

lisdexamfetamine dimesylate, 30mg, 50mg & 70mg capsules (Elvanse®)  
SMC No. (863/13)

## Shire Pharmaceutical Contracts Ltd

05 April 2013

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHS Scotland. The advice is summarised as follows:

**ADVICE:** following a full submission

**lisdexamfetamine dimesylate (Elvanse®)** is accepted for use within NHS Scotland.

**Indication under review:** as part of a comprehensive treatment programme for attention deficit/hyperactivity disorder (ADHD) in children aged 6 years of age and over when response to previous methylphenidate treatment is considered clinically inadequate.

In a multi-centre, randomised, double-blind, controlled study in children and adolescents with ADHD, treatment with lisdexamfetamine was associated with a shorter time to first response compared with a non-stimulant, centrally-acting sympathomimetic agent. A greater proportion of lisdexamfetamine treated patients achieved improvements in symptom scores and functioning than those treated with the active comparator.

Overleaf is the detailed advice on this product.

**Chairman,  
Scottish Medicines Consortium**

## Indication

As part of a comprehensive treatment programme for attention deficit/hyperactivity disorder (ADHD) in children aged 6 years of age and over when response to previous methylphenidate treatment is considered clinically inadequate.

Treatment must be under the supervision of a specialist in childhood and/or adolescent behavioural disorders.

## Dosing Information

Dosage should be individualised according to the therapeutic needs and response of the patient. Careful dose titration is necessary at the start of treatment with lisdexamfetamine.

For all patients, either starting treatment for ADHD or switching from another medication, the starting dose is 30mg taken once daily in the morning.

The daily dose may be increased by 20mg increments, at approximately weekly intervals. Lisdexamfetamine should be administered orally at the lowest effective dosage.

The maximum recommended dose is 70mg/day; higher doses have not been studied.

Treatment must be stopped if the symptoms do not improve after appropriate dosage adjustment over a one month period. If paradoxical aggravation of symptoms or other intolerable adverse events occur, the dosage should be reduced or discontinued.

Treatment must be initiated under the supervision of an appropriate specialist in childhood and/or adolescent behavioural disorders.

## Product availability date

March 2013

## Summary of evidence on comparative efficacy

Attention deficit/hyperactivity disorder (ADHD) is one of the most commonly diagnosed behavioural disorders among children and adolescents. Common features include developmentally inappropriate levels of activity and impulsivity, an impaired ability to sustain attention and a combination of both. Lisdexamfetamine is a pharmacologically inactive prodrug which following absorption undergoes hydrolysis to dexamfetamine, the active moiety. The mode of action in ADHD is not fully established, but it is thought to be due to its ability to block the reuptake of norepinephrine and dopamine into the pre-synaptic neuron and increase the release of these monoamines into the extraneuronal space.<sup>1</sup>

Evidence for the use of lisdexamfetamine in the management of children and adolescents with ADHD is from three pivotal studies.

A multi-centre, double-blind, randomised, active-controlled phase III study recruited children and adolescents (aged 6 to 17 years) with ADHD of moderate severity, ADHD Rating Scale version IV (ADHD-RS-IV) total score of  $\geq 28$  and who had a historical or current inadequate response to treatment

with methylphenidate. (The ADHD-RS-IV assesses the major symptoms of ADHD, grouped into two sub-scales: inattention and hyperactivity/impulsivity with total score ranging from 0 to 54, higher scores indicating more severe symptoms).<sup>2</sup>

Patients were randomised equally to either lisdexamfetamine (30mg to 70mg/day) or atomoxetine (10mg to 100mg/day), with stratification by country. Treatment was administered over nine weeks consisting of a four-week dose optimisation phase (titration schedules as per respective licences) followed by a five-week maintenance phase.<sup>3</sup>

The primary outcome was the time to response, assessed at each weekly visit during the study, defined as attainment of a Clinical Global Impression – Improvement (CGI-I) score of 1 (very much improved) or 2 (much improved) measured on a seven-point scale, ranging from 1 to 7 (very much worse). Patients who did not complete the study and those who completed the study without response were censored the end of the study.

In the full analysis set (FAS), defined as all randomised patients who had taken at least one dose of randomised treatment, 89% (113/127) of patients in the lisdexamfetamine group compared with 76% (102/135) of patients in the atomoxetine group met the response criterion. The median time to first response was significantly shorter for patients in the lisdexamfetamine group, 12 days (95% confidence interval [CI]: 8 to 16) compared with the atomoxetine group, 21 days (95% CI: 15 to 23),  $p=0.001$ .<sup>3</sup>

Secondary outcomes included an alternative assessment of treatment response, defined as a  $\geq 25\%$ ,  $\geq 30\%$  or  $\geq 50\%$  reduction in ADHD-RS-IV total score from baseline. Significantly more patients in the lisdexamfetamine group compared with atomoxetine were classed as responders for each threshold at each study visit.<sup>3</sup>

Quality of life was assessed using the Health Utilities Index-2 multi-attribute utility function in which scores range from 0 (health-related quality of life equivalent to death) to 1.0 (perfect health). At baseline, the mean score was 0.830 and 0.867 for patients in the lisdexamfetamine and atomoxetine groups respectively. At week 9, the respective scores were approximately 0.92. No statistical comparison was made between the groups.<sup>3</sup>

A seven-week phase III, double-blind, randomised, placebo and active controlled dose-optimisation safety and efficacy study recruited children and adolescents with ADHD of at least moderate severity, ADHD-RS-IV total score at baseline  $\geq 28$ . Randomisation was stratified by country and age group (child or adolescent) and patients were assigned to once-daily lisdexamfetamine ( $n=113$ , starting dose 30mg/day), placebo ( $n=111$ ), or osmotic-release oral system methylphenidate, OROS-MPH ( $n=112$ , starting dose 18mg/day). Doses were optimised on a weekly basis over four-weeks and patients continued for a further three-week maintenance phase. Doses were titrated to achieve at least a 30% reduction in ADHD-RS-IV total score from baseline and a CGI-I rating of one or two, with tolerable adverse effects. The study was not designed to formally compare the active treatments.<sup>4</sup>

The primary outcome of this study was the change from baseline in the investigator-rated ADHD-RS-IV total score at endpoint, analysed in the FAS, definition as per the first study. Endpoint was defined as the last on-therapy, post-randomisation treatment visit at which a valid ADHD-RS-IV total score was observed. From a mean ADHD-RS-IV total score at baseline of 41.0, 41.2 and 40.4, the least squares mean ( $\pm$  standard error [SE]) changes in ADHD-RS-IV total score from baseline to endpoint were -24.3 ( $\pm 1.2$ ), -5.7 ( $\pm 1.1$ ) and -18.7 ( $\pm 1.1$ ) for the lisdexamfetamine, placebo and OROS-MPH groups respectively. The treatment difference between lisdexamfetamine and placebo was -18.6 (95% CI: -21.5 to -15.7,  $p<0.001$ ), and between OROS-MPH and placebo was -13.0 (95% CI: -15.9 to -10.2,  $p<0.001$ ). There was no comparison between active treatments reported.<sup>4</sup>

The proportion of responders, defined by a CGI-I score of 1 or 2, at endpoint was significantly greater in the lisdexamfetamine (78%) and OROS-MPH (61%) groups compared with placebo (14%).<sup>4</sup>

Health-related quality of life was measured using the Child Health and Illness Profile, Child Edition: Parent Report Form (CHIP-CE:PRF) global T-score at up to seven weeks. This is composed of five domains (satisfaction, comfort, resilience, avoidance, and achievement) consisting of a total of 76 items. Higher scores indicate better health. The least squares mean ( $\pm$ SE) change from baseline in CHIP-CE:PRF global T-score at up to seven weeks was 8.6 ( $\pm$ 1.1), -0.2 ( $\pm$ 1.1) and 7.1 ( $\pm$ 1.1) in the lisdexamfetamine (n=78), placebo (n=80) and OROS-MPH (n=75) groups respectively. The differences between the active treatments and placebo were statistically significant.<sup>5</sup>

A phase III, double-blind, randomised, multi-centre, placebo-controlled, withdrawal extension study recruited patients from the placebo-controlled study described above and also included direct entry patients using the same criteria as the core study. Patients initially received open-label lisdexamfetamine (n=276) in a four-week dose optimisation period, followed by at least 20 weeks maintenance and then a two-week fixed-dose period. During the fixed-dose period, patients were withdrawn from the study if they experienced unacceptable side effects, required dose adjustment, or had sufficiently severe ADHD: ADHD-RS-IV total score  $>22$  or CGI-Severity score  $\geq 3$  (range from 1 [normal, not at all ill] to 7 [among the most extremely ill]). Eligible patients at this point were entered into the six-week, double-blind, randomized-withdrawal phase of the study, in which patients were assigned to continue with lisdexamfetamine (n=78) or take placebo (n=79).<sup>6</sup>

The primary outcome of the study was the proportion of patients with treatment failure during the six week randomized-withdrawal period. Treatment failure was defined as a  $\geq 50\%$  increase in ADHD-RS-IV score and  $\geq 2$  point increase in the CGI-Severity score at any visit compared with scores at the start of the randomized-withdrawal period. In the FAS, the proportion of patients with treatment failure during the randomised-withdrawal period was significantly lower in the lisdexamfetamine group compared with the placebo group (16% versus 68%,  $p < 0.001$ ). Quality of life was assessed using the CHIP-CE-PRF. In the randomized-withdrawal phase, the mean difference between lisdexamfetamine and placebo in the change from randomised-withdrawal baseline T-score in the CHIP-CE-PRF at up to 6 weeks in the randomized-withdrawal period was 6.5 (95% CI: 3.5 to 9.5) in favour of lisdexamfetamine.<sup>7</sup>

Other data were also assessed but remain commercially confidential.\*

## Summary of evidence on comparative safety

In the head to head study versus atomoxetine, similar proportions of patients in the lisdexamfetamine and atomoxetine groups experienced treatment-emergent adverse events (TEAEs): 72% (92/128) and 71% (95/134) respectively. Only a small proportion was classified as severe: 5.5% and 3.0%, respectively. The rate of discontinuation due to TEAEs was similar between the groups: 6.3% and 7.5%, respectively.<sup>3</sup>

Adverse events experienced by at least 5% of patients in either group included: abdominal pain (2.3% versus 6.0%), upper abdominal pain (2.3% versus 7.5%), constipation (6.3% versus 1.5%), diarrhoea (1.6% versus 6.7%), dry mouth (6.3% versus 3.0%), nausea (12% versus 16%), vomiting (4.7% versus 9.7%), fatigue (9.4% versus 10%), irritability (6.3% versus 2.2%), nasopharyngitis (6.3% versus 6.0%), upper respiratory tract infection (2.3% versus 6.0%), weight decrease (22% versus 6.7%), decreased appetite (26% versus 10%), headache (13% versus 16%), sedation (3.9% versus 6.0%) somnolence (3.1% versus 12%), and insomnia (12% versus 6.0%).<sup>3</sup>

In the study with OROS-MPH, TEAEs were experienced by 72% (80/111), 57% (63/110) and 65% (72/111) of patients in the lisdexamfetamine, placebo and OROS-MPH groups respectively. Most were mild or moderate in intensity.<sup>4</sup>

Common TEAEs occurring in the lisdexamfetamine, placebo and OROS-MPH groups were decreased appetite (25%, 2.7% and 15%), headache (14%, 20% and 20%), insomnia (14%, 0 and 8.1%), decreased weight (14%, 0 and 4.5%), nausea (11%, 2.7% and 7.2%) and anorexia (11%, 1.8% and 5.4%), respectively. Less than 5% of patients in each group discontinued treatment due to TEAEs: 4.5%, 3.6% and 1.8%, respectively. TEAEs leading to study drug discontinuation in the lisdexamfetamine group were vomiting, anorexia, decreased appetite, angina pectoris, tachycardia, decreased weight and insomnia. There were no serious TEAEs considered by the investigator to be related to lisdexamfetamine.<sup>4</sup>

## Summary of clinical effectiveness issues

In children and adolescents who have an inadequate clinical response to methylphenidate, the treatment options include atomoxetine and dexamfetamine. UK clinical guidelines make differing recommendations for the treatment pathway.<sup>8,9</sup> There was no consensus from feedback received from clinical experts consulted by SMC; however, Scottish prescribing data suggests that atomoxetine is prescribed more commonly than dexamfetamine in ADHD. In addition, experts advised that there was an unmet need for a longer acting second choice psychostimulant in the treatment pathway.

The clinical studies demonstrate the efficacy of lisdexamfetamine in improving the symptoms and functioning of patients with moderate to severe ADHD. Lisdexamfetamine treatment was associated with a shorter time to response compared with atomoxetine, and over the nine-week study period a greater proportion of patients achieved improved global functioning, measured by CGI-I, and symptoms, as per ADHD-RS-IV response. In the placebo-controlled study, lisdexamfetamine was superior to placebo in improving symptoms and global functioning over seven weeks. The randomised-withdrawal extension study provides evidence of longer-term efficacy, with over six months treatment in some patients. Compared with placebo, health-related quality of life was improved with treatment with lisdexamfetamine.

The outcome measures employed in the three pivotal studies (ADHD-RS-IV, and CGI) are validated for the assessment of changes in symptoms and overall function in ADHD.

In the two placebo-controlled studies, there was a higher drop-out rate in the placebo groups compared with lisdexamfetamine. The most common reason was lack of efficacy. Little risk of bias was identified in the pivotal studies.

Only the atomoxetine study specifically recruited patients with a history of clinically inadequate response to methylphenidate. Generalisability of the results of this study may be affected by the exclusion of patients who had received more than one methylphenidate treatment course.

Lisdexamfetamine is a once-daily oral preparation, thus avoiding the problems associated with administering doses during school hours. An additional advantage of importance for children who struggle with solid oral dosage forms, is that the lisdexamfetamine capsule contents can be dissolved in water and swallowed as a liquid, whereas the marketing authorisation for atomoxetine discourages this.

Since lisdexamfetamine is a prodrug requiring metabolic activation, the pharmacodynamic and kinetic properties are considered by the company to lower its abuse potential compared with equivalent

doses of dexamfetamine. The company presented an in-house analysis of postmarketing surveillance conducted in the US and found the rates of non-medical use of lisdexamfetamine to be similar to extended-release methylphenidate.<sup>10</sup>

At the time of writing, the legal status of lisdexamfetamine is under review by the Advisory Council on the Misuse of Drugs. In the interim, the Home Office and the Royal Pharmaceutical Society have advised that lisdexamfetamine should be treated as a schedule 2 controlled drug.

## Summary of comparative health economic evidence

The submitting company presented a cost-utility analysis comparing lisdexamfetamine to atomoxetine for the treatment of ADHD in children aged 6 years of age and older when response to previous methylphenidate treatment is considered clinically inadequate. A Markov model with a one-year time horizon was presented. Response and tolerance to each medicine was evaluated over the first 28 days (i.e. one cycle) of the model, with the data drawn from the results of the pivotal study. Patients who respond to therapy are assumed to continue on their current treatment and maintain their level of response until the end of the time horizon. The base case analysis assumed that no further treatment was available for non-responders and those having discontinued because of intolerance.

Utility values for adequate response and inadequate response were taken from the literature, where EQ-5D scores were evaluated by a parent or guardian of children with mild to severe ADHD. Costs for each health state included medicine acquisition and the direct medical costs of administering and monitoring the ADHD program of treatment. Medicine costs were based on the doses used within the pivotal study, while other resource use data were obtained from a prospective survey of Scottish clinicians (psychiatrists and paediatricians) involved in the treatment of patients with ADHD in NHS Scotland.

The result of the base case analysis was a cost per quality adjusted life year (QALY) of £6,969. This was based on an incremental QALY gain of 0.0104 and an incremental cost of £72 per patient over the one-year time horizon. Lisdexamfetamine use was estimated to result in a medicine acquisition cost increase of £214 per patient per year, with this figure offset by a reduction of £142 in administration and monitoring costs.

The submitting company provided an additional three-step analysis where non-responders were given an additional line of treatment. In the three-step analysis, patients who do not achieve adequate response to atomoxetine go on to receive dexamfetamine, while those who do not achieve adequate response to lisdexamfetamine begin treatment with atomoxetine. The result of the three-step analysis was a cost per QALY of £9,683. This was based on an incremental QALY gain of 0.0082 and an incremental cost of £79 per patient over the one-year time horizon. Lisdexamfetamine dimesylate use was estimated to result in a medicine acquisition cost increase of £192 per patient per year, with this figure offset by a reduction of £113 in administration and monitoring costs.

One-way sensitivity analyses were carried out where variations to the values used within the model were tested, as was the impact of using alternative data sources for the model inputs. The cost per QALY remained below £18,000 across all sensitivity analyses, with the only exception being a cost per QALY of £21,239 when an alternative set of utility values were used. However, it should be noted that the utility values used in the base case were accepted within a relevant NICE Multiple Technology Appraisal.

There are some uncertainties surrounding the economic case;



- Within the economic model, response and tolerance to each medicine was evaluated over the first 28 days. Responding patients are assumed to maintain their level of response and remain on their treatment throughout the one-year time horizon. Although this appears a reasonable assumption, the pivotal study also recorded the proportion of 'sustained responders' up until 63 days follow-up. The 63-day response rates for lisdexamfetamine and atomoxetine are lower than the response rates used in the model. Additional analysis provided by the submitting company demonstrated that the use of 63-day response rates did not alter the overall conclusions of the model.
- There is uncertainty surrounding the response rate for patients receiving dexamfetamine within the three-step analysis. SMC clinical expert responses indicate that dexamfetamine is often as effective as other treatments for ADHD, so there is some concern that the model assumes a response rate for dexamfetamine that is substantially lower than for atomoxetine in the third step of the three-step analysis. The submitting company was unable to provide this analysis, but it is unlikely to be a key driver of the results.
- The model includes the cost of consultant appointments as part of the monitoring of patients with ADHD. However, SMC clinical expert responses have indicated that follow-up appointments may not always be carried out by consultants but by junior doctors and specialty doctors also. This means that the cost saving from a lower number of follow-up appointments in the lisdexamfetamine arm may have been overestimated by the submitting company. However, further analysis was provided where it was assumed that 50% of follow up appointments are led by junior doctors and this resulted in the cost per QALY increasing to £11,112 and £13,831 for the base case and three-step analysis respectively.

In summary, despite the uncertainties highlighted above, the economic case has been demonstrated.

## Summary of patient and public involvement

A Patient Interest Group Submission was not made.

## Additional information: guidelines and protocols

The Scottish Intercollegiate Guidelines Network (SIGN) published SIGN Guideline 112: Management of attention deficit and hyperkinetic disorders in children and young people in October 2009. Psychostimulants (methylphenidate or dexamfetamine) are recommended as the first choice medication for the core symptoms of ADHD in children. They should not be used first line in patients who have a history or family history of cardiac abnormalities or (for immediate release formulations) there is a likelihood of diversion. If one psycho-stimulant fails to be effective then the other should be considered. Atomoxetine is recommended as a treatment when psychostimulant medication is not appropriate, not tolerated or is ineffective.<sup>8</sup>

The National Institute for Health and Clinical Excellence (NICE) published a clinical guideline (CG72) in September 2008: Attention deficit hyperactivity disorder: Diagnosis and management of ADHD in children, young people and adults. When it has been decided to treat a child or young person with ADHD with drugs then methylphenidate should usually be tried first in patients without significant co-morbidity or co-morbid conduct disorder. Atomoxetine should be considered in patients who have tried methylphenidate and it has been ineffective or not tolerated. If patients do not respond to methylphenidate or atomoxetine then further treatment options include: higher doses of

methylphenidate or atomoxetine; switching to dexamfetamine; further or alternative psychological treatments; or referral to a regional specialist for an alternative drug treatment.<sup>9</sup>

NICE also published a multiple technology appraisal (TA98) in March 2006: Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents. The three drugs are recommended, within their licensed indications, as options for the management of ADHD in children and adolescents. When choosing the most appropriate drug, consideration should be given to the presence of other medical conditions, adverse effect profiles, compliance issues, potential for drug diversion and/or misuse and the preferences of the child/adolescent and/or their parent or guardian. If there is more than one appropriate drug then the cheapest one should be used. Treatment should be initiated by healthcare professionals with expertise in ADHD and be based on a comprehensive assessment and diagnosis.<sup>11</sup>

All guidelines predate the availability of lisdexamfetamine.

## **Additional information: comparators**

Pharmacological therapies used in patients who have had an inadequate response to methylphenidate include atomoxetine and dexamfetamine.

## **Cost of relevant comparators**

<b>Drug</b>	<b>Dose Regimen</b>	<b>Cost per year (£)</b>
<b>Lisdexamfetamine</b>	<b>30mg to 70mg orally once daily</b>	<b>757 to 1,081</b>
Atomoxetine	10mg to 100mg orally once daily	812 to 1,083
Dexamfetamine	5mg to 20mg orally daily in two to three divided doses	245 to 981

Doses are for general comparison and do not imply therapeutic equivalence. Costs from eVadis on 04 February 2013 except lisdexamfetamine, from company submission.

## **Additional information: budget impact**

The submitting company estimated the population eligible for treatment to be 546 in all years with an estimated uptake rate of 11% in year 1 and 61% in year 5. The gross impact on the medicines budget was estimated to be £54k in year 1 and £298k in year 5. As other drugs were assumed to be displaced the net medicines budget impact is expected to be cost neutral in years 1 and 5.

Alternative Scenario: The company also submitted a budget impact template showing another scenario for the dosage of the displaced medicine. The gross impact for this scenario remained the same as above but the net medicines budget impact increases the estimated savings to £5k in year 1 and £26k in year 5. This second scenario is based on Scottish Prescribing data and may be a more accurate reflection of prescribing practice.



## References

The undernoted references were supplied with the submission. Those shaded in grey are additional to those supplied with the submission.

- 1) Shire Pharmaceutical Contracts Ltd. (draft) Summary of product characteristics Lisdexamfetamine hard capsules (Elvanse®). Received 17 January 2013.
- 2) Clinical trials.gov. Comparison of lisdexamfetamine dimesylate with atomoxetine HCl in attention-deficit/hyperactivity disorder (ADHD) subjects with an inadequate response to methylphenidate. NCT01106430. Last updated 25 January 2013. [www.clinicaltrials.gov](http://www.clinicaltrials.gov)
- 3) Shire Pharmaceutical Contracts Ltd. Data on file: Clinical study SPD489-317.
- 4) Coghill D, Banaschewski T, Lecendreux M et al. European, randomized, phase 3 study of lisdexamfetamine dimesylate in children and adolescents with attention-deficit/hyperactivity disorder. European Neuropsychopharmacology (2013)  
<http://dx.doi.org/10.1016/j.euroneuro.2012.11.012>
- 5) Clinical trials.gov. Randomized, double-blind safety and efficacy study of lisdexamfetamine dimesylate (LDX) in children and adolescents aged 6-17. NCT00763971. Last updated 27 February 2012. [www.clinicaltrials.gov](http://www.clinicaltrials.gov)
- 6) Coghill D, Banaschewski T, Lecendreux M et al. Maintenance of efficacy of lisdexamfetamine dimesylate in children and adolescents with attention-deficit/hyperactivity disorder: randomized-withdrawal design. Presented at the EUNETHYDIS 2nd International ADHD conference, 23–25 May 2012, Barcelona, Spain.
- 7) Clinical trials.gov. Double-blind, placebo-controlled, randomised withdrawal, extension, safety and efficacy study of LDX in children and adolescents aged 6-17. NCT00784654. Last updated 30 August 2012. [www.clinicaltrials.gov](http://www.clinicaltrials.gov)
- 8) Scottish Intercollegiate Guidelines Network. SIGN Guideline 112: Management of attention deficit and hyperkinetic disorders in children and young people. October 2009. [www.sign.ac.uk](http://www.sign.ac.uk)
- 9) The National Institute for Health and Clinical Excellence. Clinical guideline 72: Attention deficit hyperactivity disorder: Diagnosis and management of ADHD in children, young people and adults. September 2008. <http://www.nice.org.uk>
- 10) Data on File, Shire. Abuse Liability Assessment Report of SPD489 (lisdexamfetamine dimesylate). 2011.
- 11) The National Institute for Health and Clinical Excellence. Multiple Technology Appraisal 98: Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents. March 2006. [www.nice.org.uk](http://www.nice.org.uk)

This assessment is based on data submitted by the applicant company up to and including 15 March 2013.

*\*Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal: [http://www.scottishmedicines.org.uk/About\\_SMC/Policy\\_Statements/Policy\\_Statements](http://www.scottishmedicines.org.uk/About_SMC/Policy_Statements/Policy_Statements)*

Drug prices are those available at the time the papers were issued to SMC for consideration. These have been confirmed from the eVadis drug database. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

**Advice context:**

*No part of this advice may be used without the whole of the advice being quoted in full.*

*This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.*