Scottish Medicines Consortium
Providing advice about the status of all newly licensed medicines
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NHS SCOTLAND

fluticasone furoate/vilanterol 92/22 micrograms inhalation powder (Relvar Ellipta®) SMC No. (953/14)

GlaxoSmithKline UK

07 March 2014

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 Scotland. The advice is summarised as follows:

ADVICE: following a full submission:

fluticasone furoate/vilanterol (Relvar Ellipta®) is accepted for restricted use within NHS Scotland.

Indication under review: symptomatic treatment of adults with chronic obstructive pulmonary disease (COPD) with a forced expiratory volume in 1 second (FEV_1) <70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy.

SMC restriction: in patients with severe COPD (FEV_1 <50% predicted normal).

In a comparative, 12-week study there was no statistically significant difference between fluticasone furoate/vilanterol 92/22 micrograms and another inhaled corticosteroid/long acting beta agonist combination inhaler for change from baseline trough in 24-hour weighted-mean FEV_1.

Fluticasone furoate/vilanterol is also licensed for the treatment of asthma. SMC is due to issue advice for this indication in June 2014.

Overleaf is the detailed advice on this product.

Chairman,
Scottish Medicines Consortium

Indication

Symptomatic treatment of adults with chronic obstructive pulmonary disease (COPD) with a forced expiratory volume in 1 second (FEV_1) <70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy.

Dosing Information

Fluticasone furoate/vilanterol 92/22 micrograms, one inhalation once daily.

Patients usually experience an improvement in lung function within 16 to 17 minutes of inhaling fluticasone furoate/vilanterol.

NB: Each single inhalation provides a delivered dose [the dose leaving the mouthpiece] of 92 micrograms of fluticasone furoate and 22 micrograms of vilanterol [as trifenatate]. This corresponds to a pre-dispensed dose of 100 micrograms of fluticasone furoate and 25 micrograms vilanterol [as trifenatate]). The dose referred to in this document is the delivered dose.

Product availability date

8 January 2014.

Summary of evidence on comparative efficacy

Fluticasone furoate/vilanterol (Relvar Ellipta®) is the third inhaled corticosteroid and long acting beta-2 agonist (ICS/LABA) combination inhaler licensed for the treatment of patients with chronic obstructive pulmonary disease (COPD). The others include fluticasone propionate/salmeterol (Seretide Accuhaler®) and budesonide/formoterol fumarate dihydrate (Symbicort Turbohaler®). [1,2]

Evidence of efficacy comes from five phase III studies of varying lengths and with different outcomes and comparator arms.

One phase III, randomised, comparative study recruited patients aged ≥40 years with COPD (FEV_1 ≤ 70% of predicted normal post-bronchodilator).[3,4] Patients were former or current smokers (≥10 pack years) and had been hospitalised or had been treated with oral corticosteroids or antibiotics for COPD within three years prior to screening. A total of 702 patients entered the single-blind, placebo, run-in phase where treatment compliance was assessed. Following this, 528 eligible patients were randomised to double-blind treatment with fluticasone furoate/vilanterol 92/22 micrograms once daily (n=266) or fluticasone propionate/salmeterol 500/50 micrograms twice daily (n=262) for 12 weeks.

The primary endpoint was change from baseline trough in 24-hour weighted-mean FEV_1 on day 84 in the intention to treat (ITT) population. The weighted mean was calculated from the pre-dose FEV_1 and post-dose FEV_1 measurements at various time points on day 84 and baseline trough FEV_1 was the mean of two pre-dose assessments on day one. There was no statistically significant difference between treatment groups; change from baseline trough 24-hour weighted-mean FEV_1 on day 84 was 0.130L (standard error [SE] 0.0148) for fluticasone

furoate/vilanterol versus 0.108L (SE 0.0145) for fluticasone propionate/salmeterol group (least squares mean difference 0.022, 95% confidence interval [CI] -0.018 to 0.063).

Secondary endpoints were nested under the primary endpoint; therefore as statistical significance was not demonstrated for the primary endpoint statistical inference could not be made for secondary endpoints. The median time to onset on day one (defined as the time to an increase of 0.1L from baseline in FEV_1, calculated over 0 to 4 hours post-dose) was 16 minutes (range 5 to 240 minutes) for fluticasone furoate/vilanterol and 28 minutes (range 5 to 240 minutes) for fluticasone propionate/salmeterol. The least squares mean change from baseline in trough FEV_1 on day 85 was 0.111L (SE 0.0155) for fluticasone furoate/vilanterol and 0.088L (SE 0.0154) for fluticasone propionate/salmeterol. In both groups there were similar decreases (indicating improvement) in the total score of the St George's Respiratory Questionnaire (SGRQ) for COPD.[3]

Two replicate, phase III, randomised, double-blind, one-year studies (HZC102871 [n=1,622] and HZC102970 [n=1,633]) recruited patients aged ≥40 years with COPD (FEV_1 ≤ 70% of predicted normal post-bronchodilator), a smoking history of ≥10 pack years and a documented history of one or more COPD exacerbations in the year before screening which required systemic or oral corticosteroids or antibiotics or admission to hospital.[5] Patients entered a four-week open-label phase and received fluticasone propionate/salmeterol 250/50 micrograms twice daily, to establish adherence to treatment and a stable baseline. Patients were then randomised to once daily treatment with fluticasone furoate/vilanterol 46/22, 92/22 (licensed dose), 184/22 or vilanterol 22 micrograms for 52 weeks.

The primary endpoint was the yearly rate of moderate and severe exacerbations in the ITT population of each study and in the pooled analysis, which was predefined. Analysis used a generalised linear model, which included all randomised patients who received at least one dose of study drug. Moderate exacerbations were defined as worsening symptoms of COPD (≥2 consecutive days) necessitating treatment with oral corticosteroids or antibiotics, or both, and severe exacerbations were similar events that necessitated hospital admission. In study HZC102871 there was no statistically significant difference for the primary endpoint between the fluticasone furoate/vilanterol 184/22 and the vilanterol 22 microgram groups. Because of the statistical hierarchy that was used, significance could not be inferred for any further comparisons of the primary and secondary endpoints for this study. In study HZC102970 there were statistically significant differences for the yearly rate of moderate and severe exacerbations between the fluticasone furoate/vilanterol 46/22, 92/22 and 184/22 microgram groups versus the vilanterol 22 microgram group.

Secondary endpoints included risk in time to first moderate or severe exacerbation, yearly rate of exacerbations necessitating systemic or oral corticosteroids and change from randomisation in trough (pre-dose) FEV_1 at week 52. Results of the primary and secondary endpoints are included in the table below for the fluticasone furoate/vilanterol 92/22 microgram (licensed dose) and vilanterol 22 microgram groups only, for the individual studies and the pooled analysis.

Table: primary and secondary endpoints for fluticasone furoate/vilanterol 92/22 microgram and vilanterol 22 microgram groups only, for studies HZC102871, HZC102970 and the pooled analysis

Endpoint	Study HZC102871		Study HZC102970		Pooled analysis	
	fluticasone furoate/ vilanterol 92/22 microgram	vilanterol 22 microgram	fluticasone furoate/ vilanterol 92/22 microgram	vilanterol 22 microgram	fluticasone furoate/ vilanterol 92/22 microgram	vilanterol 22 microgram
Primary endpoint: yearly rate of moderate and severe exacerbations						
N	403	409	403	409	806	818
Least squares mean yearly rate	0.70	1.05	0.90	1.14	0.81	1.11
Ratio to vilanterol group (95% CI), p-value	0.7 (0.5 to 0.8) NA	-	0.8 (0.6 to 1.0) p=0.0244	-	0.7 (0.6 to 0.8) p<0.0001	-
Secondary endpoints						
Risk in time to first moderate or severe exacerbation						
Hazard ratio to vilanterol group (95% CI), p-value	0.7 (0.6 to 0.9) NA	-	0·8 (0·7 to 1·0) p=0.0365	-	0.8 (0.7 to 0.9) p=0.0002	
Yearly rate of exacerbations necessitating systemic or oral corticosteroids						
Least squares mean yearly rate	0.52	0.84	0.66	0.86	0.61	0.87
Ratio to vilanterol group (95% CI), p-value	0.6 (0.5 to 0.8) NA	-	0.8 (0.6 to 1.0) p=0.0411	-	0.7 (0.6 to 0.8) p<0.0001	
Change in trough (pre-dose) FEV_1 at week 52						
Least squares mean change	0.02	-0.04	0.01	-0.02	0.01	-0.03
Change from vilanterol group (95% CI), p-value	0.058 (0.03 to 0.09) NA	-	0.024 (-0.01 to 0.06) p=0.1426	-	0.04 (0.02 to 0.06) p=0.0003	

N=number (of patients) CI=confidence interval, NA=not applicable (due to statistical hierarchy used)

Additional evidence of efficacy comes from two similar 24-week placebo-controlled phase III studies (HZC112206 and HZC112207) which recruited 1,030 and 1,224 patients respectively. The studies compared fluticasone furoate/vilanterol 92/22 micrograms (and fluticasone furoate/vilanterol 46/22 micrograms in study HZC112206 and fluticasone furoate/vilanterol 184/22 micrograms in study HZC112207) with its components and placebo.[6,7] Recruitment criteria were similar to the previous studies, but unlike the one year studies, patients were not required to have a history of exacerbations for study entry and approximately three-quarters of patients had not experienced a moderate or severe exacerbation in the 12 months prior to recruitment. The co-primary endpoints were weighted mean FEV_1 (0 to 4 hour post-dose) on day 168 and the change from baseline in trough (23 to 24 hour post-dose) FEV_1 on day 169. A predefined testing hierarchy was used due to the number of treatment arms and co-primary endpoints. In study HZC112206 there were statistically significant differences in the co-primary end-points for fluticasone furoate/vilanterol 92/22 micrograms versus placebo and for the comparison versus fluticasone furoate 92 micrograms for FEV_1 (0 to 4 hour post-dose) only. In study HZC112207, as there was no statistically significant difference for the co-primary endpoints between fluticasone furoate/vilanterol 184/22 microgram and vilanterol 22 microgram, no inference could be drawn for comparisons for fluticasone furoate/ vilanterol 92/22 microgram with placebo or its components. However there were numerical differences for the co-primary endpoints in favour of fluticasone furoate/vilanterol 92/22 microgram versus placebo, vilanterol 22 micrograms and fluticasone furoate 92 micrograms.

Summary of evidence on comparative safety

In the comparative study of fluticasone furoate/vilanterol versus fluticasone propionate/salmeterol similar proportions of patients reported a non-serious adverse event (12% [32/266] versus 11% [30/262]). In the fluticasone furoate/vilanterol group the non-serious adverse events reported were; headache (7.5% [20/266]), back pain (3.8% [10/266]) and nasopharyngitis (3.0% [8/266]). In the fluticasone propionate/salmeterol group the non-serious adverse events reported were; headache (6.9% [18/262]), nasopharyngitis (4.6% [12/262]) and back pain (1.1% [3/262]). Serious adverse events occurred in six (2.3%) of fluticasone furoate/vilanterol and three (1.1%) of fluticasone propionate/salmeterol treated patients. Serious adverse events reported in the fluticasone furoate/vilanterol group included; atrial fibrillation (two patients) and angina pectoris, coronary artery disease, pneumonia, food poisoning, infective exacerbation of chronic obstructive airways disease, rectal cancer and COPD (all one patient each). Serious adverse events reported in the fluticasone propionate/salmeterol group included; pneumonia (two patients) and sialoadenitis (one patient).[4]

In the pooled analysis of the one-year studies the proportion of patients with any adverse event was 77% (621/806) in the fluticasone furoate/vilanterol 92/22 microgram group versus 70% (575/818) in the vilanterol 22 microgram group. The proportion of patients with any adverse event leading to discontinuation or withdrawal was 7.7% (62/806) and 5.5% (45/818) respectively and serious adverse events occurred in 15% of patients in both groups. On-treatment or post-treatment fatal adverse events occurred in 10 patients in the fluticasone furoate/vilanterol 92/22 microgram group and 13 patients in the vilanterol 22 microgram group. The number of patients with serious pneumonia (reported as an adverse event necessitating hospital admission) was 25 (3.1%) in the fluticasone furoate/vilanterol 92/22 microgram group and eight (1.0%) in the vilanterol 22 microgram group. There was one fatal pneumonia-related adverse event in the fluticasone furoate/vilanterol 92/22 microgram group, none in the vilanterol 22 microgram group (and seven in the fluticasone furoate/vilanterol 184/22 microgram group). [5]

Summary of clinical effectiveness issues

COPD, which is predominantly caused by smoking, is characterised by airflow obstruction that is not fully reversible and often results in exacerbations, where there is rapid and sustained worsening of symptoms beyond normal day-to-day variations. Two other ICS/LABA combination inhalers are licensed for the treatment of COPD (fluticasone propionate/salmeterol [Seretide Accuhaler®] and budesonide/formoterol fumarate dihydrate [Symbicort Turbohaler®]). Both have been accepted for use by SMC in patients with severe COPD (FEV_1 <50% predicted normal), while fluticasone propionate/salmeterol was not recommended for COPD with FEV_1 50% to <60% predicted normal. National Institute for Health and Care Excellence (NICE) guidance recommends offering an ICS plus LABA in a combination inhaler when FEV_1 <50% (and there are exacerbations or persistent breathlessness despite using short acting bronchodilators as required)[8]. When FEV_1 is ≥50% treatment is with single agent LABA or long-acting muscarinic antagonist (LAMA); however ICS plus LABA in a combination inhaler should be considered when there are persistent exacerbations or breathlessness despite maintenance therapy with a LABA. NICE recommends using FEV_1 predicted normal post-bronchodilator for diagnosis of COPD.[8] Studies comparing pre-and post-bronchodilator FEV_1 % predicted suggest that FEV_1 post-bronchodilator is around 4-8% higher than FEV_1 pre-bronchodilator.[6,7,9,10]

One study provided comparative efficacy of fluticasone furoate/vilanterol versus fluticasone propionate/salmeterol where no statistically significant difference between treatments was found for change from baseline trough in 24-hour weighted-mean FEV_1 after 12 weeks treatment.

Two studies compared annualised moderate/severe exacerbation rates for various doses of fluticasone furoate/vilanterol versus vilanterol 22 micrograms alone. While vilanterol alone does not have marketing authorisation, it was accepted as an appropriate comparator by the European Medicines Agency (EMA). In the pooled analysis (and also in one of the studies) there was a statistically significant difference in the annualised moderate/severe exacerbation rate in favour of fluticasone furoate/vilanterol 92/22 micrograms compared to vilanterol 22 micrograms. However the EMA noted that the difference between fluticasone furoate/vilanterol 92/22 micrograms and vilanterol 22 micrograms of 0.3 moderate/severe exacerbations per year (in the pooled analysis) was less than the clinically meaningful difference of one per year. However this was similar to the difference in annual exacerbation rate for ICS/LABA combination inhalers versus LABA alone, reported in a recent Cochrane review (which did not include any fluticasone furoate/vilanterol studies).[11] Overall the EMA considered the effect of fluticasone furoate/vilanterol 92/22 microgram versus vilanterol 22 microgram on moderate exacerbations to be clinically relevant but that the effect was neither statistically nor clinically relevant for severe exacerbations.

All studies required patients to complete a run-in period where adherence to treatment was assessed. Therefore only patients who were adhering to inhaled treatment were included in the studies and consequently efficacy may differ in clinical practice. Studies HZC112206 and HZC112207, which did not require patients to have a history of exacerbations for entry, have less relevance to the indication under review. There are no comparative data versus an approved dose of an ICS/LABA combination inhaler beyond treatment duration of 12 weeks. Furthermore there is a lack of efficacy or safety data beyond one year's treatment duration.

Comparative efficacy and safety data with other ICS/LABA combination inhalers are limited. The submitting company included Bayesian hierarchical mixed treatment comparisons (MTC) to

provide comparative efficacy versus budesonide/formoterol fumarate dihydrate and fluticasone propionate/salmeterol for three outcomes. The primary outcome was change from baseline in FEV_1 and secondary outcomes were annual rate of moderate/severe exacerbations and the change from baseline in SGRQ total score. Covariate analyses using length of study, age, gender, smoking history, exacerbation history and FEV_1 % predicted at baseline as covariates were reported. The FEV_1 MTC included 28 studies, exacerbation rate MTC 15 studies and SGRQ MTC 20 studies. The exacerbation rate MTC presented in the company's submission included only studies where patients were required to have a history of exacerbations as an inclusion criterion; however this restriction did not apply to the other outcomes. Generally for all of the MTC there were differences between studies in baseline characteristics and outcomes for common control arms. Results indicated that fluticasone furoate/vilanterol was broadly comparable to fluticasone propionate/salmeterol and budesonide/formoterol fumarate dihydrate for change from baseline in FEV_1 and SGRQ. However there was sufficient uncertainty in the annual rate of moderate/severe exacerbations outcome to preclude conclusions being made. No distinction was made in the MTC between FEV_1 pre- or post-bronchodilator for inclusion criteria of studies or in the FEV_1 outcome. In addition, no comparison of adverse events was performed.

Overall an increase in pneumonia (and also pneumonias resulting in hospitalisation) was observed in patients with COPD receiving fluticasone furoate/vilanterol (relative to vilanterol alone), with some events being fatal. Risk factors for pneumonia in these patients include current smokers, history of prior pneumonia, body mass index <25 kg/m^2 and an FEV_1 <50% predicted.[12] In the Cochrane review of ICS/LABA combination inhalers versus LABA alone, the odds ratio of pneumonia was 1.55 (95% 1.2 to 2.01) with a median follow-up of one year.[13] The authors concluded there was moderate quality evidence of an increased risk of pneumonia with ICS/LABA treatment.

Clinical experts consulted by SMC consider that the once daily administration of fluticasone furoate/vilanterol, compared to twice daily administration of the comparators may be more acceptable to the patient and suggest that its place in therapy might be when compliance is an issue. However the double-blind design of the studies did not allow this to be assessed.

Summary of comparative health economic evidence

The company submitted a cost-minimisation analysis of fluticasone furoate/vilanterol for the symptomatic treatment of adults with COPD with a FEV_1 <70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy. The comparators included fluticasone propionate/salmeterol and budesonide/formoterol fumarate dihydrate (which have both been accepted for use by SMC in COPD (FEV_1 <50% predicted normal). The time horizon for the analysis was five years.

The data to support comparable efficacy were based on Bayesian mixed treatment comparisons assessing the probability of non-inferiority of fluticasone furoate/vilanterol compared with fluticasone propionate/salmeterol and budesonide/formoterol fumarate dihydrate. A 12-week study directly compared fluticasone furoate/vilanterol with fluticasone propionate/salmeterol, however the purpose of this study was to demonstrate superiority and the primary superiority endpoint was not met. There were no direct clinical data versus budesonide/formoterol fumarate dihydrate.

Only drug costs were included in the analysis. Costs were presented over one to five years. The results showed that the cost of fluticasone furoate/vilanterol is £338 in year one and £1,645 over a five years time horizon compared with a cost in year one of £498 for fluticasone propionate/salmeterol and £2,422 over a five years time horizon and compared with a cost of £462 in year one for budesonide/formoterol fumarate dihydrate and £2,249 over a five years time horizon. Fluticasone furoate/vilanterol is therefore associated with cost savings of £160 and £124 in year one compared with fluticasone propionate/salmeterol and budesonide/formoterol fumarate dihydrate, respectively, and £777 and £604 over a five years time horizon compared with fluticasone propionate/salmeterol and budesonide/formoterol fumarate dihydrate, respectively. Fluticasone furoate/vilanterol would therefore be the preferred treatment on cost-minimisation grounds.

The economic case has been demonstrated for patients with an FEV_1 <50% predicted normal. However, as the comparators are not in routine use for COPD patients with FEV_1 50 % to <70% predicted normal, the case has not been demonstrated in the group of patients with less severe disease.

Summary of patient and public involvement

A Patient Interest Group Submission was not made.

Additional information: guidelines and protocols

NICE published an update to clinical guideline 101; Management of chronic obstructive pulmonary disease in adults in primary and secondary care, in June 2010.[8] The guideline includes the following recommendations:

- Offer an ICS plus LABA in a combination inhaler or single-agent LAMA in patients with COPD (FEV_1 <50%) and exacerbations or persistent breathlessness despite using short acting bronchodilators as required.
- Offer single-agent LABA or LAMA in patients with COPD (FEV_1 ≥50%)
- Consider an ICS and LABA in a combination inhaler in patients with COPD (FEV_1 ≥50%) and persistent exacerbations or breathlessness despite maintenance therapy with a LABA.
- Offer LAMA in addition to LABA plus ICS to patients with COPD who remain breathless or have exacerbations despite taking LABA plus ICS, irrespective of their FEV_1.

The following points are also included:

- Choose a drug based on the person's symptomatic response and preference, the drug's adverse effects, potential to reduce exacerbations and cost.
- Do not use oral corticosteroid reversibility tests to identify patients who will benefit from inhaled corticosteroids.
- Be aware of the potential risk of developing adverse effects (including non-fatal pneumonia) in people with COPD treated with inhaled corticosteroids and be prepared to discuss this with patients.

NICE recommends using FEV_1 predicted normal post-bronchodilator for diagnosis of COPD.

Additional information: comparators

Fluticasone propionate / salmeterol (Seretide Accuhaler®) and budesonide / formoterol fumarate dihydrate (Symbicort Turbohaler®)

Cost of relevant comparators

Drug	Dose Regimen	Cost per year (£)
fluticasone furoate/vilanterol (Relvar Ellipta®)	**92/22 micrograms once daily**	**337**
fluticasone propionate/salmeterol (Seretide Accuhaler®)	500/50 micrograms twice daily	496
budesonide / formoterol fumarate dihydrate (Symbicort Turbohaler®)	400/12 micrograms twice daily	461

Doses are for general comparison and do not imply therapeutic equivalence. Costs are from eVadis on 29 November 2013. Cost of fluticasone furoate/vilanterol (Relvar Ellipta®) obtained from the company's submission.

Additional information: budget impact

The submitting company estimated the population eligible for treatment to be 75,974 in year 1 rising to 80,276 in year 5 with an assumed market share of 2% in year 1 rising to 15% in year 5.

The gross impact on the medicines budget was estimated to be £514k, in year 1 and £4.073m in year 5. As other drugs were assumed to be displaced the net medicines budget impact is expected to be a savings of £216k, in year 1 and £1.708m in year 5.

References

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

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3. European Medicines Agency. European Public Assessment Report for fluticasone furoate 92 micrograms / vilanterol 22 micrograms (Relvar Ellipta®) EMEA/H/C/002673/0000 19 September 2013
4. www.clinicaltrials.gov
5. Dransfield M. Once-daily inhaled fluticasone furoate and vilanterol versus vilanterol only for prevention of exacerbations of COPD: two replicate double-blind, parallel-group, randomised controlled trials. The Lancet 2013; 201-13
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8. NICE. Update to Clinical guideline 101; Management of chronic obstructive pulmonary disease in adults in primary and secondary care. June 2010
9. Anzueto A, Ferguson GT, Feldman G, Chinsky K, Seibert A, Emmett A, et al. Effect of fluticasone propionate/salmeterol (250/50) on COPD exacerbations and impact on patient outcomes. 2009;6(5):320-9.
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11. Nannini LJ, Lasserson TJ, Poole P. Combined corticosteroid and long-acting beta2-agonist in one inhaler versus long-acting beta2-agonists for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2012, Issue 9. Art. No.: CD006829. DOI: 10.1002/14651858.CD006829.pub2.
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13. Nannini LJ, Lasserson TJ, Poole P. Combined corticosteroid and long-acting beta2-agonist in one inhaler versus long-acting beta2-agonists for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews* 2012, Issue 9. Art. No.: CD006829. DOI: 10.1002/14651858.CD006829.pub2.

This assessment is based on data submitted by the applicant company up to and including 14 February 2014.

Drug prices are those available at the time the papers were issued to SMC for consideration. 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.