre for Neurologic Study-Lability Scale (CNS-LS) after 12 weeks. Initial results in the AD/dementia group are published (n=134), mean change in CNS-LS score was -7.2 (p<0.001). In the TBI group (n=120) and stroke groups (n=113), mean change in CNS-LS score was -8.6 and -7.7, respectively (p<0.001).
Safety:	See prescribing data. Significant potential for interactions, especially related to CYP metabolism and potential for cardiac adverse effects including QT prolongation.
Guidance:	None.
Reviews:	None.

BNF 5. Infections

Likely CCG commissioned

Oritavancin **injection** *[Orbactiv];* The Medicines Company	
Pharmacology:	Second-generation glycopeptide antibiotic, single dose given by i.v. infusion.
Indication:	Acute bacterial skin and skin structure infections due to gram-positive bacteria, including MRSA.
Current status:	Licensed in EU March 2015. See prescribing data.
UK availability:	Uncertain due to company strategy.
Population:	In England (2013-14) there were 5,239 hospital admissions due to local infections of skin and subcutaneous tissue (~10 per 100,000 people).
Sector:	Secondary care.
Implications:	Once-weekly i.v. alternative to daily i.v. vancomycin, teicoplanin, daptomycin or oral linezolid. Vancomycin and linezolid require monitoring (blood levels, renal function, full blood counts) and linezolid has significant drug interactions. Oritavancin does not need monitoring and could reduce length of stay.
Financial:	Cost may be higher than alternatives but may be offset by reduced inpatient costs.
Tariff:	Likely HRG included.
Efficacy:	A single i.v. dose of oritavancin was non-inferior to a 7-10 day course of i.v. vancomycin in the PIII SOLO I trial (n=968). Clinical response (cessation of infection spread and absence of fever without rescue antibiotics) at 48-72 hours occurred in 82.3% on oritavancin vs. 78.9% on vancomycin, and was sustained 7-14 days after treatment ended. Investigator-assessed clinical cure occurred in 79.6% vs. 80.0% of patients. Efficacy outcomes were similar in treatment groups, including for MRSA infection. Oritavancin was non-inferior to vancomycin in the SOLO II trial (n=1,005). Clinical response (as for SOLO I) was achieved by 80% vs. 83%, respectively, 48-72 hours after treatment started (FDA primary outcome), and by 83% vs. 81%, 7-14 days after treatment stopped (EMA primary outcome).
Safety:	Common adverse events include hypersensitivity and infusion site reactions. Oritavancin can artificially prolong measures of bleeding time.
Guidance:	**NICE**: Antibiotic use, Healthcare-associated infections.
Reviews:	None.

Dalbavancin **injection** *[Xydalba]*; Durata Therapeutics	
Pharmacology:	Second-generation glycopeptide antibiotic, two doses given by i.v. infusion once weekly.
Indication:	Acute bacterial skin and skin structure infections (ABSSSI), due to gram-positive microorganisms including MRSA.
Current status:	Licensed in EU February 2015 - see prescribing data. Launched in US July 2014.
UK availability:	Uncertain due to company strategy.
Population:	In England (2013-14) there were 5,239 hospital admissions due to local infections of skin and subcutaneous tissue (~10 per 100,000 people).
Sector:	Secondary care.
Implications:	A once-weekly alternative to antibiotics given daily, e.g. i.v. ceftaroline, daptomycin, teicoplanin and vancomycin (which require monitoring of blood levels and renal function) or oral linezolid (which requires weekly full blood counts and has significant drug interactions). It could reduce length of hospital stay.
Financial:	Cost may be higher than alternatives but may be offset by reduced inpatient costs.
Tariff:	Likely HRG included
Efficacy:	In a published pooled analysis of DISCOVER 1 and 2 (n=1,312), two doses of i.v. dalbavancin (given one week apart) were non-inferior to vancomycin (given i.v. twice daily for 3 days with the option of switching to oral linezolid for a total of 10-14 days). Treatment success (early clinical response at 48-72 hours) was reported in 79.7% on dalbavancin vs. 79.8% on vancomycin/linezolid, respectively. Outcomes were similar at the end of therapy. In a PIII study (n=716), dalbavancin was non-inferior to a 14-day course of linezolid i.v./oral at 48-96 hours, and at 28 days.
Safety:	Hepatobiliary, oto- and renal- toxicity cannot be excluded. Rapid infusion can cause red-man syndrome.
Guidance:	**NICE**: Antibiotic use, Healthcare-associated infections.
Reviews:	None.

Actoxumab + bezlotoxumab injection; MSD	
Pharmacology:	Monoclonal antibodies against *Clostridium difficile (C.difficile)* producing toxin A (actoxumab) and toxin B (bezlotoxumab), given as a single infusion.
Indication:	*Clostridium difficile* associated diarrhoea (CDAD), prevention of recurrence.
Current status:	PIII
UK availability:	2016
Population:	The overall rate of *C. difficile* infection (CDI) in England, Wales and Northern Ireland was 22 per 100,000 people in 2014, a 5% decrease from 2013.
Sector:	Secondary care.
Implications:	Likely to be reserved for patients with recurrent CDI. May speed recovery and reduce morbidity with respect to diarrhoea and potential hospital admissions for complications.
Financial:	As a further treatment option, costs would be additional to antibacterial courses. Oral/i.v. metronidazole costs from ~£2 to £65, oral/i.v. vancomycin costs up to £380 and oral fidaxomicin around £1,350.
Tariff:	Likely HRG included.
Efficacy:	In a published PII study (n=200), patients still symptomatic after receiving metronidazole (i.v. or oral) or vancomycin (oral) received actoxumab + bezotoxumab or placebo. Laboratory documented recurrence rates of CDI 84 days after treatment (primary outcome) were 7% in the treated group vs. 25% for placebo (p<0.001; NNT=6) and 7% vs. 38%, respectively, among patients with >1 previous episode of CDI (p=0.006; NNT=3). The mean duration of initial hospitalisation did not differ between groups but subsequent admission rates were lower in the treatment group (9% vs. 20%, p=0.03; NNT=9). The PIII MODIFY-I (n=1,453) and MODIFY-II (n=1,203) studies completed in 2014; results are not yet available.
Safety:	Similar adverse effect rates were seen between treatment and placebo groups.
Guidance:	**NICE**: Diarrhoea and vomiting, Healthcare-associated infections.
Reviews:	None.

Cadazolid oral; Actelion	
Pharmacology:	Bacterial protein synthesis inhibitor, formulated as a powder for oral suspension.
Indication:	*Clostridium difficile* associated diarrhoea.
Current status:	PIII, with Qualified Infectious Disease Product and fast track status in the US.
UK availability:	2017
Sector:	Secondary care.
Tariff:	Likely HRG included.
Guidance:	**NICE**: Diarrhoea and vomiting, Healthcare-associated infections.
Reviews:	None.

Eravacycline injection and oral; Tetraphase	
Pharmacology:	Synthetic broad spectrum tetracycline antibacterial, given as an i.v. infusion and oral tablet.
Indication:	Intra-abdominal infections, complicated.
Current status:	PIII in EU and US with fast track and Qualified Infectious Disease Product status in US.
UK availability:	2017
Sector:	Secondary care.
Tariff:	Likely HRG included.
Guidance:	**NICE**: Antibiotic use
Reviews:	None.

Eravacycline injection and oral; Tetraphase	
Pharmacology:	Synthetic broad spectrum tetracycline antibacterial, given as an i.v. infusion and oral tablet.
Indication:	Urinary tract infections, complicated.
Current status:	PIII in EU and US with fast track and Qualified Infectious Disease Product status in US.
UK availability:	2017
Sector:	Secondary care.
Tariff:	Likely HRG included.
Guidance:	**NICE:** Antibiotic use. **SIGN:** UTI
Reviews:	None.

Omadacycline injection and oral; Paratek	
Pharmacology:	Aminomethylcycline, broad spectrum antibacterial given via injection or orally, first-in-class.
Indication:	Pneumonia, moderate to severe (refractory), community acquired.
Current status:	PIII, with Qualified Infectious Disease Product (QIDP) and fast track status in the US.
UK availability:	2017
Sector:	Secondary care initiated.
Tariff:	Likely HRG included.
Guidance:	**NICE:** Respiratory conditions: general.
Reviews:	None.

Amikacin liposomal for inhalation *[Arikayce]*; Insmed	
Pharmacology:	Aminoglycoside antibacterial formulated in small biocompatible liposomes (Sustained release Lipid Inhalation Targeting *[SLIT]* delivery technology) for inhalation via eFlow nebuliser.
Indication:	Non-tuberculous mycobacterial (NTM) lung infections.
Current status:	Filed in EU December 2014 with orphan status.
UK availability:	2016
Population:	Estimates of NTM prevalence vary and geographical variation is expected; UK incidence may range from around 0.8-1.9 per 100,000 people.
Sector:	Secondary care.
Implications:	Inhaled antibacterial treatment for NTM lung infections as an addition to standard (oral or i.v.) treatment.
Financial:	As a further treatment option it will be additional to current costs.
Tariff:	Specified high cost drug.
Efficacy:	In the PII, TARGET-NTM trial (n=89) patients received once daily *Arikayce* or placebo added to current treatment but the primary outcome measure (change in mycobacterial density from baseline to day 84) was not met. Antibacterial cultures (secondary outcome measure) were negative in 11/44 patients using *Arikayce* at day 84 (p=0.01 vs. placebo) with further negative cultures at day 186 in an open-label follow-on phase. The on-going PIII open-label CONVERT trial (target n=350) will assess *Arikayce* in patients with refractory NTM lung infection and is due to complete October 2016.
Safety:	The overall incidence of adverse effects with *Arikayce* was similar to placebo (93.2% vs. 88.9%) but serious adverse effects were more frequent with *Arikayce* (18.2% vs. 8.9%). Respiratory adverse events were most common (dysphonia, infection, cough, oropharyngeal pain and haemoptysis).
Guidance:	None.
Reviews:	None.

Likely NHSE commissioned

Amikacin liposomal for **inhalation** *[Arikayce]*; Insmed	
Pharmacology:	Aminoglycoside antibacterial formulated in small biocompatible liposomes (Sustained release Lipid Inhalation Targeting [*SLIT*] delivery technology) for inhalation via eFLow nebuliser.
Indication:	*Pseudomonas aeruginosa* pulmonary infections in patients with cystic fibrosis (CF).
Current status:	Filed in EU December 2014 with orphan status.
UK availability:	2016
Population:	The UK CF registry recorded 10,338 people with CF in 2013 (16 per 100,000 people); 34% of whom have a chronic *Pseudomonas aeruginosa* lung infection.
Sector:	Secondary care.
Implications:	*SLIT* enables amikacin to be delivered directly to the lungs via a single daily dose which takes 15 minutes to inhale. Currently, inhaled tobramycin is administered in two daily doses which take 15 minutes each to inhale. *Vantobra* (tobramycin) will be administered as two doses which take 4-5 minutes each to inhale.
Financial:	*Arikayce* is likely to be competitively priced with other available options, i.e. *Bramitob* and *TOBI*, both of which currently cost about £1,180 for 28 days treatment. *Vantobra* will be another potential alternative.
Tariff:	Specified high cost drug. Likely excluded from CF 'Year of Care' tariff.
Efficacy:	*Arikayce* was non-inferior to *TOBI* with respect to change in FEV1 at 24 weeks in the open-label PIII CLEAR-108 study (n=302). Patients received 3 cycles (alternating 28 days on/ 28 days off) of *Arikayce* once daily via the eFlow nebuliser or *TOBI* twice daily via the *PARI LC PLUS* nebuliser. Eligible patients were enrolled into the PIII open-label safety study CLEAR-110 (n=206). At the end of the sixth treatment cycle FEV1 improved from baseline by 3.39% and 1.11% with *Arikayce* and *TOBI*, respectively.
Safety:	*Arikayce* has a similar incidence of serious treatment emergent adverse events vs. *TOBI*. Respiratory adverse events were most common (haemoptysis, dysphonia, cough and oropharyngeal pain and inflammation).
Guidance:	**NICE:** Cystic Fibrosis. **NHSE**: CCP Inhaled therapy for CF.
Reviews:	None.

Tobramycin nebuliser solution *[Vantobra]*; PARI Pharma	
Pharmacology:	Aminoglycoside antibacterial for inhalation via eFlow nebuliser system.
Indication:	*Pseudomonas aeruginosa* pulmonary infection in patients aged ≥ 6 years with cystic fibrosis (CF).
Current status:	Licensed in the EU March 2015 – see prescribing data.
UK availability:	2016
Population:	The UK CF registry recorded 10,338 people with CF in 2013 (16 per 100,000 people); 34% of whom have a chronic *Pseudomonas aeruginosa* lung infection.
Sector:	Secondary care.
Implications:	The eFlow device allows low volume/high concentration tobramycin to be administered and shortens treatment time.
Financial:	Likely to be competitively priced with other available options, i.e. *Bramitob* and *TOBI*, both of which currently cost about £1,180 for 28 days treatment. *Arikayce* will be another potential alternative.
Tariff:	Specified high cost drug.
Efficacy:	EPAR data suggest a 28-day, PII bioequivalence study (n=78), compared *Vantobra* (150mg/1.5mL) given twice daily via an investigational eFlow nebuliser system with *TOBI* (tobramycin 300mg/5mL) delivered via the PARI LC PLUS nebuliser. Maximum tobramycin levels were lower than safety thresholds. Average inhalation time was 4-4.5 minutes for *Vantobra* vs. 16-17 minutes for *TOBI*.
Safety:	The most common treatment related adverse effects were respiratory in origin.
Guidance:	**NICE:** Cystic Fibrosis. **NHSE**: CCP - Inhaled therapy for CF.
Reviews:	None.

Levofloxacin nebuliser solution *[Quinsair];* Aptalis Pharma	
Pharmacology:	Quinolone antibacterial for targeted inhalation via e-Flow nebuliser technology.
Indication:	*Pseudomonas aeruginosa* pulmonary infection in patients aged ≥12 years with cystic fibrosis (CF).
Current status:	Licensed in the EU March 2015 with orphan status – see prescribing data.
UK availability:	2015
Population:	The UK CF registry recorded 10,338 people with CF in 2013 (16 per 100,000 people); 34% of whom have a chronic *Pseudomonas aeruginosa* lung infection.
Sector:	Secondary care.
Implications:	Nebulised levofloxacin will be an alternative to inhaled/nebulised colomycin, tobramycin, aztreonam and amikacin. Twice daily dosing may be important for compliance.
Financial:	Based on current prices, cost for 28 days tobramycin (*TOBI* 300mg twice daily) treatment is ~£1,180, aztreonam (75mg three times a daily) ~ £2,180 and nebulised colomycin (up to 2 million units three times a day) ~£270. *Quinsair*, with device, is likely to be competitively priced with aztreonam.
Tariff:	Specified high cost drug. Likely excluded from CF 'Year of Care' tariff.
Efficacy:	*Quinsair* was non-inferior to *TOBI* in the open-label, non-inferiority PIII MPEX-209 study (n=282). Both treatments were nebulised twice daily over a 28 day on/off treatment cycle and the primary outcome measure, relative change from baseline in percentage FEV1 after a 28 day treatment cycle, showed <4% difference between arms. This was maintained over 3 treatment cycles (to day 168). In the PIII MPEX-207 study (n=330), twice daily nebulised *Quinsair* was compared to placebo over 28 days. The primary outcome (time to first pulmonary exacerbation) was not met.
Safety:	*Quinsair* had a similar incidence of adverse effects vs. *TOBI*.
Guidance:	**NICE:** Cystic Fibrosis. **NHSE**: CCP -Inhaled therapy for CF.
Reviews:	None.

Isavuconazole injection and oral *[Cresemba]*; Basilea	
Pharmacology:	Triazole antifungal, prodrug, available as infusion (200mg) and capsules (100mg).
Indication:	Mucormycosis, when amphotericin B is inappropriate.
Current status:	Recommended for approval in EU July 2015 with orphan status. Licensed in US March 2015 – see prescribing data.
UK availability:	2016
Population:	Mucormycosis is very rare with an estimated EU prevalence of around 0.6 in 100,000 people. It affects immunocompromised patients and in 2013-14, there were <20 cases in England.
Sector:	Secondary care.
Implications:	An alternative to amphotericin (and posaconazole) for a condition which is difficult to treat and has poor prognosis. It is available in bioequivalent i.v. and oral dose forms.
Financial:	Likely to be competitively priced with other available options (e.g. liposomal amphotericin).
Tariff:	Specified high cost drug.
Efficacy:	The open-label PIII VITAL study (n=149) investigated isavuconazole in patients with invasive life-threatening fungal infections. Patients with mucormycosis (n=37) received i.v. or oral isavuconazole for a median of 84 days (range 2–882). Survival at 180 days was 53% and treatment was successful in 32% of those using ISA as the primary antifungal, and in 36% of those refractory to prior therapy. Treatment success was based on committee-assessed clinical, mycological, and radiological criteria. Of the 37 patients, 11 died and 2 had an inadequate response.
Safety:	In VITAL, the most common adverse effects were vomiting, diarrhoea, nausea, and pyrexia. Isavuconazole may shorten QT interval and monitoring of liver function is required.
Guidance:	None.
Reviews:	None.

Isavuconazole injection and oral *[Cresemba]*; Basilea	
Pharmacology:	Triazole antifungal, prodrug, available as infusion (200mg) and capsules (100mg)
Indication:	Invasive aspergillosis.
Current status:	Filed in EU July 2015 with orphan status. Launched in US April 15 – see prescribing data.
UK availability:	2016
Population:	Invasive aspergillosis is rare amongst the general population but prevalence amongst immunocompromised patients varies from 5-25%. In 2013-14, there were 965 hospital admissions in England due to aspergillosis, accounting for 1,450 finished consultant episodes.
Sector:	Secondary care via highly specialist Chronic Pulmonary Aspergillosis centres.
Implications:	Isavuconazole will compete with voriconazole, posaconazole or amphotericin B. It is available in bioequivalent i.v. and oral dose forms and may offer improved tolerability over other options.
Financial:	Likely to be competitively priced with other available options (i.e. VRC).
Tariff:	Specified high cost drug.
Efficacy:	Isavuconazole (200mg i.v. three times daily for 2 days followed by a once daily i.v. or oral dose of 200mg for up to 84 days) demonstrated non-inferiority vs. voriconazole (loading dose of 6mg/kg i.v. twice daily for 24 hours then 4mg/kg i.v. twice daily for 2 days followed by a once daily oral dose of 200mg for up to 84 days) in the PIII SECURE study (n=527). All-cause mortality at 42 days (primary outcome measure) was 18.6% vs. 20.2%, respectively (adjusted treatment difference of <10%).
Safety:	Common adverse effects include hypokalaemia and infusion related reactions. Serious adverse effects include hepatitis, cholestasis and hepatic failure. Liver function must be regularly monitored. It may also shorten QT interval.
Guidance:	None.
Reviews:	None.

Tenofovir alafenamide/ cobicistat/ elvitegravir/ emtricitabine oral; Gilead	
Pharmacology:	Tenofovir alafenamide is a prodrug of tenofovir disoproxil fumarate. Tenofovir alafenamide 10mg is co-formulated with emtricitabine 200mg, elvitegravir 150mg and cobicistat 150mg for daily use.
Indication:	HIV-1 infection.
Current status:	Filed in EU January 2015.
UK availability:	2016
Population:	In 2013, there were an estimated 107,800 people living in the UK who had HIV infection; a quarter of whom were unaware of their infection. Prevalence of HIV in the UK is estimated at 0.17%.
Sector:	Secondary care.
Implications:	Improved bioavailabity may allow for similar antiviral efficacy with lower doses of tenofovir compared to *Stribild*. This may allow for a more favourable renal, bone and cardiovascular long term safety profile.
Financial:	This will be alternative to *Stribild* (cost £1,034/month) and is likely to be competitively priced.
Tariff:	Specified high cost drug.
Efficacy:	Pooled data from two published PIII studies showed that tenofovir alafenamide co-formulation was non-inferior to *Stribild* in 1,733 treatment-naïve patients. The primary outcome, proportion of patients with <50 copies per mL of plasma HIV-1 RNA, was achieved by 92% and 90% of patients in the tenofovir alafenamide co-formulation and *Stribild* groups, respectively (p=ns).
Safety:	Non-inferiority studies in patients with renal impairment suggest tenofovir alafenamide co-formulation may have fewer unfavourable long term effects on bone density, kidney function and lipid profiles than *Stribild*. An open-label PIII safety study is ongoing.
Guidance:	**British HIV Association:** Treatment of HIV. **NHSE**: CCP- Elvitegravir/cobicistat/emtricitabine/tenofovir, CCP-Dolutegravir, CCP- Cobicistat .
Reviews:	None.

Grazoprevir/ elbasvir **oral**; MSD	
Pharmacology:	Fixed-dose combination of NS3/4a (grazoprevir 100mg) and NS5A (elbasvir 50mg) protease inhibitors.
Indication:	Hepatitis C viral (HCV) infection (genotypes 1, 4 and 6) in treatment naive and experienced patients.
Current status:	PIII
UK availability:	2016
Population:	About 214,000 people are infected with HCV in the UK; around 30% receive antivirals. The majority (90%) of HCV infections are of genotype 1 and 3.
Sector:	Secondary care.
Implications:	This clears HCV of several genotypes without need for interferon or ribavirin and over a short treatment course (12 weeks).
Financial:	This is likely to be competitively priced with other available options.
Tariff:	Likely specified high cost drug.
Efficacy:	In the placebo-controlled C-EDGE, C-SURFER studies, grazoprevir/ elbasvir achieved high rates (95-99%) of sustained virologic response 12 weeks after treatment (SVR12). The PIII C-EDGE study (n=421) included patients with cirrhotic and non-cirrhotic, treatment naive HCV of genotypes 1, 4 and 6. The PII/III C-SURFER study (n=116) included patients with treatment naive or experienced HCV of genotype 1 and advanced chronic kidney disease. In the PII open label C-SALVAGE study (n=79), grazoprevir/elbasvir with ribavirin achieved SVR12 in 96% of treatment-experienced patients with genotype 1 HCV.
Safety:	The most common adverse events reported were headache, fatigue, nausea and arthralgia.
Guidance:	**NICE**: Hepatitis. **SIGN**: Hepatitis C. **NHSE**: CCP-Hepatitis C in patients with cirrhosis. **European Association Study of the Liver**: Hepatitis C.
Reviews:	None recent.

Sofosbuvir/ velpatasvir **oral**; Gilead	
Pharmacology:	Fixed-dose combination of NS5A (velpatasvir 100mg) and NS5B protease inhibitors (sofosbuvir 400mg).
Indication:	Hepatitis C virus (HCV) infection (all genotypes) in treatment naïve and experienced patients.
Current status:	PIII
UK availability:	2016
Population:	About 214,000 people are infected with HCV in the UK; around 30% receive antivirals. The majority (90%) of HCV infections are of genotype 1 and 3.
Sector:	Secondary care.
Implications:	This fixed dose combination clears HCV for the majority of people without need for interferon. It offers broad coverage of HCV genotypes and appears to be well tolerated.
Financial:	Velpatasvir will be an additional cost to that of sofosbuvir, which currently costs £11,600/ month. The fixed dose combination was used in trials with or without ribavirin (£250-300 per month).
Tariff:	Likely specified high cost drug.
Efficacy:	Three open-label PII studies (GS-US-342-0109 [n=160], GS-US-342-0102 [n=140], ELECTRON2 [n=53]) found that once daily sofosbuvir (400mg) + velpatasvir (25mg or 100mg) +/- ribavirin for 8 or 12 weeks was effective in patients with treatment-naïve or treatment-experienced HCV, across genotypes. The rates of sustained virologic response 12 weeks after the end of therapy (SVR12) ranged from 88%- 100% among those receiving sofosbuvir 400mg + velpatasvir 100mg – the regimen selected for the ongoing PIII ASTRAL studies which are due to complete at the end of 2015.
Safety:	Common adverse events were fatigue, headache, nausea and insomnia and low haemoglobin in patients also taking ribavirin.
Guidance:	**NICE**: Hepatitis. **SIGN**: Hepatitis C. **NHSE**: CCP-Hepatitis C in patients with cirrhosis. **European Association Study of the Liver**: Hepatitis C.
Reviews:	NIHR HSRIC February 2015.

Daclatasvir/ asunaprevir/ beclabuvir **oral;** Bristol-Myers Squibb	
Pharmacology:	Fixed-dose combination of an NS5A inhibitor (daclatasvir 30mg), NS3 inhibitor (asunaprevir 200 mg) and NS5B inhibitor (beclabuvir 75mg), given twice daily.
Indication:	Hepatitis C virus (HCV) genotype 1 infection.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care.
Tariff:	Likely specified high cost drug.
Guidance:	**NICE**: Hepatitis. **SIGN**: Hepatitis C. **European Association Study of the Liver**: Hepatitis C. **NHSE**: CCP-Hepatitis C in patients with cirrhosis.
Reviews:	NIHR HSRIC February 2015.

BNF 6. Endocrine system

Likely CCG commissioned

Dapagliflozin/ saxagliptin **oral;** AstraZeneca	
Pharmacology:	Fixed-dose combination preparation containing a sodium-glucose co-transporter-2 (SGLT-2) inhibitor (dapagliflozin 10mg) and a dipeptidyl peptidase-4 (DPP-4) inhibitor (saxagliptin 5mg), taken once a day.
Indication:	Type 2 diabetes mellitus, in combination with metformin.
Current status:	Filed in EU June 2015, and in US February 2015.
UK availability:	2016
Population:	Estimated UK prevalence of diagnosed diabetes mellitus was 3.3 million people in 2014; a further 590,000 may be undiagnosed. 90% of people with diabetes have type 2 diabetes. NICE estimates that 14% of patients are on triple therapy (about 840 per 100,000).
Sector:	Primary care.
Implications:	Place in therapy for this combination is unclear. NICE does not currently recommend triple therapy with metformin, a SGLT-2 inhibitor and a DPP-4 inhibitor.
Financial:	Dapagliflozin costs £37/month and saxagliptin £32/month. A dapagliflozin/ saxagliptin preparation will have to be competitive.
Tariff:	HRG included.
Efficacy:	In a 24-week PIII study involving 534 adults not controlled on metformin 1,500mg daily, mean changes from baseline in HbA_{1c} were -1.5% with dapagliflozin/ saxagliptin, -1.2% with dapagliflozin and -0.9% with saxagliptan. 41%, 22% and 18% of patients, respectively, achieved HbA_{1c} <7% (53mmol/mol]).
Safety:	See medicines.org.uk for individual products. The EMA is currently reviewing risk of diabetic ketoacidosis with SGLT-2 inhibitors.
Guidance:	**NICE**: Diabetes, Dapagliflozin. **SIGN**: Diabetes.
Reviews:	None.

Empagliflozin/ linagliptin oral *[Glyxambi];* Boehringer Ingelheim	
Pharmacology:	Fixed-dose combination preparation taken once daily containing sodium-glucose co-transporter-2 (SGLT-2) inhibitor (empagliflozin 10mg or 25mg) and a dipeptidyl peptidase-4 (DPP-4) inhibitor (linagliptin 5mg).
Indication:	Type 2 diabetes mellitus, in combination with metformin.
Current status:	PIII in EU. Launched in US March 2015 – see prescribing data.
UK availability:	2016
Population:	Estimated UK prevalence of diagnosed diabetes mellitus was 3.3 million people in 2014; a further 590,000 may be undiagnosed. 90% of people with diabetes have type 2 diabetes. NICE estimates that 14% of patients are on triple therapy (about 840 per 100,000).
Sector:	Primary care.
Implications:	Place in therapy for this combination is unclear. NICE does not currently recommend triple therapy with metformin, a SGLT-2 inhibitor and a DPP-4 inhibitor.
Financial:	Empagliflozin costs £37/month (10mg or 25mg daily) and linagliptin £33/month. An empagliflozin/ linagliptin preparation will have to be competitive.
Tariff:	HRG included.
Efficacy:	In a published 24-week PIII study involving 686 adults not controlled on metformin 1,500mg daily, mean changes from baseline in HbA_{1c} were -1.2% with empagliflozin 25mg/ linagliptin, -1.1% with empagliflozin 10mg/ linagliptin, -0.6% with empagliflozin 25mg, -0.7% with empagliflozin 10mg and -0.7% with linagliptin 5mg ($p<0.001$ for all comparisons). In these groups, respectively, 62%, 58%, 33%, 28% and 36% of subjects with baseline HbA_{1c} ≥7% (58mmol/mol) had HbA_{1c} <7% at week 24.
Safety:	See medicines.org.uk for individual products. The EMA is currently reviewing risk of diabetic ketoacidosis with SGLT-2 inhibitors.
Guidance:	**NICE**: Diabetes, Empagliflozin. **SIGN**: Diabetes.
Reviews:	None.

Empagliflozin/ metformin oral *[Synjardy];* Boehringer Ingelheim	
Pharmacology:	Fixed-dose immediate-release combination preparation containing a sodium-glucose co-transporter-2 (SGLT-2) inhibitor (empagliflozin 5mg or 12.5mg) and an immediate-release biguanide (metformin 850mg or 1,000mg), taken twice daily.
Indication:	Type 2 diabetes mellitus – alone or in combination with other anti-diabetic medicines including insulin.
Current status:	Licensed in EU May 2015 – see prescribing data.
UK availability:	2015
Population:	Estimated UK prevalence of diagnosed diabetes mellitus was 3.3 million people in 2014; a further 590,000 may be undiagnosed. 90% of people with diabetes have type 2 diabetes. NICE estimates that 14% of patients are on triple therapy (about 840 per 100,000).
Sector:	Primary care.
Implications:	NICE has approved empagliflozin for dual therapy with metformin (if a sulfonylurea is contraindicated or not tolerated, or the person is at significant risk of hypoglycaemia), for triple therapy with metformin and a sulfonylurea or a thiazolidinedione, and for use with insulin. Canagliflozin and dapagliflozin are also available in twice-daily fixed-dose combination preparations with metformin.
Financial:	Empagliflozin costs £37/month (10mg or 25mg daily) and metformin <£2/month. The combination preparation is likely to be a similar price to empagliflozin.
Tariff:	HRG included.
Efficacy:	A pooled analysis of data from 3 pivotal PIII studies (n=1,679) showed mean treatment difference to placebo + metformin for change from baseline in HbA_{1c} after 24 weeks was -0.6% for empagliflozin 10mg daily + metformin and -0.6% for empagliflozin 25mg daily + metformin, regardless of additional background therapy.
Safety:	See prescribing data. The EMA is currently reviewing risk of diabetic ketoacidosis with SGLT-2 inhibitors.
Guidance:	**NICE**: Diabetes, Empagliflozin. **SIGN**: Diabetes.
Reviews:	**SMC**: *Synjardy* due October 2015.

Alogliptin/ pioglitazone oral *[Incresync]; Takeda*	
Pharmacology:	Fixed-dose combination preparations containing a dipeptidyl peptidase-4 (DPP-4) inhibitor (alogliptin 12.5mg or 25mg) and a thiazolidinedione (pioglitazone 30mg or 45mg).
Indication:	Type 2 diabetes mellitus, second line, alone or in combination with metformin.
Current status:	Licensed in EU September 2013 – see prescribing data.
UK availability:	Uncertain due to lack of clarity regarding marketing plans.
Population:	Estimated UK prevalence of diagnosed diabetes mellitus was 3.3 million people in 2014; a further 590,000 may be undiagnosed. 90% of people with diabetes have type 2 diabetes. NICE estimates that 14% of patients are on triple therapy (about 840 per 100,000).
Sector:	Primary care.
Implications:	This will be the first DPP-4 inhibitor plus glitazone combination product, although most DPP-4 inhibitors are licensed to be used with pioglitazone.
Financial:	28-day cost for DPP-4 inhibitors alone and in combination with metformin is £27-34. Generic pioglitazone is available (<£2/month). An alogliptin/ pioglitazone preparation will have to be competitive.
Tariff:	HRG included.
Efficacy:	In a published 26-week PIII study, mean change in HbA_{1c} from baseline (8.8%) in 655 treatment-naïve patients was -1.7% with alogliptin 25mg/ pioglitazone 30mg vs. -1.0% with alogliptin 25mg and -1.2% with pioglitazone 30mg (both p<0.001).
Safety:	See prescribing data. The MHRA has issued warnings about using pioglitazone in patients with a history of heart failure or bladder cancer.
Guidance:	**NICE**: Diabetes. **SIGN**: Diabetes.
Reviews:	None.

Omarigliptin oral; MSD	
Pharmacology:	First once-weekly dipeptidyl peptidase-4 (DPP-4) inhibitor.
Indication:	Type 2 diabetes mellitus, monotherapy, and in combination with other anti-diabetic medicines including insulin.
Current status:	PIII
UK availability:	2016
Population:	Estimated UK prevalence of diagnosed diabetes mellitus was 3.3 million people in 2014; a further 590,000 may be undiagnosed. 90% of people with diabetes have type 2 diabetes.
Sector:	Primary care.
Implications:	First once-weekly oral antidiabetic. May be attractive for some patients, but risks of accidental overdose need to be considered.
Financial:	Likely to be competitively priced to daily DPP-4 inhibitors, including sitagliptin (£33/month).
Tariff:	Likely HRG included.
Efficacy:	Data from 9 PIII studies, in about 7,500 patients, will be submitted to licensing authorities. In a 24-week PIII study involving 414 patients, omarigliptin significantly reduced mean HbA_{1c} from baseline by -0.8% vs. placebo, and was non-inferior to sitagliptin 50mg daily (treatment difference -0.02%).
Safety:	Rates of adverse events were similar with omarigliptin and sitagliptin in a PIII study. No patients had symptomatic hypoglycaemia with omarigliptin, and mean weight change at 24 weeks was 0.04 kg.
Guidance:	**NICE**: Diabetes. **SIGN**: Diabetes.
Reviews:	None.

Exenatide injection *[Bydureon];* AstraZeneca	
Pharmacology:	New suspension formulation of exenatide, a long-acting glucagon-like peptide-1 (GLP-1) agonist, given once-weekly by s.c. injection.
Indication:	Type 2 diabetes mellitus.
Current status:	PIII
UK availability:	2016
Population:	Estimated UK prevalence of diagnosed diabetes mellitus was 3.3 million people in 2014; a further 590,000 may be undiagnosed. 90% of people with diabetes have type 2 diabetes. 2,800 per 100,000 people could be eligible for GLP-1 receptor agonists.
Sector:	Primary care.
Implications:	A suspension of exenatide for once-weekly administration. Unlike *Bydureon* vials or dual chamber pen this does not need to be reconstituted prior to use. NICE recommends once-weekly exenatide (with metformin, and a sulphonylurea or pioglitazone) in patients with a body mass index (BMI) ≥35kg/m^2 and weight-related psychological or medical problems, or a BMI <35kg/m^2 and insulin is unsuitable or weight loss would be beneficial. Dual therapy with metformin or a sulphonylurea is recommended only if either drug, and pioglitazone and a dipeptidylpeptidase-4 inhibitor, is contraindicated or not tolerated.
Financial:	Likely to be priced similarly to available *Bydureon* preparations (£18.34/2mg vial or pen).
Tariff:	HRG included.
Efficacy:	In the PIII DURATION-NEO-1 trial (n=377), mean decreases in HbA_{1c} from baseline to 28 weeks were -1.4% with exenatide 2mg once-weekly vs. -1.0% with exenatide 10micrograms twice daily (p=0.007 for non-inferiority). HbA_{1c} target of <7% (53mmol/mol) was reached by 49% and 43% of patients using once-weekly vs. twice-daily exenatide (p=ns); 36% and 26% of patients achieved targets <6.5%, respectively (p=0.05; NNT=10). Reductions in mean body weight and fasting plasma glucose were similar between groups.
Safety:	See prescribing data for *Bydureon* vial/pen. 12.7% of patients given the once-weekly suspension had injection site nodules vs. 0.7% in the twice-daily exenatide group.
Guidance:	**NICE**: Diabetes, Exenatide prolonged-release. **SIGN**: Diabetes.
Reviews:	None.

Exenatide implant; Servier	
Pharmacology:	Long-acting glucagon-like peptide 1 (GLP-1) agonist delivered over 3-12 months via the DUROS device, implanted subcutaneously into the abdomen.
Indication:	Type 2 diabetes mellitus.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care initiated.
Tariff:	HRG included.
Guidance:	**NICE**: Diabetes. **SIGN**: Diabetes.
Reviews:	None.

Albiglutide injection [Eperzan]; GSK	
Pharmacology:	Glucagon-like peptide-1 (GLP-1) receptor agonist fused to human albumin, given by once-weekly s.c. injection.
Indication:	Type 2 diabetes mellitus, monotherapy, and in combination with other anti-diabetic medicines including insulin.
Current status:	Licensed in EU March 2014 – see prescribing data. Launched in Ireland and US.
UK availability:	Uncertain due to lack of clarity regarding marketing plans.
Sector:	Primary care.
Tariff:	HRG included.
Guidance:	**NICE**: Diabetes. **SIGN**: Diabetes.
Reviews:	**SMC**: Albiglutide in progress.

Insulin inhalation *[Afrezza];* Sanofi-Aventis	
Pharmacology:	Dry-powder formulation of insulin, ultra rapid-acting, first-in-class. Used at the start of a meal.
Indication:	Type 1 and 2 diabetes mellitus in adults.
Current status:	PIII in EU. Launched in US February 2015 – see prescribing data.
UK availability:	Uncertain.
Population:	Estimated UK prevalence of diagnosed diabetes mellitus was 3.3 million people in 2014; a further 590,000 may be undiagnosed. 90% of people with diabetes have type 2 diabetes. Prevalence of insulin use in patients with type 2 diabetes increased from 0.7 to 4.3 per 1,000 people between 1991 and 2010.
Sector:	Secondary care initiated.
Implications:	Needle-free insulin will be attractive to patients, especially those with needle phobia or problems injecting. *Exubera* (an inhaled insulin formulation launched in 2006 but discontinued due to poor sales) was not approved for use by NICE on cost-effectiveness grounds.
Financial:	Cost of *Afrezza* in US is $7.54/day (based on 12units/day). In 2006, *Exubera* cost £1,100 annually.
Tariff:	HRG included.
Efficacy:	A PIII study in 518 patients with type 1 diabetes using basal insulin showed that *Afrezza* was non-inferior to insulin aspart. Mean HbA_{1c} was reduced by 0.2% with *Afrezza* vs. 0.4% with insulin aspart. Fasting blood glucose and bodyweight were also reduced vs. insulin aspart (p=0.003 and p=0.01, respectively). In a PIII study involving 353 insulin-naïve patients with type 2 diabetes, *Afrezza* in combination with oral anti-diabetic medicines, decreased mean HbA_{1c} by 0.8% vs. 0.4% with oral medicines alone (p<0.001).
Safety:	Cough is the most common treatment-related adverse effect. Inhaled insulin is not recommended in patients who smoke because of unknown efficacy and safety, and concerns exist over use in people with respiratory problems. Whilst insulin doses given by injection can be adjusted by half unit increments, *Afrezza* doses can only be adjusted by 4 unit increments.
Guidance:	**NICE**: Diabetes. **SIGN**: Diabetes.
Reviews:	None.

Anamorelin oral; Helsinn	
Pharmacology:	Ghrelin receptor agonist, first-in-class.
Indication:	Anorexia/cachexia associated with non-small cell lung cancer (NSCLC).
Current status:	PIII, with fast track status in US.
UK availability:	2016
Population:	Cancer anorexia-cachexia syndrome (CACS) is characterised by involuntary weight loss, muscle atrophy and physiological changes. CACS occurs in 61% of patients with NSCLC and causes 20% of cancer deaths. In 2010, there were 42 new cases of NSCLC per 100,000 people.
Sector:	Primary and secondary care.
Implications:	Treatment options for CACS are limited, and include nutritional treatments, short-term therapy with corticosteroids, and progestogens. Anamorelin is a new therapeutic option which could reduce symptoms, improve quality of life and prolong patient independence.
Financial:	Cost is unknown. It may offset costs associated with nutritional supplements.
Tariff:	Likely HRG included.
Efficacy:	In two 12-week PIII studies (both n=477), median lean body mass (LBM) increased from baseline by 1.1kg with anamorelin vs. -0.44kg with placebo in ROMANA 1 (p<0.0001), and by 0.75kg and -0.96kg, respectively in ROMANA 2 (p<0.0001). Anamorelin increased body weight vs. placebo in both trials (2.2kg vs. 0.14kg, and 0.95kg vs. -0.57kg, respectively; both p<0.0001), and improved patient symptoms and concerns as shown by higher Functional Assessment of Anorexia-Cachexia Treatment (FAACT) subdomain scores vs. placebo (p=0.0004 in ROMANA 1 and p=0.0016 in ROMANA 2).
Safety:	Most common adverse events are hyperglycaemia and nausea.
Guidance:	**NICE**: Lung cancer, Nutrition support. **SIGN**: Lung cancer.
Reviews:	NIHR HSRIC December 2013.

Bazedoxifene/ conjugated estrogens **oral** *[Duavive];* Pfizer	
Pharmacology:	Fixed-dose combination preparation containing a selective estrogen receptor modulator (SERM) (bazedoxifine 20mg) plus conjugated estrogens (0.45mg), taken once-daily.
Indication:	Estrogen deficiency symptoms in postmenopausal women with a uterus who are unsuitable for progestin-containing therapy.
Current status:	Licensed in EU December 2014 and launched in several EU countries – see prescribing data. Launched in US February 2014 for menopausal symptoms and postmenopausal osteoporosis – see prescribing data. EU filing for postmenopausal osteoporosis withdrawn.
UK availability:	2015
Population:	Menopausal symptoms include vasomotor mood and urogenital symptoms. A 2009 postal survey of women in Scotland showed 47% had experienced hot flushes in the previous month, 46% had night sweats and 26% had vaginal dryness.
Sector:	Primary care.
Implications:	Many preparations are available for menopausal symptoms. Women vary in their tolerance to progestogens. Bazedoxifene plus conjugated estrogens (BAZ/CE) is likely to be used as a second-line option for women unable to tolerate progestin-containing preparations.
Financial:	BAZ/CE will have to compete with available options.
Tariff:	Likely HRG included.
Efficacy:	BAZ/CE has been evaluated in 5 published PIII Selective Estrogen Menopause and Response to Therapy (SMART) studies. In SMART-1 (n=3,397), SMART-4 (n=1,061) and SMART-5 (n=1,843), BAZ/CE was associated with low rates (<1%) of endometrial hyperplasia and/or endometrial thickness over 24 months that were similar to placebo. In SMART-2 (n=332), BAZ/CE reduced daily incidence of moderate-to-severe hot flushes by 74% (from 10.3 at baseline to 2.8 at week 12) vs. 51% with placebo (from 10.5 to 5.4) ($p<0.001$). In SMART-3 (n=664), BAZ/CE improved vaginal dryness vs. placebo ($p=0.05$).
Safety:	Incidence of bleeding and breast tenderness is similar to that with placebo, and significantly lower than with CE plus medroxyprogesterone acetate ($p<0.05$).
Guidance:	**NICE**: Menopause.
Reviews:	None.

Elagolix **oral;** Abbvie	
Pharmacology:	Second-generation gonadotropin-releasing hormone antagonist that allows partial estrogen suppression, first-in-class.
Indication:	Endometriosis-related pain.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care initiated, continued in primary care.
Tariff:	HRG included.
Guidance:	**NICE**: Endometriosis and fibroids.
Reviews:	None.

Odanacatib **oral**; MSD	
Pharmacology:	Selective cathepsin-K inhibitor, taken once-weekly.
Indication:	Osteoporosis in postmenopausal women, primary or secondary prevention, when bisphosphonates are contraindicated or not successful.
Current status:	PIII
UK availability:	2016
Population:	Over 2 million women are estimated to have osteoporosis in England and Wales. After the menopause, prevalence of osteoporosis increases from about 2% at 50 years of age to more than 25% at 80 years.
Sector:	Primary care.
Implications:	NICE recommends an oral bisphosphonate first-line for primary and secondary prevention of postmenopausal osteoporosis. Odanacatib will be an alternative to denosumab, teriparatide, strontium ranelate and raloxifene.
Financial:	Current annual treatment costs of existing options vary: about £200 (raloxifene 60mg/day), £370 (denosumab 60mg 6-monthly), £325 (strontium ranelate 2g/day) and £3,300 (teriparatide 20micrograms/daily). The cost of odanacatib is likely to be competitive.
Tariff:	Likely HRG included.
Efficacy:	The 5-year LOFT study (previously named POWER) in 16,713 postmenopausal women was closed early after interim analysis showed it met the primary outcome. Compared with placebo, odanacatib reduced rates of hip fracture by 47%, vertebral fracture by 72% and non-vertebral fracture by 23% (all p<0.001). Odanacatib increased bone mineral density at total hip and lumbar spine from baseline by 9.5% (p<0.001) and 11.2% (p<0.001), respectively. However, safety issues were noted which are being followed-up in a number of extension studies.
Safety:	In the LOFT study, 215 patients in the odanacatib arm reported major acute cardiovascular events vs. 194 in the placebo arm (p=ns), and 1.4% of patients given odancatib had a stroke vs. 1.1% given placebo (p=ns). As odanacatib prevents collagen breakdown, data are needed on potential effects on fracture healing and bone structure.
Guidance:	**NICE**: Osteoporosis. **SIGN**: Osteoporosis.
Reviews:	None.

Likely NHSE commissioned

Odanacatib **oral**; MSD	
Pharmacology:	Selective cathepsin-K inhibitor, taken once-weekly.
Indication:	Osteoporosis treatment in men when bisphosphonates fail or are contra-indicated (licence extension).
Current status:	PIII. A licence for use in men will only be submitted once licenced for use in postmenopausal women.
UK availability:	2017
Sector:	Secondary care and specialist endocrinology centres.
Tariff:	Likely HRG included.
Guidance:	**NICE**: Osteoporosis. **SIGN**: Osteoporosis.
Reviews:	NIHR HSRIC June 2013.

Metreleptin **injection** *[Myalept];* Aegerion	
Pharmacology:	An analogue of the human hormone leptin, given by once daily s.c. injection.
Indication:	Lipodystrophy, as an adjunct to diet to treat complications of leptin deficiency.
Current status:	PII/III in EU with orphan status. Launched in US – see prescribing data.
UK availability:	2017
Sector:	National highly specialist service provided by Addenbrooke's Hospital (National Severe Insulin Resistance Service).
Tariff:	Likely specified high cost drug.
Guidance:	**NICE**: Endocrinal, nutritional and metabolic conditions.
Reviews:	NIHR HSRIC June 2014.

BNF 7. Obstetrics, gynaecology and urinary-tract disorders

Likely CCG commissioned

ICES13 injection; Innovacell	
Pharmacology:	Autologous myoblast cell-based therapy, given by intra-sphincter muscle injection.
Indication:	Urinary stress incontinence, mild-to-moderate, second-line, in women.
Current status:	PIII in EU.
UK availability:	2017
Sector:	Secondary care.
Tariff:	Likely specified high cost drug.
Guidance:	**NICE**: Urinary incontinence
Reviews:	NIHR HSRIC May 2013.

BNF 8. Malignant disease and immunosuppression

Likely NHSE commissioned

Dinutuximab injection *[Unituxin]*; United Therapeutics	
Pharmacology:	GD2-binding monoclonal antibody. Given by i.v. infusion over 10-20 hours for 4 consecutive days every 24-32 days for up to 5 cycles, in combination with GM-CSF, interleukin-2 and isotretinoin.
Indication:	High-risk neuroblastoma, in children aged 1 year and older who receive induction chemotherapy and achieve at least a partial response, followed by autologous stem cell transplant.
Current status:	Recommended for approval in EU May 2015, with orphan status. Licensed in US March 2015, with orphan and priority review status – see prescribing data.
UK availability:	2015
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Brain cancers. Dinutuximab due April 2016.
Reviews:	NIHR HSRIC June 2014.

Brain cancer vaccine injection *[DCVax-L];* Northwest Biotherapeutics	
Pharmacology:	Immunostimulant vaccine manufactured using the patient's dendritic cells and resected tumour tissue, given by intradermal injection.
Indication:	Glioblastoma multiforme, first-line adjuvant therapy.
Current status:	PIII, with Promising Innovative Medicine and orphan status.
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Brain cancers.
Reviews:	None.

Nivolumab injection *[Opdivo];* Bristol-Myers Squibb	
Pharmacology:	Humanised monoclonal IgG4 antibody against programmed death-1 (PD-1) protein.
Indication:	Head and neck cancer, squamous cell, recurrent or metastatic, platinum-refractory (licence extension).
Current status:	PIII in EU and US.
UK availability:	2017
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Head and neck cancer. **SIGN**: Head and neck cancer.
Reviews:	None.

Crizotinib oral *[Xalkori];* Pfizer	
Pharmacology:	ALK and cMET inhibitor, first-in-class.
Indication:	Non-small cell lung cancer, advanced, first-line in ALK-positive patients (licence extension).
Current status:	Filed in EU.
UK availability:	2015
Sector:	Secondary care.
CDF:	Not included for this indication July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Lung cancer. **SIGN**: Lung cancer.
Reviews:	NIHR HSRIC February 2015.

Ceritinib oral *[Zykadia];* Novartis	
Pharmacology:	ALK inhibitor.
Indication:	Non-small cell lung cancer, ALK-positive, locally advanced or metastatic – second-line after crizotinib.
Current status:	Licensed in EU May 2015 – see prescribing data. Launched in US July 2014, with breakthrough therapy status.
UK availability:	2015
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Lung cancer. Ceritinib due January 2016. **SIGN**: Lung cancer.
Reviews:	NIHR HSRIC April 2013.

Afatinib oral *[Giotrif];* Boehringer Ingelheim	
Pharmacology:	Tyrosine kinase inhibitor irreversibly blocking epidermal growth factor receptors, including HER2.
Indication:	Non-small cell lung cancer, advanced, squamous – second-line after platinum-based chemotherapy (licence extension).
Current status:	PIII
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Lung cancer. Afatinib is recommended for locally advanced or metastatic EGFR-positive disease. **SIGN**: Lung cancer.
Reviews:	None.

Mereletinib **oral**; AstraZeneca	
Pharmacology:	Third-generation, irreversible, selective EGFR inhibitor.
Indication:	Non-small cell lung cancer, locally advanced or metastatic, EGFR and T790M mutation-positive – second-line in patients who have progressed on EGFR tyrosine kinase inhibitor therapy.
Current status:	Filed in EU June 2015. PIII in US, with breakthrough therapy, orphan and fast track status.
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Lung cancer. **SIGN**: Lung cancer.
Reviews:	NIHR HSRIC April 2015.

Necitumumab **injection**; Lilly	
Pharmacology:	Monoclonal IgG antibody that inhibits EGFR, given by i.v. infusion on day 1 and 8 every 3 weeks.
Indication:	Non-small cell lung cancer, squamous, locally advanced or metastatic, first-line.
Current status:	Filed in EU and US January 2015 with fast track status in US.
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Lung cancer. **SIGN**: Lung cancer.
Reviews:	NIHR HSRIC February 2014.

Nivolumab **injection** *[Opdivo];* Bristol-Myers Squibb	
Pharmacology:	Monoclonal IgG4 antibody against programmed death-1 (PD-1) protein, given by i.v. infusion every two weeks.
Indication:	Non-small cell lung cancer, non-squamous, advanced, second-line (licence extension).
Current status:	PIII in EU and US, with fast track status in US.
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Lung cancer. Nivolumab due September 2016. **SIGN**: Lung cancer.
Reviews:	NIHR HSRIC October 2013.

Atezolizumab **injection**; Roche	
Pharmacology:	A monoclonal antibody against programmed cell death-1 (PD-1) protein, given by i.v. infusion once every 21 days.
Indication:	Non-small cell lung cancer, PD-1-positive, second-line.
Current status:	PIII in EU. PIII in US, with breakthrough therapy and fast track status.
UK availability:	2017
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Lung cancer. **SIGN**: Lung cancer.
Reviews:	None.

Pembrolizumab injection *[Keytruda];* MSD	
Pharmacology:	Monoclonal IgG4 antibody against programmed death-1 (PD-1), given by i.v. infusion every 3 weeks.
Indication:	Non-small cell lung cancer, advanced, PD-1-positive and EGFR- or ALK-negative, with disease progression following platinum containing chemotherapy, first- and second-line (licence extensions).
Current status:	PIII in EU. Filed in US April 2015 (second-line), with breakthrough therapy and priority review status.
UK availability:	2016 (second-line) and 2017 (first-line).
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Lung cancer. **SIGN**: Lung cancer.
Reviews:	NIHR HSRIC December 2013 (second-line), NIHR HSRIC August 2015 (first-line).

Ganetespib injection; Synta	
Pharmacology:	A second-generation heat shock protein-90 inhibitor, given by i.v. infusion.
Indication:	Non-small cell lung cancer, advanced, second-line.
Current status:	PIII, with fast track status in US.
UK availability:	2017
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Lung cancer. **SIGN**: Lung cancer.
Reviews:	None.

Defactinib oral; Verastem	
Pharmacology:	FAK inhibitor.
Indication:	Malignant pleural mesothelioma, maintenance therapy in patients who have not progressed.
Current status:	PII, with orphan status in EU and US.
UK availability:	2017
Sector:	Secondary or tertiary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Lung cancer. **SIGN**: Lung cancer.
Reviews:	None.

Buparlisib oral; Novartis	
Pharmacology:	Pan-phosphatidylinositol 3-kinase (PI3K) inhibitor.
Indication:	Breast cancer, advanced, hormone receptor-positive and HER2-negative, second-line in combination with fulvestrant or hormone therapy in postmenopausal women after progression on aromatase inhibitor.
Current status:	PIII
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Breast cancer. **SIGN**: Primary breast cancer.
Reviews:	NIHR HSRIC July 2015.

Palbociclib oral *[Ibrance];* Pfizer	
Pharmacology:	Cyclin-dependent kinase 4 and 6 inhibitor.
Indication:	Breast cancer, advanced, hormone receptor-positive and HER2-negative, first-line with letrozole in postmenopausal women.
Current status:	Filed in EU August 2015. Launched in US February 2015, with breakthrough therapy and priority review status – see prescribing data.
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Breast cancer. **SIGN**: Primary breast cancer.
Reviews:	NIHR HSRIC June 2014.

Palbociclib oral *[Ibrance];* Pfizer	
Pharmacology:	Cyclin-dependent kinase 4 and 6 inhibitor.
Indication:	Breast cancer, advanced, hormone receptor-positive and HER2-negative, second-line.
Current status:	Filed in EU August 2015.
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Breast cancer. **SIGN**: Primary breast cancer.
Reviews:	NIHR HSRIC July 2015

Everolimus oral *[Afinitor]*; Novartis	
Pharmacology:	mTOR inhibitor.
Indication:	Neuroendocrine tumours, advanced, of gastrointestinal or lung origin (licence extension).
Current status:	PIII
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Cancer – general and other.
Reviews:	None recent.

Regorafenib oral *[Stivarga];* Bayer	
Pharmacology:	Multi-targeted inhibitor of angiogenic, stromal and oncogenic receptor tyrosine kinases, taken once daily for the first 21 days of each 28-day cycle.
Indication:	Hepatocellular carcinoma, unresectable, second-line after sorafenib (licence extension).
Current status:	PIII
UK availability:	2017
Sector:	Secondary care.
CDF:	Not included for this indication July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Liver cancers.
Reviews:	None.

Cediranib **oral** *[Recentin];* AstraZeneca	
Pharmacology:	An inhibitor of all three VEGF receptors (VEGFR-1,-2 and -3).
Indication:	Ovarian cancer (including fallopian tube or primary peritoneal), platinum-sensitive, second-line in combination with platinum-based chemotherapy, followed by monotherapy maintenance.
Current status:	PIII, with orphan status in EU.
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Ovarian cancer. **SIGN**: Ovarian cancer.
Reviews:	NIHR HSRIC April 2014.

Paclitaxel **injection** *[Paclical];* Oasmia	
Pharmacology:	Tubulin inhibitor. An encapsulated formulation that increases water solubility of paclitaxel, given by i.v infusion every 3 weeks for 6 cycles.
Indication:	Ovarian cancer, platinum-sensitive or partially platinum-sensitive, second- or third-line.
Current status:	PIII with orphan status in EU and US.
UK availability:	Uncertain.
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Ovarian cancer. **SIGN**: Ovarian cancer.
Reviews:	None recent.

Trifluridine/ tipiracil **oral** *[Lonsurf];* Taiho	
Pharmacology:	Trifluridine is a thymidine-based nucleoside analogue. Tipiracil prevents degradation of trifluridine by inhibiting thymidine phosphorylase.
Indication:	Colorectal cancer, metastatic, refractory, third- or fourth-line.
Current status:	Filed in EU March 2015 and in US December 2014.
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Colorectal cancer. **SIGN**: Colorectal cancer.
Reviews:	None.

Nivolumab **injection** *[Opdivo];* Bristol-Myers Squibb	
Pharmacology:	Monoclonal IgG4 antibody against programmed death-1 (PD-1) protein.
Indication:	Renal cell cancer, locally advanced or metastatic, second- or third-line (licence extension).
Current status:	PIII in EU. PIII in US, with fast track status.
UK availability:	2017
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Renal cancer.
Reviews:	NIHR HSRIC December 2014.

Apaziquone intravesical *[Neoquin];* Spectrum	
Pharmacology:	An indoloquinone mitomycin analogue prodrug metabolised to an alkylating agent by the DT-diaphorase enzyme, which is over-expressed by bladder cancer cells.
Indication:	Bladder cancer, non-muscle invasive, in patients at low or intermediate risk of progression.
Current status:	PIII in EU. PIII in US, with fast track status.
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Bladder cancer. **SIGN**: Bladder cancer.
Reviews:	None.

Atezolizumab injection; Roche	
Pharmacology:	Monoclonal antibody targeting programmed cell death-1 (PD-1). Given by i.v. infusion once every 21 days for up to 12 months.
Indication:	Bladder cancer, urothelial, locally advanced or metastatic, second-line.
Current status:	PIII in EU. PIII in the US, with fast track status.
UK availability:	2017
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Bladder cancer. **SIGN**: Bladder cancer.
Reviews:	NIHR NSRIC July 2015.

Custirsen injection; OncoGenex	
Pharmacology:	Clusterin inhibitor, given by i.v. infusion.
Indication:	Prostate cancer, metastatic castration-resistant, second-line.
Current status:	PIII in EU and US with fast track status in the US.
UK availability:	2017
Sector:	Secondary care.
CDF:	Not included May 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Prostate cancer.
Reviews:	NIHR HSRIC February 2014.

Eribulin injection [*Halaven];* Eisai	
Pharmacology:	Synthetic analogue of halichondrin B, with tubulin-based antimitotic activity, given by i.v. infusion.
Indication:	Soft tissue sarcoma, advanced, third-line (licence extension).
Current status:	Filed in EU August 2015.
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Sarcoma.
Reviews:	None.

Evofosfamide injection; Merck Serono	
Pharmacology:	A hypoxia-activated prodrug of dibromo isophoramide mustard, a potent DNA alkylator. Given by i.v. infusion over 30-60 minutes on days 1 and 8 of a 21-day cycle.
Indication:	Soft tissue sarcoma, locally advanced or metastatic, unresectable – first-line in combination with doxorubicin.
Current status:	PIII in EU, with orphan status. PIII in US, with fast track and orphan status.
UK availability:	2017
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Sarcoma.
Reviews:	NIHR HSRIC December 2014.

Sonidegib oral *[Odomzo];* Novartis	
Pharmacology:	Smoothened (Smo) protein antagonist (formerly known as erismodegib).
Indication:	Basal cell carcinoma, locally advanced or metastatic, in patients not amenable to curative surgery or radiation therapy.
Current status:	Licensed in EU August 2015. Licensed in US – see prescribing data.
UK availability:	2015
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Skin cancer. **SIGN**: Primary cutaneous squamous cell carcinoma.
Reviews:	NIHR HSRIC January 2013.

Trametinib oral *[Mekinist];* Novartis	
Pharmacology:	MEK inhibitor taken once daily. Use in combination with twice-daily dabrafenib overcomes resistance to BRAF inhibition associated with reactivation of MEK.
Indication:	Malignant melanoma, unresectable or metastatic $BRAF^{V600}$-positive, monotherapy and in combination with dabrafenib.
Current status:	Monotherapy licensed in EU June 2014 – see prescribing data. Combination therapy recommended for approval in EU July 2015. Launched in US January 2014 for mono- and combination therapy – see prescribing data.
UK availability:	2015
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Skin cancer. Trametinib in combination with dabrafenib due August 2016. **SIGN**: Cutaneous melanoma due Spring 2016. **NHS England**: Draft national chemotherapy algorithm.
Reviews:	None recent.

Cobimetinib **oral**; Roche	
Pharmacology:	MEK inhibitor, taken once-daily.
Indication:	Malignant melanoma, metastatic, BRAFV600-positive, first-line in combination with vemurafenib.
Current status:	Filed in EU September 2014 and in US December 2014 with fast track and priority review status.
UK availability:	2015
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Skin cancer. Cobimetinib due June 2016. **SIGN**: Cutaneous melanoma due Spring 2016.
Reviews:	NIHR HSRIC August 2014.

Talimogene laherparepvec **injection**; Amgen	
Pharmacology:	Oncolytic virus immunostimulant, injected into tumour sites every 2 weeks.
Indication:	Malignant melanoma, unresectable or metastatic.
Current status:	Filed in EU September 2014. Recommended for approval in US April 2015.
UK availability:	2015
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Skin cancer, Talimogene laherparapvec due July 2016. **SIGN**: Cutaneous melanoma due Spring 2016.
Reviews:	None recent.

Nivolumab **injection** *[Opdivo];* Bristol-Myers Squibb	
Pharmacology:	Monoclonal IgG4 antibody against programmed death-1 (PD-1) protein.
Indication:	Malignant melanoma, advanced, unresectable, first-line with ipilimumab (licence extension).
Current status:	PIII in EU. Filed in US June 2015, with fast track and priority review status.
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Skin cancer. Nivolumab with ipilimumab due September 2016. **SIGN**: Cutaneous melanoma due Spring 2016.
Reviews:	NIHR HSRIC December 2014.

Ipilimumab **injection** *[Yervoy];* Bristol-Myers Squibb	
Pharmacology:	Anti-CTLA-4 monoclonal antibody given by i.v. infusion every 3 weeks for 4 doses, then 3-monthly.
Indication:	Malignant melanoma, resected high-risk stage III, first-line adjuvant therapy (licence extension).
Current status:	PIII in EU. Filed in US March 2015.
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Skin cancer. Ipilimumab for first-line adjuvant therapy in progress. Ipilimumab is recommended for previously-treated and treatment-naïve advanced disease. **SIGN**: Cutaneous melanoma due Spring 2016.
Reviews:	None recent.

Vosaroxin injection *[Qinprezo];* Sunesis	
Pharmacology:	Anticancer quinolone derivative, first-in-class.
Indication:	Acute myeloid leukaemia, relapsed or refractory, second-line with cytarabine.
Current status:	PIII in EU, with orphan status. PIII in US, with fast track and orphan status.
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Blood and bone marrow cancers.
Reviews:	None recent.

Blinatumomab injection *[Blincyto];* Amgen	
Pharmacology:	Bi-specific T-cell engager (BiTE), given by daily continuous i.v. infusion for 28 days, then 2-week break.
Indication:	Acute lymphoblastic leukaemia, B-precursor, Philadelphia chromosome-negative, relapsed or refractory.
Current status:	Filed in EU October 2014, with orphan status. Licensed in US December 2014, with breakthrough therapy, orphan and priority review status – see prescribing data.
UK availability:	2015
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Blood and bone marrow cancers.
Reviews:	NIHR HSRIC June 2014.

Carfilzomib injection *[Kyprolis]*; Amgen	
Pharmacology:	Second-generation, selective and irreversible proteasome inhibitor, first-in-class, given as i.v. infusion.
Indication:	Multiple myeloma, relapsed.
Current status:	Filed in EU January 2015 (accelerated assessment and orphan). Launched in US - see prescribing data.
UK availability:	2015
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Bone and bone marrow cancers. Carfilzomib in progress.
Reviews:	NIHR HSRIC October 2013.

Panobinostat oral *[Farydak];* Novartis	
Pharmacology:	Pan-deacetylase inhibitor.
Indication:	Multiple myeloma, relapsed and/or refractory, with bortezomib and dexamethasone, in patients who have received at least two prior regimens including bortezomib and an immunomodulatory agent.
Current status:	Recommended for approval in EU June 2015, with orphan status. Licensed in US February 2015 with orphan status after accelerated assessment – see prescribing data.
UK availability:	2015
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Blood and bone marrow cancers. Panobinostat due January 2016.
Reviews:	None recent.

Ixazomib citrate **oral**; Takeda	
Pharmacology:	Second-generation reversible proteasome inhibitor.
Indication:	Multiple myeloma, relapsed and/or refractory.
Current status:	Filed in EU July 2015 with accelerated assessment and orphan status.
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Bone and bone marrow cancers. **NHS England**: Draft national chemotherapy algorithm.
Reviews:	NIHR HSRIC April 2014.

Elotuzumab **injection**; Bristol-Myers Squibb	
Pharmacology:	Monoclonal antibody that binds to the cell surface glycoprotein CS1, which is highly expressed on myeloma cells and minimally expressed on normal cells.
Indication:	Multiple myeloma, relapsed and/or refractory, second-line in combination with dexamethasone and bortezomib or lenalidomide.
Current status:	Filed in EU July 2015 with accelerated assessment and orphan status. Use with dexamethasone and lenalidomide has breakthrough therapy and orphan status in US.
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Blood and bone marrow cancers.
Reviews:	NIHR HSRIC July 2013.

Daratumumab **injection;** Janssen	
Pharmacology:	Humanised CD38 monoclonal antibody, infused once weekly for 8 weeks, then every 2 weeks for 16 weeks, and then every 4 weeks.
Indication:	Multiple myeloma, relapsed and/or refractory, second-line or greater in combination with dexamethasone and bortezomib or lenalidomide.
Current status:	PIII in EU, with orphan status. Filed in US June 2015 with breakthrough therapy status for patients who have failed three therapies.
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Bone and bone marrow cancers.
Reviews:	None.

Bendamustine injection *[Levact];* Napp	
Pharmacology:	An alkylating agent with antimetabolite activity, given by i.v. infusion for up to six cycles.
Indication:	Non-Hodgkin's lymphoma, indolent (low-grade) and mantle cell, first-line (licence extension).
Current status:	Filed in EU. Filed in US December 2011 but additional data requested October 2012.
UK availability:	2015
Sector:	Secondary care.
CDF:	Included for low-grade and mantle cell non-Hodgkin's lymphoma July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Blood and bone marrow cancers. Bendamustine in progress.
Reviews:	LCNDG April 2013.

Chlormethine topical *[Valchlor];* Actelion	
Pharmacology:	Nitrogen mustard, an alkylating agent, formulated as a 0.016% gel applied daily.
Indication:	Cutaneous T-cell lymphoma, mycosis fungoides, in patients who have had prior skin-directed therapy.
Current status:	Filed in EU July 2015, with orphan status. Available in France via an early access programme. Launched in US with orphan status – see prescribing data.
UK availability:	2016
Sector:	Secondary care.
CDF:	Not included July 2015 (updated regularly).
Tariff:	Chemotherapy is locally negotiated.
Guidance:	**NICE**: Skin cancer. **SIGN**: Primary cutaneous squamous cell carcinoma.
Reviews:	None.

Daclizumab injection *[Zinbryta];* Biogen Idec	
Pharmacology:	Interleukin-2 receptor antagonist monoclonal antibody that binds to CD25, given by monthly s.c. injection.
Indication:	Multiple sclerosis (MS), relapsing-remitting (RRMS), first- or second-line.
Current status:	Filed in EU March 2015 and in US April 2015.
UK availability:	2016
Population:	In a population of 100,000, 100 people will have MS and about 5 new cases are diagnosed each year. 80% initially have RRMS and 50% of these go on to develop secondary progressive MS within 10 years. In 2012-13, there were 38,080 hospital admissions due to MS in England.
Sector:	Secondary care.
Implications:	Offers an additional therapeutic option for patients.
Financial:	Cost unknown but annual cost of other disease-modifying therapies ranges from about £6,000 to £21,000.
Tariff:	Specified high cost drug.
Efficacy:	In the PIII DECIDE study (n=1,841), daclizumab 150mg reduced annualised relapse rate by 45% vs. i.m. interferon (IFN) beta-1a (p<0.0001). After 96 weeks, 73% of daclizumab-treated patients were relapse-free vs. 59% on IFN (p<0.0001; NNT=7), and there was a 24% reduction in risk of meaningful worsening in physical impact of MS (defined as >7.5 point worsening in the MS Impact Scale physical score) vs. IFN (p=0.018). In the published PII 1-year SELECT study (n=621), mean relapse rate was lower in patients receiving daclizumab 150mg (21%) or 300mg (23%) than in those given placebo (46%) (p<0.0001). 81% of patients were relapse-free in the daclizumab 150mg, 80% in the 300mg group vs. 64% in the placebo group (p<0.0001 and p=0.0003, respectively, vs. placebo; NNT=6 for both doses).
Safety:	In studies rates of cutaneous reactions, serious cutaneous reactions and serious infections were 37%, 2% and 4%, respectively – double the rates with IFN. Transaminase elevations more than 5 times the upper limit of normal occurred in 6% of patients given daclizumab and 3% of patients given IFN.
Guidance	**NICE**: Multiple sclerosis, Daclizumab proposed technology appraisal. **NHSE**: CCP-Disease modifying therapies for MS.
Reviews:	NIHR HSRIC August 2014.

Masitinib oral; AB Science	
Pharmacology:	Protein tyrosine kinase inhibitor targeting mast cells and macrophages.
Indication:	Multiple sclerosis, primary progressive or relapse-free secondary progressive.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care.
Tariff:	Specified high cost drug.
Guidance:	**NICE**: Multiple sclerosis. **NHSE**: CCP-Disease modifying therapies for MS.
Reviews:	None.

Ocrelizumab injection; Roche	
Pharmacology:	Second-generation, humanised anti-CD20 monoclonal antibody, given by i.v. infusion on day 1 and day 14 of each treatment cycle (every 6 months).
Indication:	Multiple sclerosis, primary-progressive and relapsing-remitting.
Current status:	PIII in EU and US.
UK availability:	2017
Sector:	Secondary care.
Tariff:	Specified high cost drug.
Guidance:	**NICE**: Multiple sclerosis. **NHSE**: CCP-Disease modifying therapies for MS.
Reviews:	NIHR HSRIC Primary-progressive and relapsing-remitting August 2014.

Inolimomab **injection** *[Leukotac];* Jazz	
Pharmacology:	Anti-interleukin-2 receptor monoclonal antibody, given by i.v. infusion.
Indication:	Acute graft-versus-host-disease, steroid-refractory, associated with haematopoietic stem cell transplant.
Current status:	PIII, with orphan status in the EU.
UK availability:	2017
Sector:	Secondary care. Blood and marrow transplantation services are provided by specialist centres.
Tariff:	Likely specified high cost drug.
Guidance:	**NICE**: Blood and bone marrow cancers.
Reviews:	None.

BNF 9. Nutrition and blood

Likely CCG commissioned

CM-4612 **oral***;* Curemark	
Pharmacology:	Proprietary modified-release formulation of proteinase enzymes.
Indication:	Autism.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care initiation, primary care continuation.
Tariff:	Likely HRG included.
Guidance:	**NICE**: Autism pathway.
Reviews:	None.

Eculizumab injection *[Soliris];* Alexion	
Pharmacology:	Recombinant humanised monoclonal IgG2/4k antibody that binds to the human C5 complement protein and inhibits the activation of terminal complement. Given by i.v infusion.
Indication:	Myasthenia gravis, generalised, severe, and refractory.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care.
Tariff:	Specified high cost drug.
Guidance:	None.
Reviews:	None.

Likely NHSE commissioned

Sebelipase alfa injection *[Kanuma];* Alexion	
Pharmacology:	A recombinant human lysosomal acid lipase, given by i.v. infusion.
Indication:	Lysosomal acid lipase (LAL) deficiency (early onset - Wolman disease, late onset - Cholesteryl Ester Storage Disease, CESD).
Current status:	Recommended for approval in EU June 2015.
UK availability:	2015
Population:	Wolman disease, estimated incidence about 1 - 2 in 1,000,000 births; CESD, UK estimated incidence is about 25 in 1,000,000 births (1 in 40,000).
Sector:	Secondary care, potentially covered by the Highly specialist metabolic disorder services commissioning.
Implications:	Wolman disease is fatal in the first 1 or 2 years of life (usually within 6 months) although bone marrow transplant may improve survival. Successful enzyme replacement therapy will be lifelong or until curative therapies are developed. CESD has very variable presentation and some patients may be managed with conventional lipid-lowering techniques.
Financial:	Likely to be high cost. Treatment will potentially be for life.
Tariff:	Specified high cost drug.
Efficacy:	In the PIII ARISE trial (n=66) patients with CESD received sebelipase or placebo on alternate weeks; primary outcome was alanine aminotransferase (ALT) level normalisation at 20 weeks. 31% in the sebelipase groups achieved the primary outcome vs. 7% in the placebo group (p<0.03; NNT=4). An open label extension indicated that response was sustained. In a PII/III open label study in 9 infants with early onset Wolman disease, 6 affected infants survived to 12 months (primary outcome).
Safety:	Main serious adverse event in trials was anaphylaxis. Other adverse effects occurring more often than placebo included headache, constipation, abdominal pain, oropharyngeal pain.
Guidance:	None.
Reviews:	None recent.

Alipogene tiparvovec **injection** *[Glybera];* UniQure/Chiesi	
Pharmacology:	Viral vector-based gene therapy injected i.m. to insert a working copy of a defective gene into muscle cells. Given as 27- 60 i.m. injections to the legs, dose dependent on body weight.
Indication:	Familial lipoprotein lipase deficiency (LPLD) in adults suffering from severe or multiple pancreatitis attacks despite dietary fat restrictions. The diagnosis has to be confirmed by genetic testing. The indication is restricted to patients with detectable levels of LPL enzyme.
Current status:	Conditional approval granted in EU subject to annual review.
UK availability:	2015
Population:	Very rare: estimated 1-2 in 1,000,000, not all of whom will be in the group covered by the indication
Sector:	Specialist centres only.
Implications:	First active therapy for this very rare condition, currently managed with strict dietary fat restriction. The small numbers and impracticality of carrying out controlled trials makes reliability of efficacy data uncertain.
Financial:	Cost extremely high. Current expectation is for a single course. Six-year data indicate reductions in frequency and severity of pancreatitis and hospitalisation which may offset cost.
Tariff:	Specified high cost drug.
Efficacy:	EPAR data (n=27) show that alipogene tiparvovec reduces blood lipid levels in some patients. However, data on pancreatitis and hospital admission rates are limited.
Safety:	Most common adverse effect is pain in the legs after administration.
Guidance:	None.
Reviews:	None recent.

Mercaptamine bitartrate **oral** *[Procysbi];* Raptor	
Pharmacology:	Glutathione synthesis stimulant, protein aggregation inhibitor in a modified-release formulation.
Indication:	Huntington's Disease (HD).
Current status:	PIII with orphan status in EU and US.
UK availability:	2016
Population:	Classic estimate of HD prevalence is between 1 in 10,000 and 1 in 20,000 people. Recent estimates in Western populations give a prevalence of 1 in 7,300 and annual incidence of 4.7- 6.9 per million.
Sector:	Secondary care.
Implications:	There are few treatments effective in HD and progressive decline is currently inevitable. Mercaptamine has shown indications of disease-modifying effects in trials, slowing the rate of motor decline. If effective, treatment will be long-term.
Financial:	Likely to be very expensive. US cost of this formulation when used for nephropathic cystinosis is about 30x the cost of the immediate-release form (*Cystagon*). In the UK, *Cystagon* costs about £9,000/year.
Tariff:	Specified high cost drug.
Efficacy:	In an on-going PII/III trial (n=96), primary outcome is change from the baseline of the Total Motor Score (TMS), of the Unified Huntington's Disease Rating Scale (UHDRS) after 18 months. At 18 months in the ITT population, compared to placebo, patients taking mercaptamine had a trend towards slower deterioration in TMS (mercaptamine, 4.51 vs. placebo, 6.68, p=0.19). In a post hoc analysis of those patients not taking tetrabenazine (n=66), the difference was significant (2.84 vs. 6.78, p=0.03). The study is continuing to a total of 3 years with all patients taking mercaptamine.
Safety:	This formulation is available elsewhere in the EU for treatment of nephropathic cystinosis - see prescribing data.
Guidance:	None.
Reviews:	None.

Biotin **oral** *[Cerenday];* MedDay	
Pharmacology:	Water-soluble vitamin, a co-enzyme in energy metabolism, dose at 10,000-fold normal requirement.
Indication:	Multiple sclerosis, primary progressive, first line.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care initiation, primary care continuation.
Tariff:	Uncertain, but could be high cost drug if in line with other treatments for multiple sclerosis.
Guidance:	**NICE**: Multiple sclerosis.
Reviews:	NIHR HSRIC April 2015.

Biotin **oral** *[Cerenday];* MedDay Pharmaceuticals	
Pharmacology:	Water-soluble vitamin, a co-enzyme in energy metabolism, dose at 10,000-fold normal requirement.
Indication:	Multiple sclerosis, permanent disability related relapses, add on therapy to current immunomodulators.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care initiation, primary care continuation.
Tariff:	Uncertain, but could be high cost drug if in line with other treatments for multiple sclerosis.
Guidance:	**NICE**: Multiple sclerosis.
Reviews:	NIHR HSRIC April 2015.

BNF 10. Musculoskeletal and joint diseases

Likely CCG commissioned

Certolizumab **injection** *[Cimzia];* UCB Pharma	
Pharmacology:	Long-acting tumour necrosis factor alpha (TNF-alpha) inhibitor for s.c. administration.
Indication:	Rheumatoid arthritis (RA), early progressive, for use in combination with methotrexate in patients not previously treated with DMARD (licence extension).
Current status:	PIII
UK availability:	2016
Population:	Annual incidence of RA in the UK is about 32 per 100,000 people.
Sector:	Secondary care.
Implications:	Another option in an increasingly crowded field.
Financial:	It will compete with other TNF-alpha inhibitors licensed for this indication. Current cost is about £8,500/ year.
Tariff:	Specified high cost drug.
Efficacy:	The PIII C-EARLY study is due to complete in July 2015. About 880 patients received certolizumab pegol or placebo in addition to methotrexate. Primary outcome is proportion in sustained remission (Disease Activity Score [Erythrocyte Sedimentation Rate] < 2.6 at both weeks 40 and 52) at week 52.
Safety:	See medicines.org.uk.
Guidance:	**NICE**: Arthritis.
Reviews:	None.

Tofacitinib **oral** *[Xeljanz];* Pfizer	
Pharmacology:	Janus kinase 3 (JAK3) inhibitor, immunosuppressant.
Indication:	Rheumatoid arthritis, second-line after failure of DMARD.
Current status:	PII with plans to file in the EU by the end of 2015.
UK availability:	2017
Sector:	Secondary care initiation, possible primary care maintenance.
Tariff:	Specified high cost drug.
Guidance:	**NICE**: Arthritis. **SIGN**: Rheumatoid arthritis
Reviews:	None recent.

Tofacitinib **oral** *[Xeljanz];* Pfizer	
Pharmacology:	Janus kinase 3 (JAK3) inhibitor, immunosuppressant.
Indication:	Rheumatoid arthritis, moderate- to-severe, methotrexate naïve.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care initiation, possible primary care maintenance.
Tariff:	Specified high cost drug.
Guidance:	**NICE**: Arthritis.
Reviews:	None recent.

Baricitinib **oral***;* Lilly	
Pharmacology:	Janus kinase (JAK) 1 and 2 inhibitor (JAK3 sparing) immunosuppressant.
Indication:	Rheumatoid arthritis, moderate-to-severe disease, second-line, combination therapy.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care initiation, possible primary care maintenance.
Tariff:	Likely specified high cost drug.
Guidance:	**NICE**: Arthritis.
Reviews:	NIHR HSRIC July 2015.

Ixekizumab injection; Lilly	
Pharmacology:	Anti–interleukin-17 monoclonal antibody, given by s.c. injection.
Indication:	Psoriatic arthritis (PsA).
Current status:	PIII
UK availability:	2016
Population:	NICE estimates prevalence of PsA is about 650 per 00,000 people or about 270,000 patients in England, of whom 6,516 will be eligible for TNF-alpha inhibitor and 1,564 will fail initial TNF-alpha inhibitor.
Sector:	Secondary care.
Implications:	Another option for patients who fail on standard drugs. Likely to compete with secukinumab.
Financial:	Likely to compete with other second and third-line drugs, so cost will have to competitive.
Tariff:	Specified high cost drug.
Efficacy:	In the 24-week PIII SPIRIT-P1 trial (n=412), ixekizumab every 2 or 4 weeks is compared to adalimumab every 2 weeks, or placebo in biologic-naïve patients. Results are not published and longer-term data will also be gathered. SPIRIT-P2 in 360 biologic-experienced patients is due to complete September 2016.
Safety:	Adverse effects include nasopharyngitis, injection site reactions, pruritus, headache and arthralgia.
Guidance:	**NICE**: Arthritis. **SIGN**: Psoriasis and PsA.
Reviews:	None.

Secukinumab injection *[Cosentyx];* Novartis	
Pharmacology:	First-in-class, fully human monoclonal antibody to interleukin-17A (IL-17A), given by s.c. injection.
Indication:	Psoriatic arthritis (PsA), after DMARDs (licence extension).
Current status:	Filed in EU and US Q2 2015.
UK availability:	2016
Population:	NICE estimates prevalence of PsA is about 650 per 00,000 people or about 270,000 patients in England, of whom 6,516 will be eligible for TNF-alpha inhibitor and 1,564 will fail initial TNF-alpha inhibitor.
Sector:	Secondary care.
Implications:	This will provide another option for patients who fail on standard drugs. It is likely to be first-in-class however similar drugs are following. It is formulated in a pre-filled pen suitable for self administration.
Financial:	More expensive than anti-TNF drugs (list price ~£18,200 for the first year, £14,600/year thereafter), but a PAS is in place for the psoriasis indication.
Tariff:	Specified high cost drug.
Efficacy:	In the PIII FUTURE 2 trial (n=397) the proportion of patients reaching ACR20 at week 24 was 29%, 51%, 54% and 15% on 75mg, 150mg, 300mg secukinumab and placebo, respectively (p<0.04 for all vs. placebo; NNT=7,3,3). 52-week data show response is maintained (51%, 64%, 64%, respectively; placebo patients transferred to active treatment). Long-term 5-year outcome data will also be collected.
Safety:	See medicines.org.uk.
Guidance	**NICE**: Arthritis. **SIGN**: Psoriasis and PsA.
Reviews:	None recent.

Tofacitinib oral *[Xeljanz];* Pfizer	
Pharmacology:	Janus kinase 3 (JAK3) inhibitor, immunosuppressant.
Indication:	Psoriatic arthritis, second line (after DMARD failure) or third-line (after biological failure).
Current status:	PIII
UK availability:	2017
Sector:	Secondary care initiation, possible primary care maintenance.
Tariff:	Specified high cost drug.
Guidance:	**NICE**: Arthritis.
Reviews:	NIHR HSRIC July 2015.

Apremilast oral *[Otezla];* Celgene	
Pharmacology:	Phosphodiesterase type 4 inhibitor, down-regulates inflammatory response.
Indication:	Psoriatic arthritis (PsA) in patients not previously treated with a disease modifying antirheumatic drug (DMARD) (licence extension).
Current status:	PIII
UK availability:	2016
Population:	UK prevalence of psoriasis is around 1.5-3%; of these, up to about 30% will have inflammatory arthritis. At least 20% of people with psoriasis have severe psoriatic arthritis with progressive joint lesions.
Sector:	Secondary care initiated, potential to continue in primary care.
Implications:	Current guidelines indicate that conventional DMARD should be used first-line in PsA, followed by biologic drugs. Therefore the place of apremilast in the sequence is currently uncertain.
Financial:	If it is used in place of parenteral biologics then cost of administration will be reduced. Assuming dose is 30mg daily, based on current list price of apremilast, cost will be about £300/month.
Tariff:	Specified high cost drug.
Efficacy:	The PALACE4 trial (n=529) compared apremilast 20 mg and 30 mg daily to placebo; primary outcome was ACR20 response at 16 weeks. Response in the apremilast groups was 28% and 30.7% vs. 15.9% for placebo (p=0.006 and p=0.001; NNT=8, 7, respectively). Follow-up data from 24 weeks, 52 weeks and 104 weeks indicate response is maintained.
Safety:	See medicines.org.uk.
Guidance:	**NICE**: Arthritis. **SMC**: (after DMARD).
Reviews:	None.

Secukinumab injection *[Cosentyx];* Novartis	
Pharmacology:	First-in-class, monoclonal antibody to interleukin-17A (IL-17A), given by s.c. injection.
Indication:	Ankylosing spondylitis (AS), second-line after DMARDs or TNF inhibitors (licence extension).
Current status:	Filed in EU and US Q2 2015.
UK availability:	2016
Population:	NICE estimates about 20,000 people in England with AS are eligible for biological drug treatment and about 6,800 of these will take up treatment. About two-thirds will respond well to standard anti-TNF drugs.
Sector:	Secondary care.
Implications:	A potential option for those not responding to standard anti-TNF drugs, for whom there are currently limited choices.
Financial:	More expensive than anti-TNF drugs (list price ~£18,200 for the first year, £14, 600/year thereafter), but a PAS is in place for the psoriasis indication.
Tariff:	Specified high cost drug.
Efficacy:	In 2 PIII studies results for the primary outcome (ASAS20 at 16 weeks) were: secukinumab 150mg and 75mg, 61% and 60% vs. 29% for placebo, p<0.001; NNT=3 (MEASURE1, n=372) and 61% and 41% vs. 28% for placebo, respectively, p<0.001; NNT=3, 8 (MEASURE2, n=220). In MEASURE1 the first month loading dose was given by i.v. infusion; in MEASURE2 it was given by s.c. injection. Both studies are ongoing to assess long-term efficacy and safety.
Safety:	See medicines.org.uk.
Guidance	**NICE**: Arthritis.
Reviews:	None recent.

Apremilast oral *[Otezla];* Celgene	
Pharmacology:	Phosphodiesterase type 4 inhibitor, down-regulates inflammatory response.
Indication:	Ankylosing spondylitis (licence extension).
Current status:	PIII
UK availability:	2017
Sector:	Secondary care initiation, primary care continuation.
Tariff:	Specified high cost drug.
Guidance:	**NICE**: Arthritis.
Reviews:	NIHR HSRIC December 2013.

Lesinurad oral; AstraZeneca	
Pharmacology:	Selective inhibitor of URAT1, a renal transporter that regulates uric acid excretion, first-in-class.
Indication:	Gout second-line in combination with a xanthine-oxidase inhibitor.
Current status:	Filed in EU January 2015.
UK availability:	2016
Population:	Estimated UK population with gout eligible for urate-lowering therapy is 472,000. Up to 25% of these may not achieve desired urate-lowering with tolerated doses of current drugs.
Sector:	Secondary care initiation, primary care continuation.
Implications:	Lesinurad can reduce urate levels in patients not responding to existing therapy. Reducing urate levels to recommended values decreases the risk of recurrent gout and end-organ damage.
Financial:	As a further treatment option it will be additional to current costs.
Tariff:	Likely HRG included.
Efficacy:	Results from 3 PIII trials are available. In CLEAR 1 (n=603) and CLEAR 2 (n=610) patients with moderate-to-severe gout and inadequate response to allopurinol were randomised to continue allopurinol with lesinurad 200mg, 400mg or placebo. Primary outcome (proportion achieving serum uric acid level of <6.0mg/dL (<360micromol/l) at 6 months) in CLEAR 1 was 54% for 200mg, 59% for 400mg, 28% for placebo (p<0.0001 for lesinurad vs. placebo; NNT=4, 3). In CLEAR 2, the primary outcome was achieved in 55%, 67% and 23%, respectively (p<0.0001 for lesinurad vs. placebo; NNT=3, 2). In the CRYSTAL (n=324) study, patients were non-responders to febuxostat and primary outcome was serum uric acid level of <5.0 mg/dL (<300 micromol/l) at 6 months. Results were 57% response for 200mg lesurinad, 76% for 400mg vs. 47% for placebo (p<0.0001; NNT=10, 4).
Safety:	Renal adverse effects noted especially at the 400mg dose; increased creatinine clearance values, usually resolving with continued treatment, occurred in up to 16% of those on this dose. Arthralgia, nasopharyngitis, and upper respiratory tract infections were also reported.
Guidance:	**NICE**: Arthritis, Lesinurad due November 2016.
Reviews:	NIHR HSRIC January 2013.

Likely NHSE commissioned

Ataluren oral *[Translarna];* PTC Therapeutics	
Pharmacology:	Dystrophin synthesis stimulant, first-in-class, granules for oral administration.
Indication:	Duchenne muscular dystrophy (DMD) resulting from a nonsense mutation (nm) in the dystrophin gene, in ambulatory patients aged 5 years and older.
Current status:	Conditional approval in EU July 2014 subject to further PIII trial results, with orphan status – see prescribing data. Launched in Germany December 2014.
UK availability:	2015
Population:	Prevalence of DMD in England is about 2,200 patients; of these, about 11.5% (250) have nonsense mutation (nmDMD) but fewer than 80 are considered eligible for ataluren.
Sector:	Specialist care.
Implications:	The first licensed drug designed to correct the effects of one of the genetic defects leading to symptoms of DMD; there is already media interest. Availability is likely to depend on the outcome of NICE guidance.
Financial:	Likely to be very high cost.
Tariff:	Specified high cost drug.
Efficacy:	In a published 48-week placebo-controlled PIIb study (n=174) using 40 or 80mg/kg ataluren daily, mean change from baseline in 6-minute walk distance (6MWD) did not reach statistical significance for either dose. Post-hoc secondary analyses suggest a possible benefit with the lower dose (difference vs. placebo 31.3m; p=0.056). 26% of patients in the 40 mg/kg group vs. 44% in the placebo group experienced persistent 10% 6MWD worsening by week 48 (hazard ratio 0.52; p=0.039; NNT=6). An open-label 96-week PIII extension study (n=220 target) is due to complete June 2017.
Safety:	Most common adverse effects include headache, nausea and vomiting. See prescribing data.
Guidance:	**NICE**: Highly Specialised Technology Guidance in preparation. **NHSE**: CCP-Ataluren.
Reviews:	None.

Drisapersen injection; BioMarin	
Pharmacology:	Dystrophin synthesis stimulant. Antisense oligonucleotide that corrects reading of faulty dystrophin gene with exon 51 mutations, given by once-weekly s.c. injection.
Indication:	Duchenne muscular dystrophy (DMD) amenable to exon 51 skipping.
Current status:	Filed in EU and US June 2015, with orphan status; also breakthrough therapy and priority review status in US.
UK availability:	2016
Population:	About 2,200 people in England have DMD, with up to 13% potentially eligible for exon 51-skipping treatment (0.5 per 100,000 people).
Sector:	Specialist care.
Implications:	Although PIII studies failed to demonstrate benefit in terms of the primary outcome, PII data showing benefit are likely to be used in licence applications.
Financial:	Likely to be very expensive and treatment will be long term.
Tariff:	Specified high cost drug.
Efficacy:	The PIII DEMAND III trial (n=186) did not meet its primary outcome of a 30m difference in 6-minute walk distance (6MWD) between active and placebo arms at 48 weeks. In the published PII DEMAND II trial (n=36), mean 6MWD increased by 31.5m from baseline with drisapersen (mean difference vs. placebo 35.09m, p=0.014) The open-label DEMAND IV extension study (n=233), was terminated as it did not meet its primary outcome; a second PIII extension study is ongoing.
Safety:	Most common adverse effects were injection site reactions, proteinuria and thrombocytopenia.
Guidance:	None.
Reviews:	None recent.

Idebenone **oral** *[Raxone];* Santhera	
Pharmacology:	Coenzyme Q10 analogue that enhances mitochondrial respiratory chain function.
Indication:	Duchenne muscular dystrophy (DMD) (licence extension).
Current status:	PIII, with orphan status in EU and US.
UK availability:	2016
Population:	Prevalence of DMD in England is about 2,200 patients.
Sector:	Specialist care.
Implications:	Cardiorespiratory failure is the leading cause of death in DMD. The only current effective treatment is glucocorticoids, but these have significant long-term adverse effects. Idebenone improves respiratory function, possibly by increasing cellular energy production. It is potentially suitable for most DMD patients.
Financial:	Likely to be expensive and will be additional to current costs.
Tariff:	Specified high cost drug.
Efficacy:	In the 52-week published PIII DELOS study (n=57) decline in percentage predicted peak expiratory flow from baseline was 3.05% with idebenone vs. 9.01% with placebo (difference 5.96%; p=0.044). Patients using concomitant glucocorticoids were excluded.
Safety:	Idebenone was well tolerated, with similar rates of adverse effects to placebo. Transient mild diarrhoea occurred in 25% of patients on idebenone vs. 12% on placebo.
Guidance:	None.
Reviews:	None.

Eteplirsen **injection**; Sarepta Therapeutics	
Pharmacology:	Dystrophin synthesis stimulant. Antisense oligonucleotide that corrects reading of faulty dystrophin gene with exon 51 mutations, for once-weekly i.v. infusion.
Indication:	Duchenne muscular dystrophy amenable to exon 51 skipping.
Current status:	PII in EU, with orphan status. Filed in US June 2015, with orphan status.
UK availability:	2017
Sector:	Specialist care.
Tariff:	Likely specified high cost drug.
Guidance:	None.
Reviews:	None.

Canakinumab **injection** *[Ilaris];* Novartis	
Pharmacology:	Interleukin 1-beta antagonist, monoclonal antibody, for s.c. injection.
Indication:	TNF-Receptor Associated Periodic Syndrome (TRAPS), first-line (licence extension).
Current status:	PIII
UK availability:	2017
Sector:	Secondary care.
Tariff:	Specified high cost drug.
Guidance:	None.
Reviews:	None.

Epratuzumab injection *[Epratucyn];* UCB Pharma	
Pharmacology:	Humanised monoclonal antibody that binds to and modulates CD22 antigen on B-cells, given by weekly i.v. infusion.
Indication:	Systemic lupus erythematosus (SLE), first-line for active moderate-to-severe disease.
Current status:	PIII in EU and US with fast-track status in US.
UK availability:	2016
Population:	Estimated UK prevalence varies from 41- 97 per 100,000 people. There is significant gender and ethnic imbalance.
Sector:	Secondary care.
Implications:	Second drug developed specifically for SLE. First available drug (belimumab) is associated with significant risk of adverse effects. Likely to be interest from patients as few effective drugs are available.
Financial:	Likely to be costly, need for i.v. infusion will add to this but it may displace belimumab. Current treatment cost is largely related to use of corticosteroids and immunosuppressant drugs, mostly available as oral generic medicines.
Tariff:	Specified high cost drug.
Efficacy:	In two PIII trials (EMBODY 1, n=793; EMBODY 2, n=792) patients were randomised to epratuzumab 600mg weekly or 1,200 mg two-weekly or placebo weekly for 4 weeks of a 12-week cycle. Primary outcome was proportion meeting a novel composite outcome (BICLA - British Isles Lupus Assessment Group (BILAG)-based Combined Lupus Assessment) at 48 weeks. These trials have completed but results not yet published. A 4-year open-label extension study (EMBODY 4, estimated n=1,400) is examining long-term adverse effects (primary outcome) and response (secondary). In the published EMBLEM PII study (n=227), 12-week BICLA response was higher in all epratuzumab groups vs. placebo.
Safety:	In the 12-week EMBLEM study, adverse event rates with epratuzumab and placebo were similar.
Guidance:	**NICE**: SLE,
Reviews:	NIHR HSRIC February 2015.

Belimumab injection *[Benlysta];* GSK	
Pharmacology:	Monoclonal antibody specific for soluble human B-lymphocyte stimulator protein (BLyS); inhibits survival of B cells. New formulation for weekly s.c. injection.
Indication:	Systemic lupus erythematosus (SLE), active autoantibody-positive, add-on therapy in adults with a high degree of disease activity despite standard therapy.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care.
Tariff:	Specified high cost drug.
Guidance:	**NICE**: SLE, belimumab in progress. **NHSE:** CCP-Rituximab for SLE.
Reviews:	None recent.

Rigerimod (forigerimod) injection *[Lupuzor];* ImmuPharma	
Pharmacology:	Immunomodulator affecting CD4 T-cells, for s.c. injection.
Indication:	Systemic lupus erythematosus (SLE).
Current status:	PIII in EU and US with fast track status in US.
UK availability:	2017
Sector:	Secondary care.
Tariff:	Specified high cost drug.
Guidance:	**NICE**: SLE. **NHSE:** CCP-Rituximab for SLE.
Reviews:	None.

Likely CCG commissioned

Aflibercept intravitreal injection *[Eylea];* Bayer	
Pharmacology:	A fully human, soluble VEGF receptor fusion protein that binds VEGF-A and placental growth factor.
Indication:	Visual impairment due to myopic choroidal neovascularisation (mCNV) of the retina (licence extension).
Current status:	Filed in EU March 2015. Licensed in Japan September 2014.
UK availability:	2015
Population:	mCNV occurs in 5-10% of patients with pathological myopia and usually affects adults aged 40-50 years. The overall prevalence of myopic CNV is estimated to be about 45 per 100,000 people.
Sector:	Secondary care. Specialised therapy.
Implications:	Alternative to ranibizumab (licensed), bevacizumab (off licence use) or vertoporfin photodynamic therapy.
Financial:	List price of aflibercept is £816 per dose, of ranibizumab is £742 per dose (PAS available).
Tariff:	Specified high cost drug.
Efficacy:	In the PIII MYRROR study (n=122), patients were randomised to aflibercept or sham injection at week 0. Patients were monitored every 4 weeks, those in the aflibercept group receiving additional doses if CNV persisted or recurred, otherwise all patients received sham injections. From week 24, all patients were eligible to receive aflibercept as-needed through to week 48. Aflibercept improved best-corrected visual acuity (BCVA) by 12.1 letters from baseline to week 24 vs. a mean decrease in BCVA of 2.0 letters with sham injections ($p<0.0001$).
Safety:	See medicines.org.uk.
Guidance:	**NICE**: Refractive errors.
Reviews:	None.

Sirolimus intravitreal injection *[Opsiria]*; Santen	
Pharmacology:	A first-in-class local immunoregulatory therapy, given 2-monthly. It forms a slowly dissolving depot in the vitreous humour and inhibits mTOR, blocking leukocyte and inflammatory cytokine activation.
Indication:	Uveitis, chronic non-infectious, posterior segment.
Current status:	Filed in EU March 2015 with orphan status.
UK availability:	2016
Population:	Chronic non-infectious uveitis affects about 40 in 100,000 people in the EU. Between 1,500 and 5,000 people are diagnosed with non-infectious posterior segment uveitis each year in England.
Sector:	Secondary care. Specialised therapy.
Implications:	Sirolimus offers another option to current therapies, which include periocular, intraocular or systemic corticosteroids, dexamethasone intravitreal implant (licensed), or immunosuppressives (unlicensed). With sirolumus, systemic exposure is minimised. It requires more frequent administration (2-monthly injections) than dexamethasone intravitreal implant (single treatment, repeated only if considered necessary).
Financial:	Cost uncertain in comparison to existing treatments. A single dexamethasone implant (*Ozurdex*) costs £870. Since more frequent injections are required with sirolimus, overall costs could be higher.
Tariff:	Likely specified high cost drug.
Efficacy:	Ongoing PIII trials (SAKURA 1 and SAKURA 2) include patients with non-infectious posterior, intermediate or panuveitis, randomised into three treatment arms, using different doses of intravitreal sirolimus. Interim results for SAKURA 1 (n=347) reported that the primary outcome of a significant proportion of patients achieving a vitreous haze score of zero at month 5 had been met.
Safety:	One-year data from the PII SAVE study (n=30) indicate that adverse events are rare. The most common adverse event was vitreous floaters. Sirolimus demonstrated a corticosteroid-sparing effect.
Guidance:	**NICE**: Eye conditions, general and other. Proposed TA - Uveitis - dexamethasone implant and sirolimus. **NHSE:** CCP-Infliximab and adalimumab for uveitis.
Reviews:	NIHR HSRIC January 2013.

Pegpleranib intravitreal injection *[Fovista];* Novartis	
Pharmacology:	Anti-PDGF pegylated aptamer, first-in-class.
Indication:	Age-related macular degeneration (wet), in combination with anti-VEGF therapy.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care. Specialised therapy.
Tariff:	Likely specified high cost drug.
Guidance:	**NICE**: Macular degeneration.
Reviews:	None.

Likely NHSE commissioned

Autologous corneal epithelial cells ocular implant *[Holoclar];* Chiesi	
Pharmacology:	Stem-cell therapy, cultured *ex vivo* from a biopsy of the patient's undamaged cornea. It replaces the damaged epithelium and creates a reservoir of limbal stem cells (LSCs) for epithelium regeneration.
Indication:	Moderate-to-severe limbal stem cell deficiency (LSCD) due to physical or chemical ocular burns.
Current status:	Licensed in EU February 2015 with orphan status - see prescribing data.
UK availability:	2016
Population:	In the EU, an estimated 3 in 100,000 people are affected by LSCD due to ocular burns. In the UK, 2,113 total corneal transplants for a variety of indications were performed in 2014.
Sector:	Secondary care. Specialised therapy.
Implications:	*Holoclar* is the first licensed product for this indication. It could replace current options (e.g. limbal allografts) with the advantage of permanently restoring corneal epithelium in a single treatment without need for donor tissues or chronic systemic immunosuppression. It will administered by specially trained surgeons. The product has a short shelf life (36 hours) and is sensitive to mechanical and temperature stress. Prophylactic systemic and topical antibiotics and corticosteroids are used post-transplant.
Financial:	Likely to be more expensive than current options, but offset by reduced cost of immunosuppressants.
Tariff:	Likely specified high cost drug.
Efficacy:	EPAR data is available from 2 uncontrolled observational studies, HLSTM01 (n=106) and HLSTM02 (n=29). In HLSTM01 (n=106), treatment success, based on the composite outcome of reduction in superficial corneal neovascularisation and epithelial defects, was reported in 72.1% of patients and failures in 27.9% ($p<0.001$; NNT=2). In HLSTM02 (n=29), success according to the subjective, overall clinical judgment of the investigator, was reported in 65.5%, and failure in 20.7% of patients; data was missing in 13.8%. Long-term efficacy data from HLSTM02 reported treatment success in 10/14 (71.4%), and 5/9 (55.6%) patients at 2 and 3 years post *Holoclar* transplant, respectively.
Safety:	Adverse effects included blepharitis, eye pain, glaucoma, conjunctival and eye haemorrhage, cataracts.
Guidance:	**NICE**: Interventional Procedure Guidance for a similar procedure using cells harvested from donors.
Reviews:	NIHR HSRIC July 2015.

BNF 12. Ear, nose and oropharynx

Likely CCG commissioned

Esketamine intratympanic gel; Auris Medical	
Pharmacology:	An NMDA antagonist of receptors in the cochlea, given as an intratympanic biodegradable gel.
Indication:	Tinnitus, inner ear.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care.
Tariff:	Likely HRG included.
Guidance:	**NICE:** Ear and hearing conditions.
Reviews:	None.

BNF 13. Skin

Likely CCG commissioned

Afamelanotide implant *[Scenesse]*; Clinuvel	
Pharmacology:	Analogue of α-melanocyte-stimulating hormone (α-MSH), delivered via a biodegradable, controlled-release, s.c. implant given up to every 2 months. First-in-class.
Indication:	Prevention of phototoxicity in erythropoietic protoporphyria (EPP).
Current status:	Licensed with orphan status in EU December 2014 – see prescribing data.
UK availability:	2015
Population:	UK prevalence is estimated to be about 1per 100,000 people.
Sector:	Specialist care.
Implications:	This is the first treatment licensed for EPP. Previous management strategies included avoiding sun exposure and use of a sunscreen.
Financial:	As first and only licensed treatment for EPP this is likely to be expensive and additional to current costs.
Tariff:	Specified high cost drug.
Efficacy:	Data from two PIII studies has been published. In both studies afamelanotide implant is compared to placebo to assess the primary outcome of the number of hours of direct exposure to sunlight without pain. In CUV039 (n=94), for afamelanotide and placebo duration of pain-free time at 6 months was 69.4 hours vs. 40.8 hours, respectively (p=0.04). In CUV029 (n=74), for afamelanotide and placebo duration of pain-free time at 9 months was 6.0 hours vs. 0.8 hours (p=0.005), and number of phototoxic reactions was 77 vs. 146 (p=0.04), respectively.
Safety:	See prescribing data.
Guidance:	None.
Reviews:	No recent reviews.

Ixekizumab injection; Lilly	
Pharmacology:	Humanised anti-interlukin-17 monoclonal antibody, given by s.c. injection.
Indication:	Plaque psoriasis, moderate-to-severe.
Current status:	Filed in EU June 2015.
UK availability:	2016
Population:	UK prevalence of psoriasis is estimated to be 1.3-2.2%, with plaque psoriasis accounting for 90% of cases. It is estimated about 230-400 per 100,000 people have moderate-to-severe disease.
Sector:	Secondary care.
Implications:	Likely to be used third-line in adults who are candidates for systemic therapy, as an alternative to available biologics.
Financial:	Cost likely to be similar to other biologics (£9,500-£13,000/year), PAS available for ustekinumab.
Tariff:	Specified high cost drug.
Efficacy:	In two ongoing PIII studies ixekizumab 160mg followed by 80mg 2-weekly or 4-weekly is compared with etanercept (50mg twice weekly) or placebo. In UNCOVER-2 (n=1,224), the co-primary outcomes were PASI-75 (75% reduction in symptoms) and static physician global assessment scores, an average assessment of all psoriatic lesions based on erythema, scale and induration, of clear to minimal (sPGA 0/1) at 12 weeks. PASI-75 was achieved by 89.7% on ixekizumab 2-weekly, 77.5% on ixekizumab 4-weekly, 41.6% on etanercept and 2.4% on placebo ($p<0.0001$ for each ixekizumab dose vs. etanercept and placebo; NNT=2, 3 vs. etanercept); sPGA0/1 was achieved by 83.2%, 72.9%, 36.0% and 2.4%, respectively ($p<0.0001$; NNT=2, 3 vs. etanercept). In UNCOVER-3 (n=1,346), for 2-weekly ixekizumab, 4-weekly ixekizumab, etanercept and placebo 12-week PASI-75 was 87.3%, 84.2%, 53.4% and 7.3%, respectively ($p<0.0001$; NNT=3 vs. etanercept) and sPGA 0/1 was 80.5%, 75.4%, 41.6% and 6.7%, respectively ($p<0.0001$; NNT=2 vs. etanercept). Results of UNCOVER-1, comparing ixekizumab to placebo are not yet published.
Safety:	Adverse effects are comparable to etanercept.
Guidance:	**NICE**: Psoriasis. **SIGN**: Psoriasis and psoriatic arthritis.
Reviews:	NIHR HSRIC April 2015.

Dimethyl fumarate oral; Almirall	
Pharmacology:	Fumaric acid derivative.
Indication:	Plaque psoriasis, moderate-to-severe.
Current status:	PIII
UK availability:	2017
Sector:	Secondary care initiation, primary care continuation.
Tariff:	Specified high cost drug.
Guidance:	**NICE**: Psoriasis. **SIGN**: Psoriasis and psoriatic arthritis.
Reviews:	NIHR HSRIC December 2013.

Biosimilar developments

What are biosimilars?

Biosimilars is the EU term for 'generic' biological medicines also known as 'follow-on' biologics in the US or 'subsequent entry' biologics in Canada. Unlike conventional 'chemical' pharmaceuticals, which are generally low molecular weight organic compounds, biologicals are large complex proteins that cannot be copied exactly. To gain a licence, the manufacturer must provide the EMA with data to show that their biosimilar is physically, chemically, biologically and clinically similar to the approved originator or reference product. These data are derived from extensive laboratory analysis of molecular characteristics, *in vitro* and *in vivo* studies in multiple species of animals and phase I studies in humans to define pharmacokinetics, pharmacodynamics and toxicity. In addition, phase III studies are performed to show clinical efficacy and safety; post-marketing risk management plans and phase IV studies assess safety in routine practice. Consequently, development of a biosimilar is more costly and protracted (up to eight years) compared to that of a standard generic medicine.

Biological drugs are expensive and biosimilars are seen as a cost-saving alternative. Marketed biosimilars are currently 5-20% cheaper than the originator products. However, they are not viewed as being interchangeable with the originator product; the MHRA recommends prescribing biological products by brand name.[1] NICE has recently reviewed their process for reviewing biosimilars.[2] They will consider biosimilars for referral to the Technology Appraisal selection process if appropriate, usually in the context of a Multiple Technology Appraisal in parallel with the originator products. Alternatively they may consider producing an 'Evidence summary new medicine'. NICE have confirmed that a Technology Appraisal and the resulting guidance, can be applied to relevant biosimilars which subsequently appear on the market.

Patent expiry of biologic drugs is the driver of biosimilar development. As for patents associated with 'chemical' generics, this is a complex and commercially sensitive area. There are situations where the UK patent for a chemical drug expired some years ago but there is currently no generic option. The same applies to biosimilar drugs which are more costly and complicated to bring to the market. There are also situations where a number of chemical generics are already licensed, and often available elsewhere in the EU, but patent extensions and legal challenges prevent marketing in the UK. The same applies to biosimilars, adding to the difficulty anticipating actual UK availability. Also, manufacturers of originator products seek to retain their market share by reformulating to simplify administration, or by offering competitive discounts.

An added uncertainty is anticipating the indication the biosimilar will be licensed for. If the originator product is licensed for a number of indications, experience suggests (from the licensing of biosimilar infliximab), that the biosimilar could be licensed for all the same indications as the originator product, irrespective of the clinical studies being undertaken. However, as the biosimilar market is a developing area there is no certainty this will also apply in the future. Bearing this in mind the indication field in the table below only includes those where clinical studies are in progress or where the licence has been granted so indication is known. Biosimilars are only listed below where there is the potential for the product to be available on the UK market in the timeframe 2015 to 2017 taking into account the patent expiry date of the originator product.

1. MHRA Drug Safety Update, February 2008.
2. NICE Position Statement. January 2015

Likely CCG commissioned

Insulin glargine LY2963016 injection *[Abasaglar];* Lilly	
Indication:	Diabetes mellitus, type 1 and 2, adults, adolescents and children aged 2 years and above. Available as 100 units/ml in 3ml cartridges for the *HumaPenSavvio* device or pre-filled pen (*Kwikpen*) devices.
Current status:	Licensed in EU September 2014 – see prescribing data.
UK availability:	2015 September
Reference product & company:	*Lantus* (Sanofi-Aventis).
Patent expiry of reference product	2015 May (expired).
Sector:	Primary care.
Implications:	This will be the first insulin biosimilar to be marketed and likely to be about 15% cheaper than the current list price for *Lantus*. Sanofi have recently launched a higher strength glargine product (*Toujeo*) which may compete for the same adult patient group. MHRA advise that, as with other biosimilar medicines, some dose adjustment may be needed if switching from *Lantus*.
Tariff:	HRG included.
Efficacy:	ELEMENT 1 in adults with type 1 diabetes (n=535) in combination with insulin lispro, the average fall in HbA1c after 6 months was 0.35% with *Abasaglar* and 0.46% with *Lantus*. In ELEMENT 2 (n=759) in adults with type 2 diabetes, HbA1c fell to below 7% in 48.8% of those given *Abasaglar* vs. 52.5% of those given *Lantus*, with an average HbA1c fall of 1.29% and 1.34%, respectively.

Insulin glargine MK-1293 **injection**; MSD	
Indication:	Diabetes mellitus, type 1 and 2.
Current status:	PIII
UK availability:	2016
Reference product & company:	*Lantus* (Sanofi-Aventis).
Patent expiry of reference product	2015 May (expired).
Sector:	Primary care.
Implications:	This is likely to be the second biosimilar insulin glargine to the market after *Abasaglar* (Lilly). It is unclear what presentations will be available.
Tariff:	HRG included.
Efficacy:	Two PIII efficacy and safety studies vs. *Lantus* are being undertaken. One study in type 2 diabetes (n=528) was completed in March 2015, results are not available. The other, in type 1 diabetes (n=500) is due to complete November 2015.

Insulin glargine [Basalog] **injection**; Mylan	
Indication:	Diabetes mellitus, type 1 and 2.
Current status:	PIII
UK availability:	2017
Reference product & company:	*Lantus* (Sanofi-Aventis).
Patent expiry of reference product	2015 May (expired).
Sector:	Primary care.
Implications:	This product is likely to be at least the third insulin glargine biosimilar on the market. It is unclear what presentations will be available.
Tariff:	HRG included.
Efficacy:	Two PIII non-inferiority efficacy and safety trials in adults with type 1 diabetes (INSTRIDE 1, n=500) and type 2 diabetes (INSTRIDE 2, n=600) comparing this product with *Lantus* are due to complete by June 2016.

Somatropin [Somatropin Biopartners] **injection**; Bioton	
Indication:	Growth disorders in adults and children given as a once weekly s.c. injection.
Current status:	Licensed in EU August 2013 - see prescribing data.
UK availability:	2016
Reference product & company:	*Genotropin* (Pharmacia).
Patent expiry of reference product	2002 (expired).
Sector:	Secondary care.
Implications:	Several somatropin biosimilar products are already available. This will be the first prolonged-release somatropin product licensed for weekly administration and may be an attractive option.
Tariff:	Specified high cost drug.
Efficacy:	In adults, a PIII placebo controlled study and a one-year safety study have been completed. In children, active comparators were shorter acting somatropin products (*Genotropin* and *Eutropin*). Results of all studies used in the licence application are available in the EPAR.

Follitropin alfa XM 17 injection *[Ovaleap];* Teva UK	
Indication:	Fertility disorders, presented as a multi-use cartridge for use with *Ovaleap* pen device.
Current status:	Licensed in EU September 2013- see prescribing data.
UK availability:	2015
Reference product & company:	*Gonal-f* (Merck Serono).
Patent expiry of reference product	2009 (expired).
Sector:	Secondary care.
Implications:	*Ovaleap* will compete with the biosimilar *Bemfola* launched in 2014 as well as the reference product *Gonal-f*. The difference in presentations may influence product choice. *Bemfola* is available as a single use pre-filled pen suitable for self administration. *Gonal-f* is available as a multidose vial requiring reconstitution and a prefilled pen device.
Tariff:	HRG included.
Efficacy:	EPAR data indicates that in a PIII study in 299 women undergoing assisted reproductive technologies comparing *Ovaleap* to *Gonal-f* the primary outcome (number of cumulus oocyte complexes retrieved) was 12.2 vs. 12.0, respectively.

Etanercept SB4 injection; Biogen	
Indication:	Rheumatoid arthritis, moderate-severe, despite methotrexate. Given by s.c. injection.
Current status:	Filed in EU January 2015.
UK availability:	2016
Reference product & company:	*Enbrel* (Pfizer)
Patent expiry of reference product:	2015 July (expired)
Sector:	Secondary care.
Implications:	Likely to be the first etanercept biosimilar to the market.
Tariff:	Specified high cost drug
Efficacy:	A published PIII study compared SB4 with *Enbrel* in 596 patients with moderate-to-severe rheumatoid arthritis already taking methotrexate; 78.1% of those given SB4 vs. 80.3% in the *Enbrel* group met ACR20 response at week 24.

Etanercept GP 2015 injection; Sandoz	
Indication:	Plaque psoriasis. Given by s.c. injection.
Current status:	PIII
UK availability:	2016
Reference product & company:	*Enbrel* (Pfizer).
Patent expiry of reference product:	2015 July (expired).
Sector:	Secondary care.
Implications:	Likely to be second etanercept biosimilar to market.
Tariff:	Specified high cost drug.
Efficacy:	The PIII EGALITY trial comparing GP 2015 with *Enbrel* in 531 patients with moderate-to-severe chronic plaque psoriasis completed in March 2015. Primary outcome is percentage of patients achieving PASI 75 (75% improvement). Results are not yet published.

Etanercept CHS 0214 injection; Baxter International	
Indication:	Rheumatoid arthritis (with inadequate response to methotrexate); Plaque psoriasis. Given by s.c. injection.
Current status:	PIII with plans to file in EU in 2016.
UK availability:	2017
Reference product & company:	*Enbrel* (Pfizer).
Patent expiry of reference product:	2015 July (expired).
Sector:	Secondary care.
Implications:	Likely to be the third etanercept biosimilar to market.
Tariff:	Specified high cost drug.
Efficacy:	The PIII RaPsOdy study comparing CHS-0214 with *Enbrel* in 424 patients with chronic plaque psoriasis inadequately treated with methotrexate is due to complete in May 2016. In another PIII study lasting 24 weeks CHS-0214 is compared with *Enbrel* in 620 patients with rheumatoid arthritis. Primary outcome is percentage achieving ACR-20 at trial end; completion is due October 2015.
Infliximab SB2 injection; Biogen	
Indication:	Rheumatoid arthritis.
Current status:	Filed in EU March 2015.
UK availability:	2016
Reference product & company:	*Remicade* (MSD).
Patent expiry of reference product:	2015 February (expired).
Sector:	Secondary care.
Implications:	There are a number of infliximab biosimilar preparations in development and one product (*Inflectra/Remsima*) is already marketed with the same indications as the originator product, despite not having clinical efficacy data for all indications.
Tariff:	Specified high cost drug.
Efficacy:	A PIII trial lasting 30 weeks in 584 patients with moderate-to-severe rheumatoid arthritis showed an ACR20 response rate of 64.6% in patients on SB2 vs. 66.0% in those on *Remicade*. A long term 52-week study was due to complete in November 2014.
Infliximab BOW 015 injection; Epirus Biopharmaceuticals	
Indication:	Rheumatoid arthritis, autoimmune disease.
Current status:	PIII for RA, PII for autoimmune disease.
UK availability:	2017
Reference product & company:	*Remicade* (MSD).
Patent expiry of reference product:	2015 February (expired).
Sector:	Secondary care.
Implications:	There are a number of infliximab biosimilar preparations in development and one product (*Inflectra/Remsima*) is already marketed with the same indications as the originator product, despite not having clinical efficacy data for all indications.
Tariff:	Specified high cost drug.
Efficacy:	A PIII trial compared BOW015 with *Remicade* in 189 patients with severe rheumatoid arthritis on methotrexate. Similar ACR20 response rates at week 16 were found; 89.8% and 86.4%, respectively.

Infliximab PF 06438179 injection; Pfizer	
Indication:	Rheumatoid arthritis.
Current status:	PIII
UK availability:	2017
Reference product & company:	*Remicade* (MSD).
Patent expiry of reference product:	2015 February (expired).
Sector:	Secondary care.
Implications:	There are a number of infliximab biosimilar preparations in development and one product (*Inflectra/Remsima*) is already marketed with the same indications as the originator product, despite not having clinical efficacy data for all indications.
Tariff:	Specified high cost drug.
Efficacy:	PIII trial started July 2014 assessing efficacy and safety of PF-06438179 vs. *Remicade* in combination with methotrexate in patients with moderately-to-severely active disease who have had an inadequate response to methotrexate. Primary outcome is proportion with ACR20 response. Expected completion date is late 2016.

Rituximab BI 695500 injection; Boehringer Ingelheim	
Indication:	Rheumatoid arthritis, moderate-to-severe.
Current status:	PIII
UK availability:	2017
Reference product & company:	*MabThera* (Roche).
Patent expiry of reference product:	2013 (expired).
Sector:	Secondary care.
Implications:	This is one of several rituximab biosimilar agents in development.
Tariff:	Specified high cost drug.
Efficacy:	Two PIII studies are both due for completion in December 2016; an efficacy, pharmacokinetics and safety study of BI 695500 vs. *MabThera* in 306 patients with rheumatoid arthritis and an open-label extension long-term safety study in 250 adult patients who have successfully completed treatment in the previous trial.

Rituximab MabionCD20 injection; Mabion	
Indication:	Rheumatoid arthritis, moderate-to-severe.
Current status:	PIII
UK availability:	2017
Reference product & company:	*MabThera* (Roche).
Patent expiry of reference product:	2013 (expired).
Sector:	Secondary care.
Implications:	This is one of several rituximab biosimilar agents in development.
Tariff:	Specified high cost drug.
Efficacy:	A PIII bioequivalence study comparing a single course of treatment of MabionCD20 and *MabThera* in 863 patients with rheumatoid arthritis is on-going and due to complete in March 2016.

Likely NHS England commissioned	
Pegfilgrastim [Neupeg/Pegasta] injection; Intas Biopharmaceuticals	
Indication:	Neutropenia, in patients with cancer undergoing chemotherapy.
Current status:	PIII in EU, filed in US December 2014.
UK availability:	2017
Reference product & company:	*Neulasta* (Amgen).
Patent expiry of reference product	2017 August.
Sector:	Secondary care.
Implications:	This product is one of a number in development.
Tariff:	Specified high cost drug.
Efficacy:	PIII trials comparing *Neupeg* with *Neulasta* are complete, results are not yet available.
Pegfilgrastim LA EP2006 injection; Sandoz	
Indication:	Neutropenia, in patients with cancer undergoing chemotherapy.
Current status:	PIII
UK availability:	2017
Reference product & company:	*Neulasta* (Amgen).
Patent expiry of reference product	2017 August.
Sector:	Secondary care.
Implications:	This product is one of a number in development.
Tariff:	Specified high cost drug.
Efficacy:	A PIII trial comparing LA EP2006 with *Neulasta* in 308 patients with breast cancer undergoing chemotherapy treatment (PROTECT 2) was completed December 2013. The primary outcome was mean duration of severe neutropenia during the first cycle of chemotherapy. Results are not yet available.
Trastuzumab CT-P6 injection *[Credima];* Hospira	
Indication:	Breast cancer, HER 2 positive, early and metastatic.
Current status:	PIII
UK availability:	2017
Reference product & company:	*Herceptin* (Roche).
Patent expiry of reference product	2014 (expired).
Sector:	Secondary care.
Implications:	There are a number of other trastuzumab biosimilars for i.v. infusion in development. However, *Herceptin* for s.c. administration is also available with which this will have to compete.
Tariff:	Chemotherapy.
Efficacy:	A PIII trial (n=532) comparing *Credima* with *Herceptin* as neoadjuvant and adjuvant treatment in patients with HER2-positive, early-stage breast cancer is ongoing with primary outcome data due December 2016. The PIII COMPARE study (n=383) compared *Credima* with *Herceptin*, both in combination with paclitaxel, as first-line therapy in metastatic breast cancer. Overall response rate (primary outcome) was 57% and 62%, respectively.

Trastuzumab PF-05280014 **injection**; Pfizer	
Indication:	Breast cancer, HER 2 positive, early and metastatic. Given by i.v. infusion.
Current status:	PIII
UK availability:	2017
Reference product & company:	*Herceptin* (Roche).
Patent expiry of reference product:	2014 (expired).
Sector:	Secondary care.
Implications:	There are a number of other trastuzumab biosimilars for i.v. infusion in development. However, *Herceptin* for s.c. administration is also available with which this will have to compete.
Tariff:	Chemotherapy.
Efficacy:	An ongoing PIII study comparing PF 05280014 to *Herceptin* as neoadjuvant treatment for patients with early stage, operable HER2-positive breast cancer is due to complete December 2016. Another ongoing PIII study is comparing PF 05280014 with *Herceptin* for first-line treatment of patients with HER2-positive metastatic breast cancer. Primary outcome data is due October 2016.

Trastuzumab ABP980 **injection**; Allergan/Amgen	
Indication:	Breast cancer, HER 2 positive, early and metastatic. Given by i.v. infusion.
Current status:	PIII
UK availability:	2017
Reference product & company:	*Herceptin* (Roche).
Patent expiry of reference product:	2014 (expired).
Sector:	Secondary care.
Implications:	There are a number of other trastuzumab biosimilars for i.v. infusion in development. However, *Herceptin* for s.c. administration is also available with which this will have to compete.
Tariff:	Chemotherapy.
Efficacy:	The PIII trial comparing ABP980 with *Herceptin* in 808 patients with early breast cancer is due to complete in March 2016.

Rituximab BI 695500 **injection**; Boehringer Ingelheim	
Indication:	Follicular lymphoma, first-line. Given by i.v. infusion.
Current status:	PIII
UK availability:	2016
Reference product & company:	*MabThera* (Roche).
Patent expiry of reference product	2013 (expired).
Sector:	Secondary care.
Implications:	The originator product is licensed in a variety of lymphomas as either first-line, treatment-resistant disease or as maintenance. There is a *MabThera* s.c. formulation for patients with follicular or Non-Hodgkin's lymphoma with which this product will have to compete.
Tariff:	Chemotherapy.
Efficacy:	A PIII study (n=530) to compare efficacy and safety of BI 695500 vs. *MabThera* was due to complete in April 2015. A PIII study (n=250) to evaluate BI 695500 vs. rituximab as a first-line immunotherapy treatment in patients with low tumour burden is due to complete March 2017.

Rituximab MabionCD20 injection; Mabion	
Indication:	Diffuse large B-cell lymphoma (DLBCL) in patients who are CD20 positive. Given by i.v. infusion.
Current status:	PIII
UK availability:	2017
Reference product & company:	*MabThera* (Roche).
Patent expiry of reference product:	2013 (expired)
Sector:	Secondary care.
Implications:	The originator product is licensed in a variety of lymphomas as either first-line, treatment-resistant disease or as maintenance. There is a *MabThera* s.c. formulation for patients with follicular or Non-Hodgkin's lymphoma with which this product will have to compete.
Tariff:	Chemotherapy.
Efficacy:	A PIII study (n=140) comparing the pharmacokinetics, efficacy, safety and immunogenicity of MabionCD20 vs. *MabThera* is due to complete March 2016.

Rituximab PF-05280586 injection; Pfizer	
Indication:	Follicular lymphoma, CD20 positive, low tumour burden. Given by i.v. infusion.
Current status:	PIII
UK availability:	2017
Reference product & company:	*MabThera* (Roche).
Patent expiry of reference product:	2013 (expired).
Sector:	Secondary care.
Implications:	The originator product is licensed in a variety of lymphomas as either first-line, treatment-resistant disease or as maintenance. There is a *MabThera* s.c. formulation for patients with follicular or Non-Hodgkin's lymphoma with which this product will have to compete.
Tariff:	Chemotherapy.
Efficacy:	A PIII study (n=394) comparing PF-05280586 vs. *MabThera* as first-line treatment in CD20-positive, low tumour burden follicular lymphoma is ongoing with primary outcome data due November 2016.

Table 2. Drugs in Prescribing Outlook 2014 - development delayed

Generic and *trade* name	Company	Indication	Reason for delay
AAV1/SERCA2a injection *Mydicar*	Celladon	Heart failure, chronic, advanced.	Development suspended following disappointing trial results.
Afatinib oral *Giotrif*	Boehringer Ingelheim	Head and neck cancer, locally advanced squamous cell.	PIII studies not due to complete until 2019.
Asunaprevir oral *Sunvepra*	Bristol-Myers Squibb	Hepatitis C infection, genotype 1 and 4, with daclatasvir.	Not filed in EU and filing in US withdrawn for commercial reasons. Development focussed on drug combinations.
Bazedoxifene/ conjugated estrogens oral *Duavive*	Pfizer	Postmenopausal osteoporosis.	EU licence application withdrawn. CHMP said there was no added value for the fixed-dose combination and there are potential unfavourable effects.
Budesonide/ formoterol inhaled *Bufomix Easyhaler*	Orion	Chronic obstructive pulmonary disease and asthma.	Launched elsewhere in the EU after licensing through the decentralised route. Progress through the UK licensing system uncertain.
Cabozantinib oral	Exelixis	Prostate cancer, metastatic castration-resistant.	Following negative trial results, the company is no longer pursuing development for this indication.
Danoprevir oral	Roche	Hepatitis C infection, treatment-naïve and -experienced.	Licence application planned for 2017 or later.
Dasiprotimut-T injection *Lympreva*	Biovest	Non-Hodgkin's lymphoma.	Not recommended for approval in EU. CHMP said the main study was inadequate to establish benefit, the effectiveness was not demonstrated and there were concerns regarding manufacture and quality control.
Diltiazem cream *Anoheal*	SLA Pharma	Anal fissure.	Following company merger this product is no longer in development.
Enobosarm oral *Ostarine*	GTXi	Cancer cachexia.	No development reported in company pipeline.
Eribulin injection *Halaven*	Eisai	Non-small cell lung cancer, advanced.	Development discontinued.
Everolimus oral *Afinitor*	Novartis	Breast cancer, second or third-line.	Development discontinued.
Everolimus oral *Afinitor*	Novartis	Breast cancer, first-line.	Development discontinued.
Fexapotide injection	Recordati	Benign prostatic hyperplasia.	Development discontinued in EU.
Fingolimod oral *Gilenya*	Novartis	Multiple sclerosis, primary progressive.	Development discontinued.
Insulin peglispro injection	Lilly	Type 1 and type 2 diabetes mellitus.	Licence application delayed to allow time for safety data collection.
Ipilimumab injection *Yervoy*	Bristol-Myers Squibb	Prostate cancer, hormone-resistant.	Development discontinued due to poor trial results.
Liraglutide injection *Saxenda*	Novo Nordisk	Obesity.	Launch plans in UK uncertain.
Lumacaftor/ ivacaftor oral *Orkambi*	Vertex	Cystic fibrosis in heterozygous F508del patients.	Plans for licence application for this indication are uncertain.

Melatonin oral *Circadin*	Nerium	Insomnia in children.	Study due to complete 2017 therefore launch anticipated 2018 or later.
Mifepristone oral *Corluxin*	Corcept Thera-peutics	Cushing's disease.	Licence application withdrawn. The CHMP provisional opinion indicated concerns about manufacture, limited effectiveness, and safety.
Peptide p277 injection *DiaPep277*	Andro-meda	Type 1 diabetes, newly-diagnosed.	Development terminated following evidence of misconduct regarding unblinding of trial data.
Ramucirumab injection *Cyramza*	Lilly	Hepatocellular carcinoma, second-line after sorafenib..	Study due to complete late 2017 therefore launch anticipated 2018 or later.
Rigosertib injection *Estybon*	Baxter	Myelodysplastic syndromes refractory, high-risk.	New trial to start with different patient subgroup following discussions with licencing authorities.
Rituximab (CT-P10) injection	Sandoz	Follicular lymphoma.	Study results not due until 2018.
Rivaroxaban oral *Xarelto*	Janssen	Prevention in patients with chronic heart failure and coronary artery disease.	Study results not due until 2017.
Safinamide oral *Xadago*	Zambon	Parkinson's disease (PD), early-stage disease.	Licence application withdrawn. CHMP said benefits in the early PD setting were not robustly shown, and did not outweigh risks. Safinamide is licensed for use in mid-to-late stage PD.
Scyllo-inositol oral	Elan	Alzheimer's disease, mild-to-moderate.	Still in PII trials, launch not anticipated before 2018.
Secukinumab injection *Cosentyx*	Novartis	Rheumatoid arthritis.	Not listed in Novartis planned licence applications, reason unknown.
Sipuleucel-T injection *Provenge*	Dendreon	Prostate cancer, castration-resistant.	Licence withdrawn for commercial reasons.
Sorafenib oral *Nexavar*	Bayer	Breast cancer, HER2-ve locally advanced/ metastatic, second-line.	Discontinued development due to failure to meet primary outcome in study.
Sorafenib oral *Nexavar*	Bayer	Renal cell carcinoma, adjuvant in resected patients at risk of relapse.	Company are no longer developing sorafenib this for this indication.
Teplizumab injection	Macro-Genics	Type 1 diabetes, prevention in very high-risk patients.	No longer listed in company pipeline and appears to have been discontinued.
Tofacitinib oral *Xeljanz*	Pfizer	Psoriasis, moderate-severe chronic plaque.	Unlikely to be available in EU before 2018.
Trastuzumab(BCD-022) injection	Biocad	Breast cancer, metastatic.	Development only underway in Russia.
Trastuzumab emtansine injection *Kadcyla*	Roche	Breast cancer, metastatic HER2+ve, first-line.	Discontinued due to disappointing trial results.
Trebananib injection	Amgen	Ovarian, fallopian tube or peritoneal cancer.	Study terminated as interim assessment indicated it is not likely to meet its primary outcome.
Volasertib injection	Boehringer Ingelheim	Acute myeloid leukaemia, in patients ineligible for intensive induction.	Based on PIII study data, the company has decided not to submit licence applications.

Table 3. Recent UK drug launches or licence extensions (Sep 2014 to Aug 2015)

Generic and *brand* name. Company.	Indication and relevant guidance. Full prescribing information can be found on the electronic medicines compendium at medicines.org.uk via *brand* name link.
BNF 1. Gastrointestinal system	
Infliximab biosimilar *Inflectra - SmPC* Hospira	***Licence:*** Crohn's disease and ulcerative colitis in adults and children. ***Guidance:*** **NICE:** Inflammatory bowel disease. **SMC:** Restricted use. **AWMSG:** Restricted use. **NTAG:** Recommended. ***Reviews:*** LMEN February 2015.
Infliximab biosimilar *Remsima - SmPC* Napp	***Licence:*** Crohn's disease and ulcerative colitis in adults and children. ***Guidance:*** **NICE:** Inflammatory bowel disease. **SMC:** Restricted use. **AWMSG:** Restricted use. **NTAG:** Recommended. ***Reviews:*** LMEN February 2015.
Methylnaltrexone *Relistor - SmPC* TMC	***Licence:*** Opioid-induced constipation in adults with chronic non-cancer pain. ***Guidance:*** **NICE:** Constipation. ***Reviews:*** NIHR HSRIC August 2014.
Prucalopride *Resolor - SmPC* Shire	***Licence:*** Chronic constipation in men when laxatives fail to provide adequate relief. ***Guidance:*** **NICE:** Constipation. ***Reviews:*** NIHR HSRIC October 2014.
Teduglutide *Revestive - SmPC* NPS	***Licence:*** Short bowel syndrome, in adults. ***Guidance:*** **NICE:** Endocrinal, nutritional and metabolic conditions. ***Reviews:*** None recent.
Cholic acid *Orphacol - SmPC* Laboratoires CTRS	***Licence:*** Inborn errors of primary bile acid synthesis [new formulation]. ***Guidance:*** **NICE:** Endocrinal, nutritional and metabolic conditions. ***Reviews:*** NIHR HSRIC March 2014.
BNF 2. Cardiovascular system	
Cangrelor *Kengrexal - SmPC* The Medicines Company	***Licence:*** Reduction of thrombotic cardiovascular events in adults with coronary artery disease undergoing percutaneous coronary intervention. ***Guidance:*** **NICE:** Acute coronary syndromes. Cangrelor. **SMC:** Not approved. **SIGN**: Acute coronary syndromes. ***Reviews:*** NICE-ES due September 2015.
Rivaroxaban *Xarelto - SmPC* Bayer	***Licence:*** Prevention of atherothrombotic events in adults after acute coronary syndrome with elevated cardiac biomarkers [2.5mg tablet formulation]. ***Guidance:*** **NICE:** Acute coronary syndromes. Rivaroxaban. **SIGN:** Acute coronary syndrome. **SMC:** Not approved. **NTAG:** Not recommended. ***Reviews:*** RDTC October 2014.
Edoxaban *Lixiana - SmPC* Daiichi Sankyo	***Licence:*** Stroke prevention in atrial fibrillation and treatment and prevention of venous thromboembolism. ***Guidance:*** **NICE:** Heart rhythm conditions. Edoxaban AF due September 2015. Embolism and thrombosis. Edoxaban VTE due August 2015. **SIGN:** VTE. Thrombotics. **SMC:** Due November 2015 for both indications. ***Reviews:*** None.
Rivaroxaban *Xarelto - SmPC* Bayer	***Licence:*** Prevention of cardiovascular complications in patients with atrial fibrillation undergoing cardioversion. ***Guidance:*** **NICE:** Heart rhythm conditions. **SIGN:** Cardiovascular disease. Thrombotics ***Reviews:*** None.
Evolocumab *Repatha SureClick - SmPC* Amgen	***Licence:*** Heterozygous familial hypercholesterolaemia (FH) / Heterozygous non-FH mixed dyslipidaemia / Homozygous FH / Primary hypercholesterolaemia or mixed dyslipidaemia in adults unable to have a statin. ***Guidance:*** **NICE:** Lipid disorders. Evolocumab due April 2016. ***Reviews:*** NIHR HSRIC April 2013.

Table 3. Recent UK drug launches or licence extensions (Sep 2014 to Aug 2015)

Generic and *brand* name. Company.	Indication and relevant guidance. Full prescribing information can be found on the electronic medicines compendium at medicines.org.uk via *brand* name link.
Midodrine *Bramox - SmPC* Brancaster	***Licence:*** Severe orthostatic hypotension due to autonomic dysfunction. ***Guidance:*** **NICE:** Cardiovascular conditions: general and other. **SMC:** Due October 2015. **AWMSG:** Due TBC. ***Reviews:*** NIHR HSRIC July 2015, NICE-ES due October 2015.
Simoctocog alfa *Nuwiq - SmPC* Octapharma	***Licence:*** Haemophilia A, treatment and prophylaxis in all age groups. ***Guidance:*** **NICE:** Blood conditions. ***Reviews:*** None.
Factor VIII/ von Willebrand factor *Voncento - SmPC* CSL Behring	***Licence:*** Prophylaxis and treatment of haemorrhage or surgical bleeding in patients with von Willebrand disease, when desmopressin treatment alone is ineffective or contraindicated. ***Guidance:*** None. ***Reviews:*** None.
BNF 3. Respiratory system	
Aclidinium bromide/ formoterol fumarate *Duaklir Genuair - SmPC* AstraZeneca	***Licence:*** Chronic obstructive pulmonary disease (COPD), [new formulation]. ***Guidance:*** **NICE:** COPD. **SMC:** Approved. ***Reviews:*** NICE-ES April 2015, RDTC March 2015, MTRAC January 2015.
Indacaterol/ glycopyrronium *Ultibro Breezhaler - SmPC* Novartis	***Licence:*** Chronic obstructive pulmonary disease (COPD) [new formulation]. ***Guidance:*** **NICE:** COPD. **SMC:** Approved. **AWMSG:** Recommended. ***Reviews:*** MTRAC January 2015, RDTC December 2014, LMEN February 2014, NICE-ES February 2014.
Tiotropium/ olodaterol *Spiolto Respimat - SmPC* Boehringer Ingelheim	***Licence:*** Chronic obstructive pulmonary disease (COPD) [new formulation]. ***Guidance:*** **NICE:** COPD. **SMC:** Due November 2015. ***Reviews:*** None.
Umeclidinium *Incruse - SmPC* GSK	***Licence:*** Chronic obstructive pulmonary disease. ***Guidance:*** **NICE:** COPD. **SMC:** Approved. **AWMSG:** Recommended. ***Reviews:*** NICE-ES January 2015.
Budesonide/ formoterol *DuoResp Spiromax - SmPC* Teva UK	***Licence:*** Asthma and chronic obstructive pulmonary disease (COPD) [new formulation]. ***Guidance:*** **NICE:** Asthma, COPD. **SIGN:** Asthma. ***Reviews:*** None.
Beclometasone/ formoterol *Fostair NEXThaler - SmPC* Chiesi	***Licence:*** Asthma [new formulation]. ***Guidance:*** **NICE:** Asthma. **SIGN:** Asthma. ***Reviews:*** NICE-ES January 2015.
Tiotropium bromide *Spiriva Respimat - SmPC* Boehringer Ingelheim	***Licence:*** Asthma. ***Guidance:*** **NICE:** Asthma. **SIGN:** Asthma. **SMC:** Approved. **AWMSG:** Due TBC. ***Reviews:*** MTRAC March 2015, NICE-ES March 2015, RDTC February 2015.
Nintedanib *Ofev - SmPC* Boehringer Ingelheim	***Licence:*** Idiopathic pulmonary fibrosis. ***Guidance:*** **NICE:** Pulmonary fibrosis, nintedanib due January 2016. **SMC:** Due October 2015. ***Reviews:*** NIHR HSRIC June 2013.

Table 3. Recent UK drug launches or licence extensions (Sep 2014 to Aug 2015)

Generic and *brand* name. Company.	Indication and relevant guidance. Full prescribing information can be found on the electronic medicines compendium at medicines.org.uk via *brand* name link.
BNF 4. Central nervous system	
Lisdexamfetamine *Elvanse Adult - SmPC* Shire	***Licence:*** Attention-deficit hyperactivity disorder in adults. ***Guidance:*** **NICE:** Attention deficit disorder. **SMC:** Due August 2015. **AWMSG:** Due TBC. ***Reviews:*** None.
Oxycodone/ naloxone *Targinact - SmPC* Napp	***Licence:*** Idiopathic restless legs syndrome. ***Guidance:*** None. ***Reviews:*** NICE-ES due December 2015.
Perampanel *Fycompa - SmPC* Eisai	***Licence:*** Primary generalised tonic-clonic seizures in patients aged ≥12 years. ***Guidance:*** **NICE:** Epilepsy. **SIGN:** Epilepsy in adults. ***Reviews:*** NIHR HSRIC March 2014.
BNF 5. Infections	
Ceftobiprole *Zevtera - SmPC* Basilea	***Licence:*** Community- and hospital-acquired pneumonia. ***Guidance:*** **NICE:** Healthcare associated infections, Respiratory conditions. **SMC:** Restricted use. ***Reviews:*** None.
Telavancin *Vibativ - SmPC* Clinigen	***Licence:*** Nosocomial pneumonia, including ventilator-associated, known or suspected to be caused by methicillin-resistant *Staphylococcus aureus.* ***Guidance:*** **NICE:** Healthcare associated infections, Respiratory conditions. **SMC:** Not approved. ***Reviews:*** NICE-ES July 2014.
Tedizolid phosphate *Sivextro - SmPC* MSD	***Licence:*** Acute bacterial skin and skin structure infections. ***Guidance:*** **NICE:** Infections: general and other. **SMC:** Restricted use. **AWMSG:** Due TBC. ***Reviews:*** None.
Para-aminosalicylic acid *GranuPAS - SmPC* Lucane	***Licence:*** Multi-drug resistant tuberculosis in adults and children aged ≥28 days. ***Guidance:*** **NICE:** Tuberculosis. ***Reviews:*** None.
Daclatasvir *Daklinza - SmPC* Bristol-Myers Squibb	***Licence:*** Hepatitis C infection. ***Guidance:*** **NICE:** Hepatitis. Daclatasvir due August 2015. **SIGN:** Hepatitis C. **SMC:** Restricted use. **AWMSG:** Restricted use. ***Reviews:*** NIHR HSRIC March 2014.
Dasabuvir *Exviera - SmPC* AbbVie	***Licence:*** Hepatitis C infection. ***Guidance:*** **NICE:** Hepatitis. **SIGN:** Hepatitis C. **SMC:** Approved. ***Reviews:*** None.
Ombitasvir/ paritaprevir/ ritonavir *Viekirax - SmPC* AbbVie	***Licence:*** Hepatitis C infection. ***Guidance:*** **NICE:** Hepatitis. *Viekirax* due November 2015. **SIGN:** Hepatitis C. **SMC:** Approved. ***Reviews:*** None.
Sofosbuvir/ ledipasvir *Harvoni - SmPC* Gilead	***Licence:*** Hepatitis C virus infection. ***Guidance:*** **NICE:** Hepatitis. *Harvoni* due November 2015. **SIGN:** Hepatitis C. **SMC:** Restricted use. **AWMSG:** Restricted use. ***Reviews:*** NIHR HSRIC August 2013.
Darunavir *Prezista - SmPC* Janssen	***Licence:*** HIV infection, in combination with cobicistat, and in children aged ≥3 years of at least 15kg bodyweight. ***Guidance:*** **NICE:** HIV and AIDs. **BHIVA:** HIV-1 infection. **SMC:** Restricted use. **AWMSG:** Recommended. ***Reviews:*** None recent.

Table 3. Recent UK drug launches or licence extensions (Sep 2014 to Aug 2015)

Generic and *brand* name. Company.	Indication and relevant guidance. Full prescribing information can be found on the electronic medicines compendium at medicines.org.uk via *brand* name link.
Darunavir/ cobicistat *Rezolsta - SmPC* Janssen	***Licence:*** HIV infection in treatment-naïve and experienced adults. ***Guidance:*** **NICE:** HIV and AIDs. **BHIVA:** HIV-1 infection. **SMC:** Approved. **AWMSG:** Due TBC. ***Reviews:*** None.
Dolutegravir/ abacavir/ lamivudine *Triumeq - SmPC* ViiV	***Licence:*** HIV infection in adults and adolescents aged ≥12 years. ***Guidance:*** **NICE:** HIV and AIDs. **BHIVA:** HIV-1 infection. **SMC:** Approved. **AWMSG:** Recommended. ***Reviews:*** None.
Raltegravir *Isentress - SmPC* MSD	***Licence:*** HIV infection in patients aged ≥ four weeks [new formulation]. ***Guidance:*** **NICE:** HIV and AIDs. **BHIVA:** HIV-1 infection. **AWMSG:** Due TBC. ***Reviews:*** None.
Posaconazole *Noxafil - SmPC* MSD	***Licence:*** Fungal infections in adults [new formulation]. ***Guidance:*** **NICE:** Infections: general and other. **SMC:** Approved. ***Reviews:*** None.
BNF 6. Endocrine system	
Canagliflozin/ metformin IR *Vokanamet - SmPC* Janssen	***Licence:*** Type 2 diabetes mellitus [new formulation]. ***Guidance:*** **NICE:** Diabetes. **SIGN:** Diabetes. **SMC:** Restricted use. ***Reviews:*** None.
Dulaglutide *Trulicity - SmPC* Lilly	***Licence:*** Type 2 diabetes mellitus. ***Guidance:*** **NICE:** Diabetes. **SIGN:** Diabetes. **SMC:** Due TBC. ***Reviews:*** NICE-ES June 2015.
Empagliflozin *Jardiance - SmPC* Boehringer Ingelheim	***Licence:*** Type 2 diabetes mellitus. ***Guidance:*** **NICE:** Diabetes. Empagliflozin. **SIGN:** Diabetes. **SMC:** Restricted use. ***Reviews:*** NICE-ES March 2014.
Exenatide *Bydureon - SmPC* AstraZeneca	***Licence:*** Type 2 diabetes mellitus [new formulation]. ***Guidance:*** **NICE:** Diabetes. **SIGN:** Diabetes. ***Reviews:*** None.
Insulin degludec/ liraglutide *Xultophy - SmPC* Novo Nordisk	***Licence:*** Type 2 diabetes mellitus [new formulation]. ***Guidance:*** **NICE:** Diabetes. **SIGN:** Diabetes. **SMC:** Due October 2015. **AWMSG:** Due TBC. ***Reviews:*** NICE-ES July 2015, RDTC May 2015.
Insulin degludec *Tresiba - SmPC* Novo Nordisk	***Licence:*** Type 1 and type 2 diabetes mellitus in adolescents and children aged ≥ one year. ***Guidance:*** **NICE:** Diabetes. **SIGN:** Diabetes. **SMC:** Not approved. ***Reviews:*** None.
Insulin glargine U300 *Toujeo - SmPC* Sanofi-Aventis	***Licence:*** Type 1 and 2 diabetes mellitus [new formulation]. ***Guidance:*** **NICE:** Diabetes. **SIGN:** Diabetes. **SMC:** Due September 2015. ***Reviews:*** NICE-ES due October 2015.
Pasireotide *Signifor - SmPC* Novartis	***Licence:*** Acromegaly. ***Guidance:*** **NICE:** Endocrinal, nutritional and metabolic conditions: general and other. **SMC:** Due September 2015. **AWMSG:** Due TBC. ***Reviews:*** None recent.
Tolvaptan *Jinarc - SmPC* Otsuka	***Licence:*** Autosomal-dominant polycystic kidney disease. ***Guidance:*** **NICE:** Kidney conditions: general and other. Tolvaptan due September 2015. **SIGN:** CKD. **SMC:** Due December 2015. ***Reviews:*** None recent.

Table 3. Recent UK drug launches or licence extensions (Sep 2014 to Aug 2015)

Generic and *brand* name. Company.	Indication and relevant guidance. Full prescribing information can be found on the electronic medicines compendium at medicines.org.uk via *brand* name link.
BNF 7. Obstetrics, gynaecology, and urinary-tract disorders	
Ethinylestradiol/ drospirenone *ELOINE - SmPC* Bayer	***Licence:*** Contraception. ***Guidance:*** **NICE:** Contraception. ***Reviews:*** None.
Levonorgestrel *Levosert - SmPC* Actavis	***Licence:*** Intrauterine contraception and heavy menstrual bleeding [new formulation]. ***Guidance:*** **NICE:** Contraception. **SMC:** Approved. ***Reviews:*** None.
Mifepristone/ misoprostol Error! Bookmark not defined. *Medabon - SmPC* Sun	***Licence:*** Termination of pregnancy. ***Guidance:*** **NICE:** Contraception. **SMC:** Approved. ***Reviews:*** None.
Follicle stimulating hormone biosimilar *Bemfola - SmPC* Finox	***Licence:*** *In vitro* fertilisation. ***Guidance:*** **NICE:** Fertility. **SMC:** Approved. **AWMSG:** Recommended. ***Reviews:*** None.
Misoprostol *Mysodelle - SmPC* Ferring	***Licence:*** Induction of labour in women with an unfavourable cervix (new formulation). ***Guidance:*** **NICE:** Intrapartum care. **SMC:** Approved. ***Reviews:*** NICE-ES March 2014.
BNF 8. Malignant disease and immunosuppression	
Bevacizumab *Avastin - SmPC* Roche	***Licence:*** Cervical cancer. ***Guidance:*** **NICE:** Cervical cancer. **SIGN:** Cervical cancer. ***Reviews:*** NIHR HSRIC May 2014.
Olaparib *Lynparza - SmPC* AstraZeneca	***Licence:*** Ovarian cancer, BRCA-mutated, maintenance treatment. ***Guidance:*** **NICE:** Ovarian cancer. Olaparib due January 2016. **SIGN:** Ovarian cancer. **SMC:** Not approved. ***Reviews:*** NIHR HSRIC June 2013.
Bortezomib *Velcade - SmPC* Janssen	***Licence:*** Mantle cell lymphoma, first-line. ***Guidance:*** **NICE:** Blood and bone marrow cancers. **SMC:** Due September 2015. ***Reviews:*** None recent.
Ibrutinib *Imbruvica - SmPC* Janssen	***Licence:*** Chronic lymphocytic leukaemia (CLL), first-line and second-plus line monotherapy / Mantle cell lymphoma (MCL), relapsed or refractory. ***Guidance:*** **NICE:** Blood and bone marrow cancers. CLL due June 2016. MCL due December 2016. **AWMSG:** MCL and CLL due TBC. ***Reviews:*** NIHR HSRIC October 2014, July 2013.
Idelalisib *Zydelig - SmPC* Gilead	***Licence:*** Chronic lymphocytic leukaemia. ***Guidance:*** **NICE:** Blood and bone marrow cancers. Idelalisib due October 2015. **SMC:** Restricted use. ***Reviews:*** NIHR HSRIC June 2013.
Idelalisib *Zydelig - SmPC* Gilead	***Licence:*** Refractory follicular lymphoma. ***Guidance:*** **NICE:** Blood and bone marrow cancers. Idelalisib. **SMC:** Approved. ***Reviews:*** NIHR HSRIC July 2013.
Lenalidomide *Revlimid - SmPC* Celgene	***Licence:*** Multiple myeloma, first-line in patients not eligible for transplant. ***Guidance:*** **NICE:** Blood and bone marrow cancers. Lenalidomide due TBC. **SMC:** Due November 2015. **AWMSG:** Due TBC. ***Reviews:*** None recent.

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Generic and *brand* name. Company.	Indication and relevant guidance. Full prescribing information can be found on the electronic medicines compendium at medicines.org.uk via *brand* name link.
Ruxolitinib *Jakavi - SmPC* Novartis	***Licence:*** Polycythemia vera, second-line. ***Guidance:*** **NICE:** Blood and bone marrow cancers. Ruxolitinib due TBC. ***Reviews:*** NIHR HSRIC April 2013.
Cabozantinib *Cometriq - SmPC* Swedish Orphan	***Licence:*** Medullary thyroid cancer. ***Guidance:*** **NICE:** Head and neck cancers. **SMC:** Not approved. **AWMSG:** Recommended. ***Reviews:*** None recent.
Lenvatinib *Lenvima - SmPC* Eisai	***Licence:*** Thyroid cancer, differentiated, radioiodine-refractory. ***Guidance:*** **NICE:** Head and neck cancers. ***Reviews:*** None.
Enzalutamide *Xtandi - SmPC* Astellas	***Licence:*** Metastatic castration-resistant prostate cancer, second-line. ***Guidance:*** **NICE:** Prostate cancer. Enzalutamide due September 2015. **SMC:** Not approved. **AWMSG:** Due TBC. ***Reviews:*** None recent.
Lanreotide *Somatuline Autogel - SmPC* Ipsen	***Licence:*** Gastroenteropancreatic-neuroendocrine tumours. ***Guidance:*** **NICE:** Stomach cancer. Pancreatic cancer. **SIGN:** Oesophageal/ gastric cancer. ***Reviews:*** NIHR HSRIC December 2014.
Ramucirumab *Cyramza - SmPC* Lilly	***Licence:*** Gastric or gastro-oesophageal junction adenocarcinoma, second-line. ***Guidance:*** **NICE:** Stomach cancer. Ramucirumab due January 2016. **SIGN:** Oesophageal and gastric cancer. ***Reviews:*** NIHR HSRIC March 2014, September 2013.
Panitumumab *Vectibix - SmPC* Amgen	***Licence:*** Metastatic colorectal cancer, wild-type RAS in adults, first-line. ***Guidance:*** **NICE:** Colorectal cancer. **SIGN:** Colorectal cancer. **SMC:** Not approved. ***Reviews:*** None recent.
Nintedanib *Vargatef - SmPC* Boehringer Ingelheim	***Licence:*** Non-small cell lung cancer in adults, second-line. ***Guidance:*** **NICE:** Lung cancer. Nintedanib. **SIGN:** Lung cancer. **SMC:** Approved. ***Reviews:*** None recent.
Nivolumab *Nivolumab BMS - SmPC* Bristol-Myers Squibb	***Licence:*** Advanced squamous non-small cell lung cancer, second-line. ***Guidance:*** **NICE:** Lung cancer. Nivolumab due May 2016. **SIGN:** Lung cancer. ***Reviews:*** NIHR HSRIC September 2013.
Paclitaxel albumin-bound *Abraxane - SmPC* Celgene	***Licence:*** Advanced non-small cell lung cancer, first-line. ***Guidance:*** **NICE:** Lung cancer. **SIGN:** Lung cancer. **SMC:** Not approved. ***Reviews:*** None recent.
Nivolumab *Opdivo - SmPC* Bristol-Myers Squibb	***Licence:*** Advanced malignant melanoma – BRAF-negative, first-line / BRAF-positive, first-line / second-line. ***Guidance:*** **NICE:** Skin cancer. Nivolumab due May 2016. ***Reviews:*** NIHR HSRIC BRAF negative, BRAF positive, second-line all December 2014.
Pembrolizumab *Keytruda - SmPC* MSD	***Licence:*** Advanced melanoma in adults, monotherapy. ***Guidance:*** **NICE:** Skin cancer. Pembrolizumab due January 2016. **SMC:** Due TBC. ***Reviews:*** NIHR HSRIC December 2013.
Pertuzumab *Perjeta - SmPC* Roche	***Licence:*** Breast cancer, HER2-positive, locally advanced, inflammatory or early stage. ***Guidance:*** **NICE:** Breast cancer. **SIGN:** Primary breast cancer. ***Reviews:*** NIHR HSRIC February 2014.
Denosumab *XGEVA - SmPC* Amgen	***Licence:*** Unresectable giant cell tumour of bone. ***Guidance:*** **NICE:** Cancer: general and other. **AWMSG:** Due TBC. ***Reviews:*** None recent.

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Generic and *brand* name. Company.	Indication and relevant guidance. Full prescribing information can be found on the electronic medicines compendium at medicines.org.uk via *brand* name link.
Dexrazoxane *Savene - SmPC* Clinigen	***Licence:*** Anthracycline extravasation. ***Guidance:*** **NICE:** Cancer: general and other. ***Reviews:*** None.
Glatiramer acetate *Copaxone - SmPC* Teva UK	***Licence:*** Multiple sclerosis [new formulation]. ***Guidance:*** **NICE:** Multiple sclerosis. **SMC:** Due December 2015. ***Reviews:*** None.
Peginterferon beta-1a *Plegridy - SmPC* Biogen	***Licence:*** Multiple sclerosis, relapsing-remitting [new formulation]. ***Guidance:*** **NICE:** Multiple sclerosis. **SMC:** Approved. **AWMSG:** Recommended. ***Reviews:*** None recent.
Ibrutinib *Imbruvica - SmPC* Janssen	***Licence:*** Waldenström's macroglobulinemia. ***Guidance:*** **NICE:** Blood conditions. ***Reviews:*** NIHR HSRIC April 2015.
Everolimus *Certican - SmPC* Novartis	***Licence:*** Prevention of organ rejection in adults receiving a heart, kidney or liver transplant. ***Guidance:*** **NICE:** Cardiovascular conditions. Kidney conditions. Liver conditions. Everolimus. ***Reviews:*** None recent.
Tacrolimus *Envarsus - SmPC* Chiesi	***Licence:*** Prevention and treatment of kidney and liver transplant rejection [new formulation]. ***Guidance:*** **NICE:** Kidney conditions. Liver conditions. **SMC:** Approved. **AWMSG:** Due TBC. ***Reviews:*** None.
BNF 9. Nutrition and blood	
Filgrastim biosimilar *Accofil - SmPC* Accord	***Licence:*** Neutropenia. ***Guidance:*** **NICE:** Blood conditions. ***Reviews:*** None.
Magnesium aspartate dihydrate *Magnaspartate - SmPC* KoRa	***Licence:*** Treatment and prevention of magnesium deficiency. ***Guidance:*** **NICE:** Endocrinal, nutritional and metabolic conditions. Blood conditions. **SMC:** Approved. **AWMSG:** Due TBC. ***Reviews:*** None.
Sapropterin *Kuvan - SmPC* Merck Serono	***Licence:*** Phenylketonuria, to include children under 4 years of age. ***Guidance:*** **NICE:** Endocrinal, nutritional and metabolic conditions. ***Reviews:*** None.
Sucroferric oxyhydroxide *Velphoro - SmPC* Fresenius Medical Care	***Licence:*** Hyperphosphataemia in patients with renal disease on dialysis. ***Guidance:*** **NICE:** Blood conditions. **SMC:** Approved. **AWMSG:** Due TBC. ***Reviews:*** NICE-ES January 2015.
BNF 10. Musculoskeletal and joint diseases	
Apremilast *Otezla - SmPC* Celgene	***Licence:*** Psoriatic arthritis, second-line. ***Guidance:*** **NICE:** Arthritis. Apremilast due October 2015. **SIGN:** Psoriasis and PsA. ***Reviews:*** NIHR HSRIC January 2013.
Golimumab *Simponi - SmPC* MSD	***Licence:*** Axial spondyloarthritis, non-radiographic, second-line. ***Guidance:*** **NICE:** Arthritis. Golimumab due October 2015. ***Reviews:*** None.
Infliximab biosimilar *Inflectra - SmPC* Hospira	***Licence:*** Rheumatoid arthritis (RA), ankylosing spondylitis, psoriatic arthritis (PsA). ***Guidance:*** **NICE:** Arthritis. **SIGN:** Early RA, Psoriasis and PsA. **SMC:** Restricted use. **AWMSG:** Restricted use. ***Reviews:*** LMEN February 2015, NIHR HSRIC RA, PsA June 2013.

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Generic and *brand* name. Company.	Indication and relevant guidance. Full prescribing information can be found on the electronic medicines compendium at medicines.org.uk via *brand* name link.
Infliximab biosimilar *Remsima - SmPC* Napp	***Licence:*** Rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis. ***Guidance:*** **NICE:** Arthritis. **SIGN:** Early RA, Psoriasis and PsA. **SMC:** Restricted use. **AWMSG:** Restricted use. ***Reviews:*** LMEN February 2015, NIHR HSRIC June 2013.
Tocilizumab *RoActemra - SmPC* Roche	***Licence:*** Rheumatoid arthritis, severe, active and progressive, methotrexate naïve. ***Guidance:*** **NICE:** Arthritis. Tocilizumab due October 2015. **SIGN:** Early RA. **SMC:** Not approved. ***Reviews:*** None recent.
Collagenase clostridium histolyticum *Xiapex - SmPC* Swedish Orphan	***Licence:*** Peyronie's disease. ***Guidance:*** **NICE:** Urological conditions: general and other. **SMC:** Not approved. ***Reviews:*** LMEN August 2015, NIHR HSRIC December 2014.
Febuxostat *Adenuric - SmPC* Menarini	***Licence:*** Prevention and treatment of hyperuricaemia in adults undergoing chemotherapy. ***Guidance:*** **NICE:** Blood conditions. ***Reviews:*** None.
BNF 11. Eye	
Aflibercept *Eylea - SmPC* Bayer	***Licence:*** Macular oedema secondary to branch retinal vein occlusion. ***Guidance:*** **NICE:** Macular oedema and retinal vein occlusion. **SMC:** Due September 2015. ***Reviews:*** NIHR HSRIC December 2014.
Dexamethasone *Ozurdex - SmPC* Allergan	***Licence:*** Diabetic macular oedema. ***Guidance:*** **NICE:** Macular oedema and retinal vein occlusion. Dexamethasone. **SMC:** Approved. ***Reviews:*** LMEN September 2014, NTAG February 2014.
Brinzolamide/ brimonidine *Simbrinza - SmPC* Alcon	***Licence:*** Open-angle glaucoma or ocular hypertension [new formulation]. ***Guidance:*** **NICE:** Glaucoma. **SIGN:** Glaucoma. **SMC:** Approved. ***Reviews:*** NICE-ES March 2015.
Tafluprost/ timolol *Taptiqom - SmPC* Santen	***Licence:*** Open angle glaucoma or ocular hypertension [new formulation]. ***Guidance:*** **NICE:** Glaucoma. **SIGN:** Glaucoma. ***Reviews:*** None.
Ciclosporin *Ikervis - SmPC* Santen	***Licence:*** Severe keratitis in adults with dry eye disease [new formulation]. ***Guidance:*** **NICE:** Eye conditions – general and other. Ciclosporin due December 2015. **SMC:** Due October 2015. ***Reviews:*** None recent.
BNF 13. Skin	
Adalimumab *Humira - SmPC* AbbVie	***Licence:*** Plaque psoriasis in children from 4 years of age and adolescents, second-line. ***Guidance:*** **NICE:** Psoriasis. **SIGN:** Psoriasis and PsA. **SMC:** Restricted use. **AWMSG:** Due TBC. ***Reviews:*** NIHR HSRIC December 2014.
Apremilast *Otezla - SmPC* Celgene	***Licence:*** Plaque psoriasis in adults, second-line. ***Guidance:*** **NICE:** Psoriasis. Apremilast due October 2015. **SIGN:** Psoriasis and PsA. **SMC:** Approved. ***Reviews:*** NIHR HSRIC January 2013.
Secukinumab *Cosentyx - SmPC* Novartis	***Licence:*** Plaque psoriasis in adults, first-line. ***Guidance:*** **NICE:** Psoriasis. Secukinumab. **SIGN:** Psoriasis and PsA. **SMC:** Approved. ***Reviews:*** None recent.

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Generic and *brand* name. Company.	Indication and relevant guidance. Full prescribing information can be found on the electronic medicines compendium at medicines.org.uk via *brand* name link.
Ustekinumab *Stelara - SmPC* Janssen	***Licence:*** Plaque psoriasis from aged ≥12 years, second-line. ***Guidance:*** **NICE:** Psoriasis. **SIGN:** Psoriasis and PsA. ***Reviews:*** NIHR HSRIC June 2013.
Infliximab biosimilar *Inflectra - SmPC* Hospira	***Licence:*** Psoriasis in adults. ***Guidance:*** **NICE:** Psoriasis. **SIGN:** Psoriasis and PsA. **SMC:** Restricted use. **AWMSG:** Restricted use. ***Reviews:*** LMEN February 2015, NIHR HSRIC June 2013.
Infliximab biosimilar *Remsima - SmPC* Napp	***Licence:*** Psoriasis in adults. ***Guidance:*** **NICE:** Psoriasis. **SIGN:** Psoriasis and PsA. **SMC:** Restricted use. **AWMSG:** Restricted use. ***Reviews:*** LMEN February 2015, NIHR HSRIC June 2013.
Bromelain *NexoBrid - SmPC* MediWound	***Licence:*** Removal of eschar in deep partial- and full-thickness thermal burns. ***Guidance:*** **NICE:** Wound management. ***Reviews:*** None.
Adalimumab *Humira - SmPC* AbbVie	***Licence:*** Hidradenitis suppurativa, second-line. ***Guidance:*** **NICE:** Skin conditions: general and other. Adalimumab due June 2016. ***Reviews:*** None.
Ivermectin *Soolantra - SmPC* Galderma	***Licence:*** Papulopustular rosacea [new formulation]. ***Guidance:*** **NICE:** Skin conditions: general and other. **SMC:** Due TBC. ***Reviews:*** NIHR HSRIC August 2014, NICE-ES due January 2016.
BNF 14. Vaccines	
Influenza vaccine *Fluenz Tetra - SmPC* AstraZeneca	***Licence:*** Prophylaxis of influenza in children and adolescents aged ≥ 24 months to ≤ 18 years. ***Guidance:*** **NICE:** Immunisation. ***Reviews:*** None.

Patent expiries 2015 - 2018

Generic medicines have a significant impact on prescribing budgets and can offset, to some extent, costs associated with the introduction of new medicines. Generic products can be marketed once the patent on the original product has expired although manufacturers may apply for a *Supplementary Protection Certificate (SPC)* to extend the effective patent life by up to 5 years (5½ years if it includes a *Paediatric Investigation Plan,* see below). Expiry dates in the table below take account of the SPC and any paediatric extension. The table also indicates where a licence for a generic/biosimilar product is in the latter stages of the EU licensing process or is already available in the EU. However, it does not follow that a generic/biosimilar product will be available in the UK as patent issues differ between countries. Patent legislation is complex and the information below should be used as a guide only.

On 26 January 2007, regulation (EC) No. 1901/2006 came into force. This provides the legislative framework to promote development of medicines for use in children. An incentive is the possibility of an extension to the duration of a SPC covering a marketed product. Before this regulation came into force, the maximum duration of an SPC was five years. Now, an SPC covering a product may be extended by six months beyond the term that would otherwise apply. This extension of the term applies to all authorised indications for the product (including the non-paediatric indications). Drugs with a granted paediatric extension are indicated.

Note that patent expiries are subject to change when new extensions (SPC or paediatric) are granted or if court decisions alter the patent status of a drug. In addition, the patent expiries listed only cover the basic, manufacturing patent. Additional patents on formulations and uses can influence when a generic or biosimilar becomes available commercially.

Drug	BNF	Patent expiry date ** = UK patent only, no SPC*	Date includes paediatric extension	Generic or biosimilar available/ in development	Commissioning route
Infliximab	1.5.3/ 10.1.3	2015 Feb	Yes	Yes	Depends on indication
Sevelamer HCl	9.5.2.2	2015 Feb		Yes	NHS England
Darifenacin	7.4.2	2015 Mar			CCG
Paricalcitol	9.6.4	2015 Mar			NHS England
Clofarabine	8.1.3	2015 May			NHS England
Glatiramer acetate (copolymer)	8.2.4	2015 May*			NHS England
Insulin glargine	6.1.1.2	2015 May	Yes	Yes	CCG
Insulin aspart biphasic	6.1.1.2	2015 Jun			CCG
Sirolimus	8.2.2	2015 Jun			NHS England
Tenecteplase	2.10.2	2015 Jun			CCG
Etanercept	10.1.3	2015 Jul	Yes		Depends on indication
Rasburicase	10.1.4	2015 Jul			NHS England
Bivalirudin	2.8.1	2015 Aug			NHS England
Strontium ranelate	6.6.2	2015 Aug			Depends on indication
Nateglinide	6.1.2.3	2015 Sep			CCG
Alitretinoin	13.5.1	2015 Oct			CCG
Palonosetron	4.6	2015 Nov			NHS England
Pimecrolimus	13.5.3	2015 Nov			CCG
Eletriptan HCl	4.7.4	2015 Dec			CCG
Frovatriptan succinate	4.7.4	2015 Dec		Yes	CCG
Lopinavir/ritonavir	5.3.1	2015 Dec			NHS England
Pemetrexed disodium	8.1.3	2015 Dec		Yes	NHS England
Botulinum toxin Type B	4.9.3	2016 Jan			Depends on indication
Emtricitabine	5.3.1	2016 Jan			NHS England
Linezolid	5.1.7	2016 Jan		Yes	CCG
Agomelatine	4.3.4	2016 Feb			CCG

Drug	BNF	Patent expiry date ** = UK patent only, no SPC*	Date includes paediatric extension	Generic or biosimilar available/ in development	Commissioning route
Oseltamivir	5.3.4	2016 Feb*		Yes	CCG
Tiotropium	3.1.2	2016 Mar	Yes		CCG
Bexarotene	8.1.5	2016 Apr			NHS England
Tolvaptan	6.5.2	2016 Apr	Yes		Depends on indication
Darbepoetin alfa	9.1.3	2016 Jun			NHS England
Telithromycin	5.1.5	2016 Jul			CCG
Voriconazole	5.2.1	2016 Jul	Yes	Yes	NHS England
Agalsidase alfa	9.8.1	2016 Aug			NHS England
Agalsidase beta	9.8.1	2016 Aug			NHS England
Adefovir dipivoxil	5.3.3.1	2016 Sep			NHS England
Ciclesonide	3.2	2016 Sep			CCG
Imatinib mesylate	8.1.5	2016 Dec	Yes	Yes	NHS England
Rupatadine	3.4.1	2017 Jan	Yes		CCG
Telmisartan/hydrochlorothiazide	2.5.5.2	2017 Jan		Yes	CCG
Velaglucerase alfa	9.8.1	2017 Jan			NHS England
Olmesartan medoxomil	2.5.5.2	2017 Feb		Yes	CCG
Bimatoprost	11.6	2017 Mar		Yes	CCG
Valganciclovir	5.3.2.2	2017 Mar	Yes	Yes	NHS England
Caspofungin	5.2.4	2017 Apr	Yes		NHS England
Entecavir	5.3.3.1	2017 Apr	Yes		NHS England
Ertapenem	5.1.2.2	2017 Apr			CCG
Melatonin	4.1.1	2017 Apr			CCG
Parecoxib	15.1.4.2	2017 Apr*			CCG
Tramadol/paracetamol	4.7.2	2017 Apr			CCG
Olopatadine	11.4.2	2017 May			CCG
Peginterferon alfa	8.2.4	2017 May*			NHS England
Tegafur/gimeracil/oteracil	8.1.3	2017 May			NHS England
Travoprost	11.6	2017 May	Yes	Yes	CCG
Nitisinone	9.8.1	2017 Jun			NHS England
Dutasteride	6.4.2	2017 Jul		Yes	CCG
Etoricoxib	10.1.1	2017 Jul*		Yes	CCG
Pregabalin	4.8.1	2017 Jul*		Yes	CCG
Bosentan	2.5.1	2017 Aug	Yes	Yes	NHS England
Estradiol/drospirenone	6.4.1.1	2017 Aug*			CCG
Norelgestromin	7.3.1	2017 Aug			CCG
Omalizumab	3.4.2	2017 Aug			NHS England
Pegfilgrastim	9.1.6	2017 Aug		Yes	NHS England
Tigecycline	5.1.3	2017 Aug			CCG
Ivabradine	2.6.3	2017 Sep			CCG
Prasugrel	2.9	2017 Sep			CCG

Drug	BNF	Patent expiry date ** = UK patent only, no SPC*	Date includes paediatric extension	Generic or biosimilar available/ in development	Commissioning route
Ezetimibe	2.12	2017 Oct		Yes	CCG
Mycophenolate mofetil E/C	8.2.1	2017 Oct			Depends on indication
Pegvisomant	6.5.1	2017 Nov			NHS England
Tadalafil	2.5.1/7.4.5	2017 Nov		Yes	Depends on indication
Abatacept	10.1.3	2017 Dec	Yes		Depends on indication
Retigabine	4.8.1	2017 Dec			CCG
Rosuvastatin calcium	2.12	2017 Dec	Yes	Yes	CCG
Abiraterone	8.3.4.2	2018 Mar			NHS England
Anidulafungin	5.2.4	2018 Mar			NHS England
Adalimumab	1.5.3 / 10.1.3	2018 Apr		Yes	Depends on indication
Enfuvirtide	5.3.1	2018 Apr			NHS England
Everolimus	8.1.5	2018 Jul			NHS England
Varicella-zoster vaccine	14.4	2018 Jul			CCG
Human papilloma virus vaccine (*Cervarix)*	14.4	2018 Sep			CCG
Vardenafil HCl	7.4.5	2018 Oct*			CCG
Aprepitant	4.6	2018 Nov			NHS England
Insulin detemir	6.1.1.2	2018 Nov			CCG
Oxycodone/naloxone	4.7.2	2018 Dec*			CCG
Solifenacin succinate	7.4.2	2018 Dec		Yes	CCG

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Erratum:

Date	*Page*	*Original entry*	*Amendment*
24/09/15	37	Exenatide implant: Long-acting glucagon-like peptide 1 (GLP-1) agonist delivered over 3-12 months via the DUROS device, implanted subcutaneously in the upper arm.	Long-acting glucagon-like peptide 1 (GLP-1) agonist delivered over 3-12 months via the DUROS device, implanted subcutaneously into the **abdomen**.
01/11/15	70	Etanercept SB4 biosimilar. Company promoting listed as Merck Serono	Company promoting is Biogen
01/11/15	14	Alirocumab. Likely HRG included.	Likley specified high cost drug.