

# NEW ZEALAND DATA SHEET

## 1. PRODUCT NAME

ZANTAC Injection 50 mg/2 mL solution for injection

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ZANTAC contains 50 mg ranitidine (as the hydrochloride) in 2 mL aqueous solution (25 mg/mL) for injection .

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

## 3. PHARMACEUTICAL FORM

Solution for injection

ZANTAC Injection is a clear, colourless to pale yellow liquid.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

ZANTAC Injection is indicated in adults for the short-term treatment of duodenal ulcer, benign gastric ulcer, post-operative ulcer, reflux oesophagitis, Zollinger-Ellison syndrome, and the following conditions where a reduction of gastric secretion and acid output is desirable: the prophylaxis of upper gastrointestinal haemorrhage from stress ulceration in seriously ill patients, the prophylaxis of recurrent haemorrhage in patients with bleeding peptic ulcers and before general anaesthesia in patients considered to be at risk of acid aspiration (Mendelson's) syndrome, particularly obstetric patients during labour. For appropriate cases ZANTAC Tablets are also available (see ZANTAC Tablet Data Sheet).

### 4.2 Dose and method of administration

#### Dose

#### Adults

ZANTAC Injection may be given as:-

- a slow (over 2 minutes) intravenous injection of 50 mg, diluted to a volume of 20 mL, every 6-8 hours.
- an intermittent intravenous infusion at 25 mg/hour for two hours, repeated at 6-8 hour intervals.
- an intramuscular injection of 50 mg every 6-8 hours.

In the prophylaxis of upper gastrointestinal haemorrhage from stress ulceration in seriously ill patients a priming dose of 50 mg as a slow intravenous injection followed by a continuous intravenous infusion of 0.125-0.250 mg/kg/h may be preferred.

In the prophylaxis of haemorrhage from stress ulceration in seriously ill patients or prophylaxis of recurrent haemorrhage in patients bleeding from peptic ulceration parenteral administration may be continued until oral feeding commences. Patients

considered to be still at risk may then be treated with ZANTAC Tablets 150 mg twice daily.

For prophylaxis of Mendelson's syndrome 50 mg by intramuscular or slow intravenous injection 45 to 60 minutes before induction of general anaesthesia.

### Children

Use in children has not been evaluated.

### Special populations

#### Elderly population

Patients over 50 years of age, see section 5.2 Pharmacokinetic properties, special patient populations, patients over 50 years of age.

#### Renal Impairment

Accumulation of ranitidine with resulting elevated plasma concentrations will occur in patients with renal impairment (creatinine clearance less than 50 mL/min). It is recommended in such patients that ZANTAC be administered in doses of 25 mg.

## **4.3 Contraindications**

ZANTAC is contraindicated in 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 as treatment with ranitidine may mask symptoms of gastric carcinoma.

Ranitidine is excreted via the kidney and so plasma levels of the medicine are increased in patients with renal impairment. The dosage should be adjusted as detailed above under section 4.2 dose and method of administration, special populations, renal impairment.

Bradycardia in association with rapid administration of ZANTAC Injection has been reported rarely, usually in patients with factors predisposing to cardiac rhythm disturbances. Recommended rates of administration should not be exceeded.

The use of higher than recommended doses of intravenous H<sub>2</sub>- antagonists has been associated with rises in liver enzymes when treatment has been extended beyond five days.

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 H<sub>2</sub>- 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 has the potential to affect the absorption, metabolism or renal excretion of other medicines. The altered pharmacokinetics may necessitate dosage adjustment of the affected medicine 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 medicines 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 medicines 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 medicines.

### 3) Alteration of gastric pH:

The bioavailability of certain medicines 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, gefitinib).

## **4.6 Fertility, pregnancy and lactation**

### Pregnancy

Like other medicines it should only be used during pregnancy if considered essential.

### Breast-feeding

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

Like other medicines it should only be used during breast-feeding if considered essential.

### Fertility

There are no data on the effects of ranitidine on human fertility. There were no effects on male and female fertility in animal studies.

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

None reported.

## **4.8 Undesirable effects**

### Summary of the safety profile

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.

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.

## Reproductive System and Breast Disorders

Reversible impotence has been reported rarely. There have been a few reports of breast symptoms and breast conditions (such as gynaecomastia and galactorrhoea).

## 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 via: <https://nzphvc.otago.ac.nz/reporting/>

## **4.9 Overdose**

Ranitidine is very specific in action and no particular problems are expected following overdosage with the medicine. 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**

Pharmacotherapeutic group: H<sub>2</sub>-receptor antagonists, ATC code: A02BA02

#### Mechanism of Action

ZANTAC 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.

### **5.2 Pharmacokinetic properties**

#### Absorption

Absorption of ranitidine after intramuscular injection is rapid and peak plasma concentrations are usually achieved within 15 minutes of administration.

#### Distribution

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

#### Biotransformation

Ranitidine is not extensively metabolised. The fraction of the dose recovered as metabolites is similar after both oral and intravenous dosing; and includes 6% of the dose in urine as the N-oxide, 2% as the S-oxide, 2% as demethyranitidine and 1 to 2% as the furoic acid analogue.

#### Elimination

Plasma concentrations decline bi-exponentially, with a terminal half-life of 2-3 hours. The major route of elimination is renal. After intravenous administration of 150 mg <sup>3</sup>H-ranitidine, 98% of the dose was recovered, including 5% in faeces and 93% in urine, of which 70% was unchanged parent medicine. After oral administration of 150 mg <sup>3</sup>H-ranitidine, 96% of the dose was recovered, 26% in faeces and 70% in urine of which 35% was unchanged parent medicine. Less than 3% of the dose is excreted in bile. Renal clearance is approximately 500 mL/min, which exceeds glomerular filtration indicating net renal tubular secretion.

### Special patient populations

#### 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.

### **5.3 Preclinical safety data**

Non-clinical data revealed no special hazard for humans based on conventional studies of safety pharmacology, repeated-dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction and development.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

- Disodium Hydrogen Orthophosphate Anhydrous
- Sodium Chloride
- Potassium Dihydrogen Orthophosphate
- Water for Injections.

### **6.2 Incompatibilities**

This medicine must not be mixed with other medicines except those mentioned in section 6.6 Special precautions for disposal and other handling.

### **6.3 Shelf life**

#### Dry shelf life

3 years.

### **6.4 Special precautions for storage**

Protect from light.

ZANTAC Injection should not be autoclaved.

Store below 25°C.

## 6.5 Nature and contents of container

ZANTAC Injection: 2 mL ampoules, boxes of five.

## 6.6 Special precautions for disposal and other handling

Although compatibility studies have only been undertaken in polyvinyl chloride infusion bags (in glass for Sodium Bicarbonate BP) and polyvinyl chloride administration sets it is considered that adequate stability would be conferred by the use of a polyethylene infusion bag.

ZANTAC Injection is compatible with the following intravenous infusion fluids:-

0.9% Sodium Chloride BP.  
5% Dextrose BP.  
0.18% Sodium Chloride and 4% Dextrose BP.  
4.2% Sodium Bicarbonate BP.  
Hartmann's Solution.

Unused admixtures should be discarded 24 hours after preparation.

## 7. MEDICINE SCHEDULE

Prescription Medicine

## 8. SPONSOR

GlaxoSmithKline NZ Limited  
Private Bag 106600  
Downtown Auckland  
NEW ZEALAND

Telephone: (09) 367 2900  
Facsimile: (09) 367 2910

## 9. DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine:  
12 May 1983

## 10. DATE OF REVISION OF THE TEXT

10 December 2018

Summary table of changes:

Section changed	Summary of new information
All	Data Sheet re-format
4.8	Included information for reporting of suspected adverse reactions
4.9	Included information for advice on the management of overdose
5.1	Added Pharmacotherapeutic group and ATC code

6.2	Added new section and statement on mixing with other medicines
9	Added date of first approval

Version:5.0

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