RANITIDINE

RAXIDE®

150mg Tablet
300mg Film-Coated Tablet
H_2 RECEPTOR ANTAGONIST

FORMULATION:
Each tablet contains:
Ranitidine (as hydrochloride), USP ..... 150mg & 300mg

DESCRIPTION:
RANITIDINE (Raxide®) 150mg or 300mg Tablet is a white to cream, round, biconvex film-coated tablet.

RAXIDE® is a brand of Ranitidine, a rapidly-acting histamine H_2 receptor antagonist used in conditions where inhibition of gastric acid secretion may be beneficial, such as gastric and duodenal ulcers.

It inhibits basal and stimulated secretion of gastric acid, reducing both the volume and the acid and pepsin content of the secretion. It has relatively long duration of action and so a single 150mg dose effectively suppresses gastric acid secretion for 12 hours.

PHARMACODYNAMICS:
Serum concentrations necessary to inhibit 50% of stimulated gastric acid secretion are estimated to be 36 to 94 ng/mL. Following a single oral dose of 150 mg, serum concentrations of ranitidine are in this range up to 12 hours. However, blood levels bear no consistent relationship to dose or degree of acid inhibition.

PHARMACOKINETICS:
Ranitidine is readily absorbed from the gastrointestinal tract with peak concentrations in plasma occurring about 2 to 3 hours after administration by mouth. The bioavailability of Ranitidine following oral administration is about 50% due to first-pass metabolism. The elimination half-life from plasma is around 2 to 3 hours and Ranitidine is weakly bound, about 15% plasma proteins.

A small proportions of Ranitidine is metabclized in the liver to the *N*-oxide, the *S*-oxide, and desmethylranitidine; The *N*-oxide is the major metabolite but accounts only for 4 to 6% of a dose. Approximately 30% of an oral dose and 70% of an intravenous dose is excreted unchanged in the urine in 24 hours; there is some excretion in the faeces. Ranitidine crosses the placental barrier and is excreted into breast milk where concentrations are reported to be higher than those in plasma. It does not readily cross the blood-brain barrier but adverse effects on the nervous system have been reported.

INDICATIONS:
Treatment of duodenal and gastric ulcer, including that associated with H. pylori, NSAID-associated peptic ulcer, post-operative ulcer, acute reflux esophagitis, Zollinger-Ellison syndrome, chronic episodic dyspepsia, symptomatic relief in gastroesophageal reflux disease, and prophylaxis of Mendelson's syndrome.

DOSAGE AND ADMINISTRATION:
Adults (including the elderly)
Usual dosage is 150 mg twice daily, taken in the morning and evening.

Duodenal ulcer, gastric ulcer:
The standard dosage regimen is 150 mg twice daily or 300mg at night. It is not necessary to time the dose in relation to meals.
In most cases of duodenal ulcer, benign gastric ulcer and post-operative ulcer, healing occurs within 4 weeks. Healing usually occurs after a further 4 weeks of treatment in those not fully healed after the initial course of therapy.

Ulcers following NSAID therapy or associated with continued NSAIDs:
8 weeks treatment may be necessary

Prevention of NSAID associated duodenal ulcers:
150 mg twice daily may be given concomitantly with NSAID therapy. In duodenal ulcer, 300 mg twice daily for 4 weeks results in healing rates which are higher than those at 4 weeks with ranitidine 150 mg twice daily or 300 mg at night. The increased dose has not been associated with an increased incidence of unwanted effects.

Duodenal ulcers associated with Helicobacter pylori infection:
For duodenal ulcers associated with Helicobacter pylori infection, ranitidine 300 mg at bedtime or 150 mg twice daily may be given with oral amoxicillin 750 mg three times daily and metronidazole 500 mg three times daily for two weeks. Therapy with ranitidine should continue for a further two weeks. This dose regimen significantly reduces the frequency of duodenal ulcer recurrence.
Maintenance treatment at a reduced dosage of 150 mg at bedtime is recommended for patients who have responded to short term therapy, particularly those with a history of recurrent ulcer.

Gastro-oesophageal reflux disease:
Symptom relief in gastro-oesophageal reflux disease. In patients with gastro-oesophageal reflux disease, a dose regimen of 150 mg twice daily for 2 weeks is recommended and this can be repeated in patients in whom the initial symptomatic response is inadequate.

Oesophageal reflux disease:
In the management of oesophageal reflux disease, the recommended course of treatment is either 150 mg twice daily or 300 mg at bedtime for up to 8 weeks or 12 weeks if necessary.
In patients with moderate to severe oesophagitis, the dosage of ranitidine may be increased to 150 mg 4 times daily for up to 12 weeks. The increased dose has not been associated with an increased incidence of unwanted effects.

Healed oesophagitis:
For long term treatment, recommended adult dose is 150 mg twice daily. Long term treatment is not indicated in management of patients with unhealed oesophagitis with or without Barrett's epithelium.

Zollinger-Ellison syndrome:
The starting dose for Zollinger-Ellison syndrome is 150 mg three times daily, and this may be increased as necessary. Doses up to 6 grams per day have been well tolerated.

Chronic episodic dyspepsia:
The standard dosage regimen for patients with chronic episodic dyspepsia is 150 mg 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 prophylaxis of recurrent haemorrhage in patients bleeding from peptic ulceration:
150 mg twice daily may be substituted for the injection once oral feeding commences.

Prophylaxis of acid aspiration (Mendelson's) syndrome:
150 mg oral dose can be given 2 hours before anaesthesia, and preferably also 150 mg the previous evening. Alternatively, the injection is also available. In obstetric patients in labour 150 mg every 6 hours, but if general anaesthesia is required it is recommended that a non-particulate antacid (e.g. sodium citrate) be given in addition. The usual precautions to avoid acid aspiration should also be taken.

Children 12 years and over
For children 12 years and over the adult dosage is given.

Children from 3 to 11 years and over 30 kg of weight
Limited pharmacokinetic data show that there are 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 oral ranitidine when correction is made for body weight.

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.

Peptic Ulcer Acute Treatment
The recommended oral dose for the treatment of peptic ulcer in children is 4 mg/kg/day to 8 mg/kg/day administered as two divided doses to a maximum of 300 mg ranitidine per day for a duration of 4 weeks. For those patients with complete healing, another 4 weeks of therapy is indicated, as healing usually occurs after eight weeks of treatment.

Gastro-Oesophageal Reflux
The recommended oral dose for the treatment of gastro-oesophageal reflux in children is 5 mg/kg/day to 10 mg/kg/day administered as two divided doses to a maximum of 600 mg (the maximum dose is likely to apply to heavier children or adolescents with severe symptoms).

Neonates
Safety and efficacy in new-born patients has not been established.

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 that the daily dose of ranitidine in such patients should be 150 mg at night for 4-8 weeks. The same dose should be used for maintenance treatment, if necessary. If an ulcer has not healed after treatment, 150 mg twice daily dosage should be instituted followed, if need be, by maintenance treatment of 150 mg at night.

CONTRAINDICATIONS:
Contraindicated to patients known to have hypersensitivity to Ranitidine.

PRECAUTIONS:
Malignancy: The possibility of malignancy should be excluded before commencement of therapy in patients with gastric ulcer (and if indications include dyspepsia; patient of middle age over with new or recently changed dyspeptic symptoms) 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 severe renal impairment.

The dosage should be adjusted as indicated under Dosage and Administration:
Renal Impairment.

Regular supervision of patients who are taking NSAID 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.

Effects on the ability to Drive or Operate Machineries: None reported.

Use in pregnancy and lactation: Ranitidine crosses the placenta and is excreted in human breast milk. Like other drugs, Ranitidine should only be used during pregnancy and nursing if considered essential.

INTERACTIONS:
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, theophylline and warfarin. There is no evidence of an interaction between Ranitidine, 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 taken after an interval of 2 hours.

ADVERSE EFFECTS:
Adverse reactions to Ranitidine are generally infrequent and are reversible following a reduction of dosage or withdrawal of therapy. The most common side effects reported have been diarrhea, dizziness, tiredness, headache and rashes. Reversible confusional states, especially in the elderly or in seriously ill patients such as those with renal failure, have occasionally occurred. Other adverse effects which have been reported rarely are hypersensitivity reactions and fever, arthralgia and myalgia, blood disorders including agranulocytosis or neutropenia and thrombocytopenia, interstitial nephritis, hepatotoxicity, and cardiovascular disorders.

Carcinogenicity. An association between H_2 receptor antagonists and gastric cancer has been proposed following individual case reports, the finding of tumors in long term high-dose animal studies, and the possibility that nitrites and nitroso compounds maybe produced; but such proposals are considered to have little clinical relevance. The excess risk of gastric cancer reported in patients taking Ranitidine decreases with time and there is no evidence for any long-term persistence of the effect.

Effects on the blood. Leucopenia, thrombocytopenia, and pancytopenia have all been reported with Ranitidine with neutropenia and agranulocytosis occurring most often.

Effects on the cardiovascular system. Bradycardia, atrioventricular block, and cardiac arrest have been reported rarely during Ranitidine therapy; a positive inotropic effect, without significant changes in heart rate or blood pressure, has also been reported in healthy subjects.

Effects on the liver. There have been some case reports of Ranitidine hepatotoxicity.

Effects on the nervous system. Ranitidine has been associated with a number of adverse neurological effects including confusion, loss of colour vision, aggressiveness, hallucinations and severe headache.

Hypersensitivity. Respiratory stridor and an urticarial rash.

OVERDOSAGE:
Ranitidine is very specific in action and no particular problems are expected.
Symptomatic and supportive therapy should be given as appropriate.

KEEP OUT OF REACH OF CHILDREN

STORAGE RECOMMENDATIONS:
Store at temperatures not exceeding 30°C. Protect from light.

CAUTION:
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph
Patient should seek medical attention immediately at the first sign of any adverse drug reaction.

AVAILABILITY:
150 mg Tablet-Aluminum Foil Strip x 4's (Box of 100's)-DR-XY26358
300 mg Film-Coated Tablet-Aluminum Foil Strip x 10's (Box of 30's)-DR-XY30701

DATE OF FIRST AUTHORIZATION:
150mg – 19-June-2000
300mg – 9-May-2005

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RAXIDE® is a registered mark of GX INTERNATIONAL, INC.

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