

Lincolnshire Prescribing and Clinical Effectiveness Bulletin

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What's new this month?

- For patients requiring treatment for perennial or seasonal allergic rhinitis always consider self-care as a first line option. Where prescribing is unavoidable, beclometasone 50 microgram nasal spray (generic/*Beconase*) should be prescribed first line. Fluticasone containing products should be restricted to a third line role. *Flixonase* nasal spray is prohibitively expensive and *Avamys* nasal spray should always be preferred (see page 4).
- Following a review of new calcium and vitamin D preparations, first line preferred products are confirmed as: *Accrete D3 tablets*, *Adcal D3 Chewable tablets*, *Adcal D3 Caplets*, *Calceos Chewable tablets*, *Evacal D3 chewable tablets*, *Natecal D3 chewable tablets* (all twice daily) and *Calci-D chewable tablets* and *theiCal-D3 chewable tablets* (once daily) (see page 6).
- Following the discontinuation of co-danthramer capsules (dantron/poloxamer), co-danthrusate 50mg/60mg (danthron/docusate) capsules are approved for use as a replacement product, solely for the treatment of constipation in terminally ill patients. Designation GREEN usually following a recommendation from a palliative care specialist (see page 8).
- NICE have now approved all three of the SGLT-2 inhibitors, canagliflozin, dapagliflozin and empagliflozin, for use as monotherapies in the treatment of type 2 diabetes (see page 10).

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SUMMARY OF PACEF DECISIONS: AUGUST 2016 UPDATE

Device, Dressing or Drug	Indication(s)	Traffic Light and <i>Joint Formulary</i> Status
Abiraterone 50mg tablets (<i>Zytiga</i>) (Janssen-Cilag Ltd)	For the treatment of metastatic castration resistant prostate cancer in adult men who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated.	RED Abiraterone (<i>Zytiga</i>) 250 mg tablets are already listed on the <i>Formulary</i> as RED for use in the treatment of castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen. The RED classification now extends to treating metastatic hormone-relapsed prostate cancer in people who have no symptoms or mild symptoms after androgen deprivation therapy has failed, and before chemotherapy is indicated.
Adalimumab injection (Humira) (AbbVie)	For the treatment of active moderate to severe hidradenitis suppurativa (acne inversa) in adult patients with an inadequate response to conventional systemic therapy.	RED Adalimumab injection (<i>Humira</i>) is already listed on the <i>Joint Formulary</i> as RED in line with licensed indications and NICE TAs. It is also licensed for the treatment of a number of conditions including: rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, Crohn's disease, paediatric Crohn's disease, ulcerative colitis and uveitis.
Beclometasone 50 microgram nasal spray (generic/ <i>Beconase</i>) (generic/GlaxoSmithKline)	For perennial and seasonal allergic rhinitis. Vasomotor rhinitis.	GREEN First line. Included in the <i>Lincolnshire Joint Formulary</i> . <i>Beconase Hayfever Relief for Adults</i> nasal spray 50mcg/dose is available to buy (GSL). <i>Beconase Hayfever</i> aqueous nasal spray 50mcg/dose is available over-the-counter from pharmacies (P).
Belimumab 120mg and 400mg solution for infusion (<i>Benlysta</i>) (GlaxoSmithKline)	For use as add-on therapy in adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity despite standard therapy	RED Approved for inclusion in the <i>Lincolnshire Joint Formulary</i> .
Budesonide 64 microgram nasal spray (generic/ <i>Rhinocort Aqua</i>) (generic/AstraZeneca)	For perennial and seasonal allergic rhinitis. Nasal polyps.	GREEN Second line. Included in the <i>Lincolnshire Joint Formulary</i> .
<i>Calci-D</i> chewable tablets (calcium carbonate 2.5g/vitamin D3 1000 i.u.) (Consilient Health)	For the prevention and treatment of calcium and vitamin D deficiency in the elderly. For use as an adjunct in osteoporosis.	GREEN Approved for inclusion in the <i>Lincolnshire Joint Formulary</i> .
Canagliflozin 100mg and 300mg tablets (<i>Invokana</i>) (Janssen Cilag)	In adults with type 2 diabetes mellitus to improve glycaemic control as monotherapy or in combination with other glucose-lowering medicinal products including insulin.	Recommended as a treatment option when an SGLT2 inhibitor is indicated in combination with metformin; designation GREEN. Also approved by NICE for triple therapy in combination with metformin and a sulfonylurea or metformin and pioglitazone; designation GREEN. Also approved by NICE for monotherapy; designation GREEN. Included in the <i>Lincolnshire Joint Formulary</i> for use within NICE criteria.

Ceritinib 150mg capsules (<i>Zykadia</i>) (Novartis Pharmaceuticals UK Ltd)	For the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously treated with crizotinib.	RED Approved for inclusion in the <i>Lincolnshire Joint Formulary</i> .
Co-danthrusate 50mg/60mg capsules (danthron/docusate)	For the treatment of constipation in the terminally ill.	GREEN usually following a recommendation from a palliative care specialist. Approved for inclusion in the <i>Lincolnshire Joint Formulary</i> .
Dapagliflozin (<i>Forxiga</i>) 5mg and 10mg tablets	In adults with type 2 diabetes mellitus to improve glycaemic control as monotherapy or in combination with other glucose-lowering medicinal products including insulin.	Recommended as a treatment option when an SGLT2 inhibitor is indicated in combination with metformin; designation GREEN. Also approved by NICE for monotherapy; designation GREEN for this indication. Included in the <i>Lincolnshire Joint Formulary</i> for use within NICE criteria.
Empagliflozin (<i>Jardiance</i>) 10mg and 20mg tablets	In adults with type 2 diabetes mellitus to improve glycaemic control as monotherapy or in combination with other glucose-lowering medicinal products including insulin.	Recommended as a treatment option when an SGLT2 inhibitor is indicated in combination with metformin; designation GREEN. Also approved by NICE for triple therapy in combination with metformin and a sulfonylurea or metformin and pioglitazone; designation GREEN. Also approved by NICE for monotherapy; designation GREEN for this indication. Included in the <i>Lincolnshire Joint Formulary</i> for use within NICE criteria.
<i>Evacal D3</i> chewable tablets (calcium carbonate 1.5g/vitamin D3 400i.u.) (Teva UK)	For the prevention and treatment of calcium and vitamin D deficiency in the elderly. For use as an adjunct in osteoporosis.	GREEN Approved for inclusion in the <i>Lincolnshire Joint Formulary</i> .
Fluticasone furoate 27.5 microgram nasal spray (<i>Avamys</i>) (GlaxoSmithKline)	Allergic rhinitis	GREEN Third line. Included in the <i>Lincolnshire Joint Formulary</i> .
Fluticasone propionate/azelastine hydrochloride 50 microgram/137 microgram nasal spray (<i>Dymista</i>) (Meda)	For perennial and seasonal allergic rhinitis.	RED-RED Not included in the <i>Lincolnshire Joint Formulary</i>
Fluticasone propionate 50 microgram nasal spray (<i>Flixonase</i>) (GlaxoSmithKline)	For perennial and seasonal allergic rhinitis.	RED-RED Not included in the <i>Lincolnshire Joint Formulary</i> .
Trametinib 0.5mg and 2mg tablets (<i>Mekinist</i>) (Novartis Pharmaceuticals UK Ltd)	For use as monotherapy and in combination with dabrafenib for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation.	RED Approved for inclusion in the <i>Lincolnshire Joint Formulary</i> . The NICE TA only covers use in combination with dabrafenib.
Voriconazole 1% eye drops (unlicensed special)	For corneal ulcers and fungal keratitis.	RED Approved for inclusion in the <i>Lincolnshire Joint Formulary</i> .

This *Bulletin* has been created specifically to convey details of decisions taken at the Prescribing and Clinical Effectiveness Forum (PACEF) to all stakeholders across the Lincolnshire Healthcare Community in both primary and secondary care. Back issues of the *PACE Bulletin* and other PACEF publications are available through the PACEF website (<http://lincolnshire-pacef.nhs.uk>). Electronic copies of the *PACE Bulletin* are circulated to a wide readership via email. If you are not currently on our distribution list and wish to receive regular copies of PACEF publications please contact Sandra France on sandra.france@ardengemcsu.nhs.uk.

Google searching can be a quick and effective way of finding back numbers of the *PACE Bulletin* relevant to a specific topic of interest. Searchers are advised to use the official version of the *Bulletin* available from the PACEF website rather than depend on a potentially unreliable draft or variant found through Google or an alternative search engine.

The *Lincolnshire Joint Formulary* is available on line and is fully searchable; it can be accessed at www.lincolnshirejointformulary.nhs.uk

RED-RED: This signifies that a product is **not recommended** for prescribing in **either** primary or secondary care. All new products are classified as RED-RED pending assessment by PACEF.
RED: This signifies that a product has been approved for use within secondary care, tertiary care or a primary care hosted specialist service only and **should not be routinely prescribed in primary care**. RED drugs may be used within ULHT or LPFT subject to approval for use within each Trust. ULHT and LPFT reserve the right to determine whether or not RED drugs will be used within their Trusts. RED classification does not automatically signify that a drug will be available within secondary/tertiary care.
AMBER: This signifies that a drug has been approved for use in primary care **subject to specialist initiation; a shared care guideline (SCG) may also be required**. The main purpose of the SCG will be to clearly define both specialist and GP responsibilities. Not all AMBER drugs that require SCGs are currently covered by formal documents; PACEF are working to rectify this.
GREEN: This signifies a product that is **approved for initiation in either primary or secondary care**.

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UPDATE: THE USE OF INTRANASAL CORTICOSTEROIDS IN PERENNIAL AND SEASONAL ALLERGIC RHINITIS

For patients requiring treatment for perennial or seasonal allergic rhinitis always consider self-care as a first line option. Where prescribing is unavoidable, beclometasone 50 microgram nasal spray (generic/*Beconase*) should be prescribed first line. Fluticasone containing products should be restricted to a third line role. *Flixonase* nasal spray is prohibitively expensive and *Avamys* nasal spray should always be preferred.

PACEF have reviewed existing guidance on the prescribing of intranasal corticosteroids. An updated cost comparison including a new section on availability over-the-counter appears below. Updated guidance is as follows:

Self-care

- Patients requiring either a systemic antihistamine or a nasal corticosteroid or both to control the symptoms of perennial or seasonal allergic rhinitis should be considered for self-care. Cetirizine 10mg and loratadine 10mg tablets are available to buy at low cost from supermarkets, other retailers and community pharmacies. *Beconase Hayfever Relief for Adults 0.05% nasal spray*, *Beconase Hayfever Aqueous Nasal Spray* (beclomethasone), *Boots Allergy Relief 50 microgram Nasal Spray*, *Pirinase Hayfever 0.05% nasal spray* (fluticasone) and *Nasacort Allergy Nasal Spray* (triamcinolone) are all available OTC from community pharmacies often for less than the prescription charge.

First Line

- Where prescribing is considered necessary, beclometasone 50 microgram nasal spray (generic/*Beconase*) is the lowest cost intranasal corticosteroid and remains the first line product of choice.

Second Line

- Budesonide 64 microgram nasal spray (generic or *Rhinocort Aqua*) is also comparatively low cost and represents an appropriate second line choice that would still be low cost in combination with an oral antihistamine. Alternatively, generic mometasone 50 microgram nasal spray could be considered. Neither of these products are available over-the-counter to buy.

Third Line

- Fluticasone containing nasal sprays are significantly more expensive than beclometasone or budesonide containing products and should only be considered for prescribing third line. Fluticasone furoate 27.5 microgram nasal spray (*Avamys*) is the fluticasone containing nasal spray of choice and is significantly lower in cost than more expensive products such as mometasone 50 microgram nasal spray (*Nasonex*), triamcinolone acetonide 55 microgram nasal spray (*Nasacort*) and fluticasone propionate 50 microgram nasal spray (*Flixonase*). Some fluticasone and triamcinolone containing products are available over-the-counter to buy (e.g. *Boots Pharmacy Hayfever and Allergy*, *Pirinase Hayfever* 0.05% nasal spray (fluticasone) and *Nasacort Allergy Nasal Spray* (triamcinolone)).
- Fluticasone propionate 50 microgram nasal spray (*Flixonase*) is prohibitively expensive in comparison to alternative intranasal corticosteroid preparations and should no longer be initiated in new patients. Despite PACEF advice *Flixonase* continues to be prescribed, in some CCGs more widely than *Avamys*. Prescribers are reminded that for new patients, fluticasone propionate 50 microgram nasal spray (*Flixonase*) should be considered to be RED-RED.
- Combination therapy of a low cost corticosteroid nasal spray with a low cost generic antihistamine, such as cetirizine 10mg or loratadine 10mg, is significantly lower in cost than fluticasone propionate/ azelastine hydrochloride 50 microgram/ 137 microgram nasal spray (*Dymista*) which remains RED-RED.

Drug	Daily dose	Cost (£) (doses)	Availability to buy
Beclometasone 50 microgram nasal spray (generic)	2 sprays into each nostril twice daily	£1.94 (200)	<i>Beconase Hayfever Relief for Adults</i> nasal spray 50mcg/dose is available to buy (GSL). <i>Beconase Hayfever aqueous nasal spray</i> 50mcg/dose is available over-the-counter from pharmacies (P).
Beclometasone 50 microgram nasal spray (<i>Beconase</i>) (GaxoSmithKline)	2 sprays into each nostril twice daily	£2.19 (200)	<i>Beconase Hayfever Relief for Adults</i> nasal spray 50mcg/dose is available to buy (GSL). <i>Beconase Hayfever aqueous nasal spray</i> 50mcg/dose is available over-the-counter from pharmacies (P).
Beclometasone 50 microgram nasal spray (<i>Nasobec</i>) (Teva UK)	2 sprays into each nostril twice daily	£3.06 (200)	<i>Beconase Hayfever Relief for Adults</i> nasal spray 50mcg/dose is available to buy (GSL). <i>Beconase Hayfever aqueous nasal spray</i> 50mcg/dose is available over-the-counter from pharmacies (P).
Budesonide 64 microgram nasal spray (generic)	1 spray into each nostril twice daily	£4.77 (120)	Not available.
Budesonide 64 microgram nasal spray (<i>Rhinocort Aqua</i>)	1 spray into each nostril twice daily	£3.49 (120)	Not available.

(AstraZeneca)			
Fluticasone furoate 27.5 microgram nasal spray (<i>Avamys</i>) (GlaxoSmithKline)	2 sprays into each nostril once daily reducing to 1 spray each nostril daily.	£6.44 (120)	Not available.
Fluticasone propionate 50 microgram nasal spray (<i>Flixonase</i>) (GlaxoSmithKline)	1 spray into each nostril twice daily	£11.01 (150)	Not available. Fluticasone propionate nasal spray 0.05% (50mcg per dose) (<i>Pirinase Hayfever 0.05% Nasal Spray</i>) is available over-the-counter from pharmacies (P). <i>Boots Allergy Relief 50 microgram Nasal Spray</i> is also available.
Azelastine hydrochloride 0.1% nasal spray (<i>Rhinolast</i>) (Meda)	1 spray into each nostril twice daily	£10.50 (150)	Not available.
Fluticasone propionate/azelastine hydrochloride 50 microgram/ 137 microgram nasal spray (<i>Dymista</i>) (Meda)	1 spray into each nostril twice daily	£ 14.80 (120)	Not available.
Mometasone 50 microgram nasal spray (generic)	2 sprays into each nostril once daily	£2.23 (140)	Not available.
Mometasone 50 microgram nasal spray (<i>Nasonex</i>) (MSD)	2 sprays into each nostril once daily	£7.68 (140)	Not available.
Triamcinolone acetonide 55 microgram nasal spray (<i>Nasacort</i>) (Sanofi)	2 sprays per nostril once daily	£7.39 (120)	Triamcinolone acetonide 55 microgram per dose (<i>Nasacort Allergy Nasal Spray</i>) is available over-the-counter from pharmacies (P).

Drug	Daily dose	Cost (30 days)	
Cetirizine 10mg tablets (generic)	One tablet daily	£0.86	Available from supermarkets for less than £1 for 30.
Loratadine 10mg tablets (generic)	One tablet daily	£0.86	Available from supermarkets for less than £1 for 30.

References:

Drug Tariff (September 2016)

MIMS (September 2016)

PACE Bulletin Volume 9 No 7 (May 2015)

UPDATED GUIDANCE ON CALCIUM AND VITAMIN D SUPPLEMENTATION

Following a review of new calcium and vitamin D preparations, first line preferred products are confirmed as: ***Accrete D3 tablets, Adcal D3 Chewable tablets, Adcal D3 Caplets, Calceos Chewable tablets, Evacal D3 chewable tablets, Natecal D3 chewable tablets (all twice daily products) and Calci-D chewable tablets and theiCal-D3 chewable tablets (both once daily products).***

- (1) There is strong evidence to suggest that elderly people living in institutionalised care are likely to benefit from calcium and vitamin D supplementation. The best evidence is around daily doses of 1200mg of calcium and 800iu of vitamin D. Evidence suggests that this can significantly reduce the risk of hip fracture, non-vertebral fracture and falls. It is strongly recommended that all ambulatory patients over the age of 65 currently resident in sheltered accommodation or care homes should be prescribed calcium and vitamin D. Prescribers are encouraged to review all patients in care homes and sheltered accommodation to ensure that calcium and vitamin D supplementation is prescribed for the ambulatory over 65s unless there are compelling reasons not to do so.
- (2) Calcium and vitamin D should be prescribed for people on or commencing systemic corticosteroid therapy at any dose for 3 months or longer.
- (3) All women on treatment for the primary or secondary prevention of osteoporotic fragility fractures should be prescribed calcium and vitamin D unless dietary intake is considered to be adequate.
- (4) Only calcium and vitamin D formulations containing an evidence based dose of each component should be prescribed (i.e. at least 1000mg of calcium and 800iu of vitamin D daily). **Following a review of new products and comparative prices, first line preferred products are confirmed as: Accrete D3 tablets, Adcal D3 Chewable tablets, Adcal D3 Caplets, Calceos Chewable tablets, Evacal D3 chewable tablets, Natecal D3 chewable tablets (all twice daily) and Calci-D chewable tablets and theiCal-D3 chewable tablets (once daily) (see cost comparison below).**

<u>Product</u>	<u>Dose</u>	<u>Price (28 days)</u>	<u>Flavour</u>
Accrete D3 tablets (calcium carbonate 1.5g(calcium 600mg)/vitamin D3 400i.u.) (Internis)	1 tablet twice daily	£2.76	
Adcal –D3 chewable tablets (calcium carbonate 1.5g (calcium 600mg)/ vitamin D3 400i.u.)(Kyowa Kirin)	1 tablet twice daily	£3.65	Lemon or Fruit
Adcal D3 Caplets (calcium carbonate 750mg (calcium 300mg)/vitamin D3 200i.u.) (Kyowa Kirin)	2 tablets twice daily	£2.95	
<i>Adcal-D3 Dissolve Effervescent tablets (calcium carbonate 1.5g (calcium 600mg)/ vitamin D3 400i.u.)(Kyowa Kirin)</i>	1 tablet twice daily	£5.99	Lemon
<i>Cacit D3 effervescent granules (calcium carbonate 1.25g (calcium 500mg)/ vitamin D3 440i.u.)(Actavis)</i>	2 sachets daily	£8.12	Lemon
Calceos chewable tabs (calcium carbonate 1.25g (calcium 500mg)/ vitamin D3 400i.u.) (Galen)	1 tablet twice daily	£3.34	Lemon
<i>Calcichew D3 Forte chewable tablets (calcium carbonate 1.25g (calcium 500mg)/ vitamin D3 400i.u.) (Takeda)</i>	1 tablet twice daily	£3.96	Lemon
<i>Calcichew D3 500mg/400iu Caplets (calcium carbonate 1.25g (calcium 500mg)/ vitamin D3 400i.u.) (Takeda)</i>	1 tablet twice daily	£4.16	
<i>Calcichew D3 1g/800iu Once Daily chewable tablets (calcium carbonate 2.5g (calcium 1g)/ Vitamin D3 800i.u.)(Takeda)</i>	1 tablet daily	£6.30	Lemon
Calci-D chewable tablets (calcium carbonate 2.5g/vitamin D3 1000 i.u.) (Consilient Health)	1 tablet daily	£2.25	
<i>Calfovit D3 sachets (calcium phosphate 3.1g (calcium 1200mg)/ vitamin D3 800i.u.) (Menarini)</i>	1 sachet daily	£4.04	Lemon
Evacal D3 chewable tablets (calcium carbonate 1.5g/vitamin D3 400i.u.) (Teva UK)	1 tablet twice daily	£2.75	
<i>Kalcipos-D chewable tablets (calcium carbonate 1.25g/vitamin D3 800 i.u.) (Meda)</i>	1 tablet daily	£3.93	
<i>Kalcipos-D Tablets (calcium carbonate 1.25g/vitamin D3 800 i.u.) (Meda)</i>	1 tablet daily	£3.93	

Natecal D3 chewable tablets (calcium carbonate 1.5g/vitamin D3 400i.u.)(Chiesi)	1 tablet twice daily	£3.39	Aniseed/peppermint
theiCal-D3 chewable tablets (calcium carbonate 2.5g/vitamin D3 880i.u.) (Stirling Anglian)	1 tablet daily	£2.76	Orange

Formulary approved products are in featured in **bold**.

Reference:

MIMS, September 2016.

RAPID DRUG ASSESSMENT: CO-DANTHRUSATE 50MG/60MG CAPSULES (DANTHRON/ DOCUSATE)

Following the discontinuation of co-danthramer capsules (dantron/poloxamer), co-danthrusate 50mg/60mg capsules as approved for use as a replacement product, solely for the treatment of constipation in terminally ill patients.

Co-danthrusate 50mg/ 60mg capsules (danthron/docusate) is a combination product containing the stimulant laxative danthron and the stool softener docusate.

In experimental animals, dantron has been associated with adenocarcinomas in the bowel and tumours in the liver. A theoretical risk of similar effects in humans cannot be excluded, which is why the product marketing authorisation is restricted solely to the treatment of constipation in terminally ill patients.

Following the discontinuation of co-danthramer capsules (dantron/poloxamer), PACEF were asked to consider the introduction of co-danthrusate 50mg/60mg capsules as a replacement product on the *Lincolnshire Joint Formulary*. A cost comparison reveals that co-danthrusate 50mg/60mg capsules are

Drug	Dose	Pack size	Cost	Cost per day
Co-danthrusate 50mg/60mg capsules	1-3 caps at night	63 capsules	£52.50	£0.83-£2.50
Co-danthrusate oral suspension 50mg/60mg per 5ml	5ml-15ml at night	200ml	£89.92	£2.25-£6.74
Co-danthramer oral suspension 25mg/200mg per 5ml	5ml-10ml at night	300ml	£146.39	£2.44-£4.88
Co-danthramer strong oral suspension 75mg/1000mg per 5ml	5ml at night	300ml	£293.62	£4.90

Reference:

Drug Tariff, October 2016

PACEF Recommendation:

Co-danthrusate 50mg/60mg capsules are lower in cost than co-danthrusate oral suspension and both strengths of co-danthramer and are approved for use through the *Lincolnshire Joint Formulary* solely for the treatment of constipation in the terminally ill. Designation GREEN usually following a recommendation from a palliative care specialist.

IN BRIEF: VORICONAZOLE 1% EYE DROPS FOR CORNEAL ULCERS AND FUNGAL KERATITIS (UNLICENSED)

Voriconazole 1% eye drops are an unlicensed antifungal eye preparation used for corneal ulcers and fungal keratitis. As this product is no longer manufactured by the ULH Aseptic Unit, it is now purchased by ULH from a specials manufacturing unit. Voriconazole 1% eye drops are approved for inclusion on the *Lincolnshire Joint Formulary*, designation RED. Any approaches to GPs to prescribe this product should be refused.

NICE UPDATE

NICE Technology Appraisal	Guidance	PACEF Recommendation
NICE Technology Appraisal 387: <i>Abiraterone for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated</i> (July 2016)	Abiraterone in combination with prednisone or prednisolone is recommended as an option for treating metastatic hormone-relapsed prostate cancer in people who have no or mild symptoms after androgen deprivation therapy has failed, and before chemotherapy is indicated.	Abiraterone (<i>Zytiga</i>) 250 mg tablets are already listed on the <i>Joint Formulary</i> as RED in line with the recommendations of NICE TA 259 for use in the treatment of castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen. The RED classification now extends to treating metastatic hormone-relapsed prostate cancer in people who have no or symptoms or mild symptoms after androgen deprivation therapy has failed, and before chemotherapy is indicated.
NICE Technology Appraisal 392: <i>Adalimumab for treating moderate to severe hidradenitis suppurativa</i> (June 2016)	Adalimumab is recommended as an option for treating active moderate to severe hidradenitis suppurativa in adults whose disease has not responded to conventional systemic therapy. Response to adalimumab should be assessed after 12 weeks of treatment, and only continue if there is clear evidence of response (defined as: a reduction of 25% or more in the total abscess and inflammatory nodule count and no increase in abscesses and draining fistulas).	Adalimumab injection (<i>Humira</i>) is already listed on the <i>Joint Formulary</i> as RED in line with licensed indications and NICE TAs. It is licensed for the treatment of a number of conditions including: rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, Crohn's disease, paediatric Crohn's disease, ulcerative colitis and uveitis. In terms of hidradenitis suppurativa, <i>Humira</i> is indicated for the treatment of active moderate to severe hidradenitis suppurativa (acne inversa) in adult patients with an inadequate response to conventional systemic HS therapy.
NICE Technology Appraisal 395: <i>Ceritinib for previously treated anaplastic lymphoma kinase positive non-small-cell lung cancer</i> (June 2016)	Ceritinib is recommended, as an option for treating advanced anaplastic lymphoma kinase positive (ALK +ve) non-small-cell lung cancer in adults who have previously had crizotinib.	RED and approved for inclusion in the <i>Lincolnshire Joint Formulary</i> . Ceritinib 150mg capsules (<i>Zykadia</i>) are licensed for the treatment of adult patients with

		anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously treated with crizotinib.
NICE Technology Appraisal 396: <i>Trametinib in combination with dabrafenib for treating unresectable or metastatic melanoma</i> (June 2016)	Trametinib in combination with dabrafenib is recommended as an option for treating unresectable or metastatic melanoma in adults with a BRAF V600 mutation.	RED and approved for inclusion in the <i>Lincolnshire Joint Formulary</i> . Trametinib 0.5mg and 2mg tablets (<i>Mekinist</i>) are licensed both as monotherapy and in combination with dabrafenib for the treatment of adult patients with un-resectable or metastatic melanoma with a BRAF V600 mutation. The NICE TA only covers use in combination with dabrafenib.
NICE Technology Appraisal 397: <i>Belimumab for treating active autoantibody-positive systemic lupus erythematosus</i> (June 2016)	Belimumab is recommended as an option as add-on treatment for active autoantibody-positive systemic lupus erythematosus.	RED and approved for inclusion in the <i>Lincolnshire Joint Formulary</i> . Belimumab solution for infusion (<i>Benlysta</i>) is licensed as add-on therapy in adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity (e.g. positive anti-dsDNA and low complement) despite standard therapy

NICE TECHNOLOGY APPRAISAL 390: CANAGLIFLOZIN, DAPAGLIFLOZIN AND EMPAGLIFLOZIN AS MONOTHERAPIES FOR TREATING TYPE 2 DIABETES (MAY 2016)

Canagliflozin, dapagliflozin and empagliflozin as monotherapies are recommended as options for treating type 2 diabetes in adults for whom metformin is contraindicated or not tolerated and when diet and exercise alone do not provide adequate glycaemic control, only if: a dipeptidyl peptidase-4 (DPP-4) inhibitor would otherwise be prescribed and a sulfonylurea or pioglitazone is not appropriate.

PACEF most recently published prescribing advice on selection of SGLT2 inhibitors in *PACE Bulletin* Vol 9 No 15 (September 2015). This guidance is now amended as follows:

PACEF Recommendation

Canagliflozin (*Invokana*) 100mg and 300mg tablets, dapagliflozin (*Forxiga*) 5mg and 10mg tablets and empagliflozin (*Jardiance*) 10mg and 20mg tablets are all recommended as treatment options when a SGLT2 inhibitor is indicated in combination with metformin and are designated as GREEN.

Canagliflozin and empagliflozin are also approved by NICE for triple therapy in combination with metformin and a sulfonylurea or metformin and pioglitazone and are designated GREEN for this indication.

In addition, canagliflozin, dapagliflozin and empagliflozin are now recommended by NICE for monotherapy and are designated GREEN for this indication.

Due to their mode of action, none of the SGLT2 inhibitors should be initiated in patients with renal impairment with an eGFR of <60 ml/min/1.73 m². However, those

patients who have previously shown they can tolerate and respond to canagliflozin or empagliflozin treatment can continue until eGFR is persistently below 45 mL/min/1.73 m².

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY: DRUG SAFETY UPDATE (JULY 2016)

Warfarin – reports of calciphylaxis

Calciphylaxis, also known as calcific uremic arteriolopathy, is a very rare but serious condition causing vascular calcification and skin necrosis. The mortality rate associated with this condition is high. It is most commonly observed in patients with end-stage renal disease on dialysis, or in those with known risk factors such as: protein C or S deficiency, hyperphosphataemia, hypercalcaemia or hypoalbuminaemia.

Cases of calciphylaxis have been reported in patients taking warfarin. Pre-existing renal disease was commonly reported in these cases, but some reports noted normal renal function. An EU-wide review of relevant evidence recently concluded that there is a reasonable possibility that on rare occasions warfarin use might lead to calciphylaxis.

Advice for healthcare professionals:

- Calciphylaxis is a very rare but serious condition that is most commonly observed in patients with known risk factors such as end-stage renal disease
- Cases have been reported in patients taking warfarin, including those with normal renal function, and evidence suggests that on rare occasions warfarin use might lead to calciphylaxis
- If calciphylaxis is diagnosed, appropriate treatment should be started and consideration should be given to stopping treatment with warfarin

Citalopram – suspected drug interaction with cocaine

The MHRA have received a Coroner's report that raised concerns about a suspected drug interaction between citalopram and cocaine after the death of a man due to subarachnoid haemorrhage. There are plausible mechanisms for an interaction between cocaine and citalopram that could lead to subarachnoid haemorrhage, including hypertension related to cocaine and an additive increased bleeding risk in combination with citalopram.

Prescribers are advised to consider the possibility of illicit drug use when prescribing drugs that have the potential to interact adversely with the drug of abuse.

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