Lincolnshire Prescribing and Clinical Effectiveness (PACE) Bulletin

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Optum in association with Lincolnshire Clinical Commissioning Groups, Lincolnshire Community Health Services, United Lincolnshire Hospitals Trust and Lincolnshire Partnership Foundation Trust

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Drug Assessments

Product	Summary	Decision
Marol®& Zytram® Tramadol sustained release tablets 75mg, 100mg, 150mg and 200mg.	**Introduction:** Tramadol modified release and sustained release products were classed RED/RED non-formulary. Review of tramadol prescribing showed significant use. If continuing use of a sustained release formulation of tramadol is clinically appropriate then significant savings could be realised by utilising lower cost brands. Review of licensed formulations identified two low cost brands Marol® & Zytram® both available in a range of different strengths 75mg (Zytram only), 100mg, 150mg and 200mg. **Further relevant information:** Marol® and Zytram® were approved when use of prolonged release formulations of tramadol is considered clinically appropriate. Patients currently receiving alternative brands of tramadol prolonged release should be reviewed and switched to either Marol® or Zytram® where possible. ULHT have indicated they do not use prolonged release and modified release tramadol and therefore these products are included on the formulary for use within primary care only.	Approved for inclusion onto the formulary as GREEN for use within primary care. To maximise cost effectiveness prescribe by brand.
Semaglutide (Ozempic ®)	**Introduction:** Semaglutide (Ozempic ®) is another Glucagon-like peptide-1 receptor agonist (GLP1) indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus (T2DM) • as an adjunct to diet and exercise • as monotherapy when metformin is considered inappropriate due to intolerance or contraindications • in addition to other medicinal products for the treatment of diabetes. It is administered subcutaneously in the abdomen, in the thigh or in the upper arm once weekly at any time of the day, with or without meals. The starting dose is 250 micrograms once weekly. After 4 weeks the dose should be increased to 500 micrograms once weekly. After at least 4 weeks with a dose of 500 micrograms once weekly, the dose can be increased to 1 mg once weekly to further improve glycaemic control. Maintenance dose: 500micrograms – 1mg once weekly **Further relevant information:** Trials demonstrate that safety and side effect profile are similar to comparators. However, there is an increased incidence of diabetic retinopathy when semaglutide is initiated in patients with a history of retinopathy receiving insulin which is considered to be associated with a rapid decline in HbA1c during the first 16 weeks of treatment. This is the fifth GLP-1 to be included onto the formulary. Dulaglutide is currently the GLP-1 preparation of choice	Approved for inclusion onto the formulary as GREEN.

Product	Summary	Decision
	because of ease of use and weekly dose schedule. Lixisenatide and liraglutide offer daily injection regimes. Exenatide is available in daily and weekly formulations, but is infrequently used because of patient acceptability, due to gastrointestinal side effects.	
Ertugliflozin 5mg & 15mg tablets (Steglatro®)	**Introduction:** New Sodium Glucose co-transporter 2 (SGLT2) inhibitor. NICE issued TA 572 27th March 2019 covering use as monotherapy or in combination with metformin for the treatment of type 2 diabetes. The recommended starting dose is 5mg once daily. In patients tolerating 5mg once daily, the dose can be increased to 15mg once daily if additional glycaemic control is needed. • When used in combination with insulin or an insulin secretagogue, a lower dose of ertugliflozin may be required to reduce the risk of hypoglycaemia. • In line with alternative SGLT-2 indibitors use is restricted in patients with renal impairment. • Initiation of ertugliflozin is not recommended in patients with an estimated glomerular filtration rate (eGFR) less than 60ml/min/1.73m^2 or creatinine clearance (CrCl) less than 60ml/min. • Ertugliflozin should be discontinued if eGFR is less than 45ml/min/1.73m^2 or CrCl is persistently less than 45ml/min. • Ertugliflozin should not be used in patients with severe renal impairment or with end stage renal disease. (ESRD). **Further relevant information:** Ertugliflozin is the fourth SGLT-2 inhibitor to be licensed for use in the UK. It has the lowest acquisition cost, £29.40 for 28 days treatment compared to £36.59 for the other three SGLT-2's (canagliflozin, dapagliflozin & empagliflozin). This cost is approximately 20% lower than the alternative SGLT-2 inhibitors. Ertugliflozin is not currently available as a fixed dose combination with metformin whereas the other 3 SGLT-2 inhibitors are. Due to its low cost PACEF approved ertugliflozin to be used first line in new patients where clinically appropriate when use of a SGLT-2 inhibitor is being considered.	Approved for inclusion onto the formulary as GREEN. Approved for use in new patients, when use of a SGLT2 inhibitor is indicated, due to its significantly lower cost.
Fusacomb Easyhaler®	**Introduction:** A new low cost breath-actuated dry powder inhaler containing a fixed dose combination of salmeterol & fluticasone propionate licensed for the treatment of asthma & COPD. The inhaler is available in two different doses salmeterol (as xinafoate) 50 microgram, with fluticasone propionate 250 microgram or salmeterol (as xinafoate) 50 microgram fluticasone propionate 500 microgram 50/500mcg. The device used is a device metered inhaler (Easyhaler®)	Fusacomb® Easyhaler® approved for inclusion on the formulary as GREEN.

<table>
<tr><th>Product</th><th>Summary</th><th>Decision</th></tr>
<tr><td></td><td>Further relevant information:

Comparative prices

<table>
<tr><th>BNF Name</th><th>Price (per inhaler)</th></tr>
<tr><td>Aerivio Spiromax 50/500mcg</td><td>£ 29.97</td></tr>
<tr><td>Airflusal Forspiro 50/500mcg</td><td>£ 29.97</td></tr>
<tr><td>Fusacomb Easyhaler 50/250mcg</td><td>£ 21.50</td></tr>
<tr><td>Fusacomb Easyhaler 50/500mcg</td><td>£ 26.99</td></tr>
<tr><td>Seretide Accuhaler 50/250mcg</td><td>£ 35.00</td></tr>
<tr><td>Seretide Accuhaler 50/500mcg</td><td>£ 32.74</td></tr>
<tr><td>Stalpex 50/500mg</td><td>£ 24.56</td></tr>
</table>

Current formulary approved products in bold.
PACEF approved Fusacomb Easyhaler for inclusion onto the formulary, as an alternative low cost fixed dose LABA/ICS combination.</td><td></td></tr>
<tr><td>Stalpex®</td><td>Introduction:
A new low cost breath-actuated dry powder inhalation containing a fixed dose combination of salmeterol & fluticasone propionate licensed for the treatment of asthma & COPD. The inhaler is available in one strength salmeterol (as xinafoate) 50 microgram, with fluticasone propionate 500 microgram (50/500mcg).
Stalpex comes as a pre-moulded plastic inhaler containing a foil strip with 60 regularly placed blister which contain the powder for inhalation.

Further relevant information:
From the dose comparison table (included in the entry for Fusacomb® EasyHaler®) Stalpex is the lowest cost option when a fixed dose combination of salmeterol 50 microgram/fluticasone propionate 500 microgram is required and a breath actuated device is the best choice for the patient.</td><td>Stalpex® approved for inclusion on the formulary as GREEN.</td></tr>
<tr><td>Haloperidol 200 microgram/ml sugar-free oral solution - Halkid®</td><td>Introduction:
New lower strength licensed haloperidol oral solution.

Further relevant information:
Two haloperidol liquid formulations included on the Lincolnshire formulary:
• Haloperidol 5mg/5ml oral solution sugar free
• Haloperidol 10mg/5ml oral solution sugar free
Halkid is significantly more expensive than the formulary approved alternatives and therefore PACEF did not approve it for routine use.

It was acknowledged that there might be certain circumstances when a low dose low volume liquid haloperidol is clinically appropriate, in which case use of Halkid would be preferable to unlicensed low dose formulations.
Further advice can be sought from Optum MMO team.</td><td>Haloperidol 200 microgram/ml sugar-free oral solution – (Halkid®) not approved for inclusion onto the formulary. Classed as RED/RED.</td></tr>
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Product	Summary	Decision
Naloxegol 12.5mg & 25mg tablets (Moventig®)	**Introduction:** Naloxegol is licensed for the treatment of opioid induced constipation in adult patients who have had an inadequate response to laxatives. NICE issued TA345 in July 2015 recommending its use within its marketing authorisation, as an option for treating opioid induced constipation in adults whose constipation has not adequately responded to laxatives. Naloxegol previously assessed by PACEF as classed as RED hospital use only. **Further relevant information:** ULHT gastroenterology service has requested a review of the current formulary classification, requesting that Naloxegol is re-classed as AMBER 2. Appropriate for prescribing in primary care following initiation by or on the advice of a specialist. Naloxegol is to be used in line with NICE guidance. PACEF approved this request.	Traffic light classification reviewed Changed to AMBER 2.

Otovent® removal from Drug Tariff May 2019

Otovent® is an auto inflation device which has been used to treat "glue ear" or otitis media with effusion (OME)
Otovent® has been removed from the Drug Tariff from 1st May 2019, which means it can no longer be prescribed on a NHS prescription.
As a result of this change, Otovent® is removed from the Lincolnshire Formulary and re-classed as RED/RED.

Review of formulary section
Modified release venlafaxine capsules

Current formulary recommendations:
When a modified release formulation is required consider either Venlablue XL capsules or Vensir XL capsules.
Drug Tariff cost of generic capsules is now linked to the cost of Vensir XL. Venlablue XL is now a more expensive alternative.

Cost (28 days' supply)	37.5mg	75mg	150mg	225mg
Vensir XL caps (Morningside)		**£ 2.60**	**£ 3.90**	**£ 21.90**
Generic capsules	£ 5.25	£ 2.60	£ 3.90	£ 47.11
Generic tablets	£ 6.60	£ 2.60	£ 3.90	£ 33.60
Efexor XL caps (Pfizer)		£ 22.08	£ 36.81	£ 47.11
Politid XL capsules (Actavis UK Ltd)		£ 23.41	£ 39.03	
Venlablue XL caps (Creo Pharma)	£ 5.25	£ 6.95	£ 9.95	
Venlalic XL tabs (DB Ashbourne Ltd)	£ 6.60	£ 2.60	£ 3.90	£ 33.60

Taking into account recent price changed, PACEF revised its formulary recommendations.
Vensir XL approved as the first line modified release venlafaxine.
Venlablue XL retained as second line option when Vensir XL not available. This advice applies for new initiations of therapy.

NICE/PHE Summary of Antimicrobial Prescribing Guidance – managing common infections

A copy of the most recent prescribing guidance produced jointly by NICE and PHE is now included on the PACEF webpage.
This provides guidance as to first/second line treatment choices for the management of common infections but also includes links to decision support tools such as FeverPAIN and Centor and links to NICE Guidelines and treatment flowcharts where available.

MEDICINES AND HEALTHCARE REGULATORY AGENCY (MHRA): DRUG SAFETY UPDATE (March 2019)

Fluoroquinolone antibiotics: New restrictions and precautions for use due to very rare reports of disabling and potentially long-lasting and irreversible side effects.

New prescribing restrictions have been put in place governing the use of Fluoroquinolone antibiotics - ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin.
Ciprofloxacin and levofloxacin are classed as AMBER 2 on the formulary.
Moxifloxacin, Ofloxacin and levofloxacin nebules (Quinsair®) are classed as RED on the formulary – hospital use only.
All of these are "restricted by indication" and should only be used in line with antibiotic guidelines.
Nalidixic acid and Norfloxacin are both non formulary and classed as RED/RED.

MHRA have issued the following advice for healthcare professionals:

- Advise patients to stop treatment at the first signs of a serious adverse reaction, such as tendinitis or tendon rupture, muscle pain, muscle weakness, joint pain, joint swelling, peripheral neuropathy and central nervous system effects and to contact their doctor for further advice.

Do not prescribe fluoroquinolones:

- For non-severe or self-limiting infections, or non-bacterial conditions
- For some mild to moderate infections (such as acute exacerbations of chronic bronchitis and chronic obstructive pulmonary disease, refer to revised indications in summary of product characteristics (SPC), unless other antibiotics that are commonly recommended for these infections are considered inappropriate.
- Ciprofloxacin or levofloxacin should no longer be prescribed for uncomplicated cystitis unless other antibiotics that are commonly recommended are considered inappropriate.
- Avoid use in patients who have had a previous serious adverse reactions with a quinolone or fluoroquinolone antibiotic.
- Prescribe with caution in people older than 60 years of age and for those with renal impairment or solid organ transplants because they are at a higher risk of tendon injury.
- Avoid use of a corticosteroid with a fluoroquinolone since co-administration could exacerbate fluoroquinolone – induced tendinitis and tendon rupture.

- Report suspected adverse drug reactions via the Yellow Card system either through the website or via the Yellow Card App.

MEDICINES AND HEALTHCARE REGULATORY AGENCY (MHRA): DRUG SAFETY UPDATE (April 2019)

Yellow fever vaccines: Reports of fatal adverse reactions: extreme caution needed in people who may be immunosuppressed and those 60 years and older.

MHRA have issued the following advice for healthcare professionals:

- As with any live attenuated vaccine, yellow fever vaccine must not be given to people who are immunosuppressed.
- Yellow fever vaccine is contraindicated in people with a history of thymus dysfunction (including myasthenia gravis and thymoma)

- Yellow fever vaccine is contraindicated in people who have had their thymus gland removed (thymectomy)
- In people aged 60 years and older, the vaccine should only be given when it is considered that there is a significant and unavoidable risk of acquiring yellow fever.
- Professional who administer a yellow fever vaccine must be familiar with any contraindications and special precautions before proceeding with immunisation.
- If there is doubt as to whether a person who is due to receive yellow fever vaccine may be immunosuppressed, immunisation should be deferred until specialist advice has been sought.
- Protocols and checklists should be strengthened to avoid inappropriate administration that can lead to severe and possible fatal adverse effects; those administering the vaccine should also be familiar with the YF Vaccine Centre code of practice.

For further information please refer to Drug Safety Update Volume 12 Issue 9 April 2019

Valproate medicines and serious harms in pregnancy- New Annual Risk Acknowledgement Form.

The MHRA have updated the Annual Risk Acknowledgement Form which should be used during annual specialist review of all women and girls of child bearing potential on valproate medicines (irrespective of indication).
An ongoing patient survey has indicated that there needs to be a more timely compliance with the valproate Pregnancy Prevention Programme to rapidly reduce and eventually eliminate the harms of valproate in pregnancy in view of serious teratogenicity.

MHRA have issued the following advice for healthcare professionals:

- Use the revised Annual risk Acknowledgment form – revised March 2019 at initiation and at annual review of all girls and women of child bearing potential on valproate medicines (irrespective of indication)
- Specialists should comply with guidance on the form if they consider there to be compelling reasons to indicate their patient is not at risk of pregnancy, including the need to document reasons for this and for the patient or responsible person to confirm these are correct.
- If the absence of pregnancy risk may change (for example the patient is pre-menarchal), the date for the next annual discussion of the risks must be documented and the patient or the patient's family or caregivers asked to contact the prescriber rapidly if the situation changes.
- There is no safe dose of valproate in pregnancy – refer to the April 2019 Drug Safety Update for key facts about the risks if pregnancies are exposed to valproate.

Produced by:

Medicines Management & Optimisation Service
Optum Health Systems Support

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T 020 7121 0560 l E info@optum.co.uk l **optum.co.uk**
10th Floor, 5 Merchant Square, Paddington, London, W2 1AS