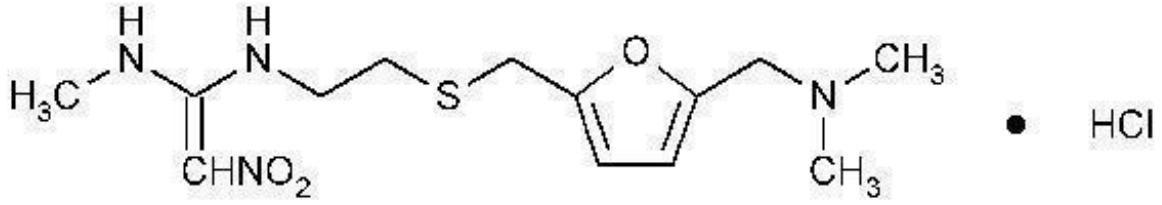
RANITIDINE- ranitidine tablet
Lake Erie Medical DBA Quality Care Products LLC

Ranitidine Tablets, USP

Rx Only

DESCRIPTION

The active ingredient in Ranitidine Tablets, USP 150 mg and Ranitidine Tablets, USP 300 mg is ranitidine hydrochloride (HCl), USP, a histamine H_2-receptor antagonist. Chemically it is N[2-[[[5-[(dimethylamino)methyl]-2-furanyl]methyl]thio]ethyl]-N'-methyl-2-nitro-1,1-ethenediamine, HCl. It has the following structure:



The empirical formula is $C_{13}H_{22}N_4O_3S{\cdot}HCl$, representing a molecular weight of 350.87. Ranitidine HCl is a white to pale yellow, granular substance that is soluble in water. It has a slightly bitter taste and sulfurlike odor.

Each Ranitidine Tablets, USP 150 mg for oral administration contains 167.4 mg of ranitidine HCl equivalent to 150 mg of ranitidine. Each tablet also contains the inactive ingredients colloidal silicon dioxide, croscarmellose sodium, hypromellose, magnesium stearate, microcrystalline cellulose, polydextrose, titanium dioxide, triethyl citrate and FD&C Yellow #6.

Each Ranitidine Tablets, USP 300 mg for oral administration contains 334.8 mg of ranitidine HCl equivalent to 300 mg of ranitidine. Each tablet also contains the inactive ingredients colloidal silicon dioxide, croscarmellose sodium, hypromellose, magnesium stearate, microcrystalline cellulose, polydextrose, titanium dioxide, triethyl citrate and D&C Yellow #10.

CLINICAL PHARMACOLOGY

Ranitidine Tablets, USP is a competitive, reversible inhibitor of the action of histamine at the histamine H_2-receptors, including receptors on the gastric cells. Ranitidine Tablets, USP does not lower serum Ca_{++} in hypercalcemic states. Ranitidine Tablets, USP is not an anticholinergic agent.

Pharmacokinetics: ***Absorption:*** Ranitidine Tablets, USP is 50% absorbed after oral administration, compared to an intravenous (IV) injection with mean peak levels of 440 to 545 ng/mL occurring 2 to 3 hours after a 150-mg dose. Absorption is not significantly impaired by the administration of food or antacids. Propantheline slightly delays and increases peak blood levels of Ranitidine Tablets, USP, probably by delaying gastric emptying and transit time. In one study, simultaneous administration of high-potency antacid (150 mmol) in fasting subjects has been reported to decrease the absorption of Ranitidine Tablets, USP.

Distribution: The volume of distribution is about 1.4 L/kg. Serum protein binding averages 15%.

Metabolism: In humans, the N-oxide is the principal metabolite in the urine; however, this amounts to <4% of the dose. Other metabolites are the S-oxide (1%) and the desmethyl ranitidine (1%). The remainder of the administered dose is found in the stool. Studies in patients with hepatic dysfunction (compensated cirrhosis) indicate that there are minor, but clinically insignificant, alterations in ranitidine half-life, distribution, clearance, and bioavailability.

Excretion: The principal route of excretion is the urine, with approximately 30% of the orally administered dose collected in the urine as unchanged drug in 24 hours. Renal clearance is about 410 mL/min, indicating active tubular excretion. The elimination half-life is 2.5 to 3 hours. Four patients with clinically significant renal function impairment (creatinine clearance 25 to 35 mL/min) administered 50 mg of ranitidine intravenously had an average plasma half-life of 4.8 hours, a ranitidine clearance of 29 mL/min, and a volume of distribution of 1.76 L/kg. In general, these parameters appear to be altered in proportion to creatinine clearance (see DOSAGE AND ADMINISTRATION).

Geriatrics: The plasma half-life is prolonged and total clearance is reduced in the elderly population due to a decrease in renal function. The elimination half-life is 3 to 4 hours. Peak levels average 526 ng/mL following a 150-mg twice daily dose and occur in about 3 hours (see PRECAUTIONS: Geriatric Use and DOSAGE AND ADMINISTRATION: Dosage Adjustment for Patients with Impaired Renal Function).

Pediatrics: There are no significant differences in the pharmacokinetic parameter values for ranitidine in pediatric patients (from 1 month up to 16 years of age) and healthy adults when correction is made for body weight. The average bioavailability of ranitidine given orally to pediatric patients is 48% which is comparable to the bioavailability of ranitidine in the adult population. All other pharmacokinetic parameter values ($t_{1/2}$, Vd, and CL) are similar to those observed with intravenous ranitidine use in pediatric patients. Estimates of C_{max} and T_{max} are displayed in Table 1.

Table 1. Ranitidine Pharmacokinetics in Pediatric Patients Following Oral Dosing

Population (age)	N	Dosage Form (dose)	C_{max} (ng/mL	T_{max} (hours)
Gastric or duodenal ulcer (3.5 to 16 years)	12	Tablets| (1 to 2 mg/kg)	54 to 492	2.0
Otherwise healthy requiring Ranitidine (0.7 to 14 years, Single dose)	10	Syrup (2 mg/kg)	244	1.61
Otherwise healthy requiring Ranitidine (0.7 to 14 years, Multiple dose)	10	Syrup (2 mg/kg)	320	1.66

Plasma clearance measured in 2 neonatal patients (less than 1 month of age) was considerably lower (3 mL/min/kg) than children or adults and is likely due to reduced renal function observed in this population (see PRECAUTIONS: Pediatric Use and DOSAGE AND ADMINISTRATION: Pediatric Use).

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 Tablets, USP are in this range up to 12 hours. However, blood levels bear no consistent relationship to dose or degree of acid inhibition.

Antisecretory Activity: ***1. Effects on Acid Secretion:*** Ranitidine Tablets, USP inhibits both daytime and nocturnal basal gastric acid secretions as well as gastric acid secretion stimulated by food, betazole, and pentagastrin, as shown in Table 2.

Table 2. Effect of Oral Ranitidine Tablets, USP on Gastric Acid Secretion

	Time After Dose, h	% Inhibition of Gastric Acid Output by Dose, mg			
		75-80	100	150	200
Basal	Up to 4		99	95	

Nocturnal	Up to 13	95	96	92	
Betazole	Up to 3		97	99	
Pentagastin	Up to 5	58	72	72	80
Meal	Up to 3		73	79	95

It appears that basal-, nocturnal-, and betazole-stimulated secretions are most sensitive to inhibition by Ranitidine Tablets, USP, responding almost completely to doses of 100 mg or less, while pentagastrin- and food-stimulated secretions are most difficult to suppress.

2. Effects on Other Gastrointestinal Secretions:

Pepsin: Oral Ranitidine Tablets, USP does not affect pepsin secretion. Total pepsin output is reduced in proportion to the decrease in volume of gastric juice.

Intrinsic Factor: Oral Ranitidine Tablets, USP has no significant effect on pentagastrin-stimulated intrinsic factor secretion.

Serum Gastrin: Ranitidine Tablets, USP has little or no effect on fasting or postprandial serum gastrin.

Other Pharmacologic Actions:

a. Gastric bacterial flora-increase in nitrate-reducing organisms, significance not known.
b. Prolactin levels-no effect in recommended oral or intravenous (IV) dosage, but small, transient, dose-related increases in serum prolactin have been reported after IV bolus injections of 100 mg or more.
c. Other pituitary hormones-no effect on serum gonadotropins, TSH, or GH. Possible impairment of vasopressin release.
d. No change in cortisol, aldosterone, androgen, or estrogen levels.
e. No antiandrogenic action.
f. No effect on count, motility, or morphology of sperm.

Pediatrics: Oral doses of 6 to 10 mg/kg per day in two or three divided doses maintain gastric pH>4 throughout most of the dosing interval.

Clinical Trials: ***Active Duodenal Ulcer:*** In a multicenter, double-blind, controlled, US study of endoscopically diagnosed duodenal ulcers, earlier healing was seen in the patients treated with Ranitidine Tablets, USP as shown in Table 3

Table 3. Duodenal Ulcer Patient Healing Rates

	Ranitidine Tablets, USP *		Placebo*	
	Number Entered	Healed / Evaluable	Number Entered	Healed / Evaluable
Outpatients				
Week 2	195	69/182 (38%) †	188	31-164 (19%)
Week 4		137/187 (73%) †		76/168 (45%)

*All patients were permitted p.r.n. antacids for relief of pain.

†P<0.0001.

In these studies, patients treated with Ranitidine Tablets, USP reported a reduction in both daytime and nocturnal pain, and they also consumed less antacid than the placebo-treated patients.

Table 4. Mean Daily Doses of Antacid

Ulcer Healed	Ulcer Not Healed

Ranitidine	0.06	0.71
Placebo	0.71	1.43

Foreign studies have shown that patients heal equally well with 150 mg b.i.d. and 300 mg h.s. (85% versus 84%, respectively) during a usual 4-week course of therapy. If patients require extended therapy of 8 weeks, the healing rate may be higher for 150 mg b.i.d. as compared to 300 mg h.s. (92% versus 87%, respectively).

Studies have been limited to short-term treatment of acute duodenal ulcer. Patients whose ulcers healed during therapy had recurrences of ulcers at the usual rates.

Maintenance Therapy in Duodenal Ulcer: Ranitidine has been found to be effective as maintenance therapy for patients following healing of acute duodenal ulcers. In 2 independent, double-blind, multicenter, controlled trials, the number of duodenal ulcers observed was significantly less in patients treated with Ranitidine Tablets, USP (150 mg h.s.) than in patients treated with placebo over a 12-month period.

Table 5. Duodenal Ulcer Prevalence

Double-Blind, Multicenter, Placebo-Controlled Trials

Multicenter Trial	Drug	Duodenal Ulcer Prevalence			No. Of Patients
		0-4 Months	0-8 Months	0-12 Months	
USA	RAN	20%*	24%*	35%*	138
	PLC	44%	54%	59%	139
Foreign	RAN	12%*	21%*	28%*	174
	PLC	56%	64%	68%	165

% = Life table estimate.

* = P<0.05 (Ranitidine Tablets, USP versus comparator).

RAN = ranitidine (Ranitidine Tablets, USP)

PLC = placebo.

As with other H_2-antogonists, the factors responsible for the significant reduction in the prevalence of duodenal ulcers include prevention of recurrence of ulcers, more rapid healing of ulcers that may occur during maintenance therapy, or both.

Gastric Ulcer: In a multicenter, double-blind, controlled, US study of endoscopically diagnosed gastric ulcers, earlier healing was seen in the patients treated with Ranitidine Tablets, USP as shown in Table 6.

Table 6. Gastric Ulcer Patient Healing Rates

	Ranitidine Tablets, USP *		Placebo*	
	Number Entered	Healed / Evaluable	Number Entered	Healed / Evaluable
Outpatients				
Week 2	92	16/183 (19%) †	94	10/83 (12%)
Week 6		50/73 (68%) †		35/69 (51%)

*All patients were permitted p.r.n. antacids for relief of pain.

†P = 0.009.

In this multicenter trial, significantly more patients treated with Ranitidine Tablets, USP became pain free during therapy.

Maintenance of Healing of Gastric Ulcers: In two multicenter, double-blind, randomized, placebo-controlled, 12-month trials conducted in patients whose gastric ulcers had been previously healed, Ranitidine Tablets, USP 150 mg h.s. was significantly more effective than placebo in maintaining healing of gastric ulcers.

Pathological Hypersecretory Conditions (such as Zollinger-Ellison syndrome):

Ranitidine Tablets, USP inhibits gastric acid secretion and reduces occurrence of diarrhea, anorexia, and pain in patients with pathological hypersecretion associated with Zollinger-Ellison syndrome, systemic mastocytosis, and other pathological hypersecretory conditions (e.g., postoperative, "short-gut" syndrome, idiopathic). Use of Ranitidine Tablets, USP was followed by healing of ulcers in 8 of 19 (42%) patients who were intractable to previous therapy.

Gastroesophageal Reflux Disease (GERD): In 2 multicenter, double-blind, placebo-controlled, 6-week trials performed in the United States and Europe, Ranitidine Tablets, USP 150 mg b.i.d. was more effective than placebo for the relief of heartburn and other symptoms associated with GERD. Ranitidine-treated patients consumed significantly less antacid than did placebo-treated patients.

The US trial indicated that Ranitidine Tablets, USP 150 mg b.i.d. significantly reduced the frequency of heartburn attacks and severity of heartburn pain within 1 to 2 weeks after starting therapy. The improvement was maintained throughout the 6-week trial period. Moreover, patient response rates demonstrated that the effect on heartburn extends through both the day and night time periods.

In 2 additional US multicenter, double-blind, placebo-controlled, 2-week trials, Ranitidine Tablets, USP 150 mg b.i.d. was shown to provide relief of heartburn pain within 24 hours of initiating therapy and a reduction in the frequency of severity of heartburn.

Erosive Esophagitis: In two multicenter, double-blind, randomized, placebo-controlled, 12-week trials performed in the United States, Ranitidine Tablets, USP 150 mg q.i.d. was significantly more effective than placebo in healing endoscopically diagnosed erosive esophagitis and in relieving associated heartburn.

The erosive esophagitis healing rates were as follows:

Table 7. Erosive Esophagitis Patient Healing Rates

	Healed / Evaluable	
	Placebo* n=229	Ranitidine Tablets, USP 150 mg q.i.d.* n=215
Week 4	43/198 (22%)	96/206 (47%) †
Week 8	63/176 (36%)	142/200 (71%) †
Week 12	92/159 (58%)	162/192 (84%) †

*All patients were permitted p.r.n. antacids for relief of pain.

†P<0.001 versus placebo.

No additional benefit in healing of esophagitis or in relief of heartburn was seen with a ranitidine dose of 300 mg q.i.d.

Maintenance of Healing of Erosive Esophagitis: In 2 multicenter, double-blind, randomized, placebo-controlled, 48-week trials conducted in patients whose erosive esophagitis had been previously healed, Ranitidine Tablets, USP 150 mg b.i.d. was significantly more effective than placebo in maintaining

healing of erosive esophagitis.

INDICATIONS AND USAGE

Ranitidine Tablets, USP is indicated in:

1. Short-term treatment of active duodenal ulcer. Most patients heal within 4 weeks. Studies available to date have not assessed the safety of ranitidine in uncomplicated duodenal ulcer for periods of more than 8 weeks.
2. Maintenance therapy for duodenal ulcer patients at reduced dosage after healing of acute ulcers. No placebo-controlled comparative studies have been carried out for periods of longer than 1 year.
3. The treatment of pathological hypersecretory conditions (e.g., Zollinger-Ellison syndrome and systemic mastocytosis).
4. Short-term treatment of active, benign gastric ulcer. Most patients heal within 6 weeks and the usefulness of further treatment has not been demonstrated.
   Studies available to date have not assessed the safety of ranitidine in uncomplicated, benign gastric ulcer for periods of more than 6 weeks.
5. Maintenance therapy for gastric ulcer patients at reduced dosage after healing of acute ulcers. Placebo-controlled studies have been carried out for 1 year.
6. Treatment of GERD. Symptomatic relief commonly occurs within 24 hours after starting therapy with Ranitidine Tablets, USP 150 mg b.i.d.
7. Treatment of endoscopically diagnosed erosive esophagitis. Symptomatic relief of heartburn commonly occurs within 24 hours of therapy initiation with Ranitidine Tablets, USP 150 mg q.i.d.
8. Maintenance of healing of erosive esophagitis. Placebo-controlled trials have been carried out for 48 weeks.

Concomitant antacids should be given as needed for pain relief to patients with active duodenal ulcer; active, benign gastric ulcer; hypersecretory states; GERD; and erosive esophagitis.

CONTRAINDICATIONS

Ranitidine Tablets, USP is contraindicated for patients known to have hypersensitivity to the drug or any of the ingredients (see PRECAUTIONS).

PRECAUTIONS

General:

1. Symptomatic response to therapy with Ranitidine Tablets, USP does not preclude the presence of gastric malignancy.
2. Since Ranitidine Tablets, USP is excreted primarily by the kidney, dosage should be adjusted in patients with impaired renal function (see DOSAGE AND ADMINISTRATION). Caution should be observed in patients with hepatic dysfunction since Ranitidine Tablets, USP is metabolized in the liver.
3. Rare reports suggest that Ranitidine Tablets, USP may precipitate acute porphyric attacks in patients with acute porphyria. Ranitidine Tablets, USP should therefore be avoided in patients with a history of acute porphyria.

Laboratory Tests: False-positive tests for urine protein with MULTISTIX® may occur during Ranitidine Tablets, USP therapy, and therefore testing with sulfosalicylic acid is recommended.

Drug Interactions: Although Ranitidine Tablets, USP has been reported to bind weakly to cytochrome P-450 *in vitro*, recommended doses of the drug do not inhibit the action of the cytochrome P-450-linked oxygenase enzymes in the liver. However, there have been isolated reports of drug interactions that

suggest that Ranitidine Tablets, USP may affect the bioavailability of certain drugs by some mechanism as yet unidentified (e.g., a pH-dependent effect on absorption or a change in volume of distribution).

Increased or decreased prothrombin times have been reported during concurrent use of ranitidine and warfarin. However, in human pharmacokinetic studies with dosages of ranitidine up to 400 mg/day, no interaction occurred; ranitidine had no effect on warfarin clearance or prothrombin time. The possibility of an interaction with warfarin at dosages of ranitidine higher than 400 mg/day has not been investigated.

In a ranitidine-triazolam drug-drug interaction study, triazolam plasma concentrations were higher during b.i.d. dosing of ranitidine than triazolam given alone. The mean area under the triazolam concentration-time curve (AUC) values in 18- to 60-year-old subjects were 10% and 28% higher following administration of 75-mg and 150-mg ranitidine tablets, respectively, than triazolam given alone. In subjects older than 60 years of age, the mean AUC values were approximately 30% higher following administration of 75-mg and 150-mg ranitidine tablets. It appears that there were no changes in pharmacokinetics of triazolam and α-hydroxytriazolam, a major metabolite, and in their elimination. Reduced gastric acidity due to ranitidine may have resulted in an increase in the availability of triazolam. The clinical significance of this triazolam and ranitidine pharmacokinetic interaction is unknown.

Carcinogenesis, Mutagenesis, Impairment of Fertility: There was no indication of tumorigenic or carcinogenic effects in life-span studies in mice and rats at dosages up to 2,000 mg/kg per day.

Ranitidine was not mutagenic in standard bacterial tests *(Salmonella, Escherichia coli)* for mutagenicity at concentrations up to the maximum recommended for these assays. In a dominant lethal assay, a single oral dose of 1,000 mg/kg to male rats was without effect on the outcome of 2 matings per week for the next 9 weeks.

Pregnancy: ***Teratogenic Effects:*** Pregnancy Category B. Reproduction studies have been performed in rats and rabbits at doses up to 160 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to Ranitidine Tablets, USP. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: Ranitidine Tablets, USP is secreted in human milk. Caution should be exercised when Ranitidine Tablets, USP is administered to a nursing mother.

Pediatric Use: The safety and effectiveness of Ranitidine Tablets, USP have been established in the age-group of 1 month to 16 years for the treatment of duodenal and gastric ulcers, gastroesophageal reflux disease and erosive esophagitis, and the maintenance of healed duodenal and gastric ulcer. Use of Ranitidine Tablets, USP in this age-group is supported by adequate and well-controlled studies in adults, as well as additional pharmacokinetic data in pediatric patients and an analysis of the published literature (see CLINICAL PHARMACOLOGY: Pediatrics and DOSADGE AND ADMINISTRATION: Pediatric Use).

Safety and effectiveness in pediatric patients for the treatment of pathological hypersecretory conditions or the maintenance of healing of erosive esophagitis have not been established.

Safety and effectiveness in neonates (less than 1 month of age) have not been established (see CLINICAL PHARMACOLOGY: Pediatrics)

Geriatric Use: Of the total number of subjects enrolled in US and foreign controlled clinical trials of oral formulations of Ranitidine Tablets, USP, for which there were subgroup analyses, 4,197 were 65 and over, while 899 were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

This drug is known to be substantially excreted by the kidney and the risk of toxic reactions to this drug

may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, caution should be exercised in dose selection, and it may be useful to monitor renal function (see CLINICAL PHARMACOLOGY: Pharmacokinetics: Geriatrics and DOSAGE AND ADMINISTRATION: Dosage Adjustment for Patients with Impaired Renal Function).

ADVERSE REACTIONS

The following have been reported as events in clinical trials or in the routine management of patients treated with Ranitidine Tablets, USP. The relationship to therapy with Ranitidine Tablets, USP has been unclear in many cases. Headache, sometimes severe, seems to be related to administration of Ranitidine Tablets, USP.

Central Nervous System: Rarely, malaise, dizziness, somnolence, insomnia, and vertigo. Rare cases of reversible mental confusion, agitation, depression, and hallucinations have been reported, predominantly in severely ill elderly patients. Rare cases of reversible blurred vision suggestive of a change in accommodation have been reported. Rare reports of reversible involuntary motor disturbances have been received.

Cardiovascular: As with other H_2-blockers, rare reports of arrhythmias such as tachycardia, bradycardia, atrioventricular block, and premature ventricular beats.

Gastrointestinal: Constipation, diarrhea, nausea/vomiting, abdominal discomfort/pain, and rare reports of pancreatitis.

Hepatic: There have been occasional reports of hepatocellular, cholestatic, or mixed hepatitis, with or without jaundice. In such circumstances, ranitidine should be immediately discontinued. These events are usually reversible, but in rare circumstances death has occurred. Rare cases of hepatic failure have also been reported. In normal volunteers, SGPT values were increased to at least twice the pretreatment levels in 6 of 12 subjects receiving 100 mg q.i.d. intravenously for 7 days, and in 4 of 24 subjects receiving 50 mg q.i.d. intravenously for 5 days.

Musculoskeletal: Rare reports of arthralgias and myalgias.

Hematologic: Blood count changes (leucopenia, granulocytopenia, and thrombocytopenia) have occurred in a few patients. These were usually reversible. Rare cases of agranulocytosis, pancytopenia, sometimes with marrow hypoplasia, and aplastic anemia and exceedingly rare cases of acquired immune hemolytic anemia have been reported.

Endocrine: Controlled studies in animals and man have shown no stimulation of any pituitary hormone by Ranitidine Tablets, USP and no antiandrogenic activity, and cimetidine-induced gynecomastia and impotence in hypersecretory patients have resolved when Ranitidine Tablets, USP has been substituted. However, occasional cases of gynecomastia, impotence, and loss of libido have been reported in male patients receiving Ranitidine Tablets, USP, but the incidence did not differ from that in the general population.

Rares cases of breast symptoms and conditions, including galactorrhea and gynecomastia, have been reported in both males and females.

Integumentary: Rash, including rare cases of erythema multiforme. Rare cases of alopecia and vasculitis.

Respiratory: A large epidemiological study suggested an increased risk of developing pneumonia in current users of histamine-2-receptor antagonists (H_2RAs) compared to patients who had stopped H_2RA treatment, with an observed adjusted relative risk of 1.63 (95% CI, 1.07 - 2.48). However, a causal relationship between use of H_2RAs and pneumonia has not been established.

Other: Rare cases of hypersensitiviy reactions (e.g., bronchospasm, fever, rash, eosinophilia), anaphylaxis, angioneurotic edema, and small increases in serum creatinine.

OVERDOSAGE

There has been limited experience with overdosage. 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 ADVERSE REACTIONS). In addition, abnormalities of gait and hypotension have been reported.

When overdosage occurs, the usual measures to remove unabsorbed material from the gastrointestinal tract, clinical monitoring, and supportive therapy should be employed.

Studies in dogs receiving dosages of Ranitidine Tablets, USP in excess of 225 mg/kg per day have shown muscular tremors, vomiting, and rapid respiration. Single oral doses of 1,000 mg/kg in mice and rats were not lethal. Intravenous LD_{50} values in mice and rats were 77 and 83 mg/kg, respectively.

DOSAGE AND ADMINISTRATION

Active Duodenal Ulcer: The current recommended adult dosage of Ranitidine Tablets, USP for duodenal ulcer is 150 mg twice daily. An alternative dosage of 300 mg once daily after the evening meal or at bedtime can be used for patients in whom dosing convenience is important. The advantages of one treatment regimen compared to the other in a particular patient population have yet to be demonstrated (see Clinical Trials: Active Duodenal Ulcer). Smaller doses have been shown to be equally effective in inhibiting gastric acid secretion in US studies, and several foreign trials have shown that 100 mg twice daily is as effective as the 150-mg dose.

Antacid should be given as needed for relief of pain (see CLINICAL PHARMACOLOGY: Pharmacokinetics).

Maintenance of Healing of Duodenal Ulcers: The current recommended adult oral dosage is 150 mg at bedtime.

Pathological Hypersecretory Conditions (such as Zollinger-Ellison syndrome):

The current recommended adult oral dosage is 150 mg twice a day. In some patients it may be necessary to administer Ranitidine Tablets, USP 150-mg doses more frequently. Dosages should be adjusted to individual patient needs, and should continue as long as clinically indicated. Dosages up to 6 g/day have been employed in patients with severe disease.

Benign Gastric Ulcer: The current recommended adult oral dosage is 150 mg twice a day.

Maintenance of Healing of Gastric Ulcers: The current recommended adult oral dosage is 150 mg at bedtime.

GERD: The current recommended adult oral dosage is 150 mg twice a day.

Erosive Esophagitis: The current recommended adult oral dosage is 150 mg four times a day.

Maintenance of Healing of Erosive Esophagitis: The current recommended adult oral dosage is 150 mg twice a day.

Pediatric Use: The safety and effectiveness of Ranitidine Tablets, USP have been established in the age-group of 1 month to 16 years. There is insufficient information about the pharmacokinetics of Ranitidine Tablets, USP in neonatal patients (less than 1 month of age) to make dosing recommendations.

The following 3 subsections provide dosing information for each of the pediatric indications.

Treatment of Duodenal and Gastric Ulcers: The recommended oral dose for the treatment of active duodenal and gastric ulcers is 2 to 4 mg/kg twice daily to a maximum of 300 mg/day. This recommendation is derived from adult clinical studies and pharmacokinetic data in pediatric patients.

Maintenance of Healing of Duodenal and Gastric Ulcers: The recommended oral dose for the maintenance of healing of duodenal and gastric ulcers is 2 to 4 mg/kg once daily to a maximum of 150

mg/day. This recommendation is derived from adult clinical studies and pharmacokinetic data in pediatric patients.

Treatment of GERD and Erosive Esophagitis: Although limited data exist for these conditions in pediatric patients, published literature supports a dosage of 5 to 10 mg/kg per day, usually given as two divided doses.

Dosage Adjustment for Patients With Impaired Renal Function: On the basis of experience with a group of subjects with severely impaired renal function treated with Ranitidine Tablets, USP, the recommended dosage in patients with a creatinine clearance <50 mL/min is 150 mg every 24 hours. Should the patient's condition require, the frequency of dosing may be increased to every 12 hours or even further with caution. Hemodialysis reduces the level of circulating ranitidine. Ideally, the dosing schedule should be adjusted so that the timing of a scheduled dose coincides with the end of hemodialysis.

Elderly patients are more likely to have decreased renal function, therefore caution should be exercised in dose selection, and it may be useful to monitor renal function (see CLINICAL PHARMACOLOGY: Pharmacokinetics: Geriatrics and PRECAUTIONS: Geriatric Use).

HOW SUPPLIED

Ranitidine Tablets, USP 150 mg are orange, round, biconvex aqueous film coated tablets debossed “IP 253” on one side and plain on the reverse.

They are available in bottles of 24, 60, 100, 180, 500 and 1000.

Ranitidine Tablets, USP 300 mg are yellow, capsule-shaped aqueous film coated tablets debossed “IP 254” on one side and plain on the reverse.

They are available in bottles of 24, 30, 100, 250, 500 and 1000.

Store at 20° - 25°C (68° - 77°F) (See USP Controlled Room Temperature) in a tight, light resistant container. Protect from light. Replace cap securely after each opening.

Manufactured by:

Amneal Pharmaceuticals of NY

Hauppauge, NY 11788

Distributed by:

Amneal Pharmaceuticals

Glasgow, KY 42141

Rev. 11-2009

Image of Label

RANITIDINE

ranitidine tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG LABEL	**Item Code (Source)**	NDC:35356-809(NDC:53746-254)
Route of Administration	ORAL	**DEA Schedule**	

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
RANITIDINE (RANITIDINE)	RANITIDINE	300 mg

Inactive Ingredients

Ingredient Name	Strength
COLLOIDAL SILICON DIOXIDE	
CROSCARMELLOSE SODIUM	
HYPROMELLOSES	

MAGNESIUM STEARATE	
CELLULOSE, MICROCRYSTALLINE	
POLYDEXTROSE	
TITANIUM DIOXIDE	
TRIETHYL CITRATE	
D&C YELLOW NO. 10	

Product Characteristics

Color	YELLOW	**Score**	no score
Shape	CAPSULE (Biconvex)	**Size**	17mm
Flavor		**Imprint Code**	IP254
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:35356-809-30	30 in 1 BOTTLE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA077824	12/16/2009	

Labeler - Lake Erie Medical DBA Quality Care Products LLC (831276758)

Establishment

Name	Address	ID/FEI	Business Operations
Lake Erie Medical DBA Quality Care Products LLC		831276758	relabel(35356-809)

Revised: 2/2013 Lake Erie Medical DBA Quality Care Products LLC