For the use of a Registered Medical Practitioner only

Rantac®

℞ Ranitidine Injection IP 50 mg / 2 ml

COMPOSITION

Each ml contains:

Ranitidine Hydrochloride IP

Equivalent to Ranitidine……..25mg

Phenol IP……..5mg (As preservative)

Buffered aqueous base……q.s.

DOSAGE FORM

Liquid Injection

Rantac Injection is a clear, colourless to yellow, non-pyrogenic liquid. The yellow colour of the liquid tends to intensify without adversely affecting potency.

THERAPEUTIC INDICATIONS

RANTAC Injection is indicated for the treatment of duodenal ulcer, benign gastric ulcer, post-operative ulcer, reflux esophagitis, Zollinger – Ellison Syndrome and the following conditions where reduction of gastric secretion and acid output is desirable.

Prophylaxis of gastrointestinal haemorrhage from stress ulceration in seriously ill patients.

Prophylaxis of recurrent haemorrhage in patients with bleeding peptic ulcers.

Prevention of acid aspiration syndrome.

PSOLOGY AND METHOD OF ADMINISTRATION

Posology

Adults (including elderly) / Adolescents (12 years and over)

RANTAC Injection may be given either as a slow (over 2 minutes) intravenous injection up to a maximum of 50mg, after dilution to a volume of 20ml per 50mg dose, which may be repeated every 6 to 8 hours; or as an intermittent intravenous infusion at a rate of 25mg per hour for two hours; the infusion may be repeated at 6 to 8 hour intervals, or as an intramuscular injection of 50mg (2ml) every 6 to 8 hours.

Prophylaxis of haemorrhage from stress ulceration or recurrent haemorrhage:

In the prophylaxis of haemorrhage from stress ulceration in seriously ill patients or the 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 RANTAC tablets 150mg twice daily.

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

Prophylaxis of Mendleson's syndrome:

In patients considered to be at risk of developing acid aspiration syndrome. RANTAC Injection 50mg may be given intramuscularly or by slow intravenous injection 45 to 60 minutes before induction of general anaesthesia.

Children / Infants (6 months to 11 years)

RANTAC Injection may be given as a slow (over 2 minutes) i.v. injection up to a maximum of 50mg every 6 to 8 hours.

Peptic Ulcer Acute Treatment and Gastro-Oesophageal Reflux

Intravenous therapy in children with peptic ulcer disease is indicated only when oral therapy is not possible.

For acute treatment of peptic ulcer disease and gastro-oesophageal reflux in paediatric patients, RANTAC injection may be administered at doses that have been shown to be effective for these disease in adults and effective for acid suppression in critically ill children. The initial dose (2.0 mg/kg or 2.5 mg/kg, maximum 50mg) may be administered as a slow intravenous infusion over 10 minutes, either with a syringe pump followed by a 3 mL flush with normal saline over 5 min, or following dilution with normal saline to 20 mL. Maintenance of pH > 4.0 can be achieved by intermittent infusion of 1.5 mg/kg every 6 h to 8 h. Alternatively treatment can be continuous, administering a loading dose of 0.45 mg/kg followed by a continuous infusion of 0.15 mg/kg/hr.

Neonates (under 1 month)

Limited pharmacokinetic data from term babies undergoing treatment with Extracorporeal Membrane Oxygenation (EMCO) suggests that plasma clearance following iv administration may be reduced (1.5-8.2 ml/min/kg) and the half-life increased in the new-born. Clearance of ranitidine appeared to be related to the estimated glomerular filtration rate in the neonates.

Patients over 50 years of age

In patients over 50 years of age, half-life is prolonged (3-4 h) 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.

Patients with renal impairment

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

Method of administration

Intravenous or intramuscular injection.

RANTAC injection has been showed to be compatible with following intravenous fluids: 0.9% Sodium chloride injection & 5% Dextrose injection.

The solution is to be inspected visually for particulate matter and discolouration prior to administration and should only be used if it is clear and free from particles.

CONTRA-INDICATIONS

Hypersensitivity to the active substance or to any of the excipients.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Malignancy

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.

Renal Disease

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

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

It has been reported that the use of higher than recommended doses of intravenous H2-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 ranitidine alone versus those who had stopped treatment, with an observed adjusted relative risk increase of 1.82 (95% CI 1.26-2.64). Post-marketing data indicate reversible mental confusion, depression, and hallucinations have been reported most frequently in severely ill and elderly patients.

DRUG INTERACTIONS

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, propanolol 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 level 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).

USE IN SPECIAL POPULATIONS

Pregnancy & Lactation:

Pregnancy

Ranitidine crosses the placenta but therapeutic doses administered to obstetric patients in labour or undergoing caesarean section have been without any adverse effect on labour, delivery or subsequent neonatal progress. Like other drugs, ranitidine should only be used during pregnancy if considered essential.

Breast-feeding

RANTAC is also excreted in human breast milk. Like other drugs, ranitidine 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.

Paediatrics:

Children/infants (6 months and above)

Limited pharmacokinetic data show that there were no significant differences in half-life (range for children 3 years and above: 1.7 - 2.2 h) and plasma clearance (range for children 3 years and above: 9 - 22 ml/min/kg) between children and healthy adults receiving intravenous ranitidine when correction is made for body weight. Pharmacokinetic data in infants is extremely limited but appears to be in line with that for older children.

Neonates (under 1 month)

Limited pharmacokinetic data from term babies undergoing treatment with Extracorporeal Membrane Oxygenation (EMCO) suggests that plasma clearance following iv administration may be reduced (1.5-8.2 ml/min/kg) and the half-life increased in the new-born. Clearance of ranitidine appeared to be related to the estimated glomerular filtration rate in the neonates.

Geriatric:

Patients over 50 years of age

In patients over 50 years of age, half-life is prolonged (3-4 h) 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.

UNDESIRABLE EFFECTS

The following convention has been utilised for the classification of undesirable effects: very common (≥ 1/10), common (≥ 1/100, <1/10), uncommon (≥ 1/1000, ≤ 1/100), rare (≥ 1/10,000, ≤ 1/1000), very rare (≤ 1/10,000). Adverse event frequencies have been estimated from spontaneous reports from post-marketing data.

Blood & Lymphatic System Disorders

Very Rare: Blood count changes (leucopenia, thrombocytopenia).These are usually reversible. Agranulocytosis or pancytopenia, sometimes with marrow hypoplasia or marrow aplasia.

Immune System Disorders

Rare: Hypersensitivity reactions (urticaria, Angioneurotic oedema, fever, bronchospasm, hypotension and chest pain).

Very Rare: Anaphylactic shock.

Not Known: Dyspnoea.

These events have been reported after a single dose.

Psychiatric Disorders

Very Rare: Reversible mental confusion, depression and hallucinations.

These have been reported predominantly in severely ill patients, in elderly and nephropatic patients.

Nervous System Disorders

Very Rare: Headache (sometimes severe), dizziness and reversible involuntary movement disorders.

Eye Disorders

Very Rare: Reversible blurred vision.

There have been reports of blurred vision, which is suggestive of a change in accommodation.

Cardiac Disorders

Very Rare: As with other H2 receptor antagonists bradycardia, A-V block, asystole and tachycardia.

Vascular Disorders

Very Rare: Vasculitis.

Gastrointestinal Disorders

Uncommon: Abdominal pain, constipation, nausea (these symptoms mostly improved during continued treatment).

Very Rare: Acute pancreatitis, diarrhoea.

Hepatobiliary Disorders

Rare: Transient and reversible changes in liver function tests.

Very Rare: Hepatitis (hepatocellular, hepatocanalicular or mixed) with or without jaundice, these were usually reversible.

Skin and Subcutaneous Tissue Disorders

Rare: Skin Rash.

Very Rare: Erythema multiforme, alopecia.

Musculoskeletal and Connective Tissue Disorders

Very Rare: Musculoskeletal symptoms such as arthralgia and myalgia.

Renal and Urinary Disorders

Rare: Elevation of plasma creatinine (usually slight; normalised during continued treatment)

Very Rare: Acute interstitial nephritis.

Reproductive System and Breast Disorders

Very Rare: Reversible impotence, breast symptoms and breast conditions (such as gynaecomastia and galactorrhoea).

Paediatric population

The safety of ranitidine has been assessed in children aged 0 to 16 years with acid-related disease and was generally well tolerated with an adverse event profile resembling that in adults. There are limited long term safety data available, in particular regarding growth and development.

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. Kindly report any suspected adverse reactions to pharmavigil@jbcpl.com

OVERDOSE

Symptoms and signs

RANTAC is very specific in action and accordingly, no particular problems are expected following overdosage with the drug.

Treatment

Symptomatic and supportive therapy should be given as appropriate.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic group: H2-receptor antagonists.

ATC code: A02BA02.

Mechanism of action

Ranitidine is a specific, rapidly acting histamine H2-antagonist. It inhibits basal and stimulated secretion of gastric acid, reducing both the volume and the acid and pepsin content of the secretion.

The clinical data available mentions the use of ranitidine in children to prevent stress ulcers. No direct evidence for prevention of stress ulcers is available. Treatment for these patients is based on the observation that pH is above 4 after administration of ranitidine. The value of this surrogate parameter in children with stress ulcers remains to be established.

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 142 L.

Metabolism

Ranitidine is not extensively metabolised. The fraction of the dose recovered as metabolites is similar after both oral and i.v. dosing; and includes 6% of the dose in urine as the N-oxide, 2& as the S-oxide, 2% as desmethylranitidine 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 IV administration of 150 mg 3H-ranitidine, 98% of the dose was recovered, including 5% in faeces and 93% in urine, of which 70% was unchanged parent drug. After oral administration of 150 mg 3H-ranitidine, 96% of the dose was recovered, 26% in faeces and 70% in urine of which 35% was unchanged parent drug. 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.

Nonclinical Toxicology

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.

Description

The active ingredient in Rantac injection is ranitidine hydrochloride (HCl), a histamine H2-receptor antagonist. Chemically it is N[2-[[[5[(dimethylamino)methyl]-2-furanyl]methyl]thio]ethyl]-N′-methyl-2-nitro-1,1-ethenediamine, hydrochloride.

INCOMPATIBILITIES:

Rantac Injection has been shown to be compatible with the following intravenous infusion fluid: 0.9% Sodium chloride Injection I.P. and 5% Dextrose Injection I.P.

PACKAGING INFORMATION: 2ml ampoule

STORAGE AND HANDLING INSTRUCTIONS:

Store at a temperature not exceeding 30°C, protected from light. Do not freeze.

Marketed by & ® Regd. Trade Mark of :
J. B. CHEMICALS & PHARMACEUTICALS LTD.
Neelam Centre, 'B' Wing, Hind Cycle Road,
Worli, Mumbai - 400 030. India.

DATE OF REVISION
September 2021

Note: This prescribing information is applicable for India Market only.