

# NEW ZEALAND DATA SHEET

## 1 PEPTISOOTHE

Ranitidine hydrochloride 150mg/10mL syrup

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 10mL of the syrup contains ranitidine hydrochloride equivalent to ranitidine 150mg.

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Peptisoothe is a clear to pale yellow syrup with a spearmint flavour.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

- the treatment of duodenal ulcer, and benign gastric ulcer, including that associated with non-steroidal anti-inflammatory agents.
- the prevention of non-steroidal anti-inflammatory agent (including aspirin) associated duodenal ulcers in patients with a history of duodenal ulceration proven by endoscopy.
- the treatment of post-operative ulcer
- the treatment of oesophageal reflux disease
- symptom relief in gastro-oesophageal reflux disease
- the treatment of Zollinger-Ellison syndrome
- the treatment of chronic episodic dyspepsia, characterised by pain (epigastric or retrosternal) which is related to meals or disturbs sleep but not associated with the above conditions.
- the prophylaxis of upper gastrointestinal haemorrhage from stress ulceration in seriously ill patients.
- the prophylaxis of recurrent haemorrhage in patients with bleeding peptic ulcers.
- before general anaesthesia in patients considered to be at risk of acid aspiration (Mendelson's syndrome), particularly obstetric patients during labour.

### 4.2 Dose and method of administration

Adults

#### **Duodenal Ulcer and Benign Gastric Ulcer**

##### Acute Treatment

The usual dosage is 150mg twice daily, taken in the morning and evening. Alternatively, patients with duodenal or gastric ulceration may be treated with a single bedtime dose of 300mg. It is not necessary to time the dose in relation to meals.

In most cases of duodenal ulcer or benign gastric ulcer, healing occurs in 4 weeks. Healing usually occurs after a further 4 weeks of treatment in those patients whose ulcers have not fully healed after the initial course of therapy.

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In duodenal ulcer 300mg twice daily for 4 weeks results in healing rates which are higher than those at 4 weeks with ranitidine 150mg twice daily or 300mg at bedtime. The increased dose has not been associated with an increased incidence of unwanted effects.

### Long Term Management

Maintenance treatment at a reduced dosage of 150mg at bedtime is recommended for patients who have responded to short-term therapy, particularly those with a history of recurrent ulcer.

Smoking is associated with a higher rate of duodenal ulcer relapse, and such patients should be advised to stop smoking. In those who fail to comply with such advice a dose of 300mg at bedtime provides additional therapeutic benefit over the 150mg dosage regimen.

### **NSAID Associated Peptic Ulceration**

#### Acute Treatment

In ulcers following non-steroidal anti-inflammatory drug therapy, or associated with continued non-steroidal anti-inflammatory drugs, 8-12 weeks treatment may be necessary with 150mg twice daily or 300mg at bedtime.

#### Prophylaxis

For the prevention of non-steroidal anti-inflammatory drug associated duodenal ulcers, ranitidine 150mg twice daily may be given concomitantly with non-steroidal anti-inflammatory therapy.

### **Postoperative Ulcer**

The standard dosage regimen for postoperative ulcer is 150mg twice daily. Most cases heal within 4 weeks. Those not fully healed after the initial 4 weeks usually do so after a further 4 weeks.

### **Gastro-Oesophageal Reflux Disease**

#### Acute reflux oesophagitis

In the management of oesophageal reflux disease, the recommended course of treatment is either 150mg twice daily or 300mg at bedtime for up to 8 weeks.

In patients with moderate to severe oesophageal reflux disease, the dosage of ranitidine may be increased to 150mg four times daily for up to twelve weeks.

#### Long-term management of reflux oesophagitis

For the long-term management of reflux oesophagitis the recommended adult oral dose is 150mg twice daily.

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### Symptom relief in gastro-oesophageal reflux disease

For the relief of symptoms associated with oesophageal acid reflux, the recommended regimen is 150mg twice daily for two weeks. This regimen may be continued for a further two weeks in those patients in whom the initial response is inadequate.

### **Zollinger-Ellison Syndrome**

In patients with Zollinger-Ellison syndrome, the starting dose is 150mg three times daily and this may be increased as necessary. Patients with this syndrome have been given increasing doses up to 6g per day and these doses have been well tolerated.

### **Chronic Episodic Dyspepsia**

For patients with chronic episodic dyspepsia the recommended course of treatment is 150mg twice daily for up to 6 weeks. Anyone not responding or relapsing shortly afterwards should be investigated.

### **Prophylaxis of Haemorrhage from Stress Ulceration in Seriously Ill Patients or the Prophylaxis of Recurrent Haemorrhage in Patients Bleeding from Peptic Ulceration**

Treatment with ranitidine syrup 150mg twice daily may be substituted for ranitidine injection once oral feeding commences in patients considered to be still at risk from these conditions.

### **Prophylaxis of Mendelson's Syndrome**

In patients thought to be at risk of acid aspiration syndrome an oral dose of 150mg can be given 2 hours before induction of general anaesthesia, and preferably also 150mg orally the previous evening.

In obstetric patients at commencement of labour, an oral dose of 150mg can be given followed by 150mg at 6 hourly intervals. It is recommended that since gastric emptying and medicine absorption are delayed during labour, any patient requiring emergency general anaesthesia should be given, in addition, a non-particulate antacid (e.g. sodium citrate) prior to induction of anaesthesia. The usual precautions to avoid acid aspiration should also be taken.

### **Children**

Experience with ranitidine in children is limited and such use has not been fully evaluated in clinical studies. It has however been used successfully in children aged 8 to 18 years in doses up to 150mg twice daily.

### **Renal Impairment**

Accumulation of ranitidine with resulting elevated plasma concentrations will occur in patients with severe renal impairment (creatinine clearance less than 50 mL/min). It is recommended that the daily dose of ranitidine in such patients should be 150mg.

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### 4.3 Contraindications

Patients known to have hypersensitivity to any component of the preparation

### 4.4 Special warnings and precautions for use

The possibility of malignancy should be excluded before commencement of therapy in patients with gastric ulcer [and if indications include dyspepsia; patients of middle age and over with new or recently changed dyspeptic symptoms] as treatment with ranitidine may mask symptoms of gastric carcinoma.

Ranitidine is excreted via the kidney and so plasma levels of the drug are increased in patients with severe renal impairment.

The dosage should be adjusted as detailed above under Dosage in Renal Impairment.

Regular supervision of patients who are taking non-steroidal anti-inflammatory drugs concomitantly with ranitidine is recommended, especially in the elderly and in those with a history of peptic ulcer.

Rare clinical reports suggest that ranitidine may precipitate acute porphyric attacks. Ranitidine should therefore be avoided in patients with a history of acute porphyria.

In patients such as the elderly, persons with chronic lung disease, diabetes or the immunocompromised, there may be an increased risk of developing community acquired pneumonia. A large epidemiological study showed an increased risk of developing community acquired pneumonia in current users of H2 receptor antagonists versus those who had stopped treatment, with an observed adjusted relative risk of 1.63 (95% CI, 1.07-2.48).

### 4.5 Interaction with other medicines and other forms of interaction

Ranitidine, at blood levels produced by standard recommended doses, does not inhibit the hepatic cytochrome P450-linked mixed function oxygenase system. Accordingly, ranitidine in usual therapeutic doses does not potentiate the actions of drugs which are inactivated by this enzyme; these include diazepam, lignocaine, phenytoin, propranolol and theophylline. There have been reports of altered prothrombin time with coumarin anti-coagulants e.g. warfarin. Due to the narrow therapeutic index, close monitoring of increased or decreased prothrombin time is recommended during concurrent treatment with ranitidine.

Because ranitidine is partially eliminated by the cationic system, it may affect the clearance of other medication eliminated by this route. High doses of ranitidine e.g. those used in the treatment of Zollinger-Ellison syndrome, may reduce the excretion of procainamide and N-acetylprocainamide resulting in increased plasma levels of these drugs.

The bioavailability of some medication may be affected by the alteration in gastric pH. This may result in either an increase e.g. triazolam, midazolam, glipizide or decrease e.g. ketoconazole, atazanavir, delaviridine, gefitinib in absorption.

There is no evidence of an interaction between ranitidine and amoxicillin and metronidazole.

If high doses (2g) of sucralfate are co-administered with ranitidine the absorption of the latter may be reduced. This effect is not seen if sucralfate is taken after an interval of 2 hours.

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### 4.6 Fertility, pregnancy and lactation

#### Category B1

Ranitidine crosses the placenta and is excreted in human breast milk.

Like other drugs it should only be used during pregnancy and nursing if considered essential.

### 4.7 Effects on ability to drive and use machines

None reported.

### 4.8 Undesirable effects

The following have been reported as events in clinical trials or in the routine management of patients treated with ranitidine. The relationship to ranitidine therapy has not been established in many cases.

#### Blood & Lymphatic

Blood count changes (leucopenia, thrombocytopenia) have occurred in a few patients. These are usually reversible. Rare cases of agranulocytosis or pancytopenia, sometimes with marrow hypoplasia or marrow aplasia have been reported.

#### Cardiovascular

As with other H<sub>2</sub> receptor antagonists, there have been rare reports of bradycardia and A-V Block. Rare cases of vasculitis have been reported.

#### Eye

There have been a few reports of reversible blurred vision suggestive of a change in accommodation.

#### Gastrointestinal

Very rare cases of diarrhoea have been reported.

#### Hepatobiliary tract & Pancreas

Transient and reversible changes in liver function-tests can occur. There have been occasional reports of hepatitis (hepatocellular, hepatocanalicular or mixed) with or without jaundice. These were usually reversible. Acute pancreatitis has been rarely reported.

#### Musculoskeletal

Musculoskeletal symptoms such as arthralgia and myalgia have been reported rarely.

#### Neurology/Psychiatry

Headache, sometimes severe and dizziness have been reported in a very small proportion of patients. Rare cases of reversible mental confusion, depression and hallucinations have been reported, predominantly in severely ill and elderly patients. In addition, reversible involuntary movement disorders have been reported rarely.

#### Non-site specific/Skin

Skin rash has been reported, including rare cases of erythema multiforme. Rare cases of alopecia have been reported.

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Hypersensitivity reactions (urticaria, angioneurotic oedema, fever, bronchospasm, hypotension, anaphylactic shock, chest pain) have been seen rarely after a single dose.

### Renal

Very rare cases of acute interstitial nephritis have been reported.

### Reproduction

Reversible impotence has been reported rarely. There have been a few reports of breast symptoms in men taking ranitidine.

### Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>

### 4.9 Overdose

Ranitidine is very specific in action and no particular problems are expected following overdosage.

Symptomatic and supportive therapy should be given as appropriate.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Ranitidine is a specific, rapidly acting histamine H<sub>2</sub>-antagonist. It inhibits basal and stimulated secretion of gastric acid, reducing both the volume and the acid and pepsin content of the secretion. Ranitidine has a relatively long duration of action and so a single 150mg dose effectively suppresses gastric acid secretion for twelve hours. Clinical evidence has shown that ranitidine combined with amoxicillin and metronidazole eradicates *Helicobacter pylori* in approximately 90% of patients. This combination therapy has been shown to significantly reduce duodenal ulcer recurrence.

*Helicobacter pylori* infects about 95% of patients with duodenal ulcer and 80% of patients with gastric ulcer.

### 5.2 Pharmacokinetic properties

The bioavailability of ranitidine is consistently about 50%. Peak concentrations in plasma, normally in the range 300-550 ng/mL, occur 2-3 hours after oral administration of a 150mg dose. Concentrations of ranitidine in plasma are proportional to dose up to and including 300mg.

Ranitidine is not extensively metabolised. Elimination of the drug is primarily by tubular secretion. The elimination half-life is 2-3 hours.

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In balance studies with 150mg 3H-ranitidine 93% of an intravenous dose was excreted in urine and 5% in faeces; 60-70% of an oral dose was excreted in urine and 26% in faeces. Analysis of urine excreted in the first 24 hours after dosing showed that 70% of the intravenous dose and 35% of the oral dose were eliminated unchanged. The metabolism of ranitidine is similar after both oral and intravenous dosing; about 6% of the dose being excreted in urine as the N-oxide, 2% as the S-oxide, 2% as desmethylranitidine and 1-2% as the furoic acid analogue.

### 5.3 Preclinical safety data

No relevant information.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Dibasic sodium phosphate dodecahydrate

Ethanol

Monobasic potassium phosphate

Purified water

Saccharin sodium

Sorbitol

Spearmint flavour 10857172

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

36 months from date of manufacture stored at or below 25°C

1 months opened stored at or below 25°C

### 6.4 Special precautions for storage

Store below 25°C.

### 6.5 Nature and contents of container

Bottles of 100mL, 150mL and 300mL

### 6.6 Special precautions for disposal

No special requirements for disposal.

## 7 MEDICINE SCHEDULE

Prescription Medicine: Bottles of 100mL, 150mL and 300mL

Pharmacy Only Medicine: Bottles of 100mL and 150mL

## 8 SPONSOR

AFT Pharmaceuticals Ltd

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# NEW ZEALAND DATA SHEET

## 9 DATE OF FIRST APPROVAL

15 March 2007

## 10 DATE OF REVISION OF THE TEXT

September 2018

## SUMMARY TABLE OF CHANGES

| <b>Date</b>          | <b>Section(s)<br/>Changed</b> | <b>Change (s)</b>  |
|----------------------|-------------------------------|--|
| 06 September<br>2018 | All                           | Reformat consistent with new Medsafe Data Sheet<br>Template. |