

Monthly briefings are produced in order to help members of the media and other interested groups understand the work and advice of the Scottish Medicines Consortium. The full advice for each drug that we have assessed can be found at [www.scottishmedicines.org](http://www.scottishmedicines.org)

SMC has this month accepted the following drugs for use within NHSScotland.

## betaine anhydrous oral powder (Cystadane®)

SMC accepted betaine anhydrous oral powder as adjunctive (add-on) treatment of homocystinuria involving deficiencies or defects in cystathionine beta-synthase (CBS), 5,10-methylene-tetrahydrofolate reductase (MTHFR) or cobalamin cofactor metabolism (cbl).

- Homocystinuria is a rare inherited disorder which causes build up in the blood and urine of a harmful type of protein called homocysteine. It is a serious life-long disease and can result in mental retardation, eye sight problems, bone abnormalities and a risk of harmful blood clotting.
- There is currently no treatment to correct the basic genetic causes of homocystinuria. The aim of treatment is to normalise the homocysteine levels by several methods including use of vitamins, special restrictive diets and supplementation of deficient products. Betaine lowers the levels of homocysteine in the body by changing it to another substance.
- The nature of this condition makes it difficult to assess the effectiveness of betaine anhydrous oral powder compared with standard therapy alone, so there are limited clinical data on its usefulness. There is evidence that the risk of harmful clotting events such as heart attack or stroke is lower in patients treated with betaine compared with that in those untreated.
- The side effects reported during treatment are mild and

## About SMC

The purpose of the Scottish Medicines Consortium (SMC) is to accept for use those newly licensed drugs that clearly represent good value for money to NHSScotland.

SMC analyses information supplied by the drug manufacturer on the health benefits of the drug and justification of its price.

Because the NHS has limited resources, SMC works to make sure that those drugs which represent good value for money are accepted for routine use as quickly as possible so that they can benefit patients.

The Consortium is made up of lead clinicians, pharmacists and health economists together with representatives of health boards, the pharmaceutical industry, the public and the Scottish Government.

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If you are interested in the work of SMC you can visit our website at:

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mainly gut related, for example, diarrhoea, stomach discomfort, nausea and vomiting. A small number of potentially life-threatening cases of severe cerebral oedema (brain swelling) have been reported although it is not clear whether this is related to therapy.

- SMC accepted betaine anhydrous oral powder for use within NHSScotland despite offering relatively poor value for money because there are no other treatment options of proven clinical benefit in this rare and potentially life-threatening condition.

## indacaterol (Onbrez Breezhaler<sup>®</sup>)

SMC accepted indacaterol for maintenance bronchodilator treatment of airflow obstruction in adults with chronic obstructive pulmonary disease (COPD).

- Chronic obstructive pulmonary disease (COPD) is the name given to several conditions (such as long-term bronchitis and emphysema) in which the airways of the lungs are blocked or narrowed. The blockage is usually caused by inflammation of the lining of the airways. Symptoms include shortness of breath after exercise, wheeze and a persistent cough which may bring up thick mucus (sputum) regularly. Measuring the maximum amount of air that a person can force out of their lungs in one second can indicate if a person has COPD and how severe the condition is. This is termed the forced expiratory volume (FEV1) and is usually expressed as a percentage of the volume that would be predicted for a patient of that age.
- Drugs to help improve symptoms and control COPD include bronchodilators to expand the airways and corticosteroids to reduce inflammation. Indacaterol is a long-acting bronchodilator which acts locally when inhaled. It is inhaled once daily.
- A number of studies showed that indacaterol is more effective than placebo (a dummy drug containing no active treatment) and other long-acting bronchodilators in improving lung function as measured by FEV1 after 12 weeks.
- The safety of indacaterol was similar to other long-acting bronchodilators, with the most common side effect being a mild cough after inhalation which did not lead to patients discontinuing the study.
- SMC accepted indacaterol for use within NHSScotland because it was similar in price or less expensive than the standard comparators used in the economic case presented by the manufacturer.

## eltrombopag (Revolade<sup>®</sup>)

SMC accepted eltrombopag for the treatment of adult chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients with no spleen who are refractory to other treatments or as second-line treatment for adult patients where surgery to remove the spleen is contraindicated. Its use is restricted to patients with severe ITP at high risk of bleeding.

- Immune thrombocytopenic purpura is a disorder in which the blood does not clot normally and can lead to an increased risk of bleeding or bruising. Patients with ITP have a lower number of a type of blood cell called platelets (which are needed to prevent bleeding) because their immune system attacks and destroys their own platelets.
- Treatment of ITP aims to increase the number of circulating platelets, and can include drugs such as corticosteroids and blood products such as immunoglobulin or surgery to remove the spleen. Eltrombopag is a new drug that works by stimulating the thrombopoietin receptor on the surface of platelets to increase the number of platelets in your blood. It is given orally as a tablet.
- A study has shown that eltrombopag was more effective than placebo (a dummy drug containing no active treatment) in increasing platelets and maintaining this level in patients with ITP who had received previous treatment. Eltrombopag also decreased the number of bleeds experienced by patients treated with it.
- In the study, more patients treated with eltrombopag experienced nausea and vomiting than patients treated with placebo. More serious side effects can include liver problems, blocked blood vessels due to clots, cataracts and bone marrow problems. There are also concerns that the condition returns when treatment is stopped.
- SMC accepted eltrombopag for use in NHSScotland because it is effective and can be given orally, and offered reasonable value for money compared with an alternative treatment.

SMC decided that the following drugs are not value for money for NHSScotland.

## betamethasone valerate medicated plaster (Betesil<sup>®</sup>)

SMC did not accept betamethasone valerate for the treatment of inflammatory skin disorders which do not respond to treatment with less potent corticosteroids.

- Eczema, psoriasis, lichenification, lichen planus, granuloma annulare, palmoplantar pustulosis and mycosis fungoides are all skin disorders caused by the body's immune system over-reacting. Symptoms include inflammation, irritation, itching and redness.
- Betamethasone valerate is a corticosteroid, a type of medicine which can interfere with the body's immune system and reduce inflammation. It can be applied as a medicated plaster directly to the affected area of skin.
- Studies have shown that betamethasone valerate medicated plasters more effectively improved the symptoms of mild to moderate plaque psoriasis compared with the same medicine applied as a cream. However, only a small number of patients were studied and the plaster was not compared with a placebo plaster (one which didn't contain active drug) or with cream covered by a dressing.

- The number of patients treated using plasters who experienced side effects was similar to that of those treated using cream. While some patients preferred the plaster, others preferred the cream.
- SMC did not accept betamethasone valerate medicated plasters for use within NHSScotland due to the uncertainty of its effectiveness compared with other standard methods of treatment used in NHSScotland. In addition, the economic case submitted by the manufacturer showed that betamethasone plasters cost more than using cream covered by a dressing (unless three or more dressings per day are required) which meant it was not considered to be value for money.

## trastuzumab (Herceptin<sup>®</sup>)

SMC did not accept trastuzumab, in combination with capecitabine or 5-fluorouracil and cisplatin, for the treatment of HER2 positive metastatic adenocarcinoma of the stomach or gastro-oesophageal junction in patients who have not received prior anti-cancer treatment.

- Adenocarcinoma is a cancer which starts in the cells of organs which make a substance for release, such as the stomach or gastro-oesophageal junction (where the gullet meets the stomach). In metastatic adenocarcinoma, the cancer cells have spread to other parts of the body. Cancer cells which have a certain type of receptor on their surface are known as HER2 positive.
- Trastuzumab is an anti-cancer drug that works by blocking the HER2 receptor. It is given in combination with capecitabine or 5-fluorouracil and cisplatin chemotherapy.
- The addition of trastuzumab to capecitabine or 5-fluorouracil and cisplatin has been shown to increase overall and progression-free survival and tumour response compared with the chemotherapy alone. However, trastuzumab was not compared with 5-fluorouracil and cisplatin plus epirubicin, the combination of treatments most commonly used in Scotland.
- The established side effects of trastuzumab include infusion reactions, and gastrointestinal, respiratory and cardiac effects.
- SMC did not accept trastuzumab for use in NHSScotland because the treatment's cost outweighed its health benefits and there were a number of uncertainties in the manufacturer's economic case which meant that the drug was not considered to be value for money.

## olanzapine long-acting injection (ZypAdhera<sup>®</sup>)

SMC did not accept olanzapine long-acting injection (LAI) for the maintenance treatment of adult patients with schizophrenia sufficiently stabilised during acute treatment with oral olanzapine.

- Schizophrenia is a common and serious mental illness, the cause of which is unknown. Symptoms include delusions (false ideas), hallucinations (seeing or hearing things that are not real) and disordered thoughts.
- Medication (known as antipsychotic drugs) is used to reduce the symptoms. It is usually taken

long term to prevent further episodes. Olanzapine LAI is an antipsychotic drug (known as an atypical antipsychotic) given as an injection once every 2 or 4 weeks depending on the desired dose. It is intended to improve compliance in patients with difficulty adhering to oral medication.

- A study has shown that olanzapine LAI prevented relapse as well as daily oral olanzapine treatment in patients whose schizophrenia had stabilised for more than 24 weeks. However, there was no evidence that adherence to treatment was improved with the injection compared with the oral treatment. There was no direct comparison of the effectiveness with that of risperidone LAI, the only other medicine of this type available as an LAI.
- The side effects of olanzapine LAI in the study were similar to those with oral olanzapine. Few patients experienced irritation at the site of the injection. The main safety concern is the risk of post-injection syndrome in approximately 2% of patients. For this reason patients must be supervised by a trained doctor or nurse for 3 hours after the injection.
- SMC did not accept olanzapine LAI for use in NHSScotland because the clinical benefits compared with other treatments used in NHSScotland were not proven in a formal, robust way and the manufacturer did not show that it was value for money compared with the range of other available treatments.

## ofatumumab (Arzerra®)

SMC did not accept ofatumumab for the treatment of chronic lymphocytic leukaemia (CLL) in patients who are refractory to fludarabine and alemtuzumab.

- CLL is the most common type of leukaemia (cancer of the white blood cells). Healthy white blood cells develop in the bone marrow and help to fight infection. In CLL, the white blood cells are not fully developed and multiply out of control, crowding out healthy blood cells that can fight infection. CLL usually develops very slowly and many people with CLL do not need treatment for months or years.
- CLL is treated by surgery, chemotherapy, radiation or a combination of these treatments. Ofatumumab is a type of anti-cancer drug called a monoclonal antibody. It binds to the abnormal cells and helps to destroy them while having no effect on healthy blood cells. Ofatumumab is given via a drip once a week for 8 weeks, followed 4-5 weeks later by a dose once every 4 weeks.
- A study has shown that 58% of patients for whom previous fludarabine and alemtuzumab treatment had been unsuccessful showed some improvement with ofatumumab. However, more than half of patients had received further therapies which could have contributed to the overall survival. Additionally, there was no direct comparison of survival in patients given ofatumumab with those receiving only best supportive care.
- In the study, ofatumumab was well tolerated. Side effects were as expected for this type of drug and included infection, low levels of white blood cells, cough, diarrhoea, shortness of breath, rash, fever, tiredness and nausea.

- SMC did not accept ofatumumab for use in NHSScotland because the treatment's cost outweighed its health benefits and there were a number of uncertainties in the manufacturer's economic case which meant that the drug was not considered to be value for money.

For drugs that have not been accepted by SMC, all NHS boards have procedures in place to consider individual requests when a doctor feels the drug would be right for a particular patient. SMC has told the manufacturers why the drug was not accepted and would be pleased to receive any resubmission.

For further information and to view the complete advice for the drugs listed above, visit our website at:

**[www.scottishmedicines.org.uk](http://www.scottishmedicines.org.uk)**