NHS Lincolnshire

Prescribing and Clinical Effectiveness Bulletin

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What's new this month:

- **Buprenorphine (BuTrans) patches have been approved as a treatment option for patients with non-malignant chronic pain who are unable to tolerate or comply with large, oral, regular doses of weak opioids (see page 3).**
- **Agomelatine (Valdoxan) tablets for major depressive disorder have been approved for use within Lincolnshire Partnership Foundation Trust only (see page 4).**
- **Prasugrel (Efient) tablets have not been approved for use (see page 5).**
- **Sevikar, a combination antihypertensive containing amlodipine and olmesartan, has been approved for use (see page 6).**
- **The NICE Clinical Guidelines on Glaucoma and Coeliac Disease are reviewed (see pages 11 to 13).**
- **The MHRA remain unconvinced of a possible link beween insulin glargine and cancer (see page 14).**

CONTENTS

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 NHS Lincolnshire website (www.lpct.nhs.uk).

SUMMARY OF PACEF DECISIONS: SEPTEMBER 2009 UPDATE

Drug	Indication(s)	Traffic Light Status
Agomelatine tablets 25mg (Valdoxan)	Major depressive disorder in adults	RED For use within LPFT only
Alitretinoin capsules 10mg and 30mg (Toctino)	Licensed for the treatment of severe, chronic hand eczema unresponsive to treatment with potent topical corticosteroids.	RED; for dermatologist use only.
Amlodipine/olmesartan tablets 5/20mg, 10/20mg and 10/40mg (Sevikar)	Hypertension	GREEN
Buprenophine patches 5 microgram /hour, 10 microgram /hour, 20 microgram/hour (BuTrans)	Licensed for the treatment of non-malignant pain of moderate intensity when an opioid is necessary for obtaining adequate analgesia.	GREEN Should only be used in patients with chronic non-malignant pain unable to tolerate or comply with large, regular doses of oral weak opioids
Cetuximab (Erbitux) intravenous infusion	Licensed for the treatment of epidermal growth factor receptor expressing metastatic colorectal cancer in combination with other antineoplastics	RED
C1-esterase inhibitor human injection (Berinert)	Licensed for the treatment of acute episodes of hereditary angioedema type I and II	RED
Gefitinib tablets 250mg (Iressa)	Licensed for locally advanced or metastatic non-small cell lung cancer with activating mutations of epidermal growth factor receptor tyrosine kinase (EGFR-TK)	RED-RED
Prasugrel tablets 5mg and 10mg (Efient)	Licensed in combination with aspirin for the prevention of atherothrombotic events in patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI).	RED-RED
Rituximab intravenous infusion (MabThera)	Licensed in combination with fludarabine and cyclophosphamide as an option for the first-line treatment of chronic lymphocytic leukaemia in people for whom fludarabine in combination with cyclophosphamide is considered appropriate.	RED
Tenofovir disoproxil tablets 245mg (Viread)	An oral nucleotide analogue licensed for the treatment of chronic hepatitis B infection with compensated liver disease, evidence of viral replication and histologically documented active liver inflammation or fibrosis.	RED

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**. Specialist initiation and shared care guidelines are not considered necessary.

REPORTING INCIDENTS TO THE NATIONAL PATIENT SAFETY AGENCY (NPSA)
The NPSA are keen to encourage the anonymous reporting of patient safety errors and systems failures both from healthcare professionals and patients. The National Reporting and Learning System (NRLS) has been set up to facilitate this process. Healthcare professionals can either report patient safety incidents through their local risk management scheme or directly into the NRLS using the eForm on the NPSA website. Please access www.npsa.nhs.uk for more information. **All healthcare professionals are encouraged to report incidents, errors and systems failures; the aim is to help the NHS to learn from things that go wrong.**

NEW DRUG ASSESSMENT: BUPRENORPHINE PATCHES (BUTRANS)

Buprenorphine (BuTrans) patches are licensed for the treatment of non-malignant pain of moderate intensity when an opioid is necessary for obtaining adequate analgesia. They are not suitable for the treatment of acute pain. The patches are available in three strengths (5 microgram per hour, 10microgram per hour and 20 microgram per hour) and are applied every seven days.

Clinical studies (mostly unpublished, small and short-term) have demonstrated the efficacy of the patch in the treatment of chronic osteoarthritis pain, low back pain and non-malignant pain when compared to sublingual buprenorphine tablets, combination paracetamol/oxycodone and paracetamol/hydrocodone tablets and placebo patches. **Non-inferiority has been demonstrated compared with codeine and modified-release tramadol.** The 5 microgram per hour patch is approximately equivalent to 30-60mg/day of oral codeine or 50mg/day of oral tramadol.

A cost comparison with oral codeine, oral tramadol and co-codamol 30/500 reveals the following:

Drug	Dose	Cost per month
Buprenorphine patch 5 micrograms/ hour (BuTrans)	**1 patch per week**	**£17.60**
Buprenorphine patches 10 micrograms/hour (BuTrans)	**1 patch per week**	**£32.02**
Buprenorphine patch 20 micrograms/hour (BuTrans)	**1 patch per week**	**£58.31**
Codeine 30mg tablets (generic)	30 - 60mg/day (equiv to 5mcg patch)	£1.51 to £3.02
Codeine 60mg tablets (generic)	60mg - 120mg/day (equiv to 10mcg patch)	£1.98 to £3.96
Codeine 60mg tablets (generic)	120mg - 240mg/day (equiv to 20mcg patch)	£3.96 to £7.92
Tramadol 50mg capsules (generic)	50mg/day (equiv to 5mcg patch)	£1.44

Tramadol 50mg capsules (generic)	100mg/day (equiv to 10mcg patch)	£2.88
Tramadol 50mg capsules (generic)	200mg/day (equiv to 20mcg patch)	£5.76
Co-Codamol 30/500 tablets	30 - 60mg codeine/day (equiv to 5mcg patch)	£1.06 to £2.12
Co-Codamol 30/500 capsules	30 - 60mg codeine/day (equiv to 5mcg patch)	£1.47 to £2.94

PACEF Recommendation

Most of the trial evidence reviewed for buprenorphine patches was either unpublished or not transferable to standard clinical practice. Nonetheless, evidence of non-inferiority to oral codeine and oral tramadol was sufficient to convince PACEF that buprenorphine (BuTrans) patches could be considered as a treatment option for patients with non-malignant chronic pain who are unable to tolerate or comply with large, oral, regular doses of weak opioids such as codeine or tramadol. Prescribers are reminded of the significant cost differential between BuTrans patches and lower cost generic oral alternatives as illustrated above. Subject to these restrictions buprenorphine patches (BuTrans) are designated GREEN.

NEW DRUG ASSESSMENT: AGOMELATINE 25MG TABLETS (VALDOXAN)

Agomelatine (Valdoxan) is a novel antidepressant agent that acts at both melatonergic and 5-HT_{2C} receptors; the mechanism by which this alleviates depression remains unclear at present. The product is licensed for the treatment of major depressive episodes in adults.

Data from short-term, small-scale clinical trials has established that agomelatine is at least equal in efficacy to sertraline, fluoxetine and venlafaxine, although the clinical significance of this remains unclear. Data on relapse prevention is also unclear, but suggests similar efficacy to existing antidepressants. Promisingly, early trial data reveals a low rate of adverse effects with agomelatine in comparison to alternatives; this may be of significance in a treatment area compromised by poor compliance rates due to poor tolerability.

A database (NEVADA) has been set up to optionally register patients being treated with agomelatine for collation of national naturalistic data to assess agomelatine outcomes in clinical practice.

A cost comparison between agomelatine and alternative antidepressants reveals that the product is comparably priced to higher cost, third line options, such as venlafaxine:

Treatment	**30 day treatment cost Minimum**	**30 day treatment cost Maximum**
Fluoxetine 20mg daily		£1.15
Citalopram 20mg daily		£1.32
Lithium 800mg daily		£2.10
Sertraline 50-200mg daily	£1.51	£3.64
Paroxetine 20-50mg	£2.58	£8.19
Moclobemide 300-600mg daily	£5.04	£10.08
Mirtazapine 30-45mg daily	£2.88	£15.84
Escitalopram 10-20mg daily	£15.98	£27.00

Duloxetine 60mg daily		£29.70
Agomelatine 25mg-50mg daily	**£41.28**	**£82.56**
Venlafaxine XL (Efexor XL) 150-225mg daily	£40.19	£64.30
Venlafaxine XL 150-225mg + Mirtazapine 30mg daily	£43.07	£67.18

PACEF Recommendation

Early evidence from small-scale, short-term studies suggests that agomelatine may have a promising future. However, further data needs to be gathered and published before this can be confirmed. As a result of this, agomelatine (Valdoxan) has been designated RED. It can be prescribed solely by specialists in mental health within Lincolnshire Partnership Foundation Trust. All patients will be registered on the NEVADA database as part of a local contribution to the developing evidence base. Agomelatine is not approved for use within primary care; any requests to GPs from specialists to prescribe should be refused. The future role of agomelatine will be determined at a later data following a review of findings emerging from NEVADA.

RAPID DRUG ASSESSMENT: PRASUGREL 5MG AND 10MG TABLETS (EFIENT)

Prasugrel (Efient) is a new antiplatelet drug with a similar mode of action to clopidogrel. It is licensed in combination with aspirin for the prevention of atherothrombotic events in patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI). Prasugrel cannot be seen as a potential substitute for clopidogrel at this stage as it does not hold the range of licenses held by the originator brand (Plavix).

Clinical evidence supporting the use of prasugrel comes from one large controlled trial which compared prasugrel with clopidogrel (both in combination with aspirin) in patients with moderate to severe acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI). This trial demonstrated that prasugrel and aspirin significantly reduced the incidence of ischaemic events (mainly non-fatal myocardial infarction) compared to clopidogrel and aspirin. However, prasugrel was also associated with an increased risk of clinically significant bleeding events; life threatening bleeds occurred in 1.4% of the prasugrel patients compared to 0.9% of the clopidogrel patients; 5 of the clopidogrel patients had a fatal bleed compared to 21 of the prasugrel patients. From this the American Food and Drug Administration (FDA) have concluded that **for every 1000 patients taking prasugrel instead of clopidogrel, 21 non-fatal myocardial infarctions and three deaths would be prevented, but 10 patients would experience major or minor bleeds, two of which would be fatal.**

A cost comparison of prasugrel and clopidogrel reveals that prasugrel is more expensive costing approximately £177 more per patient per year. As discussed in the previous issue of the *PACE Bulletin*, falling generic prices of clopidogrel are likely to widen this differential still further.

Drug	Daily dose	28 day cost
Prasugrel 5mg tablets (Efient)	5mg daily	£47.56
Prasugrel 10mg tablets (Efient	10mg daily	£47.56
Clopidogrel 75mg tablets (Plavix)	75mg daily	£33.93

PACEF Recommendation

Evidence from one clinical trial suggests that prasugrel in combination with aspirin is more effective than clopidogrel/aspirin in reducing ischaemic events in patients with ACS undergoing PCI, but with an increased risk of significant GI bleeding. As a result of this, PACEF have designated prasugrel (Efient) as RED-RED. NICE are in the process of evaluating prasugrel and will be publishing a Technology Appraisal shortly. Once the TA is published, PACEF will review this decision accordingly.

RAPID DRUG ASSESSMENT: AMLODIPINE/OLMESARTAN TABLETS 5/20MG, 5/40MG AND 10/40MG (SEVIKAR)

Sevikar is a new combination product containing the calcium channel blocker (CCB) amlodipine and the angiotensin II receptor antagonist (A2RA) olmesartan; the combination is licensed for the treatment of hypertension. Prescribed as separate components, both drugs are approved for use in county.

The cost comparison below reveals that for two of the three strengths (5mg/40mg and 10mg/40mg), Sevikar tablets are lower in cost than the individual components prescribed separately. Generic low-cost amlodipine is already available; the patent life of Olmetec extends to 2017 (see below).

Drug	Strength	Cost (28 days)
Sevikar tablets	5mg/20mg	£16.95
	5mg/40mg	£16.95
	10mg/40mg	£16.95
Amlodipine tablets	5mg	£1.09
Amlodipine tablets	10mg	£1.25
Olmesartan tablets (Olmetec)	10mg	£10.95
Olmesartan tablets (Olmetec)	20mg	£12.95
Olmesartan tablets (Olmetec)	40mg	£17.50

PACEF Recommendation

As both of the component drugs are currently approved for use in county and Sevikar, as a combination product, is usually lower in cost than the components prescribed separately, Sevikar tablets are designated GREEN and approved for use. Prescribers are reminded of the comparative cost of the A2RAs currently available in the UK and the imminence of some patent expiries (see below). At present, candesartan, telmisartan and olmesartan are all locally approved, but this is subject to review and may change as patents expire and prices change.

Drug	Dose Range (hypertension)	Cost (28 days)	Patent Expiry
Candesartan tablets (Amias)	8mg-32mg daily	£9.89 - 16.31	April 2012
Eprosartan tablets (Teveten)	600mg-800mg	£10.00 - 15.77	April 2012
Losartan tablets (Cozaar)	50mg-100mg	£12.80 - 16.18	March 2010
Olmesartan tablets (Olmetec)	10mg-40mg daily	£10.95 –17.50	Feb 2017
Telmisartan tablets (Micardis)	40mg-80mg	£12.50 -17.00	Jan 2017
Valsartan tablets (Diovan)	80mg-320mg	£13.97 – 20.23	May 2011

RAPID DRUG ASSESSMENT: C1-ESTERASE INHIBITOR HUMAN INJECTION (BERINERT)

C1-esterase inhibitor human injection (Berinert) is licensed for the treatment of acute episodes of hereditary angioedema type I and II. This drug has been in use for some time within ULHT as an unlicensed medicine. The advent of a licensed formulation has resulted in rapid adoption by the ULHT Drug and Therapeutics Committee; PACEF have formally ratified this decision.

PACEF Recommendation:
C1-esterase inhibitor human injection (Berinert) is designated RED.

NEW TRIALS IN BRIEF

ANTIBIOTIC PRESCRIBING: RESPIRATORY TRACT INFECTIONS IN CHILDREN

558 children from 61 general practices in England and Wales presenting with an acute respiratory tract infection were randomised to usual care or a consultation that incorporated the use of an interactive booklet (and take home resource) on respiratory tract infections. Rates of antibiotic prescribing were lower in the intervention group (19.5% vs. 40.8%, ARR 21.3%). No difference was found in the primary outcome of face-to-face re-consultation about the same illness during a 2 week follow up period. There was a significant difference in the proportion of parents who said that they would consult in the future if their child developed a similar illness.

PACEF Comment
Prescribers are urged to obtain copies of the interactive booklet and online training which are freely available from www.equipstudy.com

Reference
Francis NA et al. Effect of using an interactive booklet about childhood respiratory tract infections in primary care consultations on reconsulting and antibiotic prescribing: a cluster randomised controlled trial. *BMJ* 2009;339:b2885.

AMOXICILLIN IN ACUTE OTITIS MEDIA

This is a follow up study to a Dutch RCT; in the original study 240 children (aged 6 months to 2 years) with acute otitis media (AOM) were randomised to either amoxicillin or placebo. In this follow-up, questionnaires were sent to parents asking about the recurrence of AOM and subsequent referrals 3 years after the RCT. AOM had recurred in 63% of children in the amoxicillin group compared with 43% of those in the placebo group. There were no significant differences in rates of referral or ENT surgery.

PACEF Comment
Prescribers are reminded that no antibiotic or delayed antibiotic strategies are recommended for uncomplicated AOM

Reference
Bezakova N et al. Recurrence up to 3.5 years after antibiotic treatment of acute otitis media in very young Dutch children: survey of trial participants. *BMJ*;2009:338:b2525

TIOTROPIUM AND THE UPLIFT STUDY: SUB-GROUP ANALYSIS IN MODERATE COPD

The original UPLIFT study failed to show a significant effect on decline in lung function (measured as FEV1) of tiotropium versus placebo in chronic obstructive pulmonary disease (COPD) over 4 years. In a pre-specified sub-group of this study consisting of 2739 patients with GOLD stage 2 (moderate) disease, the rate of decline of mean post-bronchodilator FEV1 was lower in the tiotropium group than in the control group (43ml/yr vs. 49ml/yr, p=0.024) No difference was found in the rate of decline of pre-bronchodilator FEV1 measurements.

Reference
Decramer M et al. Effect of tiotropium on outcomes in patients with moderate chronic obstructive pulmonary disease (UPLIFT): a pre-specified subgroup analysis of a randomised controlled trial. *The Lancet*, early online publication, 28 August 2009 doi:10.1016/S0140-6736(09)61298-8

RISK OF FALLS ASSOCIATED WITH MEDICINES

This multicentre French prospective cohort study investigated the risk of falls associated with the use of medicines considered inappropriate for older people. Users of inappropriate medication were found to have an increased risk of falling, mainly due to:

- occasional or regular use of **long acting benzodiazepines**.
- regular use of other **psychotropics**.
- regular use of **anticholinergic medicines**.

Reference
Berdot S et al. Inappropriate medication use and risk of falls – A prospective study in a large community-dwelling elderly cohort. *BMC Geriatrics* 2009;9:30 doi:10.1186/1471-2318-9-30

NICE TECHNOLOGY APPRAISAL 173: *TENOFOVIR DISOPROXIL FOR THE TREATMENT OF CHRONIC HEPATITIS B* (JULY 2009)

The key recommendations are as follows:

- **Tenofovir disoproxil, within its marketing authorisation, is recommended as an option for the treatment of people with chronic HBeAg-positive or HBeAg-negative hepatitis B in whom antiviral treatment is indicated.**
- This guidance does not apply to people with chronic hepatitis B who also have hepatitis C, hepatitis D or HIV.

Tenofovir disoproxil (Viread) is an oral nucleotide analogue licensed for the treatment of chronic hepatitis B infection with compensated liver disease, evidence of viral replication and histologically documented active liver inflammation or fibrosis. The acquisition cost is £255 for 30 tablets; the standard adult dose is 245mg once daily. The optimal treatment duration is currently unknown.

PACEF Recommendation
Tenofovir disoproxil (Viread) is designated RED for this indication. Further consideration may be given to the development of shared care guideline at a later date. Tenofovir disoproxil is not approved for use within primary care; any requests to GPs from specialists to prescribe should be refused.

NICE TECHNOLOGY APPRAISAL 174: *RITUXIMAB FOR THE FIRST-LINE TREATMENT OF CHRONIC LYMPHOCYTIC LEUKAEMIA* (JULY 2009)

The key recommendations are as follows:

- **Rituximab in combination with fludarabine and cyclophosphamide is recommended as an option for the first-line treatment of chronic lymphocytic leukaemia in people for who fludarabine in combination with cyclophosphamide is considered appropriate.**
- Rituximab in combination with chemotherapy agents other than fludarabine and cyclophosphamide is not recommended for the first-line treatment of chronic lymphocytic leukaemia.

PACEF Recommendation:
Rituximab (MabThera) is designated RED for use in combination with fludarabine and cyclophosphamide as an option for the first-line treatment of chronic lymphocytic leukaemia in people for who fludarabine in combination with cyclophosphamide is considered appropriate.

NICE TECHNOLOGY APPRAISAL 175: *GEFITINIB FOR THE SECOND-LINE TREATMENT OF LOCALLY ADVANCED OR METASTATIC NON-SMALL-CELL LUNG CANCER* (TERMINATED APPRAISAL) (JULY 2009)

The key recommendations are as follows:

- **NICE is unable to recommend the use in the NHS of gefitinib for the second-line treatment of locally advance or metastatic non-small-cell lung cancer** because no evidence submission was received from the manufacturer or sponsor of the technology.

PACEF Recommendation:
Gefitinib tablets (Iressa) are designated RED-RED for this indication.

NICE TECHNOLOGY APPRAISAL 176: *CETUXIMAB FOR THE FIRST-LINE TREATMENT OF METASTATIC COLORECTAL CANCER* (AUGUST 2009)

The key recommendations are as follows:

- **Cetuximab in combination with 5-fluorouracil (5-FU), folinic acid and oxaliplatin (FOLFOX), within its licensed indication, is recommended for the first-line treatment of metastatic colorectal cancer subject to certain criteria.**
- **Cetuximab in combination with 5-FU, folinic acid and irinotecan (FOLFIRI), within its licensed indication, is recommended for the first-line treatment of metastatic colorectal cancer subject to certain criteria.**
- Patients should receive treatment with cetuximab for no more than 16 weeks. At 16 weeks, treatment with cetuximab should stop and the patient should be assessed for resection of liver metastases.

PACEF Recommendation
Cetuximab (Erbitux) is designated RED for use as part of the FOLFOX and FOLFIRI regimes for the first-line treatment of metastatic colorectal cancer subject to NICE criteria.

NICE TECHNOLOGY APPRAISAL 177: *ALITRETINOIN FOR THE TREATMENT OF SEVERE CHRONIC HAND ECZEMA* (AUGUST 2009)

The key recommendations are as follows:

Alitretinoin is recommended, within it licensed indication, as a treatment option for adults with severe chronic hand eczema that has not responded to potent topical corticosteroids if the person has:

- severe disease, as defined by the physician's global assessment (PGA) and
- a dermatology life quality index (DLQI) score of 15 or more.

Alitretinoin treatment should be stopped:

- as soon as an adequate response (hands clear or almost clear) has been achieved or
- if the eczema remains severe (as defined by the PGA) at 12 weeks or
- if an adequate response (hands clear or almost clear) has not been achieved by 24 weeks.

Only dermatologists, or physicians with experience in both managing severe chronic hand eczema and the use of systemic retinoids, should start and monitor treatment with alitretinoin.

PACEF Recommendation:
Alitretinoin (Toctino) is the first licensed oral treatment for patients with severe chronic hand eczema unresponsive to topical corticosteroids. It was reviewed by PACEF in April 2009 and designated RED for use by dermatologists only (see *PACE Bulletin* Vol 3, No 5 (May 2009). NICE TA177 supports this decision and provides further criteria for initiation (see above). Alitretinoin is not approved for use within primary care; any requests to GPs from specialists to prescribe should be refused.

NICE TECHNOLOGY APPRAISAL 178: *BEVACIZUMAB (FIRST-LINE), SORAFENIB (FIRST-AND-SECOND-LINE), SUNITINIB (SECOND-LINE) AND TEMSIROLIMUS (FIRST-LINE) FOR THE TREATMENT OF ADVANCED AND/OR METASTATIC RENAL CELL CARCINOMA* (AUGUST 2009)

The key recommendations are as follows:

- Bevacizumab, sorafenib and temsirolimus are not recommended as first-line treatment options for people with advanced and/or metastatic renal cell carcinoma.
- Sorafenib and sunitinib are not recommended as second-line treatment options for people with advanced and/or metastatic renal cell carcinoma.
- People who are currently being treated with bevacizumab (first-line), sorafenib (first-and-second-line), sunibtinib (second-line) and temsirolimus (first-line) for advanced and/or metastatic renal cell carcinoma should have the option to continue their therapy until they and their clinicians consider it appropriate to stop.

NICE CLINICAL GUIDELINE 85: *GLAUCOMA – DIAGNOSIS AND MANAGEMENT OF CHRONIC OPEN ANGLE GLAUCOMA AND OCULAR HYPERTENSION* (APRIL 2009)

The key recommendations are as follows:

Information

Patients should be provided with information on:

- Chronic open angle glaucoma (COAG), its life-long implications and prognosis for keeping their sight.
- the fact that COAG and ocular hypertension (OHT) are symptomless.
- the fact that, once lost, sight cannot be recovered, although most people treated for COAG will not go blind.
- the hereditary nature of the condition. Other family members may wish to be tested for the disease.
- how to apply eye drops and the use of compliance aids.
- the different treatment options and the need for regular monitoring.
- Driver and Vehicle Licensing Agency (DVLA) regulations.
- Letter of Vision Impairment (LVI), Referral of Vision Impairment (RVI) and Certificate of Vision Impairment (CVI) registration.

Diagnosis

At diagnosis offer:

- intraocular pressure (IOP) measurement using Goldmann applanation tonometry
- central corneal thickness (CCT) measurement.
- peripheral anterior chamber configuration and depth assessments using gonioscopy
- visual field measurement using standard automated perimetry
- optic nerve assessment, with dilatation, using stereoscopic slit lamp biomicroscopy with fundus examination.
- obtain an optic nerve head image.

Monitoring

Ongoing monitoring should include:

- Standard automated perimetry (for all people with established COAG and those suspected of having visual field defects who are being investigated for COAG).
- Supra-threshold perimetry (for those with confirmed normal visual fields with diagnosed OHT or suspected COAG).
- Goldmann applanation tonometry and Van Herick's test.
- CCT measurement and gonioscopy (when clinically indicated).
- Stereoscopic split lamp biomicroscopic examination of the optic nerve head
- A new optic nerve head image (if there is a change of status)

Treatment

- Treatment options include prostaglandin analogues, beta-blockers, carbonic anhydrase inhibitors and sympathomimetics.
- If the person is allergic to preservatives, preservative-free preparations are available.
- More than one agent may be needed concurrently.
- Check co-morbidities and potential drug interactions before offering medication.
- **Offer people newly diagnosed with early or moderate COAG and at risk of significant visual loss in their lifetime, treatment with a prostaglandin analogue.**

- **Offer surgery with pharmacological augmentation (mitomycin C or 5-fluoruracil) as indicated to people with COAG who are at risk of progressing to sight loss despite treatment.** Offer information on risks and benefits associated with surgery.

Organisation of care

- **Refer people with suspected optic nerve damage or repeatable visual field defect, or both, to a consultant ophthalmologist for consideration of a definitive diagnosis and formulation of a management plan.**
- Diagnosis of OHT and suspected COAG and formulation of a management plan should be made by a suitably trained healthcare professional (i.e. either a consultant ophthalmologist, or someone with a specialist qualification or relevant experience).

PACEF Recommendation:
In response to this Clinical Guideline and the increasing number of new products for COAG in the marketplace, PACEF are working in conjunction with ULHT ophthalmologists to devise a primary/secondary care joint formulary. This formulary will be circulated to all prescribers in the near future.

NICE CLINICAL GUIDELINE 86: *COELIAC DISEASE* (MAY 2009)

The key recommendations are as follows:

Signs, symptoms and conditions associated with coeliac disease

Signs and symptoms

- Chronic or intermittent diarrhoea
- Failure to thrive or faltering growth (in children)
- Persistent or unexplained GI symptoms including nausea and vomiting
- Prolonged fatigue ('tired all the time')
- Recurrent abdominal pain, cramping or distension.
- Sudden or unexpected weight loss
- Unexplained iron-deficiency anaemia or other unspecified anaemia

Conditions

- Autoimmune thyroid disease
- Dermatitis herpetiformis
- Irritable bowel syndrome
- Type 1 diabetes
- First degree relatives (parents, siblings or children) with coeliac disease

Serological testing should be offered to children and adults with any of the signs, symptoms and conditions listed above. Do not use serological testing for coeliac disease in infants before gluten has been introduced to the diet.
Consider offering serological testing to children and adults with any of the following:

- Addison's disease
- Amenorrhoea
- Aphthous stomatitis (mouth ulcers)
- Autoimmune liver conditions
- Autoimmune myocarditis
- Chronic thrombocytopenia purpura
- Dental enamel defects
- Depression or bipolar disorder
- Downs syndrome
- Epilepsy
- Low-trauma fracture
- Lymphoma

- Metabolic bone disease (e.g. rickets or osteomalacia)
- Microscopic colitis
- Persistent or unexplained constipation
- Persistently raised liver enzymes with unknown cause
- Polyneuropathy
- Recurrent miscarriage
- Reduced bone mineral density
- Sarcoidosis
- Sjogren's syndrome
- Turner syndrome
- Unexplained alopecia
- Unexplained sub-fertility

Dietary considerations before serological testing

People and their carers should be informed that:

- Testing (serology and biopsy if required) is accurate only if they follow a gluten-containing diet.
- When following a gluten-containing diet they should eat some gluten in more than one meal every day for at least 6 weeks before testing.
- They should not start a gluten-free diet until diagnosis is confirmed by intestinal biopsy (even if a self-test or other serological test is positive)
- If the person is unwilling to reintroduce gluten to their diet, it may be difficult to confirm a diagnosis of coeliac disease on intestinal biopsy. **This may have implications for the person's ability to access gluten-free foods on prescription.**

Delayed diagnosis of coeliac disease or undiagnosed coeliac disease can result in:

- Continuing ill health
- Long-term complications (e.g. osteoporosis, increased fracture risk, unfavourable pregnancy outcomes, increased risk of intestinal malignancy)
- Growth failure, delayed puberty and dental problems (in children0

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY (MHRA): *DRUG SAFETY UPDATES* (AUGUST/SEPTEMBER 2009)

Safety information: oseltamivir (Tamiflu) and zanamivir (Relenza) for pandemic swine flu influenza A/H1N1

Oseltamivir (Tamiflu).

- Most common side effects are nausea, vomiting, diarrhoea, abdominal pain and headache which normally occur after the initial dose but usually cease when treatment is stopped. The frequency of these adverse affects can be reduced if taken with food.
- More serious effects listed in the Summary of Product Characteristics (SPC) include neuropsychiatric disorders – convulsions and delirium, these were only included in the SPC as a precautionary measure as a clear link between these adverse events and treatment with oseltamivir has yet to be established.
- Clinically important drug interactions are unlikely however the MHRA advise that care should be taken when co-administering with medicines with a narrow therapeutic index (e.g. chlorpropamide or methotrexate).
- Dose adjustment is required for adults with severe renal insufficiency with a creatinine clearance of ≤30ml/min. Tamiflu is not recommended if creatinine clearance ≤ 10ml/min or if the patient is on dialysis.
- Patients with an existing kidney disorder should be treated with oseltamivir as per National Pandemic Flu Service treatment protocols.

Zanamivir (Relenza)

- Adverse effects are rare but may include allergic type reactions such as swelling of the face, mouth or throat, skin rash or hives.
- Acute bronchospasm or serious decline in respiratory function or both have been reported in patients with a history of asthma, chronic obstructive pulmonary disease (COPD). The MHRA advise that patients with severe asthma should not receive Relenza unless under close medical monitoring because of the risk of bronchoconstriction. Patients should be informed of the risk of bronchospasm and should have a fast acting bronchodilator available if required. Patients on maintenance inhaled bronchodilator therapy should be advised to use their bronchodilator before taking Relenza.
- Clinically significant drug interactions are unlikely.

Herbal products: safety update

- The MHRA encourage health care professionals to report any suspected adverse reactions associated with the use of herbal products. There has been a decline over the last four years in the number of reports received by the MHRA which they are attributing to confusion as to the relevance of 'yellow card' reporting arrangements in relation to herbal medicines rather than a genuine reduction in the number of incidents occurring.
- 'Yellow cards' should be used to report suspected adverse reactions to both herbal and medicinal products.

Insulin glargine: possible cancer link

Several recent observational studies have suggested a link between insulin glargine and an increased risk of certain cancers. A recent MHRA review has concluded the following:

- Type 2 diabetes is associated with an increased risk of certain types of cancers, including cancer of the breast, colon and pancreas.
- Three previously published studies have shown that metformin is associated with a lower cancer risk than either insulin or sulfonylureas. These findings have led to a hypothesis that metformin may have an anti-tumour effect whereas insulin may act as a tumour growth factor. This hypothesis remains unconfirmed.
- The MHRA have highlighted inconsistencies in the findings from the four observational studies reviewed, concluding that the results could neither confirm nor exclude a relationship between insulin glargine and cancer.
- There is a large ongoing RCT known as the Outcome Reduction with Initial Glargine Intervention or ORIGIN trial which may provide further information on potential cancer risk.

Advice for healthcare professionals:

- The European Medicines Agency has advised that there is no need to change practice at present; patients currently being treated with insulin glargine should continue with their treatment.

PACEF Recommendation:
PACEF will continue to monitor the unfolding story around insulin glargine and cancer risk. At present, no change in practice is advocated.

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