NEW ZEALAND DATA SHEET

1. PRODUCT NAME

ZANTAC 150 ranitidine (as hydrochloride) 150 mg tablets.

ZANTAC 300 ranitidine (as hydrochloride) 300 mg tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

ZANTAC 150 150 mg tablets contain ranitidine (as hydrochloride) 150 mg.

ZANTAC 300 300 mg tablets contain ranitidine (as hydrochloride) 300 mg.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

ZANTAC 150 150 mg tablets are white film-coated round tablets engraved “150” on one face and plain on the other.

ZANTAC 300 300 mg tablets are white capsule-shaped, film-coated tablets engraved “300” on one face and plain on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

1. Treatment of duodenal and gastric ulcers.

2. Prophylaxis against recurrence of duodenal and gastric ulcers.

3. Treatment of reflux oesophagitis.

4. Prophylaxis of reflux oesophagitis.

5. Treatment of Zollinger-Ellison syndrome.

6. Prophylaxis of stress induced duodenal and peptic ulcer in seriously ill patients.

4.2 Dose and method of administration

ZANTAC 150 and ZANTAC 300 tablets are administered by mouth.

1. **Treatment of duodenal and gastric ulcers:**
   300 mg taken as a single dose at bedtime, or 150 mg taken twice daily, in the morning and at bedtime for up to 8 weeks.

2. **Prophylaxis against recurrence of duodenal and gastric ulcers:**
   150 mg taken at night.

3. **Treatment of reflux oesophagitis:**
   150 mg taken twice daily in the morning and at bedtime for up to 4 weeks.

4. **Prophylaxis of reflux oesophagitis:**
   150 mg taken twice daily in the morning and at bedtime.

5. **Treatment of Zollinger-Ellison syndrome:**
   150 mg taken 3 times daily initially and increased, as necessary, to 600-900 mg/day.

6. **Prophylaxis of stress induced duodenal and peptic ulcer in seriously ill patients:**
   150 mg taken twice daily in the morning and at bedtime.

7. **Patients with renal impairment:**
   In patients with renal impairment (creatinine clearance less than 50 mL/min) it is recommended that the daily dose of ranitidine is 150 mg/day (see section 4.4).

4.3 Contraindications

Patients with known hypersensitivity to any component of the formulation.

4.4 Special warnings and precautions for use

Carcinoma

Treatment with a histamine H_2-antagonist may mask symptoms associated with carcinoma of the stomach and therefore may delay diagnosis of the condition. Accordingly, where gastric ulcer is suspected, the possibility of malignancy should be excluded before therapy with **ZANTAC 150 and ZANTAC 300** tablets is instituted.

Long-term use

The risk of ulcer recurrence is determined by many factors. In some cases, long periods of treatment may be necessary and/or repeated. Evidence from controlled clinical trials of up to 18 months continuous treatment with **ZANTAC 150 and ZANTAC 300** has not revealed any undue untoward effects.

Hepatic effects

The use of higher than recommended doses of intravenous H_2-antagonists has been associated with rises in liver enzymes when treatment has been extended beyond five days.

Porphyria

Rare clinical reports suggest that ranitidine may precipitate acute porphyric attacks. **ZANTAC 150 and ZANTAC 300** should therefore be avoided in patients with a history of acute porphyria.

Pneumonia
Agents that elevate gastric pH may increase the already present risk of nosocomial pneumonia in intubated ICU patients receiving mechanical ventilation.

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 H_2-receptor antagonists versus those who had stopped treatment, with an observed adjusted relative risk of 1.63 (95% CI, 1.07-2.48).

Use in renal impairment
Ranitidine is excreted via the kidney and in the presence of renal impairment (creatinine clearance less than 50 mL/min) plasma levels of ranitidine are increased and prolonged. Accordingly in the presence of significant renal impairment, serum levels should be monitored and dosage adjustments made. It is recommended that the daily dose of ranitidine is 150 mg/day. The clearance of ranitidine is increased during haemodialysis (see section 4.2 Patients with renal impairment).

Paediatric use
Experience with ranitidine tablets in children is limited and such use has not been fully evaluated in clinical studies.

Effects on laboratory tests
No data available.

4.5 Interaction with other medicines and other forms of interaction

Ranitidine has the potential to affect the absorption, metabolism or renal excretion of other drugs. The altered pharmacokinetics may necessitate dosage adjustment of the affected drug or discontinuation of treatment.

Interactions occur by several mechanisms including:

1) Inhibition of cytochrome P450-linked mixed function oxygenase system:
Ranitidine at usual therapeutic doses does not potentiate the actions of drugs which are inactivated by this enzyme system such as diazepam, lidocaine, phenytoin, propranolol and theophylline.

There have been reports of altered prothrombin time with coumarin anticoagulants (e.g. warfarin). Due to the narrow therapeutic index, close monitoring of increased or decreased prothrombin time is recommended during concurrent treatment with ranitidine.

2) Competition for renal tubular secretion:
Since ranitidine is partially eliminated by the cationic system, it may affect the clearance of other drugs eliminated by this route. High doses of ranitidine (e.g. such as 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.

3) Alteration of gastric pH:
The bioavailability of certain drugs may be affected. This can result in either an increase in absorption (e.g. triazolam, midazolam, glipizide) or a decrease in absorption (e.g. ketoconazole, atazanavir, delaviridine, gefitnib).

If high doses (2 g) 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 two hours.

4.6 Fertility, pregnancy and lactation

Effects on fertility
There are no data on the effects of ranitidine on human fertility. Reproduction studies performed in rats and rabbits have revealed no evidence of impaired fertility or harm to the foetus due to ranitidine.

Use in pregnancy: Category B1
The safety of ranitidine in pregnancy has not been established. Ranitidine crosses the placenta. **ZANTAC 150 and ZANTAC 300** should only be used during pregnancy if considered essential. If the administration of **ZANTAC 150 or ZANTAC 300** is considered to be necessary, its use requires that the potential benefits be weighed against possible hazards to the patient and to the foetus.

Use in lactation
Ranitidine is secreted in breast milk in lactating mothers, but the clinical significance of this has not been fully evaluated. **ZANTAC 150 or ZANTAC 300** should only be used by nursing mothers if considered essential.

4.7 Effects on ability to drive and use machines

Not applicable.

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 clear in many cases. Headache, sometimes severe, has been reported in a very small proportion of patients.

Central nervous system: Rarely, malaise, dizziness, somnolence, insomnia and vertigo. 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. There have been a few reports of reversible blurred vision suggestive of a change in accommodation. Reversible impotence has been reported rarely.

Cardiovascular: As with other H_2 - receptor antagonists rare reports of tachycardia, bradycardia, premature ventricular beats, AV block, and asystole.

Gastrointestinal: Constipation, diarrhoea, nausea/vomiting, abdominal discomfort/pain.

Hepatic: Transient and reversible changes in liver-function tests can occur. There have been occasional reports of hepatitis, hepatocellular or hepatocanalicular or mixed, with or without jaundice. These were usually reversible.

Musculoskeletal: Rare reports of arthralgias and myalgia.

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

Endocrine: Controlled studies in animals and man have shown no stimulation of any pituitary hormone by ranitidine, no anti-androgenic activity, and cimetidine-induced gynaecomastia and impotence in hypersecretory patients have resolved when ranitidine was substituted. However, occasional cases of breast conditions such as gynaecomastia and galactorrhoea, impotence and loss of libido have been reported in male patients receiving ranitidine but the incidence did not differ from that in the general population.

Integumental: Rash including rare cases of mild erythema multiforme. Rare cases of vasculitis and alopecia have been reported.

Renal: Very rare cases of acute interstitial nephritis have been reported.

Other: Rare cases of hypersensitivity reactions (eg, fever, bronchospasm, anaphylactic shock, urticaria, angioneurotic oedema, hypotension, chest pain, rash, eosinophilia), small increases in serum creatinine. Acute pancreatitis has been reported rarely.

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://pophealth.my.site.com/carmreportnz/s/

4.9 Overdose

There has been limited experience with overdosage with oral doses of ranitidine. Reported acute ingestions of up to 18 g orally have been associated with transient adverse effects similar to those encountered in normal clinical experience. See Section 4.8 Undesirable effects. Symptomatic and supportive therapy should be given as appropriate. If need be, the drug may be removed from the plasma by haemodialysis.

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: histamine H2-receptor antagonist, ATC code: A02BA02

Mechanism of action Animal experiments both *in vitro* and *in vivo* have established that ranitidine is a selective, competitive antagonist of histamine at H_2-receptor sites. Ranitidine has no significant interaction at histamine H_1-receptors, muscarinic receptors or beta-adrenoceptors. Ranitidine is a potent inhibitor of gastric secretion in the rat and dog.

All the evidence from human studies is compatible with a selective, competitive antagonism of histamine H_2-receptors by ranitidine in man. Oral administration of ranitidine inhibits both basal gastric secretions and gastric acid secretion induced by histamine, pentagastrin and other secretagogues. On a weight basis ranitidine is between 4 and 9 times more potent than cimetidine.

After oral administration of ranitidine, the plasma concentrations of ranitidine achieved are directly related to the dose administered. A plasma ranitidine concentration of 50-100 ng/mL has an inhibitory effect upon stimulated gastric acid secretion of approximately 50%.

Inhibition of pentagastrin-induced gastric acid secretion increases with dose, being approximately 90% two hours after an oral 150 mg dose and a significant effect is still evident 12 hours after this dose. In 10 patients with duodenal ulcer, 150 mg ranitidine given orally every 12 hours significantly reduced mean 24 hour hydrogen ion activity by 69% and nocturnal gastric acid output by 90% whereas cimetidine (200 mg three times daily and 400 mg at night) reduced mean 24 hour hydrogen ion activity by 48% and nocturnal gastric acid output by 70%.

Pepsin secretion is also inhibited by ranitidine, but secretion of gastric mucus is not affected. Ranitidine does not alter the secretion of bicarbonate or enzymes from the pancreas in response to secretin and pancreozymin. Reduction in gastric acid secretion induced by ranitidine 150 mg twice daily for 7 days did not cause bacterial overgrowth in the stomach.

Pulse rate, blood pressure, electrocardiogram and electroencephalogram were not significantly affected in man following recommended doses of ranitidine.

Chronic ranitidine therapy (300 mg/day for 28 days) had no effect on serum prolactin, gastrin, thyroid stimulating hormone, follicle stimulating hormone, luteinising hormone, gonadotrophins, testosterone, oestriol, progesterone or cortisol levels.

One study in 30 male duodenal ulcer patients showed a significant decrease in basal thyroxine levels after 4 weeks' treatment with 300 mg ranitidine daily, but no significant change in thyroid stimulating hormone was noted.

Clinical trials
No clinical trial data available.

5.2 Pharmacokinetic properties

Absorption
Peak plasma levels occur about 2-3 hours after oral administration of ranitidine. Absorption is not significantly altered by food or concurrent antacid administration.

Following oral administration of 150 mg ranitidine, maximum plasma concentrations (300 to 580 ng/mL) occurred after 1 to 3 hours. Two distinct peaks or a plateau in the absorption phase suggest reabsorption of drug secreted into the intestine. The absolute bioavailability of ranitidine is 50 to 60%, and plasma concentrations increase proportionally with increasing dose up to 200 mg. Bioavailability of ranitidine is approximately 50%. Serum protein binding of ranitidine in man is in the range 10-19%. The elimination half-life is approximately 2 hours.

Distribution
Ranitidine is not extensively bound to plasma proteins (15%), but exhibits a large volume of distribution ranging from 96 to 142 L.

Metabolism
The fraction of the dose recovered as metabolites includes 6% of the dose in urine as the N-oxide, 2% as the S-oxide and small amounts of desmethylranitidine and the furoic acid analogue. . The 24 hour urinary recovery of free ranitidine and its metabolites is about 40% after oral administration of the drug.

Excretion
Plasma concentrations decline bi-exponentially, with a terminal half-life of 2 to 3 hours. The major route of elimination of unchanged ranitidine is renal. Renal clearance is approximately 500 mL/min, which exceeds glomerular filtration indicating net renal tubular secretion.

Patients over 50 years of age
In patients over 50 years of age, half life is prolonged (3 to 4 hours) and clearance is reduced, consistent with the age-related decline of renal function. However, systemic exposure and accumulation are 50% higher. This difference exceeds the effect of declining renal function and indicates increased bioavailability in older patients.

Impairment of renal function requires a reduction in dosage (see Section 4.4 Special warnings and precautions for use). Impairment of liver function may increase the bioavailability of ranitidine but has no significant effect on the elimination half-life. However, in the presence of normal renal function, no dosage reduction for oral or intravenous ranitidine appears necessary in patients with hepatic impairment.

5.3 Preclinical safety data
No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Croscarmellose sodium, magnesium stearate, microcrystalline cellulose and Opadry II white YS-22-18096.

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 years.

6.4 Special precautions for storage
Store below 25ºC, keep dry. Protect from heat.

6.5 Nature and contents of container
ZANTAC 150 150 mg tablets are available in Al/Al foil blister packs of 10 (starter packs) and 60 tablets.

ZANTAC 300 300 mg tablets are available in Al/Al foil blister packs of 30 tablets.

(Note: Not all strengths or pack sizes may be marketed in New Zealand.)

6.6 Special precautions for disposal
No special requirements for disposal.

7 MEDICINE SCHEDULE

Prescription medicine.

8 SPONSOR

Pharmacy Retailing (NZ) Limited trading as Healthcare Logistics
58 Richard Pearse Drive
Airport Oaks
Auckland,
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Telephone: (09) 9185 100
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9 DATE OF FIRST APPROVAL

21 August 2025

10 DATE OF REVISION OF THE TEXT

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
New Document	NA