# TAYSIDE PRESCRIBER

# Tayside DTC Supplement No 63

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*Produced by NHS Tayside Drug and Therapeutics Committee*

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## SMC Advice Issued in November 2006

### Anastrozole (Arimidex®) – HR+ve early breast cancer after 2-3 years of initial tamoxifen

**SMC recommendation**

**Advice:** following a full submission

Anastrozole (Arimidex®) is accepted for restricted use within NHS Scotland for the adjuvant treatment of early breast cancer in hormone receptor positive postmenopausal women who have received 2 to 3 years of adjuvant tamoxifen.

In a combined analysis of two trials, switching to anastrozole after 2 years of tamoxifen therapy rather than continuing with tamoxifen resulted in a 3.1% increase in event-free survival at three years follow-up. It offers an alternative to tamoxifen after initial adjuvant treatment with tamoxifen for 2-3 years and has a different adverse effects profile. Treatment with anastrozole is restricted to initiation by a breast cancer specialist.

*Click here for SMC link*

**Tayside recommendation**

Recommended within specialist treatment pathway (GPs may prescribe under the direction of a breast cancer specialist)

***Points for consideration*:**

- Tamoxifen, letrozole, anastrozole and exemestane are licensed for the adjuvant treatment of early breast cancer; anastrozole and exemestane may be used as a switch following two to three years of tamoxifen, letrozole may be used following five years of tamoxifen; and anastrozole and letrozole may be used as an alternative to tamoxifen.
- The Scottish Intercollegiate Guidelines Network (SIGN), in the *Management of Breast Cancer in Women* guideline (number 84), recommends tamoxifen as the drug of choice and an aromatase inhibitor if there are relative contraindications or intolerance to its use. The guideline also states that postmenopausal women should be considered for a switch to an aromatase inhibitor after two to three years, or after five years of tamoxifen therapy.
- Anastrozole is the second agent to be licensed for the adjuvant treatment of early breast cancer in hormone receptor positive postmenopausal women, who have received two to three years of adjuvant tamoxifen.
- Anastrozole will be the preferred option, within NHS Tayside, over exemestane on the basis of cost.
- The NHS Tayside breast protocol is currently being updated, in light of the above.
- In the longer term, this additional licence will lead to a cost reduction of hormonal treatments in this setting.

## Docetaxel (Taxotere®) – metastatic gastric adenocarcinoma

**SMC recommendation**
**Advice:** following non-submission
Docetaxel (Taxotere®) injection concentrate in combination with cisplatin and 5-fluorouracil is not recommended for use within NHS Scotland for the treatment of patients with metastatic gastric adenocarcinoma, including adenocarcinoma of the gastroesophageal junction, who have not received prior chemotherapy for metastatic disease.
The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHS Scotland.

**Tayside recommendation**

Not recommended.

## Fludarabine (Fludara® Oral) – B-cell chronic lymphocytic leukaemia (CLL)

**SMC recommendation**
**Advice:** following a full submission
Fludarabine phosphate (Fludara®) is accepted for restricted use within NHS Scotland for the treatment of B-cell chronic lymphocytic leukaemia (CLL) in patients with sufficient bone marrow reserves. First-line treatment should only be initiated in patients with advanced disease, Rai stages III/IV (Binet stage C), or Rai stages I/II (Binet stage A/B) where the patient has disease related symptoms or evidence of progressive disease.
Fludarabine phosphate has been associated with higher response rates than chlorambucil in clinical trials. No overall survival advantage over other therapies has been demonstrated.
Fludarabine is restricted to use by specialists in haemato-oncology.
*Click here for SMC link*

**Tayside recommendation:**

Recommended within specialist treatment pathway – **HOSPITAL ONLY**

***Points for consideration:***

- Chronic lymphocytic leukaemia is the most common adult haematological malignancy and incidence increases with age. Fludarabine, a nucleoside analogue, is an anti-metabolite that is a potent inhibitor of DNA synthesis and reduces synthesis of RNA and proteins.
- Fludarabine with cyclophosphamide is the first-line treatment, within the local CLL protocol, of selected high risk patients with B-cell CLL.
- Place in treatment is in line with past treatment options in the national CLL studies.

## Lopinavir 200mg/ritonavir 50mg tablet (Kaletra®) – HIV-1

**SMC recommendation**
**Advice:** following an abbreviated submission
Lopinavir 200mg, ritonavir 50mg tablet (Kaletra®) is accepted for use in NHS Scotland for the treatment of HIV-1 infected adults and children above the age of 2 years, in combination with other antiretroviral agents. For patients for whom this drug combination is appropriate, it is associated with a reduced pill burden compared to an existing solid oral dose formulation containing these drugs at no increased cost.

**Tayside recommendation**

Recommended within specialist treatment pathway – **HOSPITAL ONLY** (HIV Clinic)

***Points for consideration:***

- Note that Kaletra® tablets are higher strength than capsules – an adult daily dose of four tablets is equivalent to six capsules.
- Unlike the capsules, Kaletra® tablets do not require refrigerated storage.
- **Locally, Kaletra® is considered as the first-line boosted protease inhibitor. The tablet is the formulation of choice. Use is restricted to the HIV clinic.**

## Rituximab (MabThera®) – severe active rheumatoid arthritis (RA)

**SMC recommendation**

**Advice:** following a full submission

Rituximab (MabThera®) is accepted for restricted use within NHS Scotland in combination with methotrexate for treatment of adult patients with severe active rheumatoid arthritis who have had an inadequate response or intolerance to other disease-modifying anti-rheumatic drugs (DMARDs) including one or more tumour necrosis factor (TNF) inhibitor. It is restricted to use by specialist physicians experienced in the diagnosis and treatment of rheumatoid arthritis.

Rituximab in combination with methotrexate improves signs and symptoms and quality of life and prevents joint damage compared to methotrexate, in adults with rheumatoid arthritis who have had an inadequate response to methotrexate and an inadequate response or intolerance to at least one TNF-antagonist.

Treatment should only be repeated in patients who continue to achieve an American College of Rheumatology (ACR) response of at least 20.

Rituximab is cost-effective if the average dosing interval for those patients who respond to initial treatment does not fall below six months.

*Click here for SMC link*

**Tayside recommendation**

Pending development of local protocol

***Points for consideration:***

- Rituximab is a monoclonal antibody that depletes CD20+ B-cells involved in the inflammatory process and reduces disease activity in rheumatoid arthritis (RA). B-cell depletion lasts up to six months, with levels returning to normal in nine to 12 months.
- The pivotal study compared a single course of rituximab (two 1000mg infusions separated by at least two weeks) plus weekly methotrexate to placebo and weekly methotrexate alone. ACR20 response was measured at 24 weeks and was achieved by 51% and 18% of patients in the rituximab and placebo groups respectively.
- Whilst rituximab has not been directly compared with TNF-antagonists, ACR responses appear similar.
- A further open-label study indicates that a repeated course of rituximab is effective and is not associated with an increase in adverse events or toxicity. The median time to rituximab retreatment was approximately 52 weeks.
- There are limited data on multiple repeat treatments with rituximab.
- In common with the TNF-antagonist infliximab, which is associated with infusion reactions that can be severe, rituximab must be administered in an environment where resuscitation facilities are available.
- The cost of one course of rituximab is £3,500 per patient. Assuming retreatment at around one year, rituximab is less expensive than TNF-antagonists. (Annual treatment with etanercept or adalimumab costs £9,300).
- Local guidelines to support the use of rituximab in the treatment of RA are currently under development by the rheumatology team.

## Sorafenib (Nexavar®) – advanced renal cell carcinoma

**SMC recommendation**

**Advice:** following a full submission

Sorafenib (Nexavar®) is not recommended for use within NHS Scotland for the treatment of patients with advanced renal cell carcinoma who have failed prior interferon-alfa or interleukin-2 based therapy or are considered unsuitable for such therapy.

Sorafenib has been compared with best supportive care and has been shown to increase progression-free survival, though the impact on overall survival is uncertain. The cost-effectiveness of sorafenib has not been demonstrated.

*Click here for SMC link*

**Tayside recommendation**

Not recommended

## Withdrawal of Becotide® and Becloforte®

The withdrawal of Becotide® and Becloforte® inhalers is planned for the third quarter of 2007. The NHS Tayside Respiratory Managed Clinical Network (MCN) is currently developing an area-wide strategy to assist practices in the switch to CFC-free beclometasone. Practices are advised to wait for this MCN guidance. Meantime, new patients should be started on a CFC-free beclometasone inhaler prescribed by brand name.

## Forthcoming SMC Advice

| Gastro-intestinal system |
|---|
| Beclometasone dipropionate 5mg (Clipper®) |
| 0.4% glyceryl trinitrate ointment (Rectogesic) |
| Mesalazine (Asacol®) |
| **Cardiovascular system** |
| Perindopril (Coversyl®) |
| Rimonabant (Accomplia®) |
| Ivabradine (Procoralan®) |
| Tachosil |
| **Respiratory** |
| Omalizumab (Xolair®) - *Resubmission* |
| **Central nervous system** |
| Buprenorphine/naloxone (Suboxone®) |
| Clostridium botulinum type A (Dysport®) |
| Donepezil orodispersible tablets (Aricept Evess®) |
| Lidocaine medicated plaster (Versatis®) |
| Rasagiline (Asilect®) - *Resubmission* |
| Varenicline (Champix®) |
| **Infections** |
| Daptomycin 500mg (Cubucin®) |
| Ertapenem (Invanz®) - *Abbreviated* |
| Tobramycin (Bramitob®) |
| **Endocrine system** |
| Parathyroid hormone (Preotact®) |
| Pioglitazone triple therapy (Actos®) |
| Triptorelin (Decapeptyl® SR) |

| Obstetrics, gynaecology & UT Disorders |
|---|
| Propiverine (Detrunorm XL®) |
| **Malignant disease & immunosuppression** |
| Busulfan IV (Busilvex®) |
| Clofarabine (Evoltra®) |
| Gemcitabine (Gemzar®) - *Resubmission* |
| Interferon beta-1b (Betaferon®) |
| Lanreotide (Somatuline® LA) |
| Mitotane (Lysodren®) |
| Natalizumab (Tysabri®) |
| Pemetrexed (Alimta®) |
| Sunitinib (Sutent) |
| Tacrolimus (Prograf®) |
| Temozolomide (Temodal®) |
| Vinorelbine (Navelbine® Oral) |
| **Nutrition & Blood** |
| Alglucosidase alfa (Myozyme®) |
| Deferasirox (Exjade®) |
| Lanthanum carbonate (Fosrenol®) |
| Pegfilgrastim (Neulasta®) |
| **Musculoskeletal and joint diseases** |
| Adalimumab (Humira®) |
| Methotrexate injection (Metoject®) |
| **Skin** |
| Azelaic acid (Finacea® 15% gel) |
| Infliximab (Remicade®) |

**Contact details:** Local implementation of SMC recommendations is being taken forward by the Tayside Medicines Unit - contact Jan Jones, Principal Pharmacist - Pharmacoeconomics (janjones@nhs.net) if you have any queries in relation to the introduction of new drugs within NHS Tayside.