The management of acute uncomplicated diarrhoea in adults involves maintenance of fluid intake and, if required, the reduction of stool frequency using an antimitotic agent. Loperamide is the agent of choice and can be supplied without a prescription for patients aged over 12. Co-phenotrope (also available without a prescription for patients aged over 16) and codeine phosphate are other options. Probiotics may also be effective.

In children under five with acute diarrhoea due to gastroenteritis, NICE recommends treatment of dehydration and fluid management but does not recommend antidiarrhoeal drugs.

The technology
Racecadotril (Hidrasec – Abbott) has been available on the continent for several years. It is a prodrug that undergoes hydrolysis to thiorphan, which inhibits enkephalinase and prolongs the actions of enkephalins. In the small intestine, this reduces hypersecretion of water and electrolytes induced by cholera toxin or inflammation. Racecadotril does not affect intestinal transit time.

It is licensed for the symptomatic treatment of acute diarrhoea in adults when causal treatment is not possible. In infants over three months old and in children, it is licensed as a complementary treatment to 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. In both age groups, racecadotril can be given as a complementary treatment if causal treatment is possible.

In adults, the recommended dose is initially 100mg, then 100mg three times daily, preferably before the main meals. Treatment should continue until two normal stools are recorded but should not exceed seven days. Dosage adjustment is not necessary for elderly patients but caution is required in patients with hepatic or renal impairment because there is little experience of its use in such cases.

Racecadotril is formulated as granules for suspension for infants and children, and capsules for oral dosage for adults. Each 50mg capsule contains 50mg of active substance (thiorphan). In infants over three months and children, granules can be taken three times daily; granules can be added to food or dispersed in water (see SPC for dosage).

20 doses (all formulations) cost £8.42

In combination with oral rehydration solution in infants and toddlers, racecadotril reduces the duration of diarrhoea by about 1 day and doubles the rate of recovery at 48 hours, regardless of the severity of dehydration or rotavirus infection.

In adults, it is as effective as loperamide but causes less constipation.

For children and infants >3 months of age racecadotril could be used as first-line treatment; it may be of use in adult patients where there is a known intolerance to loperamide.
Racecadotril

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**NEW PRODUCTS** | Racecadotril

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<table>
<thead>
<tr>
<th>Racecadotril plus ORS</th>
<th>ORS alone or with placebo</th>
<th>Analysis (intent-to-treat population)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median duration of diarrhoea</td>
<td>1.75 days</td>
<td>2.81 days</td>
</tr>
<tr>
<td><strong>Selected secondary outcomes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>responders (% with diarrhoea for less than 48 hours after adjusting for baseline dehydration and rotavirus)</td>
<td>50.3%</td>
<td>25.8%</td>
</tr>
<tr>
<td>stool output in first 24 hours (inpatient studies only; ratio of mean stool output racecadotril/placebo)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>number of diarrhoeic stools until recovery (outpatient studies only; ratio of the mean number of diarrhoeic stools racecadotril/placebo)</td>
<td></td>
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</tr>
</tbody>
</table>

**Children experiencing adverse events**

<table>
<thead>
<tr>
<th>Racecadotril plus ORS</th>
<th>ORS alone or with placebo</th>
<th>Analysis (intent-to-treat population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>children experiencing adverse events</td>
<td>11.6%</td>
<td>10.1%</td>
</tr>
</tbody>
</table>

HR = hazard ration; RR = relative risk; GMR = geometric mean ratio; NNT = number needed to treat

Table 1. Summary of the 2011 meta-analysis that compared treatment with racecadotril plus ORS with ORS alone in children; after reference 4

Children. The dose is determined according to bodyweight and taken three times daily:
- <9kg – one 10mg sachet
- 9–13kg – two 10mg sachets
- 13–27kg – one 30mg sachet
- >27kg two 30mg sachets.

It is contraindicated in children with hepatic or renal impairment.

**Clinical trials**

Children

A meta-analysis of nine randomised trials involving a total of 1384 children (median ages 11–32 months) compared treatment with racecadotril plus oral rehydration solution (ORS) with ORS alone (see Table 1). Outcomes were categorised by the degree of dehydration and the confirmed presence of rotavirus.

Racecadotril/ORS reduced the duration of diarrhoea (median 1.7 days vs 2.8 days with ORS) and almost doubled the overall rate of recovery at 48 hours (50 vs 26 per cent with ORS solution). This gives a number needed to treat of four children treated with racecadotril/ORS rather than ORS alone for one additional child to recover in 48 hours.5

In outpatients, the number of diarrhoea stools was reduced by 37 per cent and stool output was reduced in patients by 41 per cent by racecadotril/ORS compared with ORS alone. Results were similar for infants (less than one year old) and toddlers.

Adults

At least five trials comparing racecadotril with loperamide have been published.6–10 Four found no significant differences in stool frequency and/or the duration of diarrhoea.6–9 The fifth (n=61), carried out in elderly nursing home residents (mean age 82–83), found that diarrhoea was less frequent with racecadotril during four days of treatment (mean number of episodes 3.9 vs 7.3), stool output was reduced by 25 per cent and normal stools were collected significantly sooner (36 vs 63 hours).10

There was no consistent difference between racecadotril and loperamide in the incidence or duration of abdominal symptoms, eg pain or distension.6–10

**Adverse effects**

Trials in children reported no difference in the frequency of adverse effects between racecadotril and placebo.4,5 In adults, constipation was more frequent with loperamide (19–60 per cent) than racecadotril (8–16 per cent).6–10 Racecadotril may be associated with more itching (28 per cent vs none with loperamide)9 and less nausea (10 vs 20 per cent).10

**References**


**Declaration of interests**

None to declare

Steve Chaplin is a pharmacist who specialises in writing on therapeutics
Place in therapy

Acute diarrhoea can be debilitating and lead to significant dehydration. In its extremes electrolyte disturbances and renal failure can also develop and complications can be potentially life threatening. Most episodes of acute diarrhoea in the UK are mild and self-limiting. The cornerstone of management is to exclude infectious and inflammatory aetiology and, where the underlying condition requires no specific treatment, to replace fluid losses and offer treatments that alleviate loose stools.

Racemadotril has recently been licensed in the UK as a treatment for acute self-limiting diarrhoea. Thiopran is the active metabolite of racemadotril and acts as a peripheral enkephalinase inhibitor, thus increasing the availability of enkephalins.

These enkephalins activate delta-opioid receptors in the gastrointestinal tract leading to reduced cyclic adenosine monophosphate (AMP) mucosal levels, resulting in a hyposecretion of water and electrolytes in the intestinal lumen.¹

Suggested use

Unlike loperamide, which is not recommended for children under the age of four years, racemadotril does have a licence for infants over the age of three months and for children. It should always be used in conjunction with adequate fluid replacement. The maximum use should be limited to seven days in all age groups.

The evidence available suggests that adding racemadotril to O R S may reduce stool output and duration of diarrhoea in acute gastroenteritis. The safety profile of the drug is good with no significant safety concerns. In most studies comparing racemadotril with loperamide the side-effect profile is better with racemadotril (less abdominal distension, nausea and reactive constipation reported).

Racemadotril is not currently licensed for the symptomatic management of chronic diarrhoea, and only a single study to date in patients with retroviral disease and associated diarrhoea has been performed.²

There is no definite evidence that racemadotril reduces the need for intravenous rehydration, leads to more rapid discharge from hospital or helps conserve healthcare resources. There is inadequate evidence to support routine use of racemadotril among patients likely to be encountered in UK primary care; however, it is an option that may be considered in certain patients as a viable alternative to

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loperamide. Therefore, it could be provided to adult patients with suspected self-limiting diarrhoea to control symptoms where there is a known intolerance to loperamide.

Adults prone to traveller’s diarrhoea and intolerant to loperamide could also be prescribed racecadotril as an alternative. A single study from Italy also supports its use in elderly patients, and the drug therefore remains an option for elderly patients prone to abdominal pain and constipation secondary to loperamide.

For children between three months and four years of age, racecadotril could also be used as first-line treatment. Data from developing countries suggest culture-negative diarrhoea and diarrhoea proven to be secondary to rotavirus can safely be treated with racecadotril with significant symptomatic benefit.

It must be appreciated that the evidence defining the role of racecadotril in diarrhoea is somewhat inadequate and most scenarios where benefits are likely to be significant are unlikely to be encountered frequently in the UK primary care setting. No concerns regarding the safety profile of racecadotril have been raised to date.

References

Declaration of interests
None to declare.

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