TAYSIDE PRESCRIBER

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Produced by Tayside New Medicines Implementation Panel (NMIP)

In this issue:

SMC Advice Issued in August 2004

Aripiprazole (Abilify®) - schizophrenia

SMC recommendation

Advice: following a full submission.

Aripiprazole (Abilify®) is accepted for use within NHS Scotland for the treatment of schizophrenia. It is one of several atypical anti-psychotic medicines that improve symptoms of an acute relapse and reduce the risk of relapse comparable to a typical antipsychotic. The evidence of comparable efficacy to other atypical antipsychotics is limited. It is associated with a lower incidence of extra-pyramidal side effects than typical antipsychotics, and comparable to other atypicals. It is associated with less elevation of serum prolactin, less lipid abnormalities and less clinically significant weight gain over the short-term compared with other atypical antipsychotics. It does not adversely effect blood glucose nor have a clinically significant advantage compared to other antipsychotics with respect to this.

Tayside recommendation

Recommended within specialist treatment pathway

Points for consideration:

- Aripiprazole is the 8th atypical antipsychotic on the UK market. It is a partial agonist at dopamine D_2 and serotonin 5-HT_{1A} receptors and an antagonist at 5-HT_2 receptors.
- A recent Cochrane review concludes that aripiprazole 'is not much different from typical antipsychotics and atypical antipsychotics with respect to treatment response, efficacy or tolerability. In comparison with typical antipsychotics, aripiprazole may have a higher risk of insomnia, but in comparison to atypical antipsychotics, less risk of raised prolactin and prolongation of QTc interval'.
- Aripiprazole is priced competitively versus other atypical antipsychotics.
- **Aripiprazole is recommended locally, under the direction of a psychiatrist, as an alternative treatment option for the management of patients with a diagnosis of schizophrenia. It is indicated where patients on previous treatment have experienced unacceptable weight gain, symptomatic hyper-prolactinaemia (breast enlargement, production of milk, sexual dysfunction), lipid abnormalities (blood monitoring/family history) or cardiac conduction abnormalities (prolonged QTc interval).**
  It is also indicated where patients are at increased risk of developing these adverse effects.

Continued over

Aripiprazole continued

- The Mental Health Prescribing Group is currently revising the Tayside Schizophrenia algorithm to include a table of comparative side-effects to guide choice of antipsychotic agent. Measurement of side-effects using rating scales will also be recommended.
- Refer to NICE guidance No.43 for further information on the use of atypical antipsychotic drugs for the treatment of schizophrenia.

Fulvestrant (Faslodex®) – advanced breast cancer

SMC recommendation

Advice: following a full submission.

Fulvestrant is not recommended for use within NHS Scotland for the treatment of postmenopausal women with advanced breast cancer who relapse or progress following prior anti-oestrogen therapy. Fulvestrant is no more effective than aromatase inhibitors when used following the failure of tamoxifen, and it is approximately four times more expensive. There are no clinical data on the use of fulvestrant following failure of aromatase inhibitors

Tayside recommendation

Not recommended

Points for consideration:

- Fulvestrant is an injectable steroidal oestrogen antagonist from a new class of drugs known as selective oestrogen receptor down regulators (SERDs). It is a 'pure' oestrogen-receptor antagonist with no oestrogenic agonist activity.
- Adverse effects associated with fulvestrant appear to be similar in type and frequency to those of anastrozole. However, long-term safety data are required to confirm effects on oestrogen responsive tissues and whether a lack of partial agonist activity reduces the risk of oestrogen associated adverse effects, such as thromboembolic events and endometrial cancer, and increases the likelihood of adverse effects on bone density.
- Fulvestrant is not stocked by the hospital pharmacy**.**

Insulin detemir (Levemir®) – diabetes mellitus

SMC recommendation

Advice: following a full submission.

Insulin detemir is accepted for restricted use within NHS Scotland for the treatment of diabetes mellitus. Insulin detemir is an acceptable basal insulin for patients with diabetes mellitus. Its use should be targeted on patients attempting to achieve better hypoglycaemic control as there may be some benefit related to a reduced intra-individual variation in glycaemic profile for insulin detemir compared with established insulins. It appears to be cost-effective from the base-case of economic modelling, but this is limited by the degree of extrapolation involved and the associated width of the confidence intervals.

Tayside recommendation

Recommended within specialist treatment pathway

Points for consideration:

- Insulin detemir is a long-acting soluble insulin analogue which remains in solution after injection.
- Insulin detemir shows similar improvements in HbA_{1c} as isophane insulin in both type 1 and type 2 diabetic patients. A lower incidence of hypoglycaemia has been demonstrated in some trials.
- No efficacy or safety data versus insulin glargine, the only other available long-acting basal insulin, are currently available.
- Insulin detemir is the same cost as insulin glargine.
- **Insulin detemir is recommended locally as an alternative to insulin glargine in patients who are unable to achieve optimal glycaemic control with established insulins due to risk of hypoglycaemia.**

Losartan (Cozaar®) – hypertension with left ventricular hypertrophy (LVH)

SMC recommendation

Advice: following a full submission.

Losartan (Cozaar®) is accepted for use within NHS Scotland for the treatment of hypertensive patients with left ventricular hypertrophy.

In a large international trial a losartan-based regimen reduced the risk of stroke compared with a beta-blocker-based regimen in patients with hypertension and left ventricular hypertrophy (LVH), who were without clinically evident vascular disease. There are no data on benefits relative to other antihypertensive agents. The trial data are included in the British Hypertension Society guidelines and reference should be made to these with regard to treatment choices for individual patients. An economic model indicates that a losartan-based regimen is cost-effective in patients with hypertension and LVH compared with a beta-blocker-based regimen.

Tayside recommendation

Not currently recommended – pending formulary decision

Points for consideration:

- Losartan is the only antihypertensive licensed for the subset of patients with LVH.
- The BHS guidelines note that controversy remains as to whether results from the LIFE study (outlined above) reflect less effective stroke protection by beta-blockers.
- No evidence currently exists to assess whether angiotensin II receptor antagonists offer any advantage over ACE inhibitors in patients with evidence of LVH. Losartan is considerably more expensive than generic lisinopril (the locally favoured ACE inhibitor for the treatment of hypertension).
- **Low dose thiazide diuretics or beta-blockers remain local first-line treatment options for the majority of hypertensive patients.**
- Further advice on the management of hypertension is available in the Cardiovascular Guidance Notes within the Tayside Area Prescribing Guide (TAPG).
- **The place of losartan in relation to other antihypertensives will be addressed by the Formulary Committee. Prescribers are advised to await the outcome of the formulary decision.**

Montelukast 4mg paediatric granules (Singulair®) - asthma

SMC recommendation

Advice: following an abbreviated submission

Montelukast paediatric 4 mg granules (Singulair®) are accepted for use in NHS in Scotland for the treatment of asthma as add-on therapy in those patients with mild to moderate persistent asthma who are inadequately controlled on inhaled corticosteroids and in whom 'as needed' short-acting beta-agonists provide inadequate clinical control of asthma. It is also accepted for the prophylaxis of asthma in which the predominant component is exercise-induced bronchoconstriction. This formulation is suitable for the treatment of children aged 6 months to 5 years, and the licence for montelukast has been extended to include children aged 6 months to 2 years, though the Summary of Product Characteristics adds that experience in those aged 6 to 12 months is limited. Its introduction is expected to have minimal resource implications in Scotland.

Tayside recommendation

Recommended within specialist treatment pathway

Points for consideration:

- Singulair® granules are a new formulation of montelukast licensed for use in paediatric patients 6 months to 5 years of age. (Tablets are licensed in children aged 2 to 14 years).
- Singulair® 4mg paediatric granules are priced in line with the tablets (£26 for 28 days treatment with 4mg or 5mg chewable tablets).
- **Montelukast granules are recommended locally, under the direction of a paediatrician, for the treatment of chronic asthma in children under 5 years:**
  - **who require regular preventer therapy and an inhaled steroid cannot be used (ie step 2 of SIGN/BTS guideline)**
  - **who require add-on asthma therapy (ie step 3)**

Continued over

Montelukast continued

- Refer to the Respiratory Guidance Notes in the TAPG for further information on the management of chronic asthma in children.

Pimecrolimus cream (Elidel®) – atopic dermatitis

SMC recommendation
Advice: following Independent Review Panel assessment.
Not recommended for use within NHS Scotland.
Pimecrolimus cream is the first topical immunomodulator licensed for the treatment of signs and symptoms of mild-to-moderate atopic dermatitis. There is no evidence that it has clinical advantage in terms of efficacy or safety when compared with the alternative treatments, which include mild-to-moderately potent topical corticosteroids. The economic case for using this preparation is unproven.

Tayside recommendation

Not recommended

Pioglitazone (Actos®) – type 2 diabetes mellitus

SMC recommendation
Advice: following a full submission.
Pioglitazone (Actos®) is not recommended for use within NHS Scotland as monotherapy for patients with type 2 diabetes mellitus.
It is one of two peroxisome proliferator-activated receptor-γ agonists recently marketed in the UK for this indication. In controlling blood glucose, its mid range and maximum doses were non-inferior to standard sulphonylurea therapies. The economic case for pioglitazone has not been demonstrated.

Tayside recommendation

Not recommended

Points for consideration:

- Pioglitazone is also indicated for combination treatment. The above SMC advice relates only to the monotherapy indication.
- Pioglitazone is considerably more expensive than sulphonylurea therapy.

Risperidone (Risperdal®) – mania in bipolar disorder

SMC recommendation
Advice: following a full submission.
Risperidone is accepted for use within NHS Scotland for the treatment of episodes of mania in bipolar disorder.
Risperidone has similar efficacy to haloperidol in improving symptom scores, with fewer extrapyramidal side effects. In an economic model based on indirect comparison, monotherapy with risperidone appears to be cost-effective. No evidence is submitted on its cost-effectiveness profile in co-therapy.

Tayside recommendation

Recommended within specialist treatment pathway

Points for consideration:

- Risperidone is the 3rd atypical antipsychotic to be licensed for the acute treatment of mania. Unlike olanzapine, it is not currently licensed for maintenance therapy.
- No comparative safety or efficacy data versus olanzapine or quetiapine are available.
- Licensed doses of risperidone are priced slightly lower than olanzapine and quetiapine.
- Further information on the management of patients with bipolar affective disorder is available within consensus guidelines produced by the British Association of Psychopharmacology.
- A SIGN guideline on the management of bipolar affective disorder in primary and secondary care is due in Autumn 2004.

Continued over

Risperidone continued

- **The use of risperidone in the treatment of manic episodes is restricted to patients under the overall supervision of clinicians experienced in managing bipolar disorder.**

Rosiglitazone (Avandia®) – type 2 diabetes mellitus

SMC recommendation

Advice: following a resubmission.

Rosiglitazone (Avandia®) is accepted for restricted use within NHS Scotland as monotherapy for type 2 diabetes mellitus patients in whom consideration is otherwise being given to commencing insulin therapy. **It is not recommended as monotherapy for any other group of patients.**

It is one of two peroxisome proliferator-activated receptor-γ agonists recently marketed in the UK for this indication. Its use should be confined to patients who have already experienced severe hypoglycaemia or who are intolerant of metformin and sulphonylureas.

Tayside recommendation

Recommended within specialist treatment pathway

Points for consideration:

- **Rosiglitazone monotherapy is restricted to type 2 diabetic patients who would otherwise commence insulin therapy eg those intolerant of metformin and sulphonylureas, on the recommendation of the diabetic clinic.**
- Very few patients are anticipated to fall into the above category.

Funding of High Cost Secondary Care New Medicines in the Acute Services Division (ASD)

The Acute Services Division is not holding a specific sum in reserve for new medicines accepted by the SMC in 2004-05. Clinical Groups have been advised to reserve funds within their allocated prescribing budgets. NMIP will continue to provide information to Clinical Groups to allow them to consider proposals for the use of new medicines.

Contact details: Local implementation of SMC recommendations is being taken forward by the Tayside Medicines Unit – contact Jan Jones, Pharmaceutical Prescribing Adviser (jan.jones@tpct.scot.nhs.uk) if you have any queries in relation to the introduction of new drugs within NHS Tayside