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 18 **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 3).**
- **Once weekly exenatide 2mg sustained release suspension for injection in a pre-filled pen (*Bydureon*) is designated GREEN subject to a second line role after first line twice daily exenatide (*Byetta*) or once daily liraglutide (*Victoza*) (see page 3).**
- **Dulaglutide pre-filled pen (*Trulicity*) is approved for use as an alternative to once weekly exenatide (*Bydureon*) in patients intolerant to exenatide or unable to use the *Bydureon* device. Designated GREEN subject to criteria (see page 5).**
- **Meningococcal group B vaccine (*Bexsero*) is now approved for use within the context of the recently launched national vaccination programme for infants aged from two months. Designation GREEN. Preventative paracetamol should be used post-meningococcal group B vaccination to reduce the incidence of fever at 2 months and 4 months (see pages 6 and 7).**
- **Meningococcal ACWY vaccines (*Menveo* and *Nimenrix*) are designated GREEN and approved for use through the *Lincolnshire Joint Formulary* within the context of the national meningitis vaccination programme (see page 7).**
- **Prescribers are alerted to the escalating price of fusidic acid 1% modified-release eye drops. Since the discontinuation of *Fucithalmic* in August 2014 the price has continued to rise and has now reached £29.06 for 5g (*Drug Tariff*, November 2015). Prescribers are urged to ensure that, where antibiotic treatment of conjunctivitis is considered necessary, chloramphenicol 0.5% eye drops are preferred first line (£1.53 for 10ml) (see page 8).**
- **The MHRA have highlighted a low level risk of subacute cutaneous lupus erythematosus in patients taking proton pump inhibitors (PPIs) (see page 9).**

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SUMMARY OF PACEF DECISIONS: *SEPTEMBER 2015 UPDATE*

Drug	**Indication(s)**	**Traffic Light and *Joint Formulary* Status**
Aflibercept 40mg/ml solution for injection (*Eylea*) (Bayer)	For the treatment of visual impairment due to diabetic macular oedema	RED Approved for inclusion in the *Lincolnshire Joint Formulary* subject to specific NICE treatment criteria:
Dexamethasone 700 microgram intravitreal implant (*Ozurdex*) (Allergan)	For the treatment of visual impairment due to diabetic macular oedema (DME) in patients who are who are pseudophakic or who are considered insufficiently responsive to, or unsuitable for non-corticosteroid therapy.	RED Approved for inclusion in the *Lincolnshire Joint Formulary* subject to specific NICE treatment criteria:
Dulaglutide 750 microgram/0.5ml and 1.5mg/0.5ml in a pre-filled pen (*Trulicity*) (Lilly)	For the treatment of type 2 diabetes mellitus inadequately controlled by diet and exercise: as monotherapy when metformin is inappropriate, or with other hypoglycaemics including insulin, when these alone are inadequate.	GREEN Approved for inclusion in the *Lincolnshire Joint Formulary* subject to specific criteria: (1) it should only be initiated by specialist diabetes services, GPs with a special interest in diabetes or GPs with a high level of experience in the treatment of diabetes; (2) it should be reserved for those who are appropriate for weekly treatment, intolerant to once weekly exenatide or unable to use the *Bydureon* device.
Exenatide 2mg powder and solvent for sustained release suspension for injection pre-filled pen (*Bydureon*) (AstraZeneca)	For use as an adjunct to existing therapy in type 2 diabetes where glycaemic control is inadequate used either as dual therapy with metformin, a sulfonylurea or a glitazone or as triple therapy with metformin and a sulfonylurea or a glitazone.	GREEN Approved for inclusion in the *Lincolnshire Joint Formulary.* Subject to a second line role after first line twice daily exenatide (*Byetta*) or once daily liraglutide (*Victoza*)
Exenatide 2mg powder and solvent for sustained release suspension for injection pre-filled syringe (*Bydureon*) (AstraZeneca)	For use as an adjunct to existing therapy in type 2 diabetes where glycaemic control is inadequate used either as dual therapy with metformin, a sulfonylurea or a glitazone or as triple therapy with metformin and a sulfonylurea or a glitazone.	GREEN Included in the *Lincolnshire Joint Formulary.* Subject to a second line role after first line twice daily exenatide (*Byetta*) or once daily liraglutide (*Victoza*)
Meningococcal group ACWY conjugate vaccine (*Menveo*) (Novartis Vaccines)	For active immunization of children (from 2 years of age), adolescents and adults at risk of exposure to *Neisseria meningitidis* groups A, C, W135 and Y, to prevent invasive disease.	GREEN Included in the *Lincolnshire Joint Formulary.* Should be prescribed on the NHS as part of the national vaccination programme for adolescents. May also be indicated in certain high risk groups.
Meningococcal group ACWY conjugate vaccine (*Nimenrix*) (GlaxoSmithKline)	For active immunisation of individuals from the age of 12 months and above against invasive meningococcal diseases caused by *Neisseria meningitidis* group A, C, W-135 and Y.	GREEN Included in the *Lincolnshire Joint Formulary.* Should be prescribed on the NHS as part of the national vaccination programme for adolescents. May also be indicated in certain high risk groups.
Meningococcal group B vaccine (*Bexsero*) (Novartis Vaccines)	For active immunisation against invasive disease cause by *Neisseria meningitidis* group B.	GREEN Included in the *Lincolnshire Joint Formulary.* Should only be prescribed on the

		NHS as part of the national vaccination programme for infants aged from 2 months and for the management of outbreaks of invasive meningococcal disease where the vaccine may be prescribed for close contacts of cases following a request from a Public Health England consultant or nurse. May also be indicated in the same high risk groups that are currently offered ACWY conjugate vaccine.
Secukinumab 150mg injection (*Cosentyx*) (Novartis)	For the treatment of moderate to severe plaque psoriasis in adults	RED Approved for inclusion in the *Lincolnshire Joint Formulary* subject to specific NICE treatment criteria:

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

NEW FORMULATION ASSESSMENT: *EXENATIDE 2MG SUSTAINED RELEASE SUSPENSION FOR INJECTION IN A PRE-FILLED PEN (BYDUREON)*

Exenatide 2mg sustained release suspension for injection in a pre-filled pen (*Bydureon*) is designated GREEN subject to a second line role after first line twice daily exenatide (*Byetta*) or once daily liraglutide (*Victoza*).

Exenatide 2mg sustained release suspension (*Bydureon*) is indicated as an adjunct to existing therapy in type 2 diabetes (T2DM) where glycaemic control is inadequate used either as dual therapy with metformin , a sulfonylurea or a glitazone or as triple therapy with metformin and a sulfonylurea or a glitazone. Exenatide 2mg vial and syringe (*Bydureon*) has been previously evaluated by PACEF, approved for inclusion in the *Lincolnshire Joint Formulary* and designated GREEN. The product is recommended as a second line glucagon-like peptide-1 (GLP-1) agonist after first line twice daily exenatide (*Byetta*) or once

daily liraglutide (*Victoza*) 1.2mg. PACEF have now evaluated the new exenatide 2mg pre-filled pen presentation of *Bydureon.*

Exenatide 2mg (*Bydureon*) pre-filled pen is a once weekly injection administered on the same day of each week at any time of day, with or without meals. The new pre-filled pen does not require the complication of reconstitution associated with the original *Bydureon* vial and syringe presentation. This means that some patients who were unable to use *Bydureon* previously may now be able to prepare and inject using the pre-filled pen. As part of the preparation to use the pen, the powder and solvent need to be thoroughly mixed prior to injection of the dose. This involves tapping the pen against the palm of your hand up to 80 times or more in order to ensure that a uniformly cloudy suspension is formed. It may not be possible for patients with manual dexterity problems to prepare the injection for self-medication.

Both of the *Bydureon* products are priced comparably with the alternative once weekly GLP-1 agonist preparation, dulaglutide (*Trulicity*).

GLP-1 Receptor Agonist	Dose	Cost (£) per 28 days	Additional needle cost per 28 days
Dulaglutide 750 microgram/0.5ml pre-filled pen (*Trulicity*) (Lilly)	0.75mg once weekly	£73.25	£0.00
Dulaglutide 1.5mg/0.5ml pre-filled pen (*Trulicity*) (Lilly)	1.5mg once weekly	£73.25	£0.00
Exenatide 5 microgram pre-filled pen (*Byetta*) (AstraZeneca)	5 microgram twice daily	£63.69	£3.64-£16.80
Exenatide 10 microgram pre-filled pen (*Byetta*) (AstraZeneca)	10 microgram twice daily	£63.69	£3.64-£16.80
Exenatide 2mg powder and solvent for sustained release suspension for injection pre-filled syringe (*Bydureon*) (AstraZeneca)	2mg once weekly	£73.36	£0.00
Exenatide 2mg powder and solvent for sustained release suspension for injection pre-filled pen (*Bydureon*) (AstraZeneca)	2mg once weekly	£73.36	£0.00
Liraglutide 6mg/ml solution for injection pre-filled pen (*Victoza*) (Novo Nordisk)	1.2mg once daily	£73.25	£2.52-£6.24
Liraglutide 6mg/ml solution for injection pre-filled pen (*Victoza*) (Novo Nordisk)	1.8mg once daily	£109.87	£2.52-£6.24
Lixisenatide 20 microgram pre-filled pen (*Lyxumia*) (Sanofi)	20mcg daily	£57.93	£0.00

PACEF Recommendation

Exenatide 2mg sustained release suspension for injection in a pre-filled syringe (*Bydureon*) is already available through the *Lincolnshire Joint Formulary* as a second line GLP-1 agonist after first line twice daily exenatide (*Byetta*) or once daily liraglutide (*Victoza*) 1.2mg. The new pre-filled pen formulation of *Bydureon* is the same price, more convenient for the patient and is likely to replace the existing presentation soon. As a result of this, exenatide 2mg sustained release suspension for injection in a pre-filled pen (*Bydureon*) is designated GREEN and approved for use through the *Lincolnshire Joint Formulary* subject to a second line role as defined above.

NEW DRUG ASSESSMENT: *DULAGLUTIDE SOLUTION FOR INJECTION (TRULICITY)*

Dulaglutide pre-filled pen (*Trulicity*) is approved for use as an alternative to once weekly exenatide (*Bydureon*) in patients intolerant to exenatide or unable to use the *Bydureon* device.

Dulaglutide 750 microgram/0.5ml and 1.5mg/0.5ml in a pre-filled pen (*Trulicity*) holds a marketing authorisation for the treatment of type 2 diabetes mellitus (T2DM) inadequately controlled by diet and exercise: as monotherapy when metformin is inappropriate, or with other hypoglycaemics including insulin, when these alone are inadequate.

PACEF reviewed the published clinical trial programme (AWARD trials 1 to 6) which assessed the efficacy and safety of dulaglutide against exenatide 10 microgram (AWARD 1), insulin glargine (AWARD 2 and 4), metformin 1000mg (AWARD 3), sitagliptin 100mg (AWARD 4) and liraglutide 1.8mg (AWARD 6) in patients with type 2 diabetes (T2DM) who were inadequately controlled on their current therapy. The AWARD trials also investigated the use of dulaglutide as monotherapy (AWARD 3), dual therapy in combination with metformin (AWARD 5 and 6), triple therapy with metformin and glimepiride (AWARD 2), triple therapy with metformin and pioglitazone (AWARD 1) and with prandial insulin lispro (AWARD 4). The primary outcome measure in these trials was reduction in HbA1c, a disease orientated or surrogate outcome. As with the other GLP-1 agonists, there are limited data relating to patient-orientated outcomes, such as rates of macrovascular or microvascular events. A further study investigating whether dulaglutide can reduce major cardiovascular events in T2DM is expected to report in 2019.

All six of the trials demonstrated at least non-inferiority of dulaglutide against all of the comparators used. Despite the breadth of trial data at launch, there is still little comparative data between dulaglutide and other GLP-1 agonists. In the AWARD 1 study dulaglutide was compared with exenatide 10mcg twice daily in one arm of the trial. The results demonstrated that dulaglutide was statistically superior to twice daily exenatide when used in combination with pioglitazone and metformin. There is currently no head to head data versus weekly exenatide, the direct competitor to dulaglutide in the market place. Dulaglutide has also been shown to be statistically non-inferior to liraglutide 1.8mg daily (AWARD 6), a dose of liraglutide not approved by NICE.

Overall, the safety profile of dulaglutide is consistent with what has previously been seen with other GLP-1 agonists. The most common side effects are nausea, diarrhoea, vomiting and dyspepsia. Incidences of hypoglycaemia were common (≥1/100) when dulaglutide was used as monotherapy or in combination with metformin and pioglitazone and very common (≥1/10) when used with prandial insulin, metformin (dulaglutide 1.5mg only) or metformin plus glimepiride. The product SPC recommends a dose reduction for people also taking a sulfonylurea or insulin in order to reduce the risk of hypoglycaemia.

Dulaglutide, liraglutide, lixisenatide and exenatide twice daily are all licensed for use with insulin while exenatide once weekly is not. There are also differences between GLP-1 agonists in terms of use in renal impairment.

GLP-1 Receptor Agonist	Use on renal impairment
Dulaglutide 750 microgram/0.5ml and 1.5mg/0.5ml pre-filled pen (*Trulicity*) (Lilly)	No dosage adjustment is required in patients with mild or moderate renal impairment. There is very limited experience in patients with severe renal impairment (eGFR < 30 ml/min/1.73 m^2) or end stage renal disease, therefore dulaglutide is not recommended in this population.
Exenatide 5 and 10 microgram pre-filled pen (*Byetta*) (AstraZeneca)	No dosage adjustment of exenatide (*Byetta*) is necessary in patients with mild renal impairment (creatinine clearance 50 to 80 ml/min). In patients with moderate renal impairment (creatinine

	clearance 30 to 50 ml/min), dose escalation from 5 mcg to 10 mcg should proceed conservatively. Exenatide (*Byetta*) is not recommended for use in patients with end-stage renal disease or severe renal impairment (creatinine clearance <30 ml/min).
Exenatide 2mg powder and solvent for sustained release suspension for injection pre-filled syringe and pre-filled pen (*Bydureon*) (AstraZeneca)	No dose adjustment is necessary for patients with mild renal impairment (creatinine clearance 50 to 80 ml/min). Clinical experience in patients with moderate renal impairment (creatinine clearance 30 to 50 ml/min) is very limited; exenatide (*Bydureon*) is not recommended in these patients. Exenatide (*Bydureon*) is not recommended for use in patients with end-stage renal disease or severe renal impairment (creatinine clearance < 30 ml/min).
Liraglutide 6mg/ml solution for injection pre-filled pen (*Victoza*) (Novo Nordisk)	No dose adjustment is required for patients with mild or moderate renal impairment (creatinine clearance 60 to 90 ml/min and 30 to 59 ml/min, respectively). There is no therapeutic experience in patients with severe renal impairment (creatinine clearance below 30 ml/min). Liraglutide (*Victoza*) cannot currently be recommended for use in patients with severe renal impairment including patients with end-stage renal disease.
Lixisenatide 20 microgram pre-filled pen (*Lyxumia*) (Sanofi)	No dose adjustment is required for patients with mild renal impairment (creatinine clearance: 50 to 80 ml/min). There is limited therapeutic experience in patients with moderate renal impairment (creatinine clearance: 30 to 50 ml/min) and lixisenatide (*Lyxumia*) should be used with caution in this population. There is no therapeutic experience in patients with severe renal impairment (creatinine clearance less than 30 ml/min) or end-stage renal disease and therefore, it is not recommended to use lixisenatide (Lyxumia) in these populations.

The cost comparison linked to the evaluation of exenatide 2mg pre-filled pen (*Bydureon*) (see above) reveals that once weekly dulaglutide is comparably priced to once weekly exenatide.

PACEF Recommendation

PACEF recognise the convenience of the dulaglutide pre-filled pen as it is fixed dose, single-use, once weekly and ready to use without the reconstitution and suspension required before administration of once weekly exenatide (*Bydureon*). However, the lack of direct comparative data against once weekly exenatide means that the product cannot be advocated as a preferred alternative at this stage. As a result of this, dulaglutide 750 microgram/0.5ml and 1.5mg/0.5ml pre-filled pen (*Trulicity*) is designated GREEN and approved for use through the *Lincolnshire Joint Formulary* subject to the following criteria; (1) it should only be initiated by specialist diabetes services, GPs with a special interest in diabetes or GPs with a high level of experience in the treatment of diabetes; (2) it should be reserved for those who are appropriate for weekly treatment and intolerant to once weekly exenatide or unable to use the *Bydureon* device. Dulaglutide once weekly is licensed for use with insulin while exenatide once weekly is not.

CHANGE IN FORMULARY STATUS FOR MENINGOCOCCAL GROUP B VACCINE (*BEXSERO*)

Meningococcal group B vaccine (*Bexsero*) is now approved for use within the context of the recently launched national vaccination programme for infants aged from two months.

As you will be aware, over the summer, Public Health England published details of the addition to the national vaccination programme of meningococcal group B vaccine for infants aged from two months. As a result of this, from September 1st 2015 all infants born on or

after 1st July 2015 are eligible for meningococcal B vaccination administered together with other primary immunisations at 2 months, 4 months and 12 months.

PACEF Recommendation

As a result of this, meningococcal group B vaccine (*Bexsero*) is reclassified as GREEN and approved for inclusion in the *Lincolnshire Joint Formulary*. It should only be prescribed on the NHS as part of the national vaccination programme for infants aged from 2 months and for the management of outbreaks of invasive meningococcal disease where the vaccine may be prescribed for close contacts of cases following a request from a Public Health England consultant or nurse. It may also be indicated in the same high risk groups that are currently offered ACWY conjugate vaccine.

Reference: Public Health England, *Immunisation against meningococcal B disease for infants aged from two months: Information for healthcare professionals* (July 2015)

USING PARACETAMOL TO PREVENT AND TREAT FEVER AFTER MENINGOCOCCAL GROUP B VACCINATION

Preventative paracetamol should be used post- meningococcal group B vaccination to reduce the incidence of fever at 2 months and 4 months.

In conjunction with materials linked to the meninogoccal group B vaccination programme, Public Health England have also produced a useful information sheet entitled *Using paracetamol to prevent and treat fever after MenB vaccination* (July 2015). When meningococcal group B vaccine is administered with other routine vaccines at two and four months, the incidence of fever in the vaccinated children is more than 50%. Fever tends to peak around six hours after vaccination and is nearly always resolved within two days. However, giving a total of three 2.5ml doses of paracetamol suspension 120mg in 5ml spaced 4 to 6 hours apart after vaccination can reduce the incidence of fever to 20% and reduce the severity of fever in those that become feverish. The recommended dosage schedule is as follows:

Age of baby	Up to 6 months (usually at 2 and 4 months)
Dose 1	One 2.5ml (60mg) dose as soon as possible after vaccination
Dose 2	One 2.5ml (60mg) dose 4 to 6 hours after the first dose.
Dose 3	One 2.5ml (60mg) dose 4 to 6 hours after the second dose.

Paracetamol is not routinely needed after the Men B booster dose given at 12 months of age. By this age, the baby's risk of fever is the same as after other vaccines.

Reference: Public Health England, *Using paracetamol to prevent and treat fever after MenB vaccination* (July 2015).

INTRODUCTION OF A MENINGOCOCCAL ACWY IMMUNISATION PROGRAMME FOR ADOLESCENTS

Meningococcal ACWY vaccines (*Menveo* and *Nimenrix*) are designated GREEN and approved for use through the *Lincolnshire Joint Formulary* within the context of the national meningitis vaccination programme.

In August 2015, Public Health England published details of a new vaccination programme aimed at protecting adolescents against meningococcal ACWY strains (see reference below).

PACEF Recommendation:
Following the introduction of this change to the national meningitis vaccination programme, meningococcal ACWY vaccines (*Menveo* and *Nimenrix*) are designated GREEN and approved for use through the *LincoInshire Joint Formulary* within the context of the national programme.

Reference: Public Health England, *Introduction of a meningococcal ACWY immunisation programme for adolescents* (August 2015)

INCREASING PRICE OF FUSIDIC ACID 1% MODIFIED RELEASE EYE DROPS

Prescribers are alerted to the escalating price of fusidic acid 1% modified-release eye drops. Since the discontinuation of *Fucithalmic* in August 2014 the price has continued to rise and has now reached £29.06 for 5g. Prescribers are urged to ensure that where antibiotic treatment of conjunctivitis is considered necessary, chloramphenicol 0.5% eye drops are always considered first line (£1.53 for 10ml).

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY, *DRUG SAFETY UPDATE* (AUGUST 2015)

SIMEPREVIR AND SOFOSBUVIR: RISK OF SEVERE BRADYCARDIA AND HEART BLOCK WHEN TAKEN WITH AMIODARONE

Simeprevir (*Olysio*) is a direct-acting antiviral medicine licensed to treat hepatitis C in combination with other medicines, including sofosbuvir (*Sovaldi*). Amiodarone is licensed to treat severe heart-rhythm disorders in patients not responding to other treatments or when other treatments cannot be used.

The MHRA and other EU medicines regulators have reviewed the cardiac safety of simeprevir, after a similar review of bradycardia events with sofosbuvir, daclatasvir, and ledipasvir with amiodarone use. Two EU cases of bradycardia after the use of simeprevir with sofosbuvir with concomitant amiodarone use were identified. The recommendations from the review are outlined below;

Avoid concomitant use of amiodarone with simeprevir (*Olysio*) and sofosbuvir (*Sovaldi)* combination therapy, unless other antiarrhythmics cannot be given.

When treating patients with both heart rhythm disorders and hepatitis C:

- closely monitor patients taking amiodarone if they start taking the combination simeprevir and sofosbuvir; sofosbuvir and daclatasvir; and the fixed-dose combination of sofosbuvir and ledipasvir (particularly during the first weeks of treatment).
- only start amiodarone in patients taking any of these antiviral combinations when other antiarrhythmics are not tolerated or contraindicated; monitor closely (particularly during the first weeks of treatment).
- monitor patients at high risk of bradyarrhythmia continuously for 48 hours in an appropriate clinical setting after starting concomitant amiodarone and antiviral treatment.
- monitor patients who have stopped amiodarone within the last few months and need to start taking any of these antiviral combinations—this is due to the long half-life of amiodarone.

- advise patients taking amiodarone with any of these antiviral combinations to watch out for signs and symptoms of bradycardia and heart block, and to get medical help urgently if they experience any of these symptoms:
    - shortness of breath
    - light-headedness
    - palpitations
    - fainting
- continue to report any suspected adverse reactions to any medicine on a Yellow Card.

PACEF Comment:
Simeprevir 150mg capsules (*Olysio*) are approved for use on the *Lincolnshire Joint Formulary* and designated RED (i.e. for hospital use only). Clinicians are advised to avoid concomitant use of amiodarone with ledipasvir-sofosbuvir 90mg/400mg capsules (*Harvoni*), and amiodarone with sofosbuvir 400mg tablets (*Sovaldi*) and daclatasvir 30mg and 60mg tablets (*Daklinza*), unless other antiarrhythmics are inappropriate.

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY, *DRUG SAFETY UPDATE* (SEPTEMBER 2015)

PROTON PUMP INHIBITORS: VERY LOW RISK OF SUBACUTE CUTANEOUS LUPUS ERYTHEMATOSUS

Proton pump inhibitors (PPIs) are associated with very infrequent cases of subacute cutaneous lupus erythematosus (SCLE), a non-scarring dermatosis that can develop in sun-

Considering the extensive use of PPIs, very few cases of SCLE have been reported. Nevertheless, evidence from clinical literature and from cases reported to medicines regulators including via the Yellow Card Scheme supports a causal association between PPIs and SCLE. Product information is being updated to include this advice for healthcare professionals and patients or carers.

The MHRA has made the following recommendations to healthcare professionals:

If a patient treated with a proton pump inhibitor (PPI) develops lesions—especially in sun-exposed areas of the skin—and it is accompanied by arthralgia:

- advise them to avoid exposing the skin to sunlight.
- consider subacute cutaneous lupus erythematosus (SCLE) as a possible diagnosis.
- consider stopping use of the PPI unless it is imperative for a serious acid-related condition; a patient who develops SCLE with a particular PPI may be at risk of the same reaction with another.
- in most cases, symptoms resolve on PPI withdrawal; topical or systemic steroids might be necessary for treatment of SCLE only if there are no signs of remission after a few weeks or months.
- report any suspected side effect with PPIs, or to any medicine, on a Yellow Card.

PSEUDOEPHEDRINE AND EPHEDRINE: UPDATE ON MANAGING RISK OF MISUSE IN THE UK

Implementation of measures to regulate sales, together with the additional voluntary actions overseen by the pharmacy profession, has made an important contribution to managing the risk of misuse of pseudoephedrine and ephedrine in the UK.

Since April 2008, the following sales restrictions have been in place to manage the risk of misuse of pseudoephedrine and ephedrine:

- it is illegal to sell or supply any product that contains more than 720 mg pseudoephedrine or 180 mg ephedrine without a prescription
- it is illegal to sell or supply a combination of products that between them add up to more than 720 mg pseudoephedrine or 180 mg ephedrine without a prescription
- it is illegal to sell or supply a product that contains pseudoephedrine and a product that contains ephedrine in one transaction

Furthermore, the Royal Pharmaceutical Society advises that the sale and supply of these products must be made by a pharmacist or suitably trained pharmacy staff under the supervision of a pharmacist

Between June 2013 and March 2015 there have been a few reports from pharmacies of suspicious behaviour, which have been addressed according to established procedures. There has been no evidence of methylamphetamine manufacture from these medicines. The evidence suggests that restrictions are continuing to help manage the risk of misuse.

PATIENT SAFETY ALERT: *ADDRESSING ANTIMICROBIAL RESISTANCE THROUGH IMPLEMENTATION OF AN ANTIMICROBIAL STEWARDSHIP PROGRAMME* (AUGUST 2015)

Antimicrobial resistance has risen alarmingly over the last 40 years and inappropriate use of antimicrobials is a key driver. From 2010 to 2013, total antibiotic prescribing in England increased by 6%, comprised of a 4% rise in general practice and a 12% increase in hospital inpatient prescribing.

This Patient Safety Alert aims to alert the whole primary care team to the importance of antimicrobial stewardship and to signpost a range of resources collectively known under the acronym TARGET (Treat Antibiotics Responsibly, Guidance, Education and Tools). This toolkit is available from http://www.rcgp.org.uk/clinical-and-research/target-antibiotics-toolkit.aspx

Examples of items included in the toolkit are: patient information leaflets, a self-assessment checklist and an audit pack.

NICE TECHNOLOGY APPRAISAL 346: *AFLIBERCEPT FOR TREATING DIABETIC MACULAR OEDEMA* (JULY 2015)

Key recommendations are as follows:

Aflibercept solution for injection (*Eylea*) is recommended as an option for treating visual impairment caused by diabetic macular oedema only if:

- the eye has a central retinal thickness of 400 micrometres or more at the start of treatment and

- the company provides aflibercept with the discount agreed in the patient access scheme.

Notes

Afibercept (*Eylea*) has a UK marketing authorisation for the treatment of

- neovascular (wet) age-related macular degeneration (AMD)
- visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO) ,
- visual impairment due to diabetic macular oedema (DME).

PACEF Recommendation:
Afibercept is already included on the *Lincolnshire Joint Formulary* as a RED hospital only drug for the treatment of wet age-related macular degeneration (subject to criteria). It is also listed as a RED drug approved as an option for the treatment of visual impairment caused by macular oedema secondary to central retinal vein occlusion (subject to criteria). It is now designated RED for the treatment of visual impairment caused by diabetic macular oedema and approved for use through the *Lincolnshire Joint Formulary* for this indication.

NICE TECHNOLOGY APPRAISAL 349: *DEXAMETHASONE INTRAVITREAL IMPLANT FOR TREATING DIABETIC MACULAR OEDEMA* (JULY 2015)

Key recommendation:

Dexamethasone intravitreal implant is recommended as an option for treating diabetic macular oedema only if:

- the implant is to be used in an eye with an intraocular (pseudophakic) lens **and**
- the diabetic macular oedema does not respond to non-corticosteroid treatment, or such treatment is unsuitable.

Notes

Dexamethasone intravitreal implant (*Ozurdex*) is indicated for the treatment of adult patients with:

- visual impairment due to diabetic macular oedema (DME) in patients who are pseudophakic or who are considered insufficiently responsive to, or unsuitable for non-corticosteroid therapy.
- macular oedema following either Branch Retinal Vein Occlusion (BRVO) or Central Retinal Vein Occlusion (CRVO).
- inflammation of the posterior segment of the eye presenting as non-infectious uveitis.

PACEF Recommendation:
Dexamethasone intravitreal implant (*Ozurdex*) is already on the *Lincolnshire Joint Formulary* as a RED hospital only drug for the treatment of macular oedema following central retinal vein occlusion (subject to NICE criteria). It is now designated RED and included on the *Formulary* for visual impairment due to diabetic macular oedema, subject to NICE criteria.

NICE TECHNOLOGY APPRAISAL 350: *SECUKINUMAB FOR TREATING MODERATE TO SEVERE PLAQUE PSORIASIS* (JULY 2015)

Key recommendations:

Secukinumab is recommended, within its marketing authorisation, as an option for treating adults with plaque psoriasis only when:

- the disease is severe, as defined by a total Psoriasis Area Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10
- the disease has failed to respond to standard systemic therapies, for example, ciclosporin, methotrexate and PUVA (psoralen and long-wave ultraviolet radiation), or these treatments are contraindicated or the person cannot tolerate them
- the company provides secukinumab with the discount agreed in the patient access scheme.

Secukinumab treatment should be stopped in people whose psoriasis has not responded adequately at 12 weeks. Further treatment cycles are not recommended in these people. An adequate response is defined as either:

- a 75% reduction in the PASI score from when treatment started (PASI 75) or
- a 50% reduction in the PASI score (PASI 50) and a 5-point reduction in DLQI from when treatment started.

Notes

Secukinumab 150mg injection (*Cosentyx*) is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

PACEF Recommendation:
Secukinumab 150mg injection (*Cosentyx*) is designated RED and approved for inclusion in the *Lincolnshire Joint Formulary* for the treatment of moderate to severe plaque psoriasis in adults subject to NICE criteria.

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