Formulary Changes

**Duloxetine Approved as a 3rd Line Option for Diabetic Peripheral Neuropathic Pain**

The ADTC have approved the use of duloxetine (Cymbalta®) for the treatment of patients with diabetic peripheral neuropathy. It is restricted to initiation by prescribers experienced in the management of diabetic peripheral neuropathic pain as a 3rd line option.

Duloxetine is a serotonin and noradrenaline reuptake inhibitor. Its mode of action in neuropathic pain is thought to be due to potentiation of descending inhibitory pain pathways within the central nervous system.

Duloxetine was approved for use by the Scottish Medicines Consortium (SMC) in August 2006 and is also considered as a treatment option by SIGN and NICE.

There is no comparative evidence to suggest duloxetine is more effective than other treatment options for diabetic peripheral neuropathy. Duloxetine is also considerably more expensive than tricyclic antidepressants (1st line choice) and gabapentin (2nd line choice).

The normal starting and maintenance dose for duloxetine is 60mg. Some patients may benefit from a higher dose of 120mg per day in divided doses.

**Key Messages**
1. 1st line treatment choice for diabetic peripheral neuropathy is a tricyclic antidepressant (amitriptyline, nortriptyline)
2. 2nd line choice is gabapentin
3. 3rd line choice duloxetine, specialist initiation only

**References**

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**Guidance**

**Updated Fife Formulary Appendix 2E - Management of Stable Angina**

The NHS Fife Formulary Appendix 2E has been updated by the Vascular Disease MCN and has been approved for use in NHS Fife by the ADTC. Appendix 2E provides guidance on the management of patients with stable angina.

All patients diagnosed with angina should be provided with lifestyle advice and if required advised to stop smoking. Patients should be prescribed an anti-platelet (aspirin, clopidogrel), a statin (1st line choice simvastatin 40mg) and a GTN spray for use when required.

In terms of symptom control patients should initially be prescribed a beta-blocker (bisoprolol, atenolol) or if a beta-blocker is contraindicated or not tolerated a rate-limiting calcium channel blocker (verapamil, diltiazem). Ivabradine should only be prescribed in patients who are intolerant of a beta-blocker and a calcium channel blocker or if they are both contraindicated.

If patients remain symptomatic then 2nd line options are ivabradine, a non rate-limiting calcium channel blocker, nicorandil or a long-acting nitrate.

Patients who remain symptomatic after addition of a 2nd line option should be referred to cardiology for further assessment.

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**In This Issue:** FORMULARY CHANGES - DULOXETINE • GUIDANCE DOCUMENTS - STABLE ANGINA, DIABETIC FOOT INFECTIONS • PRESCRIBING OF MEDICAL DEVICES • PRESCRIBING OF COMPLEMENTARY MEDICINES/VITAMIN SUPPLEMENTS • LATEST SMC RECOMMENDATIONS • DATES FOR 2012 ADTC MEETINGS


**Guidance (contd.)**

**Management of Diabetic Foot Infections**

A new guideline on the empiric antibiotic treatment of diabetic foot infections has been authorised by the Antimicrobial Management Team and approved for use in NHS Fife by the ADTC.

Patients with mild infection should be treated for 7 days then reviewed. 1st line treatment should be with flucloxacillin or doxycycline (if penicillin allergy or known/suspected MRSA).

If there is treatment failure with flucloxacillin patients should be switched to doxycycline.

For patients with moderate or severe infections, patients should be treated for 14 days then reviewed. Initial treatment will be with i.v. antibiotics. Choice of i.v. antibiotic will depend upon if the infection is MRSA or non/MRSA or if the patient has a penicillin allergy. When suitable, patients will be switched to oral treatment with co-trimoxazole + metronidazole.

Copies of the above guidance documents can be accessed / downloaded from the ADTC website www.fifeadtc.scot.nhs.uk/or via the Fife Formulary/ADTC link on the NHS Fife intranet homepage.

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**Prescribing of Medical Devices**

Recently there have been several queries from GP practices about the prescribing of medical devices that are listed in the Drug Tariff.

One of the queries has related to the prescribing of the medical device Resperate® in the management of patients with hypertension. A recent review of evidence for the use of Resperate® appeared in the Journal of Hypertension\(^1\). The review found that Resperate® reduced both systolic and diastolic blood pressure (systolic BP reduction 3.67mmHg, diastolic BP reduction 2.51mmHg). However the trial duration was a maximum of 9 weeks and there was no improvement in heart rate or quality of life.

The British Hypertension Society in response to this review have concluded that “such small effects over very short durations of time do not provide sufficient evidence for this equipment to be recommended.”

> In general, the ADTC recommend that, as with drugs, devices should only be prescribed where the prescriber is satisfied regarding the safety and clinical effectiveness for that patient. If prescribers feel pressurised to prescribe medical devices of unproven or limited benefit they should consider seeking advice from an appropriate specialist or making a referral to secondary care.

Reference


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**Prescribing of Complimentary Medicines/ Vitamin Supplements**

Similar to prescribing of medical devices (see article above) is the prescribing of complimentary medicines/vitamin supplements for various medical conditions.

A recent example has been requests to prescribe vitamin supplements e.g. Macushield®, I-Caps® to patients with age related macular degeneration (AMD).

Dr. Styles, Consultant Ophthalmologist, has stated that there is little evidence that vitamin supplements are effective in the treatment of AMD. The only trial that has shown some benefit is the AREDS trial which showed benefits of a specific formulation of vitamins but only in patients who were non-smokers and had advanced wet macular degeneration in one eye.

Dr Styles recommends that key advice to patients should be to stop smoking and ensure a healthy diet. Patients should be advised that there is no strong evidence that vitamin supplements are beneficial in the majority of patients and for this reason they cannot be prescribed.

Generally, there tends to be a lack of scientific evidence to show that complimentary medicines/vitamin supplements are effective in the treatment of medical conditions. As these products tend to not be licensed medicines there can also be differences in formulations between different suppliers and individual doses may not be of a uniform strength.

> In general, it is recommended complimentary medicines/vitamin supplements are not prescribed to patients unless specifically recommended in the Fife Formulary or recommended by a specialist. The ADTC have confirmed that NHS Fife would support prescribers who refuse to prescribe these products to patients due to lack of evidence of efficacy. Patients should be advised, if the patient wishes to, to purchase a suitable product instead.
### SMC Recommendations

#### Medicines accepted for use by SMC

**Formulary Choices** – Products that are recommended within Fife and should be used in the majority of patients.

**Restricted Use** – Products that have been approved by the SMC for a limited indication or for a niche group of patients. Appropriate for them to be prescribed for patient groups that have been approved by the SMC / Fife ADTC.

**Not Preferred** – Products that have been approved by the SMC but agreed in Fife that suitable Formulary choices are already available. These products should only be used when Formulary products have been ineffective, not tolerated or are contra-indicated.

<table>
<thead>
<tr>
<th>Product</th>
<th>Indication assessed</th>
<th>Fife ADTC decisions &amp; comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Everolimus, 5mg, 10mg tablets (Afinitor®)</td>
<td>Treatment of unresectable or metastatic, well- or moderately-differentiated neuroendocrine tumours of pancreatic origin (pNET) in adults with progressive disease.</td>
<td>Await decision from SCAN.</td>
</tr>
<tr>
<td>Collagenase clostridium histolyticum 0.9mg powder and solvent for solution for injection (Xiapex®)</td>
<td>Treatment of Dupuytren’s contracture in adult patients with a palpable cord.</td>
<td>Add to the Formulary. Alternative to limited fasciectomy in patients with moderately severe Dupuytren’s Contracture. Specialist hospital use only.</td>
</tr>
<tr>
<td>Etanercept 10mg and 25mg powder and sterile water for solution for injection for paediatric use (Enbrel®)</td>
<td>Treatment of chronic severe plaque psoriasis in children and adolescents from the age of 6 years who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies.</td>
<td>Already in the Fife Formulary. New licensed indication noted.</td>
</tr>
<tr>
<td>Etanercept 10mg and 25mg powder and sterile water for solution for injection for paediatric use (Enbrel®)</td>
<td>Treatment of active polyarticular juvenile idiopathic arthritis in children and adolescents from the age of 2 years who have had an inadequate response to, or who have proved intolerant of, methotrexate.</td>
<td>Already in the Fife Formulary. New licensed indication noted.</td>
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<tr>
<td>Insulin detemir (Levemir®)</td>
<td>Treatment of diabetes mellitus in adults, adolescents and children aged 2 years and above. Restricted to patients unable to achieve good glycaemic control with established insulins.</td>
<td>Already in the Fife Formulary. New licensed indication noted.</td>
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<tr>
<td>Dexametomidine 100 micrograms/mL concentrate for solution for infusion (Dexdor®)</td>
<td>For sedation in adult intensive care unit (ICU) patients requiring a sedation level not deeper than arousal in response to verbal stimulation (corresponding to Richmond Agitation-Sedation Scale [RASS] 0 to -3).</td>
<td>Formulary - Add to restricted list. Restricted to use in patients who do not achieve adequate sedation with propofol.</td>
</tr>
<tr>
<td>Exenatide, 5 micrograms &amp; 10 micrograms, solution for injection, prefilled pen (Byetta®)</td>
<td>Adjunctive therapy to basal insulin with or without metformin and/or pioglitazone in adults with type 2 diabetes who have not achieved adequate glycaemic control with these agents.</td>
<td>Already in Fife Formulary. New licensed indication noted. Specialist initiation only.</td>
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<tr>
<td>Tobramycin 28mg inhalation powder, hard capsules (TOBI Podhaler®)</td>
<td>Suppressive therapy of chronic pulmonary infection due to Pseudomonas aeruginosa in adults and children aged 6 years and older with cystic fibrosis.</td>
<td>Tobramycin already in Fife Formulary. New formulation noted. Use restricted to patients where tobramycin nebulised solution is unsuitable. Hospital use only.</td>
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<tr>
<td>Alteplase, 10mg, 20mg, 50mg, powder and solvent for solution for injection and infusion (Actilyse®)</td>
<td>The fibrinolytic treatment of acute ischaemic stroke. Treatment must be started as early as possible within 4.5 hours after onset of the stroke symptoms and after exclusion of intracranial haemorrhage.</td>
<td>New indication noted. Hospital use only.</td>
</tr>
<tr>
<td>Dexamethasone 700 microgram intravitreal implant (Ozurdex®)</td>
<td>Treatment of adult patients with macular oedema following either branch retinal vein occlusion or central retinal vein occlusion.</td>
<td>Add to the Fife Formulary. Specialist, hospital use only. In CRVO Patients: Alternative to ranibizumab in patients who would prefer less frequent administration. In BRVO Patients: For use in patients where laser therapy has failed or in patients where laser therapy is inappropriate i.e. patients with dense macular haemorrhage.</td>
</tr>
<tr>
<td>Pregabalin oral solution (Lyrica®)</td>
<td>Treatment of peripheral and central neuropathic pain in adults, as adjunctive therapy in adults with partial seizures with or without secondary generalization and the treatment of Generalised Anxiety Disorder (GAD) in adults.</td>
<td>New formulation noted. Pregabalin is already in the Fife Formulary for use as a 3rd line option in the treatment of peripheral neuropathic pain. (after TCA, gabapentin). The oral solution can be used as an alternative to capsules in patients with swallowing problems. The oral solution may also be considered 2nd line but only in patients unable to swallow gabapentin tablets/capsules.</td>
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**Medicines not recommended by SMC**

- **Bevacizumab (Avastin®)** is not recommended in combination with capecitabine for first-line treatment of patients with metastatic breast cancer in whom treatment with other chemotherapy options including taxanes or anthracyclines is not considered appropriate. Lack of clinical benefits compared to cost, lack of robust economic analysis.
- **Ipilimumab (Yervoy®)** is not recommended for treatment of advanced (unresectable or metastatic) melanoma in adults who have received prior therapy. Lack of clinical benefits compared to cost, lack of robust economic analysis.
- **Belatacept (Nulojix®)** is not recommended, in combination with corticosteroids and a mycophenolic acid, for prophylaxis of graft rejection in adults receiving a renal transplant. It is recommended to add an interleukin-2 receptor antagonist for induction therapy to this belatacept-based regimen. Lack of clinical benefits compared to cost, lack of robust economic analysis.
- **Triptorelin pamoate (Salvacyl®)** is not recommended for reversible reduction of testosterone to castrate levels in order to decrease sexual drive in adult men with severe sexual deviations. Non-submission by the manufacturer.
- **Vandetanib (Caprelsa®)** is not recommended for treatment of aggressive and symptomatic medullary thyroid cancer (MTC) in patients with unresectable locally advanced or metastatic disease. Non-submission by the manufacturer.

**Dates for 2012 ADTC Meetings**

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<td>17th October</td>
<td>28th September</td>
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<td>19th December</td>
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The information provided in this bulletin is correct at the time of publishing but is subject to change as new clinical information becomes available.

If you require this newsletter in alternative formats please telephone 01592 226915

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or visit our website: www.fifeadtc.scot.nhs.uk