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 8; Number 20 **December 2014**

MERRY CHRISTMAS AND HAPPY NEW YEAR TO ALL OUR READERS

What's new this month?

- **Effective immediately, the Lincolnshire PACEF website has moved to: http://lincolnshire-pacef.nhs.uk/lincolnshire-prescribing-and-clinical-effectiveness-forum-pacef . Alternatively, go to http://lincolnshire-pacef.nhs.uk and follow the commissioning link to the PACEF section (see page 3).**
- **PACEF are unconvinced by the poor quality evidence base behind sodium hyaluronate 0.1%/dexpanthenol 2% eye drops *(Hylo-Care*) for the treatment of dry eye. The product is designated RED-RED and is not approved for inclusion in the *Lincolnshire Joint Formulary* (see page 3).**
- ***DuoResp Spiromax* 160/4.5mcg and 320/9mcg inhalers offer an equivalent lower cost alternative to *Symbicort Turbohaler* at the 200/6mcg and 400/12mcg strengths respectively. Both strengths of *DuoResp Spiromax* are designated GREEN and approved for inclusion in the *Lincolnshire Joint Formulary*. Prescribers should consider *DuoResp Spiromax* in new patients aged 18 and over where combination ICS/LABA therapy is indicated for the treatment of asthma or COPD (see page 5).**
- **Beclometasone/formoterol 100/6microgram dry powder inhaler (*Fostair NEXThaler*) is designated GREEN and approved for inclusion in the *Lincolnshire Joint Formulary* within licensed indications (i.e. where combination ICS/LABA therapy is indicated for the treatment of asthma in adults). It is identically priced to the *Fostair* MDI which holds a wider marketing authorisation including the treatment of COPD (see page 7).**
- **Canagliflozin and metformin tablets 50mg/850mg and 50mg/1000mg (V*okanamet*) are approved for use only when triple therapy requiring a SGLT-2 inhibitor component is indicated and renal function is considered satisfactory. *Vokanamet* tablets are designated GREEN for this limited indication and approved for inclusion in the *Lincolnshire Joint Formulary* (see page 7).**
- **While the *Freestyle Libre Glucose Monitoring System* may represent a significant innovation in the monitoring of blood glucose in adults with diabetes, it is not currently available through the *Drug Tariff* and cannot be prescribed on the NHS. The product is designated RED-RED and not approved for inclusion on the *Lincolnshire Joint Formulary* (see page 8).**
- **The *Otovent* autoinflation device is designated GREEN for the treatment of otitis media with effusion in young children and approved for inclusion in the *Lincolnshire Joint Formulary*. It should be prescribed for a maximum period of two weeks' only (see page 8).**

CONTENTS

SUMMARY OF PACEF DECISIONS: *NOVEMBER 2014 UPDATE*

Drug	Indication(s)	Traffic Light and Joint Formulary Status
Beclometasone/ formoterol dry powder inhaler 100microgram/ 6microgram *(Fostair NEXThaler)* (Chiesi)	For the regular treatment of asthma in adults.	GREEN Approved for inclusion in the *Lincolnshire Joint Formulary.* Equivalent cost to the *Fostair* metered dose inhaler with a narrower range of licensed indications.
Budesonide/ formoterol fumarate breath actuated dry powder inhaler 160/4.5 and 320/9 (*DuoResp Spiromax*) (Teva)	An inhaled corticosteroid / long-acting bronchodilator combination product licensed for the treatment of asthma and chronic obstructive pulmonary disease in adults	GREEN Approved for inclusion in the *Lincolnshire Joint Formulary.* Lower cost equivalent to *Symbicort Turbohaler .*
Canagliflozin/metformin 50mg/850mg and 50mg/1000mg tablets *(Vokanamet)*	For adults aged 18 years and older with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control: • in patients not adequately controlled on their maximally tolerated doses of metformin alone • in patients on their maximally tolerated doses of metformin along with other glucose-lowering medicinal products including insulin, when these do not provide adequate glycaemic control • in patients already being treated with the combination of canagliflozin and metformin as separate tablets.	GREEN. For use only when triple therapy requiring a SGLT-2 inhibitor component is indicated and renal function is considered satisfactory. Approved for inclusion in the *Joint Formulary.*
Freestyle Libre Glucose Monitoring System (Abbott Diabetes Care)	For the measurement of interstitial fluid glucose levels in adults aged 18 years and older with diabetes.	RED-RED Not approved for inclusion in the *Lincolnshire Joint Formulary*.
Otovent autoinflation device	For the treatment of otitis media with effusion in young children	GREEN Approved for inclusion in the *Joint Formulary.*
Prasugrel 5mg and 10mg tablets	For the prevention of atherosclerotic	AMBER without shared care.

(*Efient*) (Lilly)	events in adults with acute coronary syndrome undergoing primary or delayed percutaneous coronary intervention.	Included in the *Lincolnshire Joint Formulary.*
Sodium hyaluronate 0.1% eye drops (Hylo-Tear) (Scope)	For the treatment of dry eyes	GREEN Approved for inclusion in the *Joint Formulary.* Third Line (hyaluronate preparation)
Sodium hyaluronate 0.2% eye drops (Hylo-Forte) (Scope)	For the treatment of dry eyes	GREEN Approved for inclusion in the *Joint Formulary.* Third Line (hyaluronate preparation)
Sodium hyaluronate 0.1% and dexpanthenol 2% eye drops *(Hylo-Care)* (Scope)	For the treatment of dry eyes	RED-RED. Not approved for inclusion in the *Lincolnshire Joint Formulary.*

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); follow the commissioning link to PACEF. 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

IMPORTANT CHANGES TO THE PACEF WEBSITE

Effective immediately, the Lincolnshire PACEF website has moved to:

http://lincolnshire-pacef.nhs.uk/lincolnshire-prescribing-and-clinical-effectiveness-forum-pacef

Alternatively go to http://lincolnshire-pacef.nhs.uk and follow the commissioning link to the PACEF section. This will be the new home for all PACEF publications in 2015. We are planning a complete refresh of the website early in the New Year. We apologise for any inconvenience caused by the temporary loss of the website earlier in December; we have now resolved these problems and normal service has been resumed.

NEW DRUG ASSESSMENT: *SODIUM HYALURONATE 0.1% AND DEXPANTHENOL 2% EYE DROPS (HYLO-CARE)*

Sodium hyaluronate 0.1% and dexpanthenol 2% eye drops *(Hylo-Care*) are part of a range of sodium hyaluronate containing eye preparations manufactured by Scope. Other products in the range include: sodium hyaluronate 0.1% eye drops (*Hylo-Tear*) and 0.2% eye drops (*Hylo-Forte*). Both *Hylo-Tear* and *Hylo-Forte* have previously been evaluated and approved for use by PACEF as third line treatment for dry eye; designation GREEN (see *PACE Bulletin* Vol 7 No 6 (June 2013).

Hyaluronic acid is found naturally in the human body, mainly in connective tissue, but also in vitreous body and synovial fluid and in the tear fluid of the eye. It has water retaining properties and provides a low resistance to blinking. This makes it highly effective at entrapping water and preventing evaporation which prolongs any beneficial effects. There is

very limited clinical evidence to support the use of sodium hyaluronate eye preparations in the treatment of dry eye. The evidence that is available confirms a longer duration of action and a superior affect in terms of relief of symptoms and prevention of further corneal damage. There is no clinical evidence to inform the debate over optimum strength.

Hylo-Care eye drops contain the same concentration of sodium hyaluronate as *Hylo-Tear* with the addition of 2% dexpanthenol. Dexpanthenol is a vitamin B5 derivative reported to have a beneficial effect on wound healing rates. PACEF reviewed two small published trials of very short duration involving sodium hyalouronate/dexpanthenol combination eye preparations other than *Hylo-Care*. These studies were conducted in clinical populations that did not mirror those in whom the products would be used locally. For example, one study assessed the use of a higher strength dexpanthenol product (5%) following corneal surgery. The only study submitted using the *Hylo-Care* product was an animal study which did not constitute a high enough level of evidence for PACEF consideration.

A cost comparison of the sodium hyaluronate eye preparations available is provided below. Products already approved for inclusion in the *Lincolnshire Joint Formulary* are highlighted in **bold**:

Product	**Preservative free (as listed *MIMS*)**	**Sodium hyaluronate content**	**Price**
***Artelac Rebalance* eye drops**		**0.15%**	**£4.00 10ml**
Artelac Splash eye drops SDU	√	0.2%	£7.00(30) £11.20 60
Clinitas eye drops SDU	√	0.4%	£5.70 (30)
Hyabak eye drops	√	0.15%	£7.99 10ml
***Hylo - Tear* eye drops**	√	**0.1%**	**£8.50 10ml**
***Hylo – Forte* eye drops**	√	**0.2%**	**£9.50 10ml**
Hylo – Care eye drops	√	0.1% + dexpanthenol 2%	£10.30 10 ml
Lubristil eye drops	√	0.15%	£4.99 (20)
***Lumecare Sodium Hyaluronate* eye drops**		**0.15%**	**£3.97 10ml**
Ocusan eye drops	√	0.2%	£5.31 (20)
Optive Fusion eye drops		0.1% + carmellose sodium 0.5% + glycerol 0.9%	£7.49 10ml
***Oxyal* eye drops**		**0.15%**	**£4.15 10ml**
Rohto Dry Eye Relief eye drops		0.2% + tamarind seed polysaccharide 0.2%	£4.10 10ml £4.75 (20)
Vismed Gel ophthalmic gel	√	0.3%	£7.95 10ml £5.98 (20)
Vismed eye drops	√	0.18%	£6.81 10ml £5.10 (20)

PACEF Recommendation:

PACEF recommend that, where a sodium hyaluronate preparation is indicated, a product of low acquisition cost should be preferred, such as *Artelac Rebalance* eye drops (0.15% sodium hyaluronate), *Lumecare Sodium Hyaluronate* eye drops (0.15% sodium hyaluronate) or *Oxyal* eye drops (0.15% sodium hyaluronate). PACEF recognize that *Hylo* products have the advantage of longer expiry dates after opening which enables the administration of the full 300 doses from each container and reduces wastage. These products are also the sodium hyaluronate products of choice

at recognised centres of excellence in ophthalmology such as Moorfields , Birmingham and Midland Eye Centre and Manchester Royal Eye Hospital. As a result of this both *Hylo-Tear* eye drops (sodium hyaluronate 0.1%) and *Hylo-Forte* eye drops (sodium hyaluronate 0.2%) are designated GREEN and already included in the Lincolnshire Joint Formulary. *Hylo-Forte* eye drops should be reserved for those who have failed to respond to the 0.1% strength. PACEF are unconvinced by the poor quality evidence base behind sodium hyaluronate 0.1%/dexpanthenol 2% eye drops *(Hylo-Care*) for the treatment of dry eye. The product is designated RED-RED and is not approved for inclusion in the *Lincolnshire Joint Formulary.* GPs are advised to refuse any requests from ophthalmologist to prescribe this product.

NEW DRUG ASSESSMENT: *BUDESONIDE/FORMOTEROL FUMARATE DIHYDRATE BREATH ACTUATED DRY POWDER INHALER 160MICROGRAM/4.5 MICROGRAM AND 320MICROGRAM/9MICROGRAM (DUORESP SPIROMAX)*

DuoResp Spiromax is a new lower cost combination inhaled corticosteroid (ICS)/ long-acting beta agonist (LABA) formulation containing budesonide and formoterol in a breath actuated dry powder inhaler. It is being marketed by Teva as a lower cost alternative to the *Symbicort Turbohaler* for the treatment of asthma and chronic obstructive pulmonary disease (COPD) in adults. The *Spiromax* device uses new cyclone technology to enable delivery of the active substance to the lungs and is claimed to be easy to use.

The efficacy of both budesonide and formoterol as single agents and in combination is well established with the *Symbicort Turbohaler* already widely prescribed. Having reviewed the comparative trials, PACEF were convinced that they demonstrate bioequivalence between:

- *DuoResp Spiromax* 160/4.5microgram and *Symbicort Turbohaler* 200/6microgram
- *DuoResp Spiromax* 320/9microgram and *Symbicort Turbohaler* 400/12microgram

There was insufficient data presented to the marketing authority to demonstate that the lower strength *DuoResp Spiromax* 80/4.5microgram inhaler was bioequivalent to *Symbicort Turbohaler* 100/6microgram. As a result of this, *DuoResp Spiromax* 80/4.5microgram has not been given a marketing authorisation and *DuoResp Spiromax* inhalers are only licensed for use in those aged 18 years and over. Conversely, *Symbicort Turbohalers* 200/6 and 400/12 are licensed for use in children aged 12 years and over.

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Since the launch of the *Symbicort Turbohaler*, there has been a change in the requirement for labelling of inhaled products with a new stipulation that the strength of each component must be expressed in terms of the delivered dose rather than the metered dose. *DuoResp Spiromax* is the first product range to have to comply with these new requirements. The table below illustrates the equivalence of the *DuoResp Spiromax* and *Symbicort Turbohaler* products in terms of both delivered dose and metered dose, although PACEF acknowledge that the change from metered dose to delivered dose may cause confusion:

Product	Delivered dose	Metered dose
DuoResp Spiromax	160/4.5	200/6
Symbicort Turbohaler	160/4.5	200/6
DuoResp Spiromax	320/9	400/12
Symbicort Turbohaler	320/9	400/12

The table below summarizes the range of ICS/LABA combination products currently available on the NHS alongside their licensed indications. Formulary approved products are highlighted in bold:

Product	LABA	ICS	Licensed indications	Age range
Fostair	**Beclometasone dipropionate**	**Formoterol fumarate**	**Asthma maintenance and reliever COPD**	**Adults aged over 18 years**
Symbicort	**Budesonide**	**Formotrerol fumarate dihydrate**	**Asthma maintenance and reliever COPD**	**Adults & children aged over 6 years.***
Flutiform	**Fluticasone propionate**	**Formoterol fumarate dihydrate**	**Asthma prophylaxis**	**Adults and children aged over 12 years.**
Relvar Elipta	Fluticasone furoate	Vilanterol	Asthma prophylaxis COPD	Adults and children aged over 12 years.
Seretide	**Fluticasone propionate**	**Salmeterol**	**Asthma prophylaxis COPD ****	**Adults and children aged over 5 years*****

* applies to lower strength 100/6 formulation: age limit raised to children aged over 12 years for higher 200/6 & 400/12 strengths.
** applies to 500 strength *Accuhaler* only.
*** applies to lower strength *Seretide 100 Accuhaler*; age limit raised to 12 years for higher strengths.

A cost comparison between equivalent strengths of *DuoResp Spiromax* and *Symbicort Turbohaler* reveals that *DuoResp Spiromax* offers equivalent treatment for more than 20% less:

Drug	Daily dose	Cost (£) (doses)
DuoResp Spiromax 160mcg/4.5mcg	1-2 puffs twice daily	£29.97(120)
Symbicort Turbohaler 200/6	1-2 puffs twice daily	£38.00 (120)
DuoResp Spiromax 320mcg/9mcg	1-2 puffs twice daily	£29.97 (60)
Symbicort Turbohaler 400/12	1-2 puffs twice daily	£38.00 (60)

PACEF Recommendation:

PACEF acknowledge that *DuoResp Spiromax* 160mcg/4.5mcg and 320mcg/9mcg inhalers offer an equivalent lower cost alternative to *Symbicort Turbohaler* at the 200mcg/6mcg and 400mcg/12mcg doses respectively. As a result of this both strengths of *DuoResp Spiromax* are designated GREEN and approved for inclusion in the *Lincolnshire Joint Formulary*. Prescribers should consider *DuoResp Spiromax* in new patients aged 18 and over where combination ICS/LABA therapy is indicated for the treatment of asthma or COPD. Open generic prescriptions for *DuoResp Spiromax* 160/4.5mcg and 320/9mcg inhalers and *Symbicort Turbohaler* 200/6mcg and 400/12mcg are not recommended as both products can be supplied interchangeably unless the brand is specified. This could result in the patient inadvertently receiving an inhaler that they have not been trained to use.

RAPID DRUG ASSESSMENT: *BECLOMETASONE/ FORMOTEROL DRY POWDER 100MICROGRAM/ 6MICROGRAM (FOSTAIR NEXTHALER)*

Beclometasone/formoterol 100/6microgram dry powder inhaler (*Fostair NEXThaler*) holds a marketing authorisation for the treatment of asthma where use of a combination product (ICS/LABA) is considered appropriate (i.e. the patient is not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short-acting beta2-agonist or the patient is already adequately controlled on both inhaled corticosteroids and long-acting beta2-agonists). Within this context the Fostair NEXThaler is licensed for use in adult patients only.

PACEF have already approved the *Fostair* metered dose inhaler (beclometasone/formoterol 100/6microgram) for use. The MDI formulation has a wider marketing authorisation and is also licensed for the symptomatic treatment of patients with severe COPD (FEV1 < 50% predicted normal) and a history of repeated exacerbations, who have significant symptoms despite regular therapy with long-acting bronchodilators.

The *Fostair NEXThaler* is priced the same as the MDI at equivalent dosage and has the advantage that it does not require cool storage before dispensing and has an expiry date of 6 months after opening compared to 5 months for the MDI.

PACEF Recommendation:
Beclometasone/formoterol 100/6microgram dry powder inhaler (*Fostair NEXThaler*) is designated GREEN and approved for inclusion in the *Lincolnshire Joint Formulary* within licensed indications (i.e. where combination ICS/LABA therapy is indicated for the treatment of asthma in adults). It is identically priced to the *Fostair* MDI which holds a wider marketing authorisation including the treatment of COPD.

RAPID DRUG ASSESSMENT: *CANAGLIFLOZIN/METFORMIN 50MG/850MG AND 50MG/1000MG TABLETS (VOKANAMET)*

Canagliflozin 100mg and 300mg tablets (*Invokana*) has been approved by NICE for use as part of dual therapy, triple therapy or in combination with insulin in the treatment of type 2 diabetes. PACEF have evaluated both of the SGLT2 inhibitors, canagliflozin and dapagliflozin, and both are approved for inclusion in the *Lincolnshire Joint Formulary* with dapagliflozin preferred on the grounds of cost. Canagliflozin should be reserved for use only when triple therapy requiring a SGLT-2 inhibitor component is indicated or when the patient has predicted deteriorating renal function (see *PACE Bulletins* Vol 7 No 14 and Vol 8 No 14).

Canagliflozin has now been launched by Janssen as a combination product with metformin (known as *Vokanamet*); it is available in two strengths - canagliflozin 50mg/ metformin 850mg and 50mg/1000mg. Combination products can help to improve patient adherence with therapy by reducing the tablet burden. A cost comparison confirms that the combination product is no more expensive than canagliflozin 100mg and 300mg tablets prescribed alone.

PACEF Recommendation:
PACEF have previously acknowledged that canagliflozin at the 100mg dose has the advantage over dapagliflozin that it can be used in patients with predicted deteriorating renal function (between 45 and 60ml/min). However, as metformin is contra-indicated in this patient group, *Vokanamet* cannot be approved for this indication. As a result of this canagliflozin and metformin tablets 50mg/850mg and 50mg/1000mg (*Vokanamet*) are approved for use only when triple therapy requiring a SGLT-2 inhibitor component is indicated and renal function is considered satisfactory *Vokanamet* tablets are designated GREEN for this limited indication and approved for inclusion in the *Lincolnshire Joint Formulary*.

RAPID DEVICE ASSESSMENT: *FREESTYLE LIBRE GLUCOSE MONITORING SYSTEM*

The *Freestyle Libre Glucose Monitoring System* has just been launched by Abbott Diabetes Care for the measurement of interstitial fluid glucose levels in adults aged 18 years and older with diabetes. The system works by using a sensor which is placed on the back of the upper arm and a small thin filament which is inserted just below the skin into the interstitial fluid. The sensor is designed to remain in place for two weeks and in that time it records a glucose reading every 15 minutes. The sensor stores data for up to eight hours. The readings are downloaded from the sensor by scanning the device with the result reader which has the appearance of a normal blood glucose meter. Among the options for data presentation are:

- A daily graph showing a trend line and when results fall within the target range. This information can be viewed at 7, 14, 30 or 90 days.
- An average glucose reading over a period of time.
- The time spent at target as well as time above and below target.
- The number of low blood glucose events over a time period of 7, 14, 30 or 90 days.

Abbott are promoting this device as a lower cost alternative to continuous glucose meters. It may also have a future role in patients who need to test frequently or those who are needle or lancet phobic.

The reader and sensors are not currently available on the NHS and are not prescribable. However, the product can be purchased by members of the public direct from the company website. Samples of sensors and readers have also been supplied to virtually all secondary care trusts.

PACEF Recommendation:
While the *Freestyle Libre Glucose Monitoring System* may represent a significant innovation in the monitoring of blood glucose in adults with diabetes, it is not currently available through the *Drug Tariff* and cannot be prescribed on the NHS. The product is designated RED-RED and not approved for inclusion on the *Lincolnshire Joint Formulary.* This decision will be subject to review should the *Drug Tariff* status of the product change.

NEW DEVICE ASSESSMENT: *OTOVENT AUTOINFLATION DEVICE FOR GLUE EAR*

The *Otovent* autoinflation device is promoted to treat 'glue ear' or otitis media with effusion (OME). In OME, the middle ear becomes filled with serous or mucoid (but not purulent) fluid causing deafness. A high proportion of cases of OME (around 50%) remit spontaneously within 3 months and over 95% within a year. It occurs typically in pre-school children, becoming less common after the age of 6.

The Otovent device consists of a nasal tube and 5 latex balloons. The nasal tube fits into the neck of the balloon at one end while the other end is pressed to one nostril while the other nostril is closed. The child then blows into the device, inflating the balloon and increasing pressure in the nasopharynx. It is recommended that the patient repeats this process two to three times a day. Each balloon can be used for 3 to 4 days.

PACEF reviewed the results of a Cochrane systematic review published in 2013 which included 8 trials involving 702 patients. The authors concluded that, in the absence of adverse effects, it is reasonable to consider autoinflation whilst awaiting natural resolution of OME. NICE have also advised that autoinflation may be considered during the active observation period in children with OME who are likely to cooperate with the procedure.

Otovent is available in the *Drug Tariff* at a price of £4.90 per pack (including 5 balloons sufficient for 2 to 3 weeks treatment).

PACEF Recommendation:
The *Otovent* autoinflation device is designated GREEN for the treatment of otitis media with effusion in young children and approved for inclusion in the *Lincolnshire Joint Formulary*. It should be prescribed for a maximum period of two weeks' only

Reference:
Trent Medicines Information Service: *Prescribable Devices – Autoinflation device (Otovent)* (November 2014)

NICE TECHNOLOGY APPRAISAL 317: *PRASUGREL WITH PERCUTANEOUS CORONARY INTERVENTION FOR TREATING ACUTE CORONARY SYNDROME* (JULY 2014)

Key points

Prasugrel 10 mg in combination with aspirin is recommended as an option within its marketing authorisation, that is, for preventing atherothrombotic events in adults with acute coronary syndrome (unstable angina [UA], non-ST segment elevation myocardial infarction [NSTEMI] or ST segment elevation myocardial infarction [STEMI]) having primary or delayed percutaneous coronary intervention.

Prasugrel (*Efient*) is an oral inhibitor of platelet activation and aggregation. It works by irreversible binding of its active metabolite to the P2Y12 class of adenosine diphosphate receptors on platelets. It has a marketing authorisation when co-administered with aspirin for the prevention of atherosclerotic events in adults with ACS undergoing primary or delayed percutaneous coronary intervention.

PACEF Recommendation:
Prasugrel 5mg and 10mg tablets (*Efient*) are currently designated AMBER without shared care. Prasugrel should only be prescribed by a GP following initiation by a cardiologist. The use of prasugrel and ticagrelor is detailed in *PACE Bulletin* Vol 7 No 9 (June 2013) *Guidance on the prescribing of aspirin, clopidogrel, prasugrel and ticagrelor for the prevention of atherothrombotic events in patients with acute coronary syndromes*. This guidance remains current, but is under review.

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY: *DRUG SAFETY UPDATE* (OCTOBER 2014)

INTERFERON-BETA: RISK OF THROMBOTIC MICROANGIOPATHY AND RISK OF NEPHROTIC SYNDROME

Interferon beta-1a and interferon beta-1b are immunomodulatory drugs indicated for the treatment of remitting-relapsing multiple sclerosis. There have been reports of thrombotic microangiopathy and nephrotic syndrome linked to interferon beta treatment. A European review was triggered by reports of thrombotic microangiopathy and nephrotic syndrome associated with interferon beta treatment. The review suggested that there may be an association between interferon beta treatment and thrombotic microangiopathy and between interferon beta treatment and nephrotic syndrome.

Healthcare professionals should be vigilant for the early signs of these conditions and treat promptly if they occur.

Clinical features of **thrombotic microangiopathy** include:

- thrombocytopenia
- new onset hypertension
- fever
- central nervous system symptoms (e.g., confusion and paresis)
- impaired renal function

Clinical features of **nephrotic syndrome** include: oedema, proteinuria, and impaired renal function especially in patients at high risk of renal disease.

PACEF comment
Interferon beta preparations (e.g. *Avonex*, *Rebif*, *Betaferon* and *Extavia*) are not currently approved for use in Lincolnshire through the *Joint Formulary*: designation is RED-RED. However, there are some neighbouring acute Trusts where these products are in use and may be prescribed for Lincolnshire patients. Whilst prescribing remains the responsibility of secondary care, patients may contact their GP for advice when becoming unwell.

DEXAMETHASONE 4MG/ML INJECTION (ORGANON LABORATORIES LIMITED): REFORMULATION WITH CHANGES IN NAME, CONCENTRATION, STORAGE CONDITIONS AND PRESENTATION

From October 2014, dexamethasone 4 mg/ml injection (Organon Laboratories Limited) will be replaced with a new formulation called dexamethasone 3.8 mg/ml solution for injection (Aspen Pharma Trading Limited). As a result, the storage conditions, presentation, and packaging of the product will change.

Dexamethasone 4 mg/ml injection is indicated for general and local glucocorticoid injection therapy (e.g. joint inflammation) and for any acute condition in which intravenous glucocorticoids may be life-saving (e.g. severe asthma, severe allergic reactions, and cerebral oedema). The 4 mg/ml injection has been reformulated to harmonise formulations available across the European Union and to improve the manufacturing process. Aspen Pharma Trading Limited has taken over the licence from Organon Laboratories Ltd. All orders placed from October 2014 onwards will be supplied with the new formulation called dexamethasone 3.8 mg/ml solution for injection (PL 39699/0060; Aspen Pharma Trading Limited). The old formulation, dexamethasone 4 mg/ml injection (PL 00065/0106R; Organon Laboratories Limited), will no longer be available.

The reformulation will result in the following changes:

- Concentration: the concentration of the active substance in the reformulated product will be 3.8 mg/ml dexamethasone, which is equivalent to 5.0 mg/ml of dexamethasone sodium phosphate. The dose recommendations have not changed. However, due to the change in concentration, the dilutions will need to be amended. A dosing card has been developed to help administer the reformulated product.
- Storage conditions: the reformulated product must be stored in the refrigerator at 2 to 8°C to reduce the potential for particle formation. The old formulation is associated with a very low risk of particle transfer to patients; no serious safety concerns are associated with the use of the old formulation.
- Presentation: the reformulated product will be available in a glass vial containing 1 ml of solution for injection.
- Packaging: the carton of the reformulated product will be clearly marked “New formulation”, “Change in concentration”, and “Store in a refrigerator”.

DRUGS AND DRIVING: CLARIFICATION FOR WALES, SCOTLAND AND NORTHERN IRELAND

The MHRA *Drug Safety Update* (July 2014) reported on a new traffic offence of driving with certain controlled drugs above specified limits in the blood. This new offence will be enforceable in England, Wales, and Scotland, but not Northern Ireland where the introduction of a similar offence is still under consideration.
The new offence does not replace any existing offences of driving whilst impaired by drugs, including licensed medicines. The new regulations are expected to come into force in March 2015.

EUROPEAN MEDICINES AGENCY: *PRAC RECOMMENDS STRENGTHENING THE RESTRICTIONS ON THE USE OF VALPROATE IN WOMEN AND GIRLS*

The EMA's Pharmacovigilance and Risk Assessment Committee (PRAC) has recommended that restrictions on the use of sodium valproate should be strengthened due to the risk of malformations and developmental problems in children exposed to valproate in the womb. It is recommended that:

- Valproate should not be used to treat epilepsy or bipolar disorder in girls or in women who are pregnant or who can become pregnant, unless other treatments are ineffective or not tolerated.
- Women for whom valproate is the only option after trying other treatments should use effective contraception and treatment should be started and supervised by a doctor experienced in treating these conditions.
- Women who have been prescribed valproate should not stop taking their medicine without first consulting their doctor.

Acknowledgements

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