General Commissioning Policy

Treatment	Racecadotril (Hidrasec®; Abbott)
For the treatment of	Complementary symptomatic treatment of acute diarrhoea in infants (older than 3 months) and children, together with oral rehydration, and the usual support measures, when these measures alone are insufficient to control the clinical condition. In adults it is indicated for the symptomatic treatment of acute diarrhoea. Note this is licensed in adults but the evidence has not been considered in this review.
Background	Racecadotril (Hidrasec®) is an enkephalinase inhibitor licensed for symptomatic treatment of acute diarrhoea in infants, children and adults. There is limited evidence that combining racecadotril with oral rehydration solution leads to shorter duration of symptoms among children presenting for hospital care. There is inadequate evidence to support routine racecadotril use among patients likely to be encountered in UK primary care.
Commissioning position	Racecadotril is not recommended for the treatment of acute diarrhoea. There is a lack of evidence to show that this treatment will reduce hospital admissions or reduce hospital stay or improve recovery rate.
Effective from	September 2016
Summary of evidence / rationale	**NICE Clinical Guideline; Diarrhoea and vomiting in children: diarrhoea and vomiting caused by gastroenteritis: diagnosis, assessment and management in children younger than 5 years. April 2009. http://publications.nice.org.uk/diarrhoea-and-vomiting-in-children- cg84/guidance** Racecadotril was not considered when these guidelines were developed as it was not licensed. Oral rehydration salt solution is the main treatment recommended as part of this clinical guideline. **Scottish Medicines Consortium (SMC) advice: Racecadotril December 2012** **http://www.scottishmedicines.org.uk/General/Homepage_Search_Results?p=0&r=20&q=racecadotril&search=Search** SMC cannot recommend use in the symptomatic treatment of acute diarrhoea in adults due to the manufacturer has not made a submission. SMC does not recommend racecadotril in the treatment of acute diarrhoea in infants older than 3 months and in children, together with oral rehydration and the usual support measures, when these measures alone are insufficient to control the clinical condition. Racecadotril was significantly better than placebo in reducing mean stool output at 48 hours in children with acute diarrhoea treated in hospital. There is insufficient evidence that it improves recovery rate.

Notes

1. This Policy will be reviewed in the light of new evidence, or guidance from NICE.
2. General Commissioning Policies are agreed by the Planning and Commissioning Committee on behalf of NHS Hull CCG.

Regional Drug & Therapeutics Centre New drug evaluation: Racecadotril granules for acute diarrhoea in children
http://www.nyrdtc.nhs.uk/docs/nde/NDE_120_Racecadotril.pdf
Racecadotril (Hidrasec®) is an enkephalinase inhibitor licensed for symptomatic treatment of acute diarrhoea in infants, children and adults. There is limited evidence that combining racecadotril with oral rehydration solution leads to shorter duration of symptoms among children presenting for hospital care.
There is no robust evidence that racecadotril reduces the need for intravenous rehydration, leads to more rapid discharge or helps conserve healthcare resources. There is inadequate evidence to support routine racecadotril use among patients likely to be encountered in UK primary care.

Clinical Evidence

Racecadotril in the treatment of acute watery diarrhoea in children. Salazar-Lindo et al
NEJM 2000; 343:463-7
This was a randomised, double blind, placebo-controlled study to assess whether or not treatment with racecadotril and oral rehydration therapy is more effective than treatment with oral rehydration alone in hospitalized children
with acute watery diarrhoea. 135 boys aged 3 to 35 months who had diarrhoea for 5 days duration or less were randomised to receive either racecadotril (1.5mg/kg orally every 8 hours) or placebo in addition to oral rehydration solution.
The primary end point was the 48 hour stool output, duration of diarrhoea and total intake of oral rehydration solution.
The mean 48-hour stool output was 92+/-12g per kg in the racecadotril group and 170+/-15 g/kg in the placebo group ($p<0.001$). The total stool output was
157=/- 27g/kg in the racecadotril group and 331+/- 27g/kg in the placebo group ($p<0.001$). The median duration of diarrhoea was significantly less ($p<0.001$) in the racecadotril group (28 hours regardless of rotavirus status) than in the placebo group (72 and 52 hours, respectively, for rotavirus-positive and rotavirus-negative patients). The intake of oral rehydration solution was
significantly lower in the racecadotril group than in the placebo group ($p<0.001$).

Efficacy and tolerability of racecadotril in acute diarrhoea in children. Cezard JP et al.
Gastroenterology 2001 March;120(4): 799-805
This is a randomised, placebo-controlled clinical trial to assess the efficacy of racecadotril to treat diarrhoea in children. 172 children aged 3 months to 4 years with acute diarrhoea (3 or more watery stools within the last 24 hours) were randomised to receive either racecadotril 1.5mg/kg three times a day or placebo. Oral rehydration solution administered as required during the first 24 hours. Treatment was continued until resolution of diarrhoea (occurrence of 2 stools of normal consistency or 12 hours without a bowel movement) or until 5 days of treatment.
The primary outcome was 48 hour stool output (g), and secondary outcomes were 24 hour stool output; recovery rate; food and ORS intake.

	Racecadotril	Placebo	
Mean 48hr stool	7g/hr	16g/hr	P=0.001
Mean 24 hr stool output	11g/hr	18g/hr	P=0.015
Recovery within 5 days Males Females	 88% 90%	 79% 82%	

Both groups had similar intake of food and ORS. However ORS intake decreased more rapidly in racecadotril group; patients requiring ORS on the second day,
19% and 35% in racecadotril and placebo respectively. The most common adverse effect was vomiting seen in 7 patients receiving racecadotril and 3 receiving placebo.

Use of racecadotril as outpatient treatment for acute gastroenteritis: a prospective, randomised, parallel study.
Santos M et al J Pediatr. 2009 July; 155(1):62-7

This study was to compare the efficacy of therapy with racecadotril plus ORS versus ORS alone in children with gastroenteritis in an outpatient setting care. The study included 189 patients, ages 3 to 36 months, with acute gastroenteritis: 94 were administered ORS alone and 94 received ORS and racecadotril. The primary outcome was the number of bowel movements in 48 hours after starting treatment.

There was no significant difference in the primary outcome between the two groups, 48 hours after starting treatment (4.1+/-2.7 bowel movements in the ORS group vs. 3.8 +/-2.4 bowel movements in the ORS+ racecadotril group.

There was no difference found in the average duration of gastroenteritis (4.7 +/- 2.2 days in the ORS group, 4+/- 2.1 days in the ORS + racecadotril group; p=0.15.

Effects of racecadotril in the management of acute diarrhoea in infants and children
Cojocaru B et al
Arch Pediatr. 2002 Aug; 9(8): 774-9

Racecadotril and rehydration were compared with rehydration alone n children aged 3 months to 3 years who had acute diarrhoea and were evaluated in the emergency department. The primary endpoint was the number of medical examinations during the week after starting treatment. Secondary endpoints were the number of stools during the first 48 hours, the duration of the diarrhoea and the weight on day 7.

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 average weight gain was similar in the racecadotril and control groups: 4.4% versus 3.5%, respectively.

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