trolav, Gastrulcer; Pep-Rani; Peptab; Peptifar; Quardin†; Ran†; Ranitine; Stacer; Ulcecur†; Ulcerol†; Zantac, Rus.: Aciloc (Ацилок); Histac (Гистак); Ranigast (Ранигасн); Ranisan (Ранисан); Rantac (Рантак); Ulran (Ульран)†; Zantac (Зантак); Zoran (Зоран); S.Afr.: Gl-Tak†; Histak; Ranihexal; Ranteen†; Ulcaid, Ultak Zantac, Singopore: Gastran†; Histac, Hyzan; Lumaren; Neoceptin-R; Rani†; Ranidine; Ratic; Xanidine; Zantac, Zendhin; Zoran†; Spain: Alquen, Arcid, Ardoral; Coralen; Denulcer; Tagus, Lake; Meticel†; Quantor; Ran H2; Ranidin; Ranix, Ranuber; Rubiulcer; Tanidina; Terposen; Toriol; Underacid; Zantac; Swed.: Artonil; Inside; Rani-Q; Zantac; Switz.: Ranimed; Ranisfar; Ulcidine; Zantic; Article; Histac; Hatic; Ranicd; Ranidine; Rantac; Ratic; Ratic; Vlac; Xanidine; Zanamet; Zantac; Zantido; Zantli, Turk: Ranitak; Ranitah; Ranitan†; Ranitan†; Ranitan†; Ranitak; Ranitak; Ranitah; Ranitan†; Ranitan†; Ranitan†; Ranitan†; Ranitak; Ranitak; Ranitah;

**Multi-ingredient:** Arg.: Duo Vizerul†; Euciton Reflux; Megalex; *India*: Aciloc RD; *Mex.*: Ergex.

### Ranitidine Bismuth Citrate (BAN, USAN)

A complex of ranitidine and bismuth citrate; GR-122311X; Ranitidin Bizmut Sitrat; Ranitidin Bizmutreks; Ranitidina y bismuto, citrato de; Ranitidine Bismutrex. N-[2-({5-[(Dimethylamino)methyl]furfury}thio)-ethyl]-N'-methyl-2-nitro-1,1-ethenediamine, compound with bismuth(3+) citrate (1:1).

Ранитидин Висмут Цитрат

 $C_{13}H_{22}N_4O_3S, C_6H_5BiO_7 = 712.5.$  CAS - 128345-62-0. ATC - A02BA07.ATC Vet - QA02BA07.

# **Adverse Effects and Precautions**

Ranitidine bismuth citrate would be expected to combine the adverse effects of both bismuth compounds (p.1711) and ranitidine (p.1766). Blackening of the tongue and faeces is common, and gastrointestinal disturbances, headache, mild anaemia, and altered liver enzyme values have been reported. Rarely, hypersensitivity reactions (including anaphylaxis), have occurred.

Ranitidine bismuth citrate should not be given to patients with moderate to severe renal impairment. It is not suitable for long-term or maintenance therapy because of the risk of bismuth accumulation. As with other antisecretory drugs, the possibility of malignancy should be considered when giving ranitidine bismuth citrate to patients with gastric ulcers since the drug may mask symptoms and delay diagnosis.

### Interactions

Ranitidine bismuth citrate would be expected to have the interactions of bismuth compounds (p.1712), and ranitidine (p.1766).

# **Pharmacokinetics**

After oral doses, ranitidine bismuth citrate dissociates into its ranitidine and bismuth components in the stomach. For the pharmacokinetics of ranitidine, see p.1766, and for those of bismuth, see p.1712.

# ♦ References

- Lacey LF, et al. Comparative pharmacokinetics of bismuth from rantitidine bismuth citrate (GR122311X), a novel anti-ulcerant and tripotassium dicitrato bismuthate (TDB). Eur J Clin Pharmacol 1994; 47: 177–80.
- Koch KM, et al. Pharmacokinetics of bismuth and ranitidine following single doses of ranitidine bismuth citrate. Br J Clin Pharmacol 1996; 42: 201–5.
- Koch KM, et al. Pharmacokinetics of bismuth and ranitidine following multiple doses of ranitidine bismuth citrate. Br J Clin Pharmacol 1996; 42: 207–11.

# **Uses and Administration**

Ranitidine bismuth citrate is a complex of ranitidine with bismuth and citrate, which releases ranitidine and bismuth in the gastrointestinal tract and therefore possesses both the actions of the bismuth compounds (p.1712) and of ranitidine (p.1767). It has been used in the management of peptic ulcer disease (p.1702), and may be given with antibacterials for the eradication of *Helicobacter pylori* infection and the prevention of relapse of peptic ulcer disease.

Doses are 400 mg twice daily orally; treatment has usually been given for 4 to 8 weeks for duodenal ulceration and for 8 weeks for benign gastric ulceration. Ranitidine bismuth citrate should not be used for maintenance therapy, and a maximum of 16 weeks of treatment (two 8-week courses or four 4-week courses) may be given in a 12-month period. For duodenal ulceration where *H. pylori* infection is present, ranitidine bismuth citrate has been given as part of a 7-day triple therapy regimen, typically combined with any two of clarithromycin 500 mg twice daily, amoxicillin 1 g twice daily, or metronidazole 400 mg twice daily. Alternatively, a 14-day dual therapy regimen of ranitidine bismuth citrate combined with clarithromycin 500 mg two or three times daily has been used. In both regimens ranitidine bismuth citrate alone may be continued to a total of 28 days.

# ♦ References.

- Bardhan KD, et al. GR122311X (ranitidine bismuth citrate), a new drug for the treatment of duodenal ulcer. Aliment Pharmacol Ther 1995; 9: 497–506.
- Peterson WL, et al. Ranitidine bismuth citrate plus clarithromycin is effective for healing duodenal ulcers, eradicating H.pylori and reducing ulcer recurrence. Aliment Pharmacol Ther 1996; 10: 251–61.

- Anonymous. Pylorid, H. pylori and peptic ulcer. Drug Ther Bull 1996; 34: 69–70.
- van der Wouden EJ, et al. One-week triple therapy with ranitidine bismuth citrate, clarithromycin and metronidazole versus two-week dual therapy with ranitidine bismuth citrate and clarithromycin for Helicobacter pylori infection: a randomized, clinical trial. Am J Gastroenterol 1998; 93: 1228–31.

#### **Preparations**

Proprietary Preparations (details are given in Part 3)

Arg.: Pylorid†, Austria: Helirad, Pylorisin; Belg.: Pylorid†, Braz.: Pylorid, Cz.: Eradipak†, Denm.: Pylorid†, Fin.: Pylorid†, Gr.: Pylorid†, Hong.: Pylorid†, Fin.: Pylorid†, Ital.: Elicodil†, Pylorid†, Nex.: Azanplus; Neth.: Pylorid†, Norw.: Pylorid; Port.: Pylorid†, Spain: Pylorid; Switz.: Pylorid†, Thai.: Pylorid†, Turk.: Pylorid†, UK: Pylorid†, Venez.: Pylorid†

Multi-ingredient: Austral.: Pylorid-KA.

## Rebamipide (rINN)

Rebamipida; Rébamipide; Rebamipidum. ( $\pm$ )- $\alpha$ -(p-Chlorobenzamido)-1,2-dihydro-2-oxo-4-quinolinepropionic acid.

Ребамипид

 $C_{19}H_{15}CIN_2O_4 = 370.8.$ CAS — 90098-04-7; 111911-87-6.

### **Profile**

Rebamipide is stated to possess cytoprotective properties and is used in the treatment of peptic ulcer disease (p.1702) and gastritis in usual oral doses of 100 mg three times daily. It has also been used rectally for the treatment of intestinal inflammation. Rebamipide eye drops are under investigation in the treatment of dry eye.

#### ♦ References

- Makiyama K, et al. Efficacy of rebamipide enemas in active distal ulcerative colitis and proctitis: a prospective study report. Dig Dis Sci 2005; 50: 2323–9.
- Miyata M, et al. Successful treatment of severe pouchitis with rebamipide refractory to antibiotics and corticosteroids: a case report. World J Gastroenterol 2006; 12: 656–8.
- Miwa H, et al. Effect of a gastro-protective agent, rebamipide, on symptom improvement in patients with functional dyspepsia: a double-blind placebo-controlled study in Japan. J Gastroenterol Hepatol 2006; 21: 1826–31.

# Preparations

Proprietary Preparations (details are given in Part 3)
Indon.: Mucosta; Jpn: Mucosta; Philipp.: Mucosta; Thai.: Mucosta

# Renzapride (BAN, rINN)

$$\label{eq:attention} \begin{split} &\text{ATL-1251; BRL-24924A; Renzaprida; Renzapridum. } (\pm)\text{-endo-4-}\\ &\text{Amino-$N-(1-azabicyclo[3.3.1]non-4-yl)-5-chloro-$o-anisamide.} \end{split}$$

 $C_{16}H_{22}CIN_3O_2 = 323.8.$ CAS — 88721-77-1; 112727-80-7.

$$\begin{array}{c|c} CH_3 \\ O \\ N \end{array}$$

# **Profile**

Renzapride is a substituted benzamide with prokinetic actions on gastrointestinal motility. It also has 5-HT<sub>4</sub> agonist and 5-HT<sub>3</sub> antagonist activity. It is under investigation for the management of gastrointestinal disorders including irritable bowel syndrome.

# ♦ References.

- Tack J, et al. Pilot study of the efficacy of renzapride on gastrointestinal motility and symptoms in patients with constipation-predominant irritable bowel syndrome. Aliment Pharmacol Ther 2006; 23: 1655–65.
- George AM, et al. Clinical trial: renzapride therapy for constipation-predominant irritable bowel syndrome—multicentre, randomized, placebo-controlled, double-blind study in primary healthcare setting. Aliment Pharmacol Ther 2008; 27: 830–7.

#### Revaprazan (HNN)

Révaprazan; Revaprazán; Revaprazanum. *N-*(4-Fluorophenyl)-4,5-dimethyl-6-[(1*RS*)-1-methyl-3,4-dihydroisoquinolin-2(1*H*)-yl]pyrimidin-2-amine.

Ревапразан

 $C_{22}H_{23}FN_4 = 362.4.$ CAS — 199463-33-7.

### Revaprazan Hydrochloride (USAN, rINNM)

Hidrocloruro de revaprazán; Révaprazan, Chlorhydrate de; Revaprazani Hydrochloridum; YH-1238; YH-1885. N-(4-Fluorophenyl)-5,6-dimethyl-4-[(1RS)-1-methyl-3,4-dihydroisoquinolin-2(1H)-y]pyrimidin-2-amine hydrochloride.

Ревапразана Гидрохлорид

 $C_{22}H_{23}FN_4$ , HCI = 398.9. CAS - 178307-42-1.

#### **Profile**

Revaprazan is a proton pump inhibitor that is under investigation for the management of gastric and duodenal ulceration, functional dyspepsia, and gastro-oesophageal reflux disease.

#### ◊ References.

- Sorbera LA, et al. Revaprazan hydrochloride. Drugs Of The Future 2004; 29: 455.
- 2. Yu K-S, et al. Pharmacokinetic and pharmacodynamic evaluation of a novel proton pump inhibitor, YH1885, in healthy volunteers. J Clin Pharmacol 2004; 44: 73–82.

## Rhubarb

Chinese Rhubarb; Korzeń rzewienia; Rabarbaro; Rabarbarų šaknys; Rabarberrot; Raparperinjuuri; Ravent; Rebarbara-gyökértörzs; Reveňový kořen; Rhabarber; Rhei radix; Rhei Rhizoma; Rheum; Rhubarb Rhizome; Rhubarbe; Ruibarbo.

Ревень Аптечный

**Description.** Indian rhubarb (Himalayan rhubarb) consists of the dried rhizome and roots of *Rheum emodi*, *R. webbianum*, or some other related species of *Rheum*. Rhapontic rhubarb (Chinese rhapontica) consists of the dried rhi-

Rhapontic rhubarb (Chinese rhapontica) consists of the dried rhizomes of *R. rhaponticum*. It may occur as an adulterant of rhubarb, and pharmacopoeias specify a test to confirm its absence. Garden rhubarb, of which the leaf-stalks are used as food, is derived from *R. rhaponticum*.

**Pharmacopoeias.** In *Chin., Eur.* (see p.vii), and *Jpn. Chin.* and *Jpn* also permit *Rheum tanguticum*, and *Jpn* also permits *R. coreanum*.

**Ph. Eur. 6.2** (Rhubarb). The whole or cut, dried underground parts of *Rheum palmatum* or of *R. officinale* or of hybrids of these two species or of a mixture. The underground parts are often divided; the stem and most of the bark with the rootlets are removed. It contains not less than 2.2% of hydroxyanthracene derivatives, expressed as rhein  $(C_{15}H_8O_6 = 284.2)$ , calculated with reference to the dried drug. Protect from light.

# **Adverse Effects and Precautions**

As for Senna, p.1769.

# **Uses and Administration**

Rhubarb is an anthraquinone stimulant laxative used similarly to senna (p.1770). It also exerts an astringent action due to the presence of gallic acid derivatives and tannins.

**Homoeopathy.** Rhubarb has been used in homoeopathic medicines under the following names: Rheum; Rhei radix; Rheum palmatum.