Prucalopride ‘Not Recommended’ for the Treatment of Constipation

After a resubmission, prucalopride has not been recommended, by the Scottish Medicines Consortium (SMC), July 2011, for the symptomatic treatment of chronic constipation in women.

**What is Prucalopride?**
Prucalopride is a serotonin 5-HT4 receptor agonist which stimulates colonic motility. It is only licensed for the symptomatic treatment of chronic constipation in adult women in whom laxatives have failed to provide adequate relief.

If treatment is ineffective after 4 weeks then ongoing treatment should be reconsidered.

**SMC Advice**
In the resubmission, the SMC were asked to consider the use of prucalopride in women after lifestyle interventions and a therapeutic trial of two or more laxatives from different classes have failed to provide adequate relief.

The SMC did not approve the use of prucalopride due to insufficient evidence of clinical and economic benefits.

Some of the key concerns raised were –
1. Short term trials (maximum of 12 weeks)
2. No comparison against other drugs used for the treatment of constipation
3. Prucalopride is relatively expensive compared to alternative laxatives. Prucalopride costs £39-£60 per patient per 28 days compared to £4 for ispaghula husk, £0.56 for senna and £5 - £15 for macroalg 3350.
4. The primary outcome measure, 3 or more spontaneous complete bowel movements per week was only achieved in a 1/3rd of patients prescribed prucalopride.

A recent article in the Drugs and Therapeutics Bulletin2 also questions the benefits of prucalopride.

**Local Advice**
In line with SMC advice, NHS Fife has not approved the use of prucalopride. If a clinician considers prucalopride may be of benefit in one of their patients then an Individual Patient Treatment Request (IPTR) form should be submitted and be approved prior to prescribing. The clinician must prove the exceptionality of the case for prescribing prucalopride in that one individual. Copies of the IPTR form can be downloaded from the ADTC website.

A recent review of PRISMS prescribing data showed prucalopride has already been prescribed 21 times in primary care (Jan. – March 2011) at a cost of £1800 for that quarter without any IPTR submissions having been made.

**Key Messages**
- Prucalopride is not approved within NHS Fife for the treatment of chronic constipation.
- Prucalopride is only licensed for use in adult women where other laxatives have been ineffective.
- In each individual case, an IPTR should be submitted and be approved before prescribing prucalopride.

**References**
1. SMC advice (653/10), June 2011. www.scottishmedicines.org.uk/SMC_Advice/Advice/653_10_prucalopride_Resolor/prucalopride_Resolor
2. What role for prucalopride in constipation?, DTB, Vol.49, No 8, 93-95, August 2011.

**Updated Pioglitazone Safety Advice**
The MHRA have recently issued new advice regarding the risk of bladder cancer with pioglitazone.

- The MHRA advise that pioglitazone should not be prescribed to the following groups of patients –
  1. Patients with current active bladder cancer or a history of bladder cancer
  2. Patients with uninvestigated macroscopic haematuria
- Patients should be advised to promptly seek the attention of their physician if the patient develops symptoms of macroscopic haematuria, dysuria or urinary urgency.
- Risk factors for developing bladder cancer include the following – increasing age, current or ex-smoker, previous exposure to chemotherapy agents e.g. cyclophosphamide, previous irradiation of the pelvic region.
- The MHRA also advises that all patients initiated on pioglitazone should be reviewed after 3-6 months to assess the benefits of ongoing prescribing of pioglitazone.

Dr. Chalmers, Diabetologist, has confirmed there is no need to change current practice in prescribing pioglitazone as long as the high-risk patient groups mentioned above are excluded.

**References**
1. MHRA Drug Safety Update, Volume 5, issue 1, August 11.
www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON125962
# 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>Ticagrelor film-coated tablets (Brilique®)</td>
<td>Co-administered with aspirin, for the prevention of atherothrombotic events in adult patients with acute coronary syndromes (unstable angina, non ST elevation myocardial infarction [NSTEMI] or ST elevation myocardial infarction [STEMI]); including patients managed medically, and those who are managed with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).</td>
<td>Defer decision until place in therapy is clarified from tertiary centres in Lothian and Tayside.</td>
</tr>
<tr>
<td>Ferric carboxymaltose 50mg iron/ML solution for injection/infusion (Ferinject®)</td>
<td>Restricted use for the treatment of iron deficiency when oral iron preparations are ineffective or cannot be used. The diagnosis must be based on laboratory tests. SMC restriction: use is restricted to administration by intravenous infusion within the licensed indication in non-haemodialysis-dependent patients with chronic kidney disease. The manufacturer’s economic case did not consider the cost-effectiveness of bolus injections or use in haemodialysis patients.</td>
<td>Add to restricted list. Ferrinject® may be used 1st line as an IV infusion in non-haemo-dialysis-dependent patients in patients where attendance at a day case unit is impractical or in patients allergic to Cosmofer®.</td>
</tr>
</tbody>
</table>
| Triptorelin (Decapeptyl SR®) 22.5mg powder and solvent for suspension for injection | • Treatment of patients with locally advanced, non-metastatic prostate cancer, as an alternative to surgical castration.  
• Treatment of metastatic prostate cancer. | New formulation noted. |
| Omalizumab (Kolvair®) 75mg, 150mg solution for injection as prefilled syringe | Restricted use in adults, adolescents (12 years of age and older) and children (6 to <12 years of age) with convincing IgE (immunoglobulin E) mediated asthma. SMC restriction: Use is restricted to patients who are prescribed chronic systemic steroids and in whom all other treatments have failed. The response to omalizumab treatment should be assessed in all patients at 16 weeks and treatment should be discontinued in patients who have not shown a marked improvement in overall asthma control. | New formulations noted. Restricted use only in patients at Step 5 of BTS/SIGN Asthma Guidance. Hospital, specialist use only. |
| Sunitinib (Sutent®) | Treatment of unresectable or metastatic, well-differentiated pancreatic neuroendocrine tumours with disease progression in adults. | Await decision from SCAN. |
| Filgrastim, 30 million units (300 micrograms)/0.5mL, 48 million units (480 micrograms)/0.5mL, solution for injection or infusion in pre-filled syringe (Zarzio®) | • Reduction in the duration of neutropenia and the incidence of febrile neutropenia in patients treated with established cytotoxic chemotherapy for malignancy (with the exception of chronic myeloid leukaemia and myelodysplastic syndromes) and reduction in the duration of neutropenia in patients undergoing myeloablative therapy followed by bone marrow transplantation considered to be at increased risk of prolonged severe neutropenia. The safety and efficacy of filgrastim are similar in adults and children receiving cytotoxic chemotherapy.  
• Mobilisation of peripheral blood progenitor cells (PBPC).  
• In children and adults with severe congenital, cyclic, or idiopathic neutropenia with an absolute neutrophil count (ANC) of ≤ 0.5 x 10⁹/L, and a history of severe or recurrent infections, long term administration of filgrastim is indicated to increase neutrophil counts and to reduce the incidence and duration of infection-related events.  
• Treatment of persistent neutropenia (ANC ≤ 1.0 x 10⁹/L) in patients with advanced HIV infection, in order to reduce the risk of bacterial infections when other therapeutic options are inappropriate. | Not preferred. NHS Fife Formulary choice is Neupogen®. Filgrastim products should be prescribed by brand name only, due to differences in bioavailability. |
Medicines not recommended by SMC
These products should not normally be prescribed within NHS Fife.

Tocofersolan oral solution (Vedrop®) is not recommended for vitamin E deficiency due to digestive malabsorption in paediatric patients suffering from congenital chronic cholestasis or hereditary chronic cholestasis. Not able to assess economic benefits.

Quetiapine (Seroquel/Seroquel XL) is not recommended for the treatment of major depressive episodes in bipolar disorder. Lack of economic benefits.

Tadalafil (Adcirca®) is not recommended for use for the treatment of pulmonary arterial hypertension (PAH). Non-submission by manufacturer.

Updated Guidance
Paediatric Antibiotic Guidance for the Management of Serious Infections in Children in Hospital
After a recent review of the paediatric antibiotic guidance it has been agreed that the current guidance from 2008 is still valid and requires no changes. The guidance document will be next reviewed in June 2012. Copies of the guidance document can be accessed from the ADTC website www.fifeadt.scot.nhs.uk/ by clicking on the link for antibiotic guidance on the left hand side of the home page.

Addiction Services
Guidance documents relating to the prescribing and treatment of patients with addiction have recently been reviewed and updated.

The guidance documents cover a range of topics to help improve the care of patients with addictions in both primary and secondary care. The documents cover the following topics –

- Management of drug misusers in hospital
- Inpatient management of patients with alcohol withdrawal
- Methadone tolerance testing
- Methadone titration in opioid dependence
- Benzodiazepine prescribing in patients with benzodiazepine dependence
- Detoxification of people with alcohol dependence in the community
- Community detoxification using buprenorphine or lortetidine
- Guidance for the use of unlicensed/ offLabel medicines within NHS Fife addiction services

Copies of the guidance documents can be accessed from the ADTC website www.fifeadt.scot.nhs.uk/ by clicking on the link for guidance documents/formulary appendices on the left hand side of the home page and then clicking on the link for addiction services.

NICE Multiple Technology Assessment (MTA) 223
NHS Healthcare Improvement Scotland (NHS HIS) have confirmed that NICE Multiple Technology Assessment (MTA) 223 - ‘Cilostazol, nafidrofuryl oxalate, pentoxifylline and inositol nicotinate for the treatment of intermittent claudication in people with peripheral arterial disease’ is as applicable in Scotland as the rest of the UK.

Key Recommendations
- Nafidrofuryl is recommended as an option in the treatment of intermittent claudication in people with peripheral arterial disease for whom vasodilator therapy is considered appropriate.
- Cilostazol, pentoxifylline and inositol nicotinate are not recommended.
- Patients currently being prescribed cilostazol, pentoxifylline or inositol nicotinate should be reviewed and a decision be made if their treatment should be stopped or where appropriate switched to nafidrofuryl instead.

Formulary Changes
Memantine
In line with NICE Multiple Technology Assessment 217, March 2011, memantine has been added to the Fife Formulary as an option in the treatment of Alzheimer’s disease in the following circumstances –

- For patients with moderate Alzheimer’s disease only when cholinesterase inhibitors are not tolerated.
- For patients with severe Alzheimer’s disease.
- Treatment should be initiated by a specialist only.
Formulary Compliance - Infections

The ADTC have reviewed primary care prescribing data to monitor compliance with Fife Formulary recommendations for BNF Chapter 5 infections.

The ADTC noted the following –

• Overall prescribing of antibiotics still remains relatively high compared to other Health Boards in Scotland.
• Relative prescribing volume of drugs for the treatment of UTIs is one of the highest in Scotland.
• The compliance rate with the Fife Formulary is high with prescribing of Fife Formulary recommended drugs in most sub-sections being 90 – 100%.

A few key areas where improvement can be made are:

<table>
<thead>
<tr>
<th>BNF sub-section</th>
<th>Non-formulary drugs being prescribed</th>
<th>Formulary Choices</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cephalosporins, cephamycins and other beta-lactams</td>
<td>Cephalosporins</td>
<td>Alternative agents e.g. penicillins, tetracyclines, macrolides</td>
<td>The rate of prescribing of cephalosporins is decreasing over time but cephalosporins still account for approximately £50k p.a. of prescribing in primary care. Cephalosporins are not recommended for general prescribing in primary care due to their C. Difficile potential. Cephalosporins should only be prescribed in primary care if formulary choices are unsuitable / ineffective and it has been recommended by secondary care.</td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>Minocycline</td>
<td>Doxycycline Tetracycline</td>
<td>Minocycline accounts for £38k p.a. of prescribing in primary care. Minocycline is non-formulary as it is associated with higher risk of serious side-effects compared to alternative formulary tetracyclines.</td>
</tr>
<tr>
<td>Antituberculous drugs</td>
<td>Cycloserine</td>
<td>Trimethoprim Nitrofurantoin</td>
<td>Cycloserine is no longer recommended for the long-term prophylaxis of UTIs. Patients being prescribed cycloserine for UTIs should be reviewed and switched to alternative treatments instead.</td>
</tr>
</tbody>
</table>

Prescribers are reminded that formulary choices should be prescribed first line with alternatives only being prescribed where formulary choices are contra-indicated, not tolerated or are ineffective.

Updated Advice on Paracetamol Dosing in Children

The dosing of paracetamol products for use in children has recently been updated. The updated dosing has a larger number of narrower age bands and defines an exact dose per age band. This will ensure that an accurate dose for a child’s age is given.

New doses for different age groups are:

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Age</th>
<th>Dose</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant paracetamol suspension (120mg/5ml)</td>
<td>3 - 6 months</td>
<td>2.5ml</td>
<td>Four times daily</td>
</tr>
<tr>
<td></td>
<td>6 - 24 months</td>
<td>5ml</td>
<td>Four times daily</td>
</tr>
<tr>
<td></td>
<td>2 - 4 years</td>
<td>7.5ml</td>
<td>Four times daily</td>
</tr>
<tr>
<td></td>
<td>4 - 6 years</td>
<td>10ml</td>
<td>Four times daily</td>
</tr>
<tr>
<td>Paracetamol six plus suspension (240mg/5ml or 250mg/5ml)</td>
<td>6 - 8 years</td>
<td>5ml</td>
<td>Four times daily</td>
</tr>
<tr>
<td></td>
<td>8 - 10 years</td>
<td>7.5ml</td>
<td>Four times daily</td>
</tr>
<tr>
<td></td>
<td>10-12 years</td>
<td>10ml</td>
<td>Four times daily</td>
</tr>
</tbody>
</table>

The default doses for paracetamol suspension which were on the Fife e-Formulary for the EMIS prescribing system have been removed so that prescribers can enter the exact dose dependant on the child’s age.

Dates for 2011 ADTC Meetings

<table>
<thead>
<tr>
<th>ADTC meeting</th>
<th>Deadline for submission of papers and agenda items</th>
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</thead>
<tbody>
<tr>
<td>12th October</td>
<td>26th September</td>
</tr>
<tr>
<td>21st December</td>
<td>5th December</td>
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</table>

Contact the Clinical Effectiveness Pharmacist on 01592 226915 for advice on making a formulary submission or for clarification on the process for approval of guidance documents.

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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