Arden and Greater East Midlands Commissioning Support Unit in association with
Lincolnshire Clinical Commissioning Groups, Lincolnshire Community Health Services,
United Lincolnshire Hospitals Trust and Lincolnshire Partnership Foundation Trust

Lincolnshire Prescribing and Clinical Effectiveness Bulletin

Volume 9; Number 20 **November 2015**

What's new this month?

- **The PACEF website is now easier to use following a recent update and review. The web address continues to be http://lincolnshire-pacef.nhs.uk (see page 4).**
- **Lincolnshire Community Health Services have recently published an update of their clinical guideline on the diagnosis and management of heart failure. The updated version can be accessed through the PACEF website (see page 4).**
- **A Home Office Circular (127/2015) has been published introducing the new mandatory requisition form for Schedule 2 and 3 controlled drugs and new approved wording for instalment prescribing. Ketamine is also to be rescheduled from a Schedule 4 to a Schedule 2 CD. These changes come into force from November 30th 2015 (see page 4).**
- **A range of new lower cost oral contraceptive agents are reviewed (see page 5).**
- **Levonorgestrel 1.5mg tablets (*Emerres*) are approved for use as the preferred levonorgestrel product for emergency contraception within 72 hours of unprotected intercourse (UPI) or contraceptive failure. The product should be prescribed by brand (see page 6).**
- **The MHRA have highlighted the risk of severe hypertension and associated cerebrovascular and cardiovascular events associated with mirabegron (*Betmiga*) (see page 6).**
- **Following reports of diabetic ketoacidosis in patients treated with SGLT2 inhibitors for type 2 diabetes, the European Medicines Agency has started a review of canagliflozin, dapagliflozin and empagliflozin. The aim of the review is to evaluate the risk of diabetic ketoacidosis in these patients (see page 8).**
- **Public Health England have published updated guidelines for malaria prevention in travellers from the UK (see page 8).**
- **A range of shared care guidelines have been updated and reviewed (see page 9).**

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SUMMARY OF PACEF DECISIONS: *OCTOBER 2015 UPDATE*

Drug	Indication(s)	Traffic Light and *Joint Formulary* Status
Bevacizumab infusion (*Avastin*) (Roche)	For the treatment of relapsed, platinum-resistant epithelial ovarian, fallopian tube or primary peritoneal cancer	RED Included in the *Lincolnshire Joint Formulary* for this indication subject to New Cancer Drugs Fund List criteria.
Desogestrel 75 microgram tablets (generic/ *Cerelle* (Consilient)/ *Nacrez* (Teva)/ *Zelleta* (Morningside))	Oral contraception	GREEN lower cost. Approved for inclusion in the *Lincolnshire Joint Formulary.*
Desogestrel 75 microgram tablets (*Aizea* (Besins)/ *Cerazette* (MSD)/ *Desomono* (MedRx)/ *Desorex* (Somnex)/ *Feanolla* (Lupin))	Oral contraception	RED-RED higher cost. Not included in the *Lincolnshire Joint Formulary.*
Ethinylestradiol 20 microgram/desogestrel 150 microgram tablets (*Bimizza* (Morningside)/ *Gedarel 20/150* (Consilient)/ *Lestramyl 20/150* (Mylan))	Oral contraception	GREEN lower cost. Approved for inclusion in the *Lincolnshire Joint Formulary.*
Ethinylestradiol 20 microgram/desogestrel 150 microgram tablets (Munalea 20/150 (Lupin)/ Mercilon (MSD))	Oral contraception	RED-RED higher cost. Not included in the *Lincolnshire Joint Formulary.*
Ethinylestradiol 30 microgram/desogestrel 150 microgram tablets (*Cimizt* (Morningside)/*Gedarel 30/15* (Consilient)/ *Lestramyl* (Mylan))	Oral contraception	GREEN lower cost. Approved for inclusion in the *Lincolnshire Joint Formulary.*
Ethinylestradiol 30 microgram/desogestrel 150 microgram tablets (*Alenvona* (Actavis)/ *Munalea 30/150* (Lupin)/ *Marvelon* (MSD))	Oral contraception	RED-RED higher cost. Not included in the *Lincolnshire Joint Formulary.*
Ethinylestradiol 30 microgram/drosperidone 3mg tablets *Acondro* (Mylan)/ *Dretine* (Teva)/ *Lucette* (Consilient)/ *Yacella* (Morningside))	Oral contraception	GREEN lower cost. Approved for inclusion in the *Lincolnshire Joint Formulary.*
Ethinylestradiol 30 microgram/drosperidone 3mg tablets (*Cleosensa* (Actavis)/ *Yasmin* (Bayer))	Oral contraception	RED-RED higher cost. Not included in the *Lincolnshire Joint Formulary.*
Ethinylestradiol 20 microgram/ gestodene 75 microgram tablets (*Aidulan 20/75* (Lupin)/ *Millinette 20/75* (Consilient)/ *Sunya 20/75* (Stragen))	Oral contraception	GREEN lower cost. Approved for inclusion in the *Lincolnshire Joint Formulary.*
Ethinylestradiol 20 microgram/ gestodene 75 microgram tablets (*Femodette* (Bayer))	Oral contraception	RED-RED higher cost. Not included in the *Lincolnshire Joint Formulary.*
Ethinylestradiol 30 microgram/gestodene 75 microgram tablets (*Aidulan 30/75* (Lupin)/ Millinette 30/75 (Consilient)/ *Katya 30/75* (Stragen))	Oral contraception	GREEN lower cost. Approved for inclusion in the *Lincolnshire Joint Formulary.*
Ethinylestradiol 30 microgram/gestodene 75 microgram tablets (*Femodene* (Bayer))	Oral contraception	RED-RED higher cost. Not included in the *Lincolnshire Joint Formulary.*
Ethinylestradiol 30 microgram/	Oral contraception	GREEN lower cost.

levonorgestrel 150 microgram tablets (*Levest* (Morningside)/ *Rigevidon* (Consilient))		Approved for inclusion in the *Lincolnshire Joint Formulary.*
Ethinylestradiol 30 microgram/ levonorgestrel 150 microgram tablets (*Elevin* (MedRx)/ *Erlibelle* (Actavis)/ *Maexeni* (Lupin)/ *Microgynon 30* and *Microgynon 30 ED* (Bayer)/ *Ovranette* (Pfizer))	Oral contraception	RED-RED higher cost. Not included in the *Lincolnshire Joint Formulary.*
Ethinylestradiol 35 microgram/ norgestimate 250 microgram tablets (*Lizinna* (Morningside)	Oral contraception	GREEN lower cost. Approved for inclusion in the *Lincolnshire Joint Formulary.*
Ethinylestradiol 35 microgram/ norgestimate 250 microgram tablets (*Cilest 35/250* (Jannsen-Cilag))	Oral contraception	RED-RED higher cost. Not included in the *Lincolnshire Joint Formulary.*
Levonorgestrel 1.5mg tablet (*Emerres)* (Morningside)	For emergency contraception within 72 hours of unprotected intercourse (UPI) or contraceptive failure	GREEN Preferred first line. Approved for inclusion in the *Lincolnshire Joint Formulary.*
Mirabegron 25mg and 50mg tablets (*Betmiga*) (Astellas)	For urinary frequency, urgency and urge incontinence.	GREEN Included in the *Lincolnshire Joint Formulary.* Reserved for treatment of the symptoms of overactive bladder in those for whom antimuscarinics are contraindicated or clinically ineffective or have unacceptable side effects.
Pembrolizumab infusion (*Keytruda*)	For the treatment of advanced (unresectable or metastatic) melanoma in adults.	RED Included in the *Lincolnshire Joint Formulary* for this indication.
Ruxolitinib 5mg and 15mg tablets (*Jakavi*) (Novartis)	For the treatment of polycythaemia vera that is resistant to hydroxycarbamide or for people who cannot tolerate hydroxycarbamide	RED-RED. Not included in the *Lincolnshire Joint Formulary* for this indication.
Ulipristal 30mg tablets (*EllaOne*) (HRA Pharma)	For emergency contraception within 120 hours (5 days) of unprotected intercourse (UPI) or contraceptive failure	GREEN Included in the *Lincolnshire Joint Formulary.* Should only be used when patients present between 72 and 120 hours after UPI or contraceptive failure.
Vedolizumab 300mg injection (*Entyvio*) (Takeda)	For the treatment of adult patients with moderate to severe active Crohn's disease in those inadequately responsive or intolerant of conventional therapy or a tumour necrosis factor-alpha (TNFα) antagonist. For the treatment of adult patients with moderate to severe active ulcerative colitis in those inadequately responsive or intolerant of conventional therapy or a tumour necrosis factor-alpha (TNFα) antagonist.	RED Included in the *Lincolnshire Joint Formulary* for both indications subject to NICE criteria for initiation, review and discontinuation.

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@gemcsu.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.**

PACEF WEBSITE NEWS

The PACEF website is now easier to use following a recent update and review. The web address continues to be http://lincolnshire-pacef.nhs.uk

UPDATED CLINICAL GUIDANCE FOR THE DIAGNOSIS AND MANAGEMENT OF HEART FAILURE (SEPTEMBER 2015)

Lincolnshire Community Health Services have recently published an update of their clinical guideline on the diagnosis and management of heart failure. All recommendations have been approved by PACEF and all key products are available through the *Lincolnshire Joint Formulary.* The updated text can be accessed through the PACEF website. Any specific queries should be addressed to Jane Scrafton, Heart Failure Professional Lead and Complex Case Manager at LCHS (email: jane.scrafton@lincs-chs.nhs.uk)

CHANGES TO CONTROLLED DRUG LEGISLATION: *NEW MANDATORY REQUISITION FORM FOR SCHEDULE 2 AND 3 CONTROLLED DRUGS, APPROVED WORDING FOR INSTALMENT PRESCRIBING AND RECLASSIFICATION OF KETAMINE FROM SCHEDULE 4 TO SCHEDULE 2*

A Home Office Circular (127/2015) has been published introducing the new mandatory requisition form for Schedule 2 and 3 controlled drugs and new approved wording for instalment prescribing. Ketamine is also to be rescheduled from a Schedule 4 to a Schedule 2 CD. These changes come into force from November 30th 2015.

Mandatory Use of Requisition Forms

Use of the standardised FP10CDF requisition form becomes a legal requirement from 30th November 2015. This requisition form is available from the NHSBSA website (http://www.nhsbsa.nhs.uk/PrescriptionServices/1120.aspx) and can be completed electronically before printing or a blank form can be printed and completed manually. Either way, a paper copy must be signed manually by the authorising prescriber. The forms can be downloaded from the website and saved locally, but electronically completed forms cannot be saved as all details will be reset to prevent saving of confidential prescriber details. Requisitions that do not use this form after November 30th 2015 will not be accepted.

Sections B and C of the requisition form must be completed including the following:

- name, address and profession/occupation of the authorising prescriber within the practice.
- the purpose for which the drug is required.
- total quantity of drug to be supplied.
- signature of the prescriber.
- the practitioner's prescriber code and the practice code.

The prescriber signing the form must be the same practitioner who has provided their name and prescriber code. Section A is for the wholesaler to complete. The regulations allow requisitions for Schedule 2 and 3 CDs to be handwritten or computer generated.

Obtaining Controlled Drug stock from a wholesaler

CDs can be ordered electronically from a wholesaler but the practice still has to provide the wholesaler with a signed requisition form FP10CDF on delivery of the CDs; the mandatory requisition form must be used from 30th November 2015. Requisitions cannot be faxed because a fax has not been signed by the prescriber and therefore does not meet the legal requirements.

Rescheduling of ketamine

Ketamine is to be rescheduled from Part I of Schedule 4 to Schedule 2 to the 2001 Regulations from 30th November 2015 with the effect that all the requirements applicable to Schedule 2 drugs, including record keeping, witnessing of destruction and prescribing will apply to the use of ketamine from this date.

Approved wording for instalment prescribing

The new Home Office approved wording for instalment prescribing is as follows:

1. Please dispense instalments due on pharmacy closed days on a prior suitable day.
2. If an instalment's collection day has been missed, please still dispense the amount due for any remaining day(s) of that instalment.
3. Consult the prescriber if 3 or more consecutive days of a prescription have been missed.
4. Supervise consumption on collection days.
5. Dispense daily doses in separate containers.

RAPID COST COMPARISON: *NEW LOWER COST ORAL CONTRACEPTIVES*

Local guidance on preferred lower cost oral contraceptives has been updated to include all new products.

Following review of a wide range of recently launched lower cost oral contraceptive preparations, PACEF have updated the list of preferred products as follows:

	Available products	**Preferred Lower Cost Product(s)**
Desogestrel 75 microgram tablets	Desogestrel 75 microgram tablets (generic) *Aizea* *Cerazette* *Cerelle* *Desomono* *Desorex* *Feanolla* *Nacrez* *Zelleta*	Desogestrel 75 microgram tablets (generic) – first choice *Cerelle* *Nacrez* *Zelleta*
Ethinylestradiol 20 microgram/desogestrel 150 microgram tablets	*Bimizza,* *Gedarel 20/150* *Lestramyl 20/150,* *Mercilon* *Munalea 20/150*	*Bimizza* *Gedarel 20/150* *Lestramyl 20/150*
Ethinylestradiol 30 microgram/desogestrel 150 microgram tablets	*Alenvona* *Cimizt* *Gedarel 30/150* *Lestramyl 30/150* *Marvelon*	*Cimizt* *Gedarel 30/150* *Lestramyl 30/150*

	Munalea 30/50	
Ethinylestradiol 30 microgram/drosperidone 3mg tablets	*Acondro* *Cleosensa* *Dretine* *Lucette* *Yacella* *Yasmin*	*Acondro* *Dretine* *Lucette* *Yacella*
Ethinylestradiol 20 microgram/gestodene 75 microgram tablets	*Aidulan 20/75* *Femodette* *Millinette 20/75* *Sunya 20/75*	*Aidulan 20/75* *Millinette 20/75* *Sunya 20/75*
Ethinylestradiol 30 microgram/gestodene 75 microgram tablets	*Aidulan 30/75* *Femodene* *Katya 30/75* *Millinette 30/75*	*Aidulan 30/75* *Katya 30/75* *Millinette 30/75*
Ethinylestradiol 30 microgram/ levonorgestrel 150 microgram tablets	*Elevin* *Erlibelle* *Levest* *Maexeni* *Microgynon 30 and Microgynon 30 ED* *Ovranette* *Rigevidon*	*Levest* (specify 'Morningside') *Rigevidon*
Ethinylestradiol 35 microgram/ norgestimate 250 microgram tablets	*Lizinna* *Cilest*	*Lizinna*

RAPID COST COMPARISON: *LEVONORGESTREL 1.5MG TABLETS (EMERRES)*

Levonorgestrel 1.5mg tablets (Emerres) are approved for use as the preferred levonorgestrel product for emergency contraception within 72 hours of unprotected intercourse (UPI) or contraceptive failure. The product should be prescribed by brand.

Another lower cost brand of levonorgestrel 1.5mg tablets (*Emerres*) has just been launched by Morningside. In common with the *Upostelle* and *Levonelle 1500* brands, *Emerres* holds a marketing authorisation for emergency contraception within 72 hours of unprotected intercourse (UPI) or contraceptive failure. A cost comparison of the three levonorgestrel 1.5mg products reveals the following:

	Dose	**Pack Size**	**Cost**
Levonorgestrel 1.5mg tablet (*Emerres)* (Morningside)	**One tablet as soon as possible after intercourse (preferably within 12 hours and no later than 72 hours).**	**1**	**£3.65**
Levonorgestrel 1.5mg tablet (*Levonelle 1500*) (Bayer)	One tablet as soon as possible after intercourse (preferably within 12 hours and no later than 72 hours).	1	£5.20
Levonorgestrel 1.5mg tablet (*Upostelle*) (Consilient Health)	One tablet as soon as possible after intercourse (preferably within 12 hours and no later than 72 hours).	1	£4.42
Ulipristal 30mg tablet (*EllaOne*) (HRA Pharma)	One tablet as soon as possible after intercourse (no later than 120 hours or 5 days).	1	£14.05

PACEF Recommendation

The *Emerres* brand of levonorgestrel 1.5mg tablets is significantly lower in price than *Upostelle* and *Levonelle 1500* and should be preferred first line. As the *Drug Tariff* reimbursement price is based around the originator brand, *Levonelle 1500*, savings will only be achieved if *Emerres* is prescribed by brand. Levonorgestrel 1.5mg tablets (*Emerres*) are approved for use through the *Lincolnshire Joint Formulary* and designated GREEN. Ulipristal 30mg tablets (*EllaOne*) are also on *Formulary* as an alternative to levonorgestrel with the advantage that they can be used up to 120 hours (5 days) after unprotected sex or contraceptive failure. Due to the higher cost of ulipristal 30mg tablets (*EllaOne*), they should only be used when patients present between 72 and 120 hours after UPI or contraceptive failure.

MHRA, *DRUG SAFETY UPDATE* (OCTOBER 2015)

MIRABEGRON (*BETMIGA*): RISK OF SEVERE HYPERTENSION AND ASSOCIATED CEREBROVASCULAR AND CARDIAC EVENTS

Mirabegron (*Betmiga*) is a beta 3-adrenoceptor agonist used in the management of urinary frequency, urgency, and incontinence in overactive bladder syndrome. An EU-wide review of the latest safety data for mirabegron has led to new measures to help reduce the risks of severe hypertension. It was already known that mirabegron could increase blood pressure. However, cases of severe hypertension have been reported since launch, which include hypertensive crisis associated with reports of cerebrovascular and cardiac events (mainly transient ischaemia attack or stroke), some with a clear temporal relation to mirabegron use.

As a result of this mirabegron is now contraindicated in patients with severe uncontrolled hypertension (systolic blood pressure ≥180 mm Hg or diastolic blood pressure ≥110 mm Hg, or both). Regular monitoring of blood pressure in patients on mirabegron is important, especially in patients with pre-existing hypertension.

Data are limited regarding the use of mirabegron in patients with stage 2 hypertension (i.e., systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥100 mm Hg) and it should be used with caution in this group.

Mirabegron is not recommended in patients with severe renal impairment (i.e., GFR 15–29 mL/min/1.73 m2) or in those with moderate hepatic impairment (i.e. Child-Pugh Class B) who are also taking strong inhibitors of cytochrome P450 3A such as itraconazole, ketoconazole, ritonavir, or clarithromycin. The dose of mirabegron in patients with mild to moderate renal impairment (i.e., GFR 30–89 mL/min/1.73 m2) or those with mild hepatic impairment (i.e., Child-Pugh Class A) who are also taking strong inhibitors of cytochrome P450 3A should be reduced to 25 mg once daily.

Key updated safety advice for healthcare professionals:

- Mirabegron is contraindicated in patients with severe uncontrolled hypertension (systolic blood pressure ≥180 mm Hg or diastolic blood pressure ≥110 mm Hg, or both)
- Blood pressure should be measured before starting treatment and monitored regularly during treatment, especially in patients with hypertension
- Please report suspected side effects to mirabegron on a Yellow Card.

PACEF Comment

Mirabegron 25mg and 50mg tablets (*Betmiga*) are designated GREEN and available through the *Lincolnshire Joint Formulary*; the product should be reserved for

treatment of the symptoms of overactive bladder in those for whom antimuscarinics are contraindicated or clinically ineffective or have unacceptable side effects.

EUROPEAN MEDICINES AGENCY: *REVIEW OF SGLT2 INHIBITORS FOR DIABETES BEGINS*

Following reports of diabetic ketoacidosis in patients treated with SGLT2 inhibitors for type 2 diabetes, the European Medicines Agency has started a review of canagliflozin, dapagliflozin and empagliflozin. The aim of the review is to evaluate the risk of diabetic ketoacidosis in these patients.

Diabetic ketoacidosis occurs when the body is unable to use blood glucose because insulin levels are too low. Instead it breaks down fat as an alternative source of energy, causing a build-up of ketones as a by-product. Diabetic ketoacidosis most commonly occurs in type 1 diabetics, but can be a complication in type 2 diabetes. The symptoms of diabetic ketoacidosis include difficulty breathing, confusion, feeling very thirsty, vomiting, abdominal pain, nausea, loss of appetite and unusual tiredness. Patients experiencing such symptoms should seek urgent medical attention.

PUBLIC HEALTH ENGLAND, *UPDATED ADVISORY COMMITTEE ON MALARIA PREVENTION GUIDELINES ON MALARIA PREVENTION IN UK TRAVELLERS* (SEPTEMBER 2015)

The Advisory Committee on Malaria Prevention have produced an updated version of their malaria prevention guidelines for UK travellers. Key changes for 2015 are as follows:

- Guidance on the use of insect repellent and sun protection.
- Clarification on the use of hydroxychloroquine.
- Updated guidance on the use of anticoagulants with antimalarials.
- Updated guidance on the use of doxycycline in epilepsy.
- Changes to recommendations for Vietnam and Malaysian Borneo and clarification on the recommendations for India.
- New malaria maps for India and South Africa.
- Clarification of advice for travelloers moving through areas where different antimalarials are recommended.

Despite safety concerns, mefloquine is still considered to be an extremely effective antimalarial and continues to be recommended for travellers to high risk areas.

The full text guideline is available from the PHE website at https://www.gov.uk/government/publications/malaria-prevention-guidelines-for-travellers-from-the-uk

SHARED CARE GUIDELINES

PACEF have recently approved updated and revised versions of the following shared care guidelines:

- *Cinacalcet in the management of secondary hyperparathyroidism in adult patients with end-stage renal disease on dialysis and hypercalcaemia of primary hyperparathyroidism or parathyroid carcinoma*
- *Lanthanum in the management of hyperphosphataemia in adult patients receiving haemodialysis or peritoneal dialysis who did not respond to or were unable to tolerate treatment with sevelamer and for controlling hyperphosphataemia associated with chronic kidney disease* (CKD)

All shared care guidelines can be accessed through the PACEF website (see above). Any queries or problems arising with shared care should be reported to Cathy Johnson, Interface Lead Pharmacist **(cathy.johnson@ardengemcsu.nhs.uk)**

NICE TECHNOLOGY APPRAISAL 352: *VEDOLIZUMAB FOR TREATING MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE AFTER PRIOR THERAPY* (AUGUST 2015)

Key recommendations are as follows:

Vedolizumab is recommended as an option for treating moderately to severely active Crohn's disease only if:

- a tumour necrosis factor-alpha inhibitor has failed (that is, the disease has responded inadequately or has lost response to treatment) or
- a tumour necrosis factor-alpha inhibitor cannot be tolerated or is contraindicated.
- Vedolizumab is recommended only if the company provides it with the discount agreed in the patient access scheme.

Vedolizumab should be given as a planned course of treatment until it stops working or surgery is needed, or until 12 months after the start of treatment, whichever is shorter. At 12 months, people should be reassessed to determine whether treatment should continue. Treatment should only continue if there is clear evidence of ongoing clinical benefit. For people in complete remission at 12 months, consider stopping vedolizumab, resuming treatment if there is a relapse. People who continue vedolizumab should be reassessed at least every 12 months to decide whether continued treatment is justified.
People whose treatment with vedolizumab is not recommended in this NICE guidance, but was started within the NHS before this guidance was published, should be able to continue treatment until they and their NHS clinician consider it appropriate to stop.

Notes

Vedolizumab injection (*Entyvio*) holds UK marketing authorisations for the treatment of adult patients with moderate to severe active Crohn's disease and moderate to severe active ulcerative colitis in those inadequately responsive or intolerant of conventional therapy or a tumour necrosis factor-alpha (TNFα) antagonist. It has now been approved for use by NICE for both of these indications.

PACEF Recommendation:
Vedolizumab injection (*Entyvio*) is designated RED within NICE criteria for the treatment of adult patients with either moderate to severe active Crohn's disease or moderate to severe active ulcerative colitis. It should be reserved for those inadequately responsive or intolerant of conventional therapy or a tumour necrosis factor-alpha (TNFα) antagonist. It is approved for inclusion in the *Lincolnshire Joint Formulary* for these indications.

NICE TECHNOLOGY APPRAISAL 353: *BEVACIZUMAB FOR TREATING RELAPSED, PLATINUM- RESISTANT EPITHELIAL OVARIAN, FALLOPIAN TUBE OR PRIMARY PERITONEAL CANCER* (AUGUST 2015)

Key recommendation is as follows:

NICE is unable to make a recommendation about the use in the NHS of bevacizumab for treating relapsed, platinum-resistant epithelial ovarian, fallopian tube or primary peritoneal cancer because no evidence submission was received from Roche Products for the

technology.

Notes

Bevacizumab (*Avastin*) is a recombinant monoclonal antibody licensed for use in conjunction with a range of chemotherapy agents to treat a number of malignant conditions most of which are not NICE approved, some of which are approved through the National Cancer Drug Fund List. It is included on the *Lincolnshire Joint Formulary* for the treatment of age related macular degeneration in line with local guidance (unlicensed indication).

PACEF Recommendation:
Bevacizumab infusion (*Avastin*) is designated RED for the treatment of relapsed, platinum-resistant epithelial ovarian, fallopian tube or primary peritoneal cancer as it is approved for use through the National Cancer Drug Fund List. It is currently included in the *Lincolnshire Joint Formulary* for this indication.

NICE TECHNOLOGY APPRAISAL 356: *RUXOLITINIB FOR TREATING POLYCYTHAEMIA VERA* (TERMINATED APPRAISAL)(SEPTEMBER 2015)

Key recommendation is as follows:

NICE is unable to make a recommendation about the use in the NHS of ruxolitinib for treating polycythaemia vera that is resistant to hydroxycarbamide or for people who cannot tolerate hydroxycarbamide because no evidence submission was received from Novartis Pharmaceuticals for the technology.

Notes

Ruxolitinib tablets (*Jakavi*) have a UK marking authorisation for the treatment of adult patients with polycythaemia vera who are resistant to or intolerant of hydroxyurea.
They are also licensed for the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis (also known as chronic idiopathic myelofibrosis), post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis.
Ruxolitinib is currently approved for use through the *Lincolnshire Joint Formulary* for the treatment of symptomatic splenomegaly in primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis, if the criteria specified by the National Cancer Drugs Fund List are met.

PACEF Recommendation:
Ruxolitinib 5mg and 15mg tablets (*Jakavi*) are designated RED-RED for the treatment of polycythaemia vera and are not included in the *Lincolnshire Joint Formulary* for this indication.

NICE TECHNOLOGY APPRAISAL 357: *PEMBROLIZUMAB FOR TREATING ADVANCED MELANOMA AFTER DISEASE PROGRESSION WITH IPILIMUMAB* (OCTOBER 2015)

Key recommendation is as follows:

Pembrolizumab is recommended as an option for treating advanced (unresectable or metastatic) melanoma in adults only after the disease has progressed with ipilimumab and, for BRAF V600 mutation-positive disease, a BRAF or MEK inhibitor.

Notes

Pembrolizumab infusion (*Keytruda*) has a UK marketing authorisation as monotherapy for the treatment of advanced (unresectable or metastatic) melanoma in adults.

PACEF Recommendation:
Pembrolizumab infusion (*Keytruda*) is designated RED for the treatment of advanced (unresectable or metastatic) melanoma in adults and is approved for inclusion in the *Lincolnshire Joint Formulary* for this indication.

Acknowledgements

Many thanks to: Cathy Johnson, Interface Lead Pharmacist and Sharon Hayler, Prescribing Adviser from Arden GEM Commissioning Support Unit for their help with the preparation of this *Bulletin.*

Stephen Gibson
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