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 10; Number 17 **December 2016**

Merry Christmas and Happy New Year to all our readers

What's new this month?

- **A range of new buprenorphine once-weekly transdermal patches have been launched as competitors to the originator brand, *BuTrans*. *Butec*, *Panitaz*, *Reletran*s and *Sevodyne* once weekly patches are all lower cost than *BuTran*s and should be considered preferentially; all of the products have been designated GREEN and approved for use through the *Lincolnshire Joint Formulary*. Patients currently prescribed *BuTrans* transdermal patch should be considered for therapeutic switch to a lower cost product. The potential saving across Lincolnshire is in excess of £0.7Mpa. In order to realise these savings, all prescribing of buprenorphine patches should be by preferred lower cost brand name (see page 5).**
- **Two new buprenorphine twice-weekly transdermal patches, *Bupeaze* and *Hapoctasin*, have also been launched as competitors to the originator brand, *Transtec*. Both products are lower cost that *Transtec* and should be considered preferentially; both products are designated AMBER without shared care and are approved for use through the *Lincolnshire Joint Formulary*. People currently prescribed *Transtec* transdermal patches for non-cancer related pain should be considered for therapeutic switch to one of the lower cost products. The potential saving across Lincolnshire is in excess of £85,000pa. In order to realise these savings, prescribing of buprenorphine patches should be by preferred lower cost brand name (see page 7).**
- **Pending advice from the Joint Committee on Vaccination and Immunisation (JCVI), human papillomavirus 9-valent vaccine (*Gardasil 9*) has not been approved for use through the *Lincolnshire Joint Formulary* and is designated RED-RED. In the unlikely event that a patient specifically requests *Gardasil 9* vaccine for their child, standard *Gardasil* should be offered in accordance with national guidance (see page 9).**
- **Guidance on preferred low paraffin emollients has been reviewed in response to another incident in which a patient was overcome by fire while smoking in bed. The investigating Fire Officer concluded that the *E45* cream being used by the patient for a dry skin condition helped to fuel the blaze. Low paraffin alternatives recommended include *Balneum* cream, *Balneum Plus* cream and *Dermol l*otion. (see page 10).**
- **Prescribers are reminded of the risk of confusion between 0.5mg and 5mg strengths of warfarin. Peterborough and Stamford Hospitals NHS Foundation Trust are in the process of reducing the use of both strengths with a view to possible future withdrawal in favour of 1mg and 3mg tablets only (see page 11).**

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SUMMARY OF PACEF DECISIONS: *OCTOBER 2016 UPDATE*

Device, Dressing or Drug	Indication(s)	Traffic Light and *Joint Formulary* Status
Abiraterone 250mg tablets (*Zytiga*) (Janssen-Cilag Ltd)	For castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen	RED Approved for inclusion in the Lincolnshire Joint Formulary.
Aflibercept 40mg per ml (*Eylea*) (Bayer plc)	For treating visual impairment caused by macular oedema after branch retinal vein occlusion	RED Approved for inclusion in the *Lincolnshire Joint Formulary* for this indication. The product is already approved for use in accordance with NICE guidance on wet age-related

		macular degeneration and visual impairment caused by macular oedema secondary to central retinal vein occlusion.
Azacitidine 25mg/ml powder for suspension for injection (*Vidaza*) (Celgene Ltd)	For the treatment of adult patients who are not eligible for haematopoietic stem cell transplantation with acute myeloid leukaemia with 20- 30% bone marrow blasts and multi-lineage dysplasia	RED-RED. Not approved for inclusion in the *Lincolnshire Joint Formulary* for this indication
Balneum Cream (liquid paraffin 5.35% plus urea 5%) (Almirall)	For pruritis, eczema, dermatitis, scaling skin conditions	GREEN Included in the *Lincolnshire Joint Formulary.* Preferred low paraffin content emollient in those at risk of immolation due to smoking or home oxygen therapy or both.
Balneum Plus Cream (liquid paraffin 1% plus urea 5% plus lauromacrogols 3%) (Almirall)	For pruritis, eczema, dermatitis, scaling skin conditions	GREEN Included in the *Lincolnshire Joint Formulary.* Preferred low paraffin content emollient in those at risk of immolation due to smoking or home oxygen therapy or both.
Bosutinib 100mg and 500mg tablets (*Bosulif*) (Pfizer Ltd)	For previously treated chronic myeloid leukaemia	RED. Approved for use through the *Lincolnshire Joint Formulary.*
Buprenorphine patches 5mcg/hour, 10mcg/hour and 20mcg/hour (*Butec*) (Qdem)	For non-malignant moderate chronic pain when an opioid is necessary. Once weekly patch.	GREEN Approved at Step 2 of the *Pain Ladder* for patients with non-malignant moderate chronic pain who are unable to tolerate or comply with large oral regular doses of opioids such as codeine or tramadol. Included in the *Lincolnshire Joint Formulary* for use subject to these criteria. **Should be prescribed by brand.**
Buprenorphine patches 5mcg/hour, 10mcg/hour, 15mcg/hour and 20mcg/hour (*BuTrans*) (Napp)	For non-malignant moderate chronic pain when an opioid is necessary. Once weekly patch.	RED-RED Re-designated from GREEN to RED-RED as a range of lower cost options are now available. To be removed from the *Lincolnshire Joint Formulary.* All existing patients on *BuTrans* patches should be reviewed and switched to an alternative lower cost product wherever possible.
Buprenorphine patches 5mcg/hour, 10mcg/hour, and 20mcg/hour (*Panitaz*) (Dr Reddy's)	For non-malignant moderate chronic pain when an opioid is necessary. Once weekly patch.	GREEN Approved at Step 2 of the *Pain Ladder* for patients with non-malignant moderate chronic pain who are unable to tolerate or comply with large oral regular doses of opioids such as codeine or tramadol. Included in the *Lincolnshire Joint Formulary* for use subject to these criteria. **Should be prescribed by brand.**
Buprenorphine patches 5mcg/hour, 10mcg/hour, 15mcg/hour and 20mcg/hour (*Reletrans*) (Sandoz)	For non-malignant moderate chronic pain when an opioid is necessary. Once weekly patch.	GREEN Approved at Step 2 of the *Pain Ladder* for patients with non-malignant moderate chronic pain who are unable to tolerate or comply with large oral regular doses of opioids such as codeine or tramadol. Included in the *Lincolnshire Joint Formulary* for use subject to these criteria. **Should be prescribed by brand.**

Buprenorphine patches 5mcg/hour, 10mcg/hour and 20mcg/hour (*Sevodyne*) (Aspire)	For non-malignant moderate chronic pain when an opioid is necessary. Once weekly patch.	GREEN Approved at Step 2 of the *Pain Ladder* for patients with non-malignant moderate chronic pain who are unable to tolerate or comply with large oral regular doses of opioids such as codeine or tramadol. Included in the *Lincolnshire Joint Formulary* for use subject to these criteria. **Should be prescribed by brand.**
Buprenorphine transdermal patches 35mcg/hour, 52.5mcg/hour and 70mcg/hour (*Bupeaze*) (Dr Reddy's)	For moderate to severe chronic cancer pain and severe pain unresponsive to non-opioid analgesics. Twice weekly patch	AMBER without shared care. Approved for inclusion in the *Lincolnshire Joint Formulary*. **Should be prescribed by brand.**
Buprenorphine transdermal patch 35mcg/hour, 52.5mcg/hour and 70mcg/hour (*Hapoctasin*) (Actavis)	For moderate to severe chronic cancer pain and severe pain unresponsive to non-opioid analgesics. Twice weekly patch	AMBER without shared care. Approved for inclusion in the *Lincolnshire Joint Formulary*. **Should be prescribed by brand.**
Buprenorphine transdermal patches 35mcg/hour, 52.5mcg/hour and 70mcg/hour (*Transtec*) (Napp)	For moderate to severe chronic cancer pain and severe pain unresponsive to non-opioid analgesics. Twice weekly patch	Re-designated from AMBER to RED-RED as two lower cost options are now available. To be removed from the *Lincolnshire Joint Formulary.* All existing patients on *BuTrans* patches should be reviewed and considered for an alternative lower cost product.
Cabazitaxel 40mg per ml concentrate and solvent for solution for infusion (*Jevtana*) (Sanofi)	For the treatment of hormone-refractory prostate cancer in patients who have previously been treated with a docetaxel-containing regimen (in combination with prednisone or prednisolone).	RED Already approved for use through the *Lincolnshire Joint Formulary* in accordance with the *National Cancer Drugs Fund List.*
Crizotinib 200mg and 400mg capsules (*Xalkori*) (Pfizer Ltd)	For untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer	RED. Approved for inclusion in the *Lincolnshire Joint Formulary*.
Dermol lotion (liquid paraffin 2.5%) (Dermal)	Dry or scaling skin conditions , eczema and dermatitis	GREEN Included in the *Lincolnshire Joint Formulary.* Preferred low paraffin content emollient in those at risk of immolation due to smoking or home oxygen therapy or both.
Human papillomavirus 9-valent vaccine (*Gardasil 9*) (Sanofi Pasteur MSD)	For active immunisation of individuals from the age of 9 against the following HPV diseases: • Premalignant lesions and cancers affecting the cervix, vulva, vagina and anus caused by vaccine HPV types. • Genital warts (*Condyloma acuminata*) caused by specific HPV types.	RED-RED Not approved for inclusion in the *Lincolnshire Joint Formulary*.
Lumacaftor-ivacaftor 125mg tablets (*Orkambi*)	For the treatment of cystic fibrosis in patients aged 12 years and older who are homozygous for the F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene	RED-RED. Not approved for inclusion in the *Lincolnshire Joint Formulary*.
Nivolumab 10mg/ml concentrate for solution for infusion (*Opdivo*) (Bristol Myers Squibb)	For use in combination with ipilimumab as an option for treating advanced (unresectable or metastatic) melanoma in adults	RED. Approved for inclusion in the *Lincolnshire Joint Formulary* for this indication. Nivolumab is already designated RED and available on the

		Lincolnshire Joint Formulary for the treatment of advanced (unresectable or metastatic) melanoma in adults.
Pegaspargase 750 units/ml solution for injection/infusion (*Oncaspar*)	For treating acute lymphoblastic leukaemia in children, young people and adults.	RED Approved for inclusion in the *Lincolnshire Joint Formulary* for this indication. Previously approved for use subject to National Cancer Drugs Fund criteria.
Pemetrexed 100mg and 500mg powder for solution for infusion (*Alimta*)(Eli Lilly and Company Ltd)	For maintenance treatment for non-squamous non-small-cell lung cancer after pemetrexed and cisplatin	RED. Approved for inclusion in the *Lincolnshire Joint Formulary* for this indication.
Ramucirumab 10mg/ml concentrate for solution for infusion (*Cyramza*) (Eli Lilly and Company Ltd)	For use in combination with docetaxel in the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer with disease progression after platinum-based chemotherapy.	RED-RED. Not approved for inclusion in the *Lincolnshire Joint Formulary* for this indication.
Secukinumab 150mg solution for injection (*Cosentyx*) (Novartis Pharmaceuticals UK Ltd)	For active ankylosing spondylitis after treatment with non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors.	RED Approved for inclusion in the *Lincolnshire Joint Formulary* for this indication. Already approved for use designation RED for the treatment of moderate to severe plaque psoriasis.
Trifluridine/tipiracil tablets 15mg/6.14mg and 20mg/8.19mg (*Lonsurf*) (Servier Laboratories Ltd)	For the treatment of adult patients with metastatic colorectal cancer (CRC) who have been previously treated with, or are not considered candidates for, available therapies including fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, anti-VEGF agents, and anti-EGFR agents.	RED Approved for inclusion in the *Lincolnshire Joint Formulary* for this indication. Formerly approved for use through the *Lincolnshire Joint Formulary* in accordance with the *National Cancer Drugs Fund List.*

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.**

REVIEW: *BUPRENORPHINE ONCE WEEKLY TRANSDERMAL PATCHES (BUTEC/ BUTRANS/ PANITAZ/ RELETRANS/ SEVODYNE)*

A range of new buprenorphine once-weekly transdermal patches have been launched as competitors to the originator brand, *BuTrans*. *Butec*, *Panitaz*, *Reletrans* and *Sevodyne* once weekly patches are all lower cost than *BuTrans* and should be considered preferentially; all of the products have been designated GREEN and approved for use through the *Lincolnshire Joint Formulary*. Patients currently prescribed *BuTrans* transdermal patch should be considered for therapeutic switch to a lower cost product. The potential saving across Lincolnshire is in excess of £0.7Mpa. In order to realise these savings, all prescribing of buprenorphine patches should be by preferred lower cost brand name.

Buprenorphine transdermal patches 5mcg/hour, 10mcg/hour, 15mcg/hour and 20mcg/hour are applied to a different area of skin every 7 days for the treatment of non-malignant moderate chronic pain when an opioid is necessary. The use of buprenorphine transdermal patches is approved at Step 2 of the *Pain Ladder* for patients with non-malignant moderate chronic pain who are unable to tolerate or comply with large oral regular doses of weak opioids such as codeine, co-codamol or tramadol. A range of new lower cost once weekly buprenorphine patches are now available, all less costly than the originator brand, *BuTrans* (see cost comparison). In order to gain a marketing authorisation, all of these products have had to demonstrate bioequivalence to the originator brand.

	Strength	Cost (28 days – 4 patches)
Buprenorphine transdermal patch (*Butec*) (Qdem)	**5 microgram per hour**	**£7.92**
Buprenorphine transdermal patch (*Butec*) (Qdem)	**10 microgram per hour**	**£14.20**
Buprenorphine transdermal patch (*Butec*) (Qdem)	**20 microgram per hour**	**£25.86**
Buprenorphine transdermal patch (*BuTrans*) (Napp)	5 microgram per hour	£17.60
Buprenorphine transdermal patch (*BuTrans*) (Napp)	10 microgram per hour	£31.55
Buprenorphine transdermal patch (*BuTrans*) (Napp)	15 microgram per hour	£49.15
Buprenorphine transdermal patch (*BuTrans*) (Napp)	20 microgram per hour	£57.46
Buprenorphine transdermal patch (*Panitaz*) (Dr Reddy's)	**5 microgram per hour**	**£9.86**
Buprenorphine transdermal patch (*Panitaz*) (Dr Reddy's)	**10 microgram per hour**	**£17.67**
Buprenorphine transdermal patch (*Panitaz*) (Dr Reddy's)	**20 microgram per hour**	**£32.18**
Buprenorphine transdermal patch (*Reletrans*) (Sandoz)	**5 microgram per hour**	**£8.80**
Buprenorphine transdermal patch (*Reletrans*) (Sandoz)	**10 microgram per hour**	**£15.78**
Buprenorphine transdermal patch (*Reletrans) (Sandoz)*	**15 microgram per hour**	**£24.58**
Buprenorphine transdermal patch (*Reletrans*) (Sandoz)	**20 microgram per hour**	**£28.73**
Buprenorphine transdermal patch (*Sevodyne*) (Aspire)	**5 microgram per hour**	**£7.92**
Buprenorphine transdermal patch (*Sevodyne*) (Aspire)	**10 microgram per hour**	**£14.20**
Buprenorphine transdermal	**20 microgram per hour**	**£25.86**

patch (*Sevodyne) (Aspire)*		

Lower cost products are highlighted in **bold.**

Trent Medicines Information Centre reviewed both the *BuTrans* and *Transtec* formulations in September 2012. A review of trials involving lower dose buprenorphine patches (*BuTrans*) for chronic non-cancer pain found that efficacy was similar to tramadol or co-codamol and that the patches had a considerable placebo effect. As a result of this and the comparatively high cost of the patch formulations, oral weak opioid analgesics such as codeine phosphate, co-codamol 15/500, co-codamol 30/500 and tramadol capsules 50mg are preferred as first line and second line weak opioid therapy in chronic non-cancer pain with buprenorphine patches confined to patients unable to tolerate or comply with oral weak opioids or who experience swallowing difficulties necessitating non-oral administration.

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PACEF Recommendation:

Buprenorphine once weekly transdermal patches *Butec*, *Panitaz*, *Reletrans* and *Sevodyne* are all lower cost than *BuTrans* and should be considered preferentially; all of the products have been designated GREEN and approved for use through the *Lincolnshire Joint Formulary*. Patients currently prescribed *BuTrans* transdermal patch should be reviewed and considered for therapeutic switch to a lower cost product. Potential CCG savings are tabulated below. Buprenorphine patches 5mcg/hour, 10mcg/hour, 15mcg/hour and 20mcg/hour (*BuTrans*) have been re-designated from GREEN to RED-RED on the *Joint Formulary* and should no longer be initiated in new patients. The use of buprenorphine transdermal patches is approved at Step 2 of the *Pain Ladder* for patients with non-malignant moderate chronic pain who are unable to tolerate or comply with large oral regular doses of weak opioids such as codeine, co-codamol or tramadol.

Potential Annual Savings from 100% switch

	Potential Annual Saving from 100% switch from *BuTrans* transdermal patches to a lower cost equivalent product
Lincolnshire East CCG	£246,712
Lincolnshire West CCG	£167,564
South Lincolnshire CCG	£110,460
South West Lincolnshire CCG	£189,748

REVIEW: *BUPRENORPHINE TWICE WEEKLY TRANSDERMAL PATCHES (BUPEAZE/ HAPOCTASIN//TRANSTEC)*

Two new buprenorphine twice-weekly transdermal patches, *Bupeaze* and *Hapoctasin*, have been launched as competitors to the originator brand, *Transtec*. Both products are lower cost that *Transtec* and should be considered preferentially; both products are designated AMBER without shared care and are approved for use through the *Lincolnshire Joint Formulary*. People currently prescribed *Transtec* transdermal patches for non-cancer related pain should be considered for therapeutic switch to one of the lower cost products. The potential saving across Lincolnshire is in excess of £85,000pa. In order to realise these savings, prescribing of buprenorphine patches should be by preferred lower cost brand name.

Buprenorphine patches 35mcg/hour, 52.5mcg/hour and 70mcg/hour (*Bupeaze*/ *Hapoctasin*/*Transtec*) are applied twice weekly and are indicated for moderate to severe chronic cancer pain and severe pain unresponsive to non-opioid analgesics. A cost

comparison reveals that both *Bupeaze* and *Hapoctasin* patches are lower price than *Transtec*, the brand leader.

	Strength	Cost (28 days – 8 patches assuming one patch every 96 hours)
Buprenorphine transdermal patch (*Bupeaze*) (Dr Reddy's)	**35 microgram per hour**	**£23.70**
Buprenorphine transdermal patch (*Bupeaze*) (Dr Reddy's)	**52.5 microgram per hour**	**£35.56**
Buprenorphine transdermal patch (*Bupeaze*) (Dr Reddy's)	**70 microgram per hour**	**£47.42**
Buprenorphine transdermal patch (*Hapoctasin*) (Actavis)	**35 microgram per hour**	**£18.96**
Buprenorphine transdermal patch (*Hapoctasin*) (Actavis)	**52.5 microgram per hour**	**£28.46**
Buprenorphine transdermal patch (*Hapoctasin*) (Actavis)	**70 microgram per hour**	**£37.92**
Buprenorphine transdermal patch (*Transtec*) (Napp)	35 microgram per hour	£31.60
Buprenorphine transdermal patch (Transtec) (Napp)	52.5 microgram per hour	£47.42
Buprenorphine transdermal patch (*Transtec*) (Napp)	70 microgram per hour	£63.20

Lower cost products are highlighted in **bold.**

PACEF Recommendation:
Buprenorphine transdermal patches 35mcg/hour, 52.5mcg/hour and 70mcg/hour (*Bupeaze*/*Hapoctasin*) are designated AMBER without shared care and are approved for inclusion in the *Lincolnshire Joint Formulary*. In particular, the 70mcg/hour patches should only be prescribed on the advice of a specialist. Equivalent strength *Transtec* transdermal patches are now prohibitively expensive and are no longer recommended; designation RED-RED and removed from the *Lincolnshire Joint Formulary*. Existing patients receiving *Transtec* patches for moderate to severe chronic cancer pain should continue to be prescribed the *Transtec* product. Patients prescribed *Transtec* for non-cancer related pain should be reviewed and considered for switch to a lower cost alternative patch (*Bupeaze* or *Hapoctasin*). All patch formulations are premium price and should only be used in patients who are insufficiently responsive to or intolerant of oral opioids or who experience swallowing difficulties necessitating non-oral administration. Prescribers should ensure that patients have a realistic view of the goals of therapy and that there is no expectation that ever increasing doses will be prescribed beyond a pre-agreed maximum. In order to realise savings, prescribing of buprenorphine patches should be by preferred lower cost brand name.

Potential Annual Savings from 100% switch

	Potential Annual Saving from 100% switch from *Trantec* transdermal patches to a lower cost equivalent product (*Hapoctasin*)
Lincolnshire East CCG	£27,726
Lincolnshire West CCG	£31,739
South Lincolnshire CCG	£14,233
South West Lincolnshire CCG	£14,536

RAPID DRUG ASSESSMENT: *HUMAN PAPILLOMAVIRUS 9-VALENT VACCINE (GARDASIL 9)*

The newly launched human papillomavirus 9-valent vaccine (*Gardasil 9*) is indicated for active immunisation of individuals from the age of 9 against the following HPV diseases:

- Premalignant lesions and cancers affecting the cervix, vulva, vagina and anus caused by vaccine HPV types.
- Genital warts (*Condyloma acuminata*) caused by specific HPV types.

The 4 valent HPV vaccine (*Gardasil*) is the vaccine currently advocated through the national childhood immunisation schedule. The Joint Committee on Vaccination and Immunisation (JCVI) are currently evaluating the new vaccine, but it has not yet been approved for use on the NHS.

PACEF Recommendation:
Pending advice from the JCVI, human papillomavirus 9-valent vaccine (*Gardasil 9*) has not been approved for use through the *Lincolnshire Joint Formulary* and is designated RED-RED. In the unlikely event that a patient specifically requests *Gardasil 9* vaccine for their child, standard *Gardasil* should be offered in accordance with national guidance.

SHARED CARE UPDATE: SHARED CARE GUIDELINE – METHOTREXATE IN DERMATOLOGY AND RESPIRATORY (AUGUST 2016)

PACEF have approved the following shared care guideline for use:

- Shared Care Guideline: *Methotrexate in Dermatology and Respiratory* (August 2016).

The guideline can be accessed through the PACEF website (http://lincolnshire-pacef.nhs.uk) or directly by contacting:

Cathy Johnson, Interface Lead Pharmacist (cathy.johnson@ardengemcsu.nhs.uk)

MEDICINES AND HEALTHCARE REGULATORY AGENCY: *DRUG SAFETY UPDATE* (SEPTEMBER 2016)

LEVONORGESTREL- CONTAINING EMERGENCY HORMONAL CONTRACEPTION: ADVICE ON INTERACTIONS WITH HEPATIC ENZYME INDUCERS AND CONTRACEPTIVE EFFICACY

Levonorgestrel-containing emergency contraception

Levonorgestrel-containing emergency contraception is used to prevent unintended pregnancy when taken within 72 hours (3 days) of unprotected intercourse or failure of a contraceptive method. The sooner it is taken after having unprotected sex, the more effective it will be. It is available with or without a prescription as a single 1500 microgram tablet, or on prescription as two 750 microgram tablets taken as a single dose.

Concomitant use of liver enzyme inducers (mainly CYP3A4) increases the metabolism of levonorgestrel. This decrease in plasma levonorgestrel may reduce contraceptive efficacy of levonorgestrel-containing emergency hormonal contraceptives. Elevated levels of CYP3A4 enzymes can persist for up to 4 weeks after cessation an enzyme-inducing medicine.

Examples of enzyme inducers that reduce plasma levonorgestrel levels include: barbiturates, primidone, phenytoin, carbamazepine, rifampicin, rifabutin, ritonavir, efavirenz and griseofulvin. Herbal remedies that contain St John's wort (*Hypericum perforatum*) also reduce levonorgestrel levels.

For women unable or unwilling to use a copper intrauterine device, a woman seeking emergency contraception who has used a hepatic enzyme inducer in the past 4 weeks, should double the usual dose of levonorgestrel (from 1.5mg to 3mg, 2 packs) to compensate for the reduced plasma levonorgestrel levels. No increased risk of side effects is expected from the higher dose in these circumstances.

A patient information sheet is available from:
https://assets.publishing.service.gov.uk/media/57d7d2d840f0b6533a000046/Levonorgestrelpatientsheet.pdf

Ulipristal acetate

Ulipristal acetate emergency contraception (*EllaOne*) is not recommended in women who are using enzyme-inducing drugs or who have stopped them in the last 4 weeks.

Summary

Women seeking emergency contraception who have used cytochrome P450 3A4 (CYP3A4) enzyme inducers within the last 4 weeks, should:

- preferably use a non-hormonal emergency contraceptive (i.e. a copper intrauterine device). A copper IUD may be fitted up to 5 days after unprotected intercourse and, if available, may be an appropriate method of emergency contraception for some women.
- if this is not an option, double the usual dose of levonorgestrel from 1.5mg to 3mg (or 2 packs).

For these women:

- provide advice on highly effective ongoing contraception that is not affected by hepatic enzyme-inducing drugs (see guidance from the Faculty of Sexual and Reproductive Health).
- advise them to have a pregnancy test to exclude pregnancy after use of levonorgestrel-containing emergency contraception.
- advise them to seek prompt medical advice if they do become pregnant.

NHS ENGLAND, *ALERT ISSUED FOLLOWING ACCIDENTAL DEATH OF A PATIENT LINKED TO E45 CREAM*

Guidance on preferred low paraffin emollients has been reviewed in response to another incident in which a patient was overcome by fire while smoking in bed. The investigating Fire Officer concluded that the *E45* cream being used by the patient for a dry skin condition helped to fuel the blaze. Low paraffin alternatives recommended include *Balneum* cream, *Balneum Plus* cream and *Dermol* lotion.

In a recent case publicised by NHS England, the Coroner recorded a verdict of accidental death in a terminally ill patient who caught fire in his bed when smoking while covered with *E45* cream. Following an investigation, the Fire Officer concluded that the most likely cause of the fire was the deceased lighter, coupled with the fact that his bedding and clothing were covered in *E45* emollient residue. This would have increased the fuel load and acted as an accelerant, increasing the intensity and speed with which the fire had taken hold. Despite the

best efforts of the patient's friend and the fire crew the patient was pronounced dead on arrival at hospital.

PACEF Recommendations:

(1) Emollients with high paraffin content can constitute a fire risk, particularly in people who are smokers or who are receiving oxygen therapy. No or low paraffin content products are preferable in these high risk groups.
(2) Products with a particularly high paraffin content, such as emulsifying ointment, 50% liquid paraffin or 50% white soft paraffin (WSP) ointment are known to be particularly high risk and are not recommended in this patient group.
(3) Previously *E45* cream was considered as a lower risk emollient due to its relatively low paraffin content; following this incident the status of *E45* cream has been reconsidered. E45 cream contains liquid paraffin 12.6% and white soft paraffin (WSP) 14.5%, a total paraffin content of 27.1%. PACEF issued advice in March 2016 (*PACE Bulletin* Vol 10 No 5) in response to locally reported incidents recommending use of products with a paraffin content of 30% or less.
(4) Following this most recent incident, local guidance for patients with mild dry skin requiring treatment with an emollient with low paraffin content is as follows:

***Balneum* Cream (liquid paraffin 5.35% plus urea 5%) or *Balneum Plus* Cream (liquid paraffin 1.0% plus urea 5% and lauromacrogols 3%).**

When an antimicrobial is required consider: *Dermol* lotion (liquid paraffin 2.5%).

All three products are already included on the *Lincolnshire Joint Formulary.*

RISK OF CONFUSION BETWEEN O.5MG AND 5MG STRENGTHS OF WARFARIN

Prescribers are reminded of the risk of confusion between 0.5mg and 5mg strengths of warfarin. Peterborough and Stamford Hospitals NHS Foundation Trust are in the process of reducing the use of both strengths with a view to possible future withdrawal in favour of 1mg and 3mg tablets only.

The Medicines Governance and Medication Safety Officer from Peterborough and Stamford Hospitals NHS Foundation Trust have notified PACEF of the intention of the Trust to reduce the usage and possibly withdraw both the 0.5mg and 5mg strength of warfarin tablets. This is in response to two fatalities recorded as a result of confusion between the two strengths. The Hospital's current warfarin policy advises that only warfarin 1mg and 3mg tablets should be prescribed and that all doses should be calculated and adjusted using these strengths only.

Standard advice from the National Patient Safety Agency (NPSA) issued in July 2007 recommends that:

- Patients should use the least number of tablets each day.
- Constant daily dosing and not alternate day dosing should be preferred.
- Treatment regimens should not require the use of half tablets.

PACEF Recommendation
GPs in South Lincolnshire CCG are alerted to the ongoing Peterborough review of the role of warfarin 0.5mg and 5mg tablets and possible changes to prescribing policy that may be implemented in the future. All prescribers should be mindful of the risk of confusion between 0.5mg and 5mg strengths of warfarin.

NICE TECHNOLOGY APPRAISALS

NICE Technology Appraisal	Guidance	PACEF Recommendation
TA259 *Abiraterone for castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen (July 2016)*	Abiraterone in combination with prednisone or prednisolone is recommended as an option for the treatment of castration- resistant metastatic prostate cancer in adults previously treated with a docetaxel-containing regimen.	Abiraterone 250mg tablets (*Zytiga*) are designated RED for this indication and approved for use through the *Lincolnshire Joint Formulary.*
TA398 *Lumacaftor–ivacaftor for treating cystic fibrosis homozygous for the F508del mutation* (July 2016)	Lumacaftor–ivacaftor is not recommended for treating cystic fibrosis in people 12 years and older who are homozygous for the F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.	Lumacaftor-ivacaftor 125mg tablets (*Orkambi*) are designated RED-RED and not approved for inclusion in the *Lincolnshire Joint Formulary*.
TA399 *Azacitidine for treating acute myeloid leukaemia with more than 30% bone marrow blasts* (July 2016)	Azacitidine is not recommended for the treatment of acute myeloid leukaemia in people with more than 30% bone marrow blasts.	Azacitidine 25mg/ml powder for suspension for injection (*Vidaza*) is designated RED-RED for this indication and is not approved for inclusion in the *Lincolnshire Joint Formulary*.
TA400 *Nivolumab in combination with ipilimumab for treating advanced melanoma (*July 2016)	Nivolumab in combination with ipilimumab is recommended as an option for treating advanced (unresectable or metastatic) melanoma in adults	Nivolumab 10mg/ml concentrate for solution for infusion (*Opdivo*) is designated RED for this indication and approved for inclusion in the *Lincolnshire Joint Formulary.*
TA391 *Cabazitaxel for hormone-relapsed metastatic prostate cancer treated with docetaxel* (August 2016)	Cabazitaxel in combination with prednisone or prednisolone is recommended as an option for treating metastatic hormone-relapsed prostate cancer in people whose disease has progressed during or after docetaxel chemotherapy	Cabazitaxel 40mg per ml concentrate and solvent for solution for infusion (*Jevtana*) is already designated RED for this indication in accordance with the *National Cancer Drugs Fund List*
TA401 *Bosutinib for previously treated chronic myeloid leukaemia* (August 2016)	Bosutinib is recommended as an option for the treatment of chronic, accelerated and blast phase Philadelphia chromosome positive chronic myeloid leukaemaia in adults.	Bosutinib 100mg and 500mg tablets (*Bosulif*) is designated RED for this indication and approved for use through the *Lincolnshire Joint Formulary.*
TA402 *Pemetrexed maintenance treatment for non-squamous non-small-cell lung cancer after pemetrexed and cisplatin* (August 2016)	Pemetrexed is recommended as an option for the maintenance treatment of locally advanced or metastatic non-squamous non-small cell lung cancer in adults	Pemetrexed 100mg and 500mg powder for solution for infusion (*Alimta*) is designated RED for this indication and approved for use through the *Lincolnshire Joint Formulary.*
TA403 *Ramucirumab for previously treated locally advanced or metastatic non-small-cell lung cancer* (August 2016)	Ramucirumab, in combination with docetaxel, is not recommended for treating locally advanced or metastatic non-small cell lung cancer in adults whose disease has progressed after platinum-based chemo-therapy.	Ramucirumab 10mg/ml concentrate for solution for infusion (*Cyramza*) is designated RED-RED for this indication and not approved for inclusion in the *Lincolnshire Joint Formulary*.
TA405 *Trifluridine–tipiracil for previously treated metastatic colorectal cancer* (August 2016)	Trifluridine–tipiracil is recommended as an option for the treatment of metastatic colorectal cancer.	Trifluridine/tipiracil tablets 15mg/6.14mg and 20mg/8.19mg (*Lonsurf*) are designated RED and approved for use through the *Lincolnshire Joint Formulary* for this indication. The product was previously approved for this indication through the *Joint Formulary* subject to New Cancer Drugs Fund List criteria.
TA406 *Crizotinib for untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer* (September 2016)	Crizotinib is recommended for untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer in adults.	Crizotinib 200mg and 400mg capsules (*Xalkori*) are designated RED and approved for inclusion in the *Lincolnshire Joint Formulary*.
TA407 *Secukinumab for active ankylosing spondylitis after treatment with non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors* (September 2016)	Secukinumab is recommended for treating active ankylosing spondylitis in adults whose disease has responded inadequately to conventional therapy (non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors)	Secukinumab 150mg solution for injection (*Cosentyx*) is designated RED for this indication and approved for use through the *Lincolnshire Joint Formulary*. Secukinumab is already designated RED for the treatment of moderate to severe plaque psoriasis.
TA408 *Pegaspargase for treating acute lymphoblastic leukaemia* (September 2016)	*Pegaspargase, as part of antineoplastic combination therapy, is recommended as an option for treating acute lymphoblastic leukaemia in children,*	Pegaspargase 750 units/ml solution for injection/infusion (*Oncaspar*) is designated RED and approved for use through the *Lincolnshire Joint*

	young people and adults only when they have untreated newly diagnosed disease.	*Formulary.* The product was previously approved for this indication through the *Joint Formulary* subject to New Cancer Drugs Fund List criteria.
TA409 *Aflibercept for treating visual impairment caused by macular oedema after branch retinal vein occlusion* (September 2016	Aflibercept is recommended as an option for treating visual impairment in adults caused by macular oedema after branch retinal vein occlusion	Aflibercept 40mg per ml (*Eylea*) is designated RED for this indication and approved for use through the *Lincolnshire Joint Formulary*. The product is already approved for use in accordance with NICE guidance on wet age-related macular degeneration and visual impairment caused by macular oedema secondary to central retinal vein occlusion.

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