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

racecadotril 10mg, 30mg granules for oral suspension (Hidrasec Infants®, Hidrasec Children®) SMC No. (818/12)

Abbott Healthcare Products Ltd.

04 July 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 resubmission:

racecadotril (Hidrasec Infants®, Hidrasec Children®) is not recommended for use within NHS Scotland.

Indication under review: Complementary symptomatic treatment of acute diarrhoea in infants older than three months and in children, together with oral rehydration and the usual support measures, when these measures alone are insufficient to control the clinical condition and when causal treatment is not possible. If causal treatment is possible racecadotril can be administered as a complementary treatment.

In a meta-analysis, racecadotril was significantly better than placebo in reducing the duration of diarrhoea and stool output in children with acute diarrhoea. There is insufficient evidence that it improves recovery rate.

The submitting company did not present a sufficiently robust clinical and economic analysis to gain acceptance by SMC.

Overleaf is the detailed advice on this product.

Chairman,
Scottish Medicines Consortium

Indication

Complementary symptomatic treatment of acute diarrhoea in infants (older than three months), and in children, together with oral rehydration, and the usual support measures, when these measures alone are insufficient to control the clinical condition and when causal treatment is not possible.

If causal treatment is possible, racecadotril can be administered as a complementary treatment.

Dosing Information

Racecadotril 10mg or 30mg granules for oral suspension (Hidrasec Infants® or Hidrasec Children®) is administered via the oral route, together with oral rehydration.

The recommended dose is determined according to body weight: 1.5mg/kg per dose (corresponding to 1 to 2 sachets).

In infants less than 9kg: one 10mg sachet three times daily
In infants from 9kg to 13kg: two 10mg sachet three times daily
In children from 13kg to 27kg: one 30mg sachet three times daily
In children of more than 27kg: two 30mg sachet three times daily

The duration of treatment in the clinical trials with children was five days. Treatment should be continued until two normal stools are recorded. Treatment should not exceed seven days. Long-term treatment with racecadotril is not recommended. There are no clinical trials in infants under 3 months of age. The granules can be added to food, dispersed in a glass of water, or in the feeding bottle, mixing well, and followed by immediate administration.

Product availability date

17 October 2012

Summary of evidence on comparative efficacy

Acute diarrhoea is the main symptom of gastroenteritis and most episodes in children in Scotland are mild and can be treated at home, although annually around 10% of children under five years require treatment from a healthcare service. Rotavirus is the leading cause of severe, dehydrating gastroenteritis among children and almost all children in both industrialised and developing countries have been infected by the age of five. In July 2013, a rotavirus immunisation programme was introduced into the routine childhood immunisation programme of infants aged 2 and 3 months in Scotland.

Racecadotril is the first in a new class of drugs for acute diarrhoea that reduce intestinal secretion of water and electrolytes by inhibiting the breakdown of encephalins which are endogenous opioid peptides. It does not increase intestinal transit time. Racecadotril is licensed to be used in addition to oral rehydration treatment (ORT) when this and the usual support measures are insufficient to control the condition. The submitting company has requested that SMC considers the use of racecadotril when positioned for use in infants and

young children aged 3 months to 5 years, presenting to general practitioners (GPs), Accident and Emergency or out of hours settings with acute diarrhoea.

The key evidence presented by the submitting company to support the use of racecadotril in infants and children aged 3 months to 5 years was from a meta-analysis of nine clinical studies.[1] This assessed the efficacy of racecadotril plus ORT versus ORT alone or with placebo in children (aged one month to 15 years) with acute gastroenteritis whatever the presumed origin. The meta-analysis included individual patient data from nine randomised controlled studies in a total of 1,384 patients. These studies were conducted in France (n=2), Spain (n=2), Guatemala (n=1), India (n=1), Mexico (n=2) and Peru (n=1): four studies were in inpatients and five in outpatients. Studies had an acceptable methodology quality which was defined by a Chalmers Score >50. The original search included studies identified by 31 December 2010.

The main outcome assessed was the duration of diarrhoea defined as the duration from first dose of study drug to the last unformed stool before recovery. Recovery was defined as the occurrence of two consecutive formed stools or no stools for 12 hours. The median duration of diarrhoea was significantly shorter in the racecadotril group than the comparator group: 1.75 days versus 2.81 days respectively. At any time, twice as many racecadotril than comparator patients had recovered: hazard ratio 2.04 (95% confidence interval [CI]: 1.85 to 2.32).

The other outcomes included stool output which was only assessed in inpatient studies (n=637) and number of diarrhoeic stools only assessed in outpatient studies (n=695). Racecadotril significantly reduced stool output (geometric mean ratio for racecadotril versus comparator was 0.59 [95% CI: 0.51 to 0.74]) and number of diarrhoea stools (mean ratio for racecadotril versus comparator was 0.63 [95% CI: 0.47 to 0.85]). The level of dehydration and presence or absence of rotavirus infection were significant predictors of duration of diarrhoea and stool output. For the number of diarrhoeic stools, significant predictors were baseline number of diarrhoeic stools and presence or absence of Rotavirus infection. There was an additional analysis on response rate (defined arbitrarily as the percentage of patients with diarrhoea for <48 hours) which was 50% and 26% in the racecadotril and placebo groups respectively. Statistical testing measured the level of heterogeneity among studies and generally this was found to be small.

An updated, unpublished analysis, presented in the submission, included an additional two studies (one from Bolivia and one from Italy) in a total of 1,506 patients.[2] The results were similar in this analysis: median duration of diarrhoea was 1.75 days versus 2.67 days respectively (hazard ratio 2.08 [95% CI: 1.86 to 2.32]; for stool output the geometric mean ratio was 0.60 (95% CI: 0.42 to 0.83); and for the number of diarrhoeic stools the mean ratio was 0.59 (95% CI: 0.46 to 0.76). Additional analysis on response rate (diarrhoea for <48 hours) found that 52% of racecadotril and 26% of placebo patients were classified as responders: risk ratio 1.91 (95% CI: 1.61 to 2.25). Sensitivity analysis on duration of diarrhoea found that the treatment effect was larger in non-European than European studies.

Although the meta-analysis included nine clinical studies of racecadotril in children with acute diarrhoea, only three randomised studies were performed in Europe. One study was performed in France in 172 children (aged 3 months to 4 years) who were randomised to receive racecadotril 1.5mg/kg (n=89) or placebo (n=83) orally three times daily for five days or less if the child had recovered.[3] All patients received rehydration either orally or via a nasogastric tube. If intravenous (iv) rehydration was required for less than 12 hours, the patient could be included in the study when this was completed. Patients stayed in hospital for at least 48 hours. The primary outcome was mean stool output at 48 hours, as grams (g) per hour, calculated by dividing the total output by the number of hours (maximum of 48) till recovery. For the full data

set, the stool output rate was 9g/hour versus 15g/hour respectively, with an estimated ratio of 60% (95% CI: 43% to 88%). A significant reduction in stool output with racecadotril was also reported at 24 hours, a secondary outcome. However, racecadotril did not improve recovery rate at five days which was reported according to gender and was numerically lower for racecadotril than placebo.

Another study was performed in 189 outpatients (aged 3 months to 3 years) in Spain.[4] Patients were randomised equally to receive racecadotril plus ORT or ORT alone every eight hours at doses of 10mg if weight <9kg; 20mg if weight ≥9kg and ≤13kg; 30mg if weight >13kg. Treatment with racecadotril was stopped when the child had two bowel movements of normal consistency or had no bowel movements for 12 hours or after seven days, whichever came first. The primary outcome was the average number of bowel movements at 48 hours and was not significantly different between the racecadotril plus ORT and ORT groups: 3.8 versus 4.1. There was no significant difference between racecadotril plus ORT and ORT in the following secondary outcomes: average duration of diarrhoea was 4.0 versus 4.7 days respectively, and subsequent visits to the emergency department or doctor by day seven, 17 versus 19 respectively.

Another single centre open-label randomised controlled study was performed in France in 164 children (aged 3 months to 3 years).[5] Patients were randomised alternately to receive racecadotril three times daily at doses of 10mg if ≤9kg and 20mg if >9kg body weight until cessation of diarrhoea (no stools for at least 12 hours) for up to seven days or to control group who received no treatment. If weight loss was <5%, ORT was given at home; if >10%, they received iv rehydration in hospital. If weight loss was between 5% and 10%, they initially received ORT in the emergency department and were reviewed after four hours and depending on prespecified criteria, were discharged or admitted to hospital for ORT or iv rehydration as required. The primary outcome was the number of medical examinations (by the treating physician or at hospital) during the week after starting treatment and was analysed in the PP population (n=154). The racecadotril group had significantly fewer additional medical visits than the control group between days two and seven: 18% (14/76) versus 35% (27/78). No meaningful conclusion could be drawn regarding the reasons for the additional visits as the published report cited the most common reason as “same episode of diarrhoea”. Also more than one reason was recorded per child. These additional medical visits resulted in hospital admission in two patients in the racecadotril group and in eight patients in the control group. The secondary outcome of duration of diarrhoea was significantly shorter in patients treated with racecadotril compared with control: 97 hours versus 138 hours respectively. The mean number of stools produced during the first 48 hours was 6.8 in the racecadotril group versus 9.5 in the control group, ($p < 0.001$).

The updated meta-analysis included one additional European study. This was an observational, retrospective review of 61 children (aged ≤5 years) admitted to a single Italian centre.[6] Twenty-six patients were treated with racecadotril plus ORT and retrospectively compared with 35 patients previously treated with ORT alone. Discharge rate within 24 hours of admission was achieved in 65% (17/26) racecadotril plus ORT patients and 40% (14/35) ORT patients ($p=0.0499$). There was no significant difference in number of patients discharged between 24 and 48 hours or in parenteral rehydration due to persisting or worsening symptoms.

Quality of life was not investigated in any of the studies described previously.

Summary of evidence on comparative safety

In the published meta-analysis, only the incidence of adverse events was compared between the racecadotril and placebo groups and no significant difference was found: 12% (81/698) racecadotril patients and 10% (70/695) control patients.[1]

The Summary of Product Characteristics (SPC) for racecadotril gives clinical study safety data for the treatment of acute diarrhoea by racecadotril in 860 children and by placebo in 441 children.[7] No comparative safety data are available. Refer to the Summary of Product Characteristics (SPC) for details of adverse effects.

The SPC also notes that racecadotril should not be administered in the presence of bloody or purulent stools and fever (as these may indicate the presence of invasive bacteria or other severe disease) or in antibiotic-associated diarrhoea. Racecadotril sachets contain sucrose and are contraindicated in children with fructose intolerance, glucose-galactose malabsorption syndrome, and saccharase-isomaltase deficiency. The sucrose content should be taken into account in children with diabetes.

Summary of clinical effectiveness issues

Racecadotril has been available for use for a number of years in some countries in Europe (e.g. France since 1999) and beyond (e.g. India since 2001). The submitting company has requested that SMC considers the use of racecadotril when positioned for use in infants and young children aged 3 months to 5 years, presenting to GPs, accident and emergency departments or out of hours settings with acute diarrhoea. Although studies in the meta-analysis could include patients aged 1 month to 15 years, the median age of patients was 12 months (range from 1 to 71 months) and so generally supports the selective positioning.[1]

Results from the meta-analysis found that the addition of racecadotril to ORT significantly reduced the following clinically important outcomes: duration of diarrhoea, mean stool output at 48 hours, measured as stool output in inpatients and number of diarrhoeic stools in outpatients. The latter is a surrogate outcome and there are difficulties associated with accurately measuring stool output in young children, including the complication of separation of urine. There was no assessment of other clinically important outcomes including improvement in hydration status, need for intravenous fluids, hospital admission and length of hospital stay. There were a number of issues with individual studies in the meta-analysis including methodological problems. Duration of diarrhoea was not the primary outcome in all studies and, in some, this outcome was not significantly improved with racecadotril versus control. There was also heterogeneity in patient populations, country and outcomes reported but the use of individual patient data helped to address this for the outcomes measured.

There is a lack of evidence of benefit which can readily be extrapolated to Scottish clinical practice. The studies included in the meta-analysis were from a range of developed and developing countries. The causes of diarrhoea are likely to vary from country to country and there can be marked variation across a country. The meta-analysis found that country (European or other) did not affect the duration of diarrhoea.[1] In the updated meta-analysis, sensitivity analysis found that the treatment effect was greater in non-European countries.[2]

Racecadotril is licensed for treatment up to seven days duration and it would be helpful to have had follow up data beyond this time; however, the previously described studies completed follow up on day seven.

There have been no studies with racecadotril in the UK. Clinical experts consulted by SMC have advised that the current practice of rehydration (usually oral) is sufficient in almost all cases of acute diarrhoea in children.

Most UK and international guidance advises that further research is needed to determine the place of racecadotril in therapy.

Summary of comparative health economic evidence

The company submitted a cost utility analysis comparing racecadotril plus ORT to ORT alone, for the treatment of acute diarrhoea in children aged 3 months to 5 years. The economic model used in the analysis was a simple decision tree which modelled a cohort of patients over a 4-day time horizon. This was considered to be the length of an acute episode of diarrhoea (including GP and secondary care).

In the model, patients consulted a GP for acute diarrhoea. The probability of GP re-consultation following the initial visit for acute diarrhoea and the probability of referral to secondary care post GP re-consultation were derived from a UK GP database and were estimated to be 9.2% and 23.6% respectively in the ORT alone arm. For those patients receiving racecadotril + ORT, the probability of GP re-consultation was estimated to be 6.2% based on the relative risk of responding to treatment (RR 0.67) derived from a meta-analysis. Those patients that experience a second GP consultation are referred to secondary care or continue on racecadotril + ORT for the duration of the model. Finally, patients referred to secondary care attend A&E or incur an inpatient stay. The only difference between the treatment arms was the lower probability of GP re-consultation applied to patients in the racecadotril + ORT arm of the model.

The clinical evidence used in the economic evaluation came from the results of an individual patient data meta-analysis described above, which included nine published studies. Responder rates from the meta-analysis were used to calculate the relative risk of GP re-consultation. The 0.67 relative risk of GP re-consultation was applied to patients who receive racecadotril + ORT.

Drug acquisition costs were included in the analysis. For those patients receiving racecadotril + ORT, the company estimated the weighted cost per course based on Scottish diarrhoea referral data in patients aged 3 months to 5 years. Treatment duration per course was assumed to be 4 days for both treatment arms, and the numbers of sachets used per day were calculated according to three weight/age categories, <9kg (1 year), 9-13kg (1-3 years) and >13kg (3-5 years). For the ORT treatment arm, costs were calculated simply by multiplying the total daily cost by the duration of treatment. Resource use was included in the analysis and consisted of primary and secondary care costs including GP visits, diagnostic tests, cost of A&E attendance and the cost of an inpatient day on children's ward. The company assumed a 2 day mean length of stay. Administration and adverse event costs were not included.

Utility values for acute rotavirus diarrhoea in children aged up to 5 years in the UK were taken from a published study. Scottish data were applied to these values to estimate utility scores for both moderate cases and severe cases which lead to GP consultation and hospitalisation. The

key utilities were 0.737 for moderate cases of diarrhoea resulting in GP consultation and 0.318 for severe cases resulting in hospitalisation. Resolved diarrhoea was valued at 0.94 and taken from a Centre for Health Economics discussion paper. This estimate was elicited from the general population aged less than 25 years. Based on the adjusted utility estimates, the quality-adjusted life-years (QALYs) for the four possible outcomes were calculated.

The base case results indicated that racecadotril + ORT was dominant versus ORT alone, resulting in cost savings of £131 per 100 children and a QALY gain of 0.0038 per 100 children. The net savings were based on a £727 incremental drug cost which was offset by £115 savings in total re-consultation costs and £743 savings in total referral costs. The reduction in GP consultations contributes to savings in the form of fewer GP visit costs and diagnostic tests for those patients in the racecadotril + ORT arm. The company provided a range of sensitivity analyses including one-way, scenario and threshold analysis.

A number of weaknesses were noted with the analysis:

- The relative risk of re-consulting the GP post prescription (0.67) is based on statistically significant responder rates which have been derived from the meta-analysis (includes 9 published studies) and is the sole basis of the QALY gain in the analysis. In addition, the results are particularly sensitive to changes in this parameter. When the relative risk increases to 0.75 and relative risk of referral to secondary care at second GP is assumed to equal 1, the incremental cost-effectiveness ratio (ICER) increases to £27,008 per QALY.
- Results of the one-way sensitivity analysis indicate that the ICER is particularly sensitive to the relative risk of referral to secondary care at second GP visit. Varying this parameter by +25% to 1.25 increased the ICER to £68,647 per QALY**.**
- In the meta-analysis, five out of the nine studies were conducted in developing countries. Therefore some uncertainty exists in relation to the generalisability of results to patients in Scotland. It should be noted that the company has conducted a sub analysis of the meta-analysis which included only the three RCTs conducted in Europe. Results maintained a statistically significant effect for the primary outcome measures versus ORT + placebo. Based on this analysis, a relative risk of 0.70 was calculated. Sensitivity analysis indicated that racecadotril continued to dominate ORT alone, resulting in incremental savings of £53 and 0.0034 QALYs per 100 patient cohort.
- The definition of “responder” is attributed to patients whose diarrhoea is short i.e. lasting less than 2 days. However, this definition appears to be arbitrarily set as the company do not provide any rationale for it. This outcome measure serves as a proxy for GP re-consultation and, therefore, it is uncertain how robust this outcome measure is.

Due to the uncertainties outlined above, the economic case has not been demonstrated.

Summary of patient and public involvement

A Patient Interest Group Submission was not made.

Additional information: guidelines and protocols

The most recent World Health Organisation (WHO) Model List of Essential Medicines for Children (intended for use for children up to 12 years of age) was published in 2011 and does not include racecadotril. Recommended treatments for diarrhoea are oral rehydration salts and zinc sulphate, (due to the prevalence of zinc deficiency in malnourished children).[8] An application to add racecadotril to the essential list of medicines had been assessed and rejected by WHO in 2007. The evidence presented was from two hospital-based studies, in Peru and in France. The Expert Committee concluded that the evidence base was limited and that the value of racecadotril therapy outside of the hospital setting, and in less severely affected infants was not clear. Concerns were also raised about the possibility of unpublished negative trials.

In 2012 the World Gastroenterology Organisation published Global Guidelines; acute diarrhoea in adults and children: a global perspective. [9] These guidelines state that ORT is a cost-effective method of managing acute gastroenteritis and it reduces hospitalisation requirements in both developed and developing countries. It states that in paediatrics, in general, anti-diarrhoeals have no practical benefits for children with acute or persistent diarrhoea. It notes that racecadotril is an encephalinase inhibitor (non-opiate) with anti-secretory activity that has been found useful in children with diarrhoea, and is now licensed in many countries in the world for use in children.

In 2009 the National Institute for Health and Care Excellence (NICE) published clinical guideline 84: Diarrhoea and vomiting in children. Diarrhoea and vomiting caused by gastroenteritis diagnosis, assessment and management in children younger than 5 years.[10] The guidance states that anti-diarrhoeal treatments should not be used. It notes that racecadotril (at that time) was not licensed for use in the UK but was used elsewhere in Europe. It states that there was evidence that racecadotril had an antidiarrhoeal effect but further research is required to examine the possible clinical and health economic benefits that might be associated with its use in the UK.

In 2008 the European Society for Paediatric Gastroenterology, Hepatology and Nutrition/European Society for Paediatric Infectious Diseases published Evidence-based Guidelines for the Management of Acute Gastroenteritis in Children in Europe.[11] It notes that racecadotril may be considered in the management of acute gastroenteritis. However, well-designed prospective studies of efficacy and safety should be carried out in outpatient children.
It states that in three relatively small randomised controlled trials with some methodological problems, two conducted in hospitalised children, in developed and developing countries, racecadotril was effective in reducing the volume and frequency of stool output and in reducing the duration of diarrhoea (particularly in children with rotavirus diarrhoea). There is evidence in favour of the use of racecadotril over placebo or no intervention to reduce the stool output in children with acute gastroenteritis. However, this evidence is based mainly on inpatient data, and does not take into account safety concerns that can be resolved either in studies involving large cohorts of children or in postmarketing surveillance evaluation, which is mandatory before therapy with racecadotril can be recommended.

In 2003 the Centers for Disease Control and Prevention, in their Morbidity and Mortality Weekly Report: Managing Acute Gastroenteritis Among Children, Oral Rehydration, Maintenance, and Nutritional Therapy, stated the following: Racecadotril, an encephalinase inhibitor, preserves

the anti-secretory activity of encephalins and does not slow intestinal transit or promote bacterial overgrowth. [12] Its use has demonstrated promise in two controlled clinical trials among children, among whom it significantly reduced stool output when compared with placebo. Although the majority of cases of acute diarrhoea require no adjunctive therapy, racecadotril might prove to be a useful adjunct. More studies are needed.

Additional information: comparators

Both loperamide and co-phenotrope (Lomotil®) are licensed for acute diarrhoea in children over four years. However current guidelines do not recommend the use of anti-diarrhoeals in children. Therefore there are no relevant comparators to racecadotril in children under 12 years.

Cost of relevant comparators

Drug	Dose Regimen	Cost per course (£)
racecadotril	**Orally 1.5mg/kg three times daily**	**Up to 18**

Costs from eVadis on 1 May 2014. Costs are based on up to 7 days treatment for the dose range for children aged 3 months to 11 years, one 10mg sachet three times daily to two 30mg sachets three times daily; the cost of racecadotril is the same for both strengths of sachets.

Additional information: budget impact

The submitting company estimated the population eligible for treatment to be 4,209 in all five years, with an estimated uptake rate of 0.50% in year 1 and 39.80% in year 5. The gross impact on the medicines budget was estimated to be £331 in year 1 and £26k in year 5. As no other drugs were assumed to be displaced, the net medicines budget impact is expected to remain as £331 in year 1 and £26k in year 5.

References

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

1. Lehert P, Cheron G, Calatayud GA, et al. Racecadotril for childhood gastroenteritis: an individual patient data meta-analysis. Dig Liver Dis. 2011 43; 9:707-13.

2. **Commercial in Confidence*

3. Cezard JP, Duhamel JF, Meyer M et al. Efficacy and tolerability of racecadotril in acute diarrhea in children. Gastroenterology. 2001; 120 (4):799-805.

4. Santos M, Maranon R, Miguez C, Vazquez P, Sanchez C. Use of racecadotril as outpatient treatment for acute gastroenteritis: a prospective, randomized, parallel study. J Pediatr. 2009; 155: 62-7.

5. Cojocaru B, Boquet N, Timsit S et al. Effect of Racecadotril in the treatment of acute diarrhoea in infants and young children Arch Pediatr 2002; 8: 774-9

6. Manfredi M, Bizzarri B, de'Angelis L. Racecadotril at the beginning of pediatric gastroenteritis: a small experience of a primary level hospital. Clin Microbiology 2013;2(1)

7. Abbott Healthcare Products Limited. Summary of product characteristics for racecadotril 10mg/30mg granules for oral suspension (Hidrasec Infants/Children ®) last updated 09.04.2014.

8. WHO Model List of Essential Medicines for Children (3rd list) March 2011

9. World Gastroenterology Global Guidelines. Acute diarrhea in adults and children: a global perspective, February 2012

10. National Institute for Health and Care Excellence (NICE) clinical guideline 84: Diarrhoea and vomiting in children: Diarrhoea and vomiting caused by gastroenteritis diagnosis, assessment and management in children younger than 5 years. April 2009

11. Guarino A, Albano F, Ashkenazi S et al. European Society for Paediatric Gastroenterology, Hepatology, and Nutrition/European Society for Paediatric Infectious Diseases Evidence-based Guidelines for the Management of Acute Gastroenteritis in Children in Europe Journal of Pediatric Gastroenterology and Nutrition 2008 46:S81–S184

12. Centers for Disease Control and Prevention Morbidity and Mortality Weekly Report Managing Acute Gastroenteritis Among Children Oral Rehydration, Maintenance, and Nutritional Therapy November 21, 2003 / Vol. 52 / No. RR-16 http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5216a1.htm

This assessment is based on data submitted by the applicant company up to and including 13 May 2014.

*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

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.