SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

DOTRIVEL 30 mg CHILDREN, oral powder in sachet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Racecadotril ..... 30 mg
Per sachet.

Excipient with known effect: each sachet contains **2,939.50 mg of sucrose**.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral powder in sachet.
White powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

As an adjunct to oral rehydration, symptomatic treatment of **acute diarrhoea in children**.

The degree of oral or intravenous rehydration must be adapted to diarrhoea severity, age, and individual patient characteristics.

4.2 Posology and method of administration

Oral use.

DOTRIVEL 30 mg is indicated in **children weighing ≥13 kg**.

Posology

The usual daily dose is based on **1.5 mg/kg per dose**, up to a maximum of **three doses per day**.

Practical dosing:

- **Children 13 to 27 kg:** 1 sachet (30 mg), **three times daily**
- **Children >27 kg:** 2 sachets (30 mg each), **three times daily**

Method of administration

The powder may be mixed with food, or dissolved in water or a bottle, stirred well, and administered immediately.

Day 1: an initial dose, then depending on the time of administration, up to three doses in total, preferably at the start of the three main meals.
Following days: three doses per day, preferably at the start of each main meal.

Maximum daily dose: **three doses**.

Treatment should continue until **two consecutive formed stools**, without exceeding **7 days**.

Special populations

- No studies conducted in children with **hepatic or renal impairment**.

4.3 Contraindications

- Hypersensitivity to the active substance or any excipient listed in section 6.1.

4.4 Special warnings and precautions for use

- DOTRIVEL is **only adjunctive therapy**; it **does not replace** oral rehydration.
- Rehydration must be systematic in children with acute diarrhoea to prevent or treat dehydration.
- In severe or prolonged diarrhoea, significant vomiting, or refusal to feed, **IV rehydration** should be considered.
- Bloody or purulent stools with fever may indicate **invasive bacterial diarrhoea** → systemic antibacterial therapy should be considered.

Racecadotril should **not** be used in:

- **Antibiotic-associated diarrhoea** (not evaluated)
- **Prolonged or uncontrollable vomiting** (reduced bioavailability)
- **Hepatic or renal impairment** (no data available)

Excipients (sucrose):

- Contraindicated in patients with **fructose intolerance**, **glucose–galactose malabsorption**, or **sucrase–isomaltase deficiency**.
- Each sachet contains **2.9395 g of sucrose**; if daily intake exceeds **5 g**, consider in diabetic or low-sugar diets.

Hypersensitivity events:

- Mild skin reactions reported; however, severe and potentially life-threatening reactions may occur.
- Cases of **angioedema** (face, tongue, lips, extremities) reported; if airway obstruction occurs, emergency treatment is required.
- Racecadotril must be discontinued immediately and **must not be re-administered** after severe hypersensitivity.

Bradykinin-mediated angioedema:

- Racecadotril and certain drug classes (especially **ACE inhibitors**) may trigger angioedema.
- Co-administration with ACE inhibitors increases risk; rigorous benefit–risk assessment required.

Severe cutaneous adverse reactions (SCAR):

- **DRESS** syndrome reported.
- Treatment must be stopped promptly if symptoms occur; racecadotril must **never** be reintroduced in affected patients.

4.5 Interaction with other medicinal products

Not recommended

Medicines linked to bradykinin-mediated angioedema, such as:

- ACE inhibitors (e.g., **perindopril**, **ramipril**)
- Angiotensin II receptor blockers (**candesartan**, **irbesartan**)
- mTOR inhibitors
- DPP-4 inhibitors (gliptins)
- Estramustine
- Sacubitril
- Recombinant alteplase
- Racecadotril itself

These may cause severe, even fatal, angioedema.

Other interactions

- Concomitant use with **loperamide** or **nifuroxazide** does not alter racecadotril pharmacokinetics.

4.6 Fertility, pregnancy and lactation

Pregnancy

Animal studies show no reproductive toxicity; however, clinical data in pregnant women are very limited.
Use should be avoided during pregnancy as a precaution.

Breast-feeding

No data on excretion in human milk.
Racecadotril should not be used during breast-feeding due to neonatal GI immaturity and pharmacological profile.

Fertility

No effects observed in animal fertility studies.

4.7 Effects on ability to drive and use machines

Racecadotril has **no or negligible** influence on the ability to drive or operate machinery.

4.8 Undesirable effects

Clinical trials: **860 infants/children** treated with racecadotril vs **441** with placebo.
Severe cutaneous adverse reactions (SCAR), including **DRESS**, have been reported.

Adverse reactions:

System organ class	Frequency	Adverse reaction
Skin and subcutaneous tissue disorders	Uncommon	Rash, erythema
	Frequency not known	Urticaria, angioedema (face, lips, tongue, eyelids), erythema multiforme, erythema nodosum, papular rash, pruritus, prurigo, DRESS
Immune system disorders	Frequency not known	Anaphylactic shock

Reporting: via FRILAB pharmacovigilance portal (www.frilab.ch).

4.9 Overdose

In reported overdose cases, no adverse reactions were observed.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: **Other antidiarrhoeals – Intestinal antisecretory agent** (ATC code: **A07XA04**).
Racecadotril is a **prodrug** hydrolysed to **thiorphan**, a potent **enkephalinase inhibitor**.
It protects endogenous enkephalins from degradation, prolonging their action in the small intestine and reducing excessive secretion.
Does **not** modify baseline intestinal secretion or motility.
Clinical studies: **40–46% reduction** in stool output in children during the first 48 hours; shorter diarrhoea duration and lower rehydration needs.
Does not prolong QT/QTc at therapeutic or supratherapeutic doses.

5.2 Pharmacokinetic properties

Absorption: rapid; plasma activity detected within 30 minutes; food delays Tmax by 1.5 h.

Distribution: not significantly bound to blood cells; Vd ~66.4 L/kg; ~90% of thiorphan bound to albumin.

Biotransformation: racecadotril → thiorphan → inactive metabolites; biological half-life ~3 h; no accumulation.

Elimination: mainly renal (81.4%); faecal (≈8%); pulmonary <1%.
Pharmacokinetics altered in hepatic/renal impairment, but no safety data available for paediatric use.

5.3 Preclinical safety data

- High safety margins in monkeys and dogs (up to 1250 mg/kg/day).
- No immunotoxicity in short-term mouse studies; high-dose long-term studies showed infections, but clinical relevance is unclear.
- No mutagenic or clastogenic potential.
- No reproductive toxicity.
- Juvenile rat studies: no significant effects at up to 160 mg/kg/day (≈35× paediatric dose)

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose, colloidal silicon dioxide, polyvinylpyrrolidone.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and contents of container

3 g oral powder sachets (LDPE/Aluminium/LDPE/Paper), box of **16**.

6.6 Special precautions for disposal

No special requirements.

Unused medicinal product or waste material must be disposed of in accordance with local regulations.

7. MARKETING AUTHORISATION HOLDER

FRILAB SA
17, rue des Pierres du Niton
1207 Geneva, Switzerland

8. MANUFACTURER

Athena Drug Delivery Solutions Pvt. Ltd.
A-1 to A-5, M.I.D.C., Chemical Zone, Ambernath (W), District Thane-421501, India

9. DATE OF REVISION OF THE TEXT

October 2024

10. DOSIMETRY

Not applicable.

PRESCRIPTION AND DISPENSING CONDITIONS

List I.