SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Nizatidine 300mg capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Nizatidine 300mg

Excipients with known effect: Propylene glycol.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsules, Hard

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of the following diseases where reduction of gastric acid is indicated:

Duodenal ulcer

Benign gastric ulcer

Prevention of duodenal or benign gastric ulcer recurrence

Gastric oesophageal reflux disease (including erosions, ulcerations and associated heartburn)

Gastric and/or duodenal ulcer associated with concomitant use of non-steroidal anti-inflammatory drugs

4.2 Posology and method of administration

Method of administration
For oral administration.

Posology
Adults:

1. For treatment of duodenal ulcer, the recommended daily dose is 300mg in the evening. Treatment should continue for four weeks, although this period may be reduced if healing is confirmed earlier by endoscopy. Most ulcers will heal within four weeks, but if complete ulcer healing has not occurred after four weeks therapy, patients should continue therapy for a further four weeks.
2. For the treatment of benign gastric ulcer, the recommended daily dose is 300mg in the evening for four or, if necessary, eight weeks. Prior to treatment with nizatidine, care should be taken to exclude the possibility of gastric cancer.
   If preferred, the 300mg daily dose for the treatment of duodenal or benign gastric ulcer may be given as two divided doses of 150mg in the morning and evening.
3. For the prevention of duodenal or benign gastric ulcer recurrence (prophylactic maintenance therapy), the recommended daily dose is 150mg in the evening.
4. For the treatment of gastric oesophageal reflux disease, the recommended dosage is from 150mg twice daily, up to 300mg twice daily. Therapy for up to 12 weeks is indicated for erosions and ulcerations, and associated heartburn.
5. For the treatment of gastric and/or duodenal ulcer associated with concomitant use of non-steroidal anti-inflammatory drugs, the recommended daily dose is 300mg daily (either 300mg at bedtime or 150mg twice daily, in the morning and in the evening) for up to 8 weeks. In most patients, the ulcers will heal within 4 weeks. During treatment, the use of non-steroidal anti-inflammatory drugs may continue.

The elderly: Age does not significantly influence efficacy or safety. Normally dosage modification is not required, except in patients who have moderate to severe renal impairment (creatinine clearance less than 50ml/min).

Paediatric population: The safety and efficacy of nizatidine in children has not been established. No data are available.

Patients with impaired renal function: For patients who have moderate renal impairment (creatinine clearance less than 50ml/min) or patients who have severe renal impairment (creatinine clearance less than 20ml/min), the dosage should be reduced as follows.

DOSAGE RECOMMENDED		
Indications	***Moderate Renasl Impairment***	***Severe Renal Impairment***
Duodenal ulcer	150mg in the evening	150mg on alternate days
Benign gastric ulcer	150mg in the evening	150mg on alternate days
Prevention of duodenal or benign gastric ulcer recurrence	150mg in the evening on alternate days	150mg in the evening every third day
Gastric oesophageal reflux disease	From 150mg daily, up to 150mg twice daily	From 150mg on alternate days, up to 150 mg daily
Gastric and/or duodenal ulcer associated with concomitant use of non-steroidal anti-inflammatory drugs	150mg in the evening	150mg on alternate days

4.3 Contraindications

Hypersensitivity to the active substance, any other H2-receptor antagonists or to any of the excipients listed in section 6.1

4.4 Special warnings and precautions for use

As nizatidine is partially metabolised by the liver and principally excreted by the kidneys, patients with impaired liver or kidney function should be treated with caution. (See 'Posology and method of administration' section).

Symptomatic response to nizatidine therapy does not preclude the presence of gastric malignancy.

Excipients:

- This medicine contains 0.98 mg propylene glycol in each dosage unit, which is equivalent to 1.96 mg/kg/day.

4.5 Interaction with other medicinal products and other forms of interaction

There is evidence that oral nizatidine does not affect the serum levels of concomitantly administered aminophylline, theophylline, chlordiazepoxide, diazepam, lidocaine, phenytoin, ibuprofen, metoprolol, warfarin or lorazepam.

Nizatidine does not inhibit the hepatic cytochrome P450-linked drug metabolizing enzyme system, but may increase absorption of salicylates when they are used in very high dosage. However, nizatidine and other histamine H_2-receptor antagonists can reduce the gastric absorption of drugs whose absorption is dependent on an acidic gastric pH. Approximately 35% of nizatidine is bound to plasma protein. Warfarin, diazepam, paracetamol, propantheline, phenobarbital and propranolol did not affect plasma protein binding of nizatidine *in vitro*.

Absorption of nizatidine is not clinically significantly affected by food intake, anticholinergic agents or antacids.

4.6 Fertility, pregnancy and lactation

Pregnancy: The safety of nizatidine for use during pregnancy has not been established. Animal studies have shown no evidence of impaired fertility or teratogenicity

attributable to nizatidine. Nizatidine should only be used in pregnant women, or in those planning pregnancies, if considered absolutely necessary, and then with caution.

Breast-feeding: Studies conducted in lactating women have shown that 0.1% of the administered oral dose of nizatidine is secreted in human milk in proportion to plasma concentrations. Because of the growth depression in pups reared by lactating rats treated with nizatidine, nizatidine should be administered to nursing mothers only if considered absolutely necessary.

4.7 Effects on ability to drive and use machines

There is no influence of nizatidine on the ability to drive or use machines.

4.8 Undesirable effects

In large scale clinical trials, sweating and urticaria were significantly more common in patients treated with oral nizatidine when compared with placebo. In these trials, 1.9% of treated patients experienced somnolence, compared to 1.6% of placebo patients (non-significant).

In the same trials, patients treated with both nizatidine and placebo had mild, transient, asymptomatic elevations of transaminases or alkaline phosphatase; rare instances of marked elevations (>500iu/l) occurred in nizatidine-treated patients. The overall rate of occurrences of elevated liver enzymes and elevations to 3 times the upper limit of normal, however, did not differ significantly from placebo. All abnormalities were reversible after discontinuation of nizatidine. Since introduction, hepatitis and jaundice have been reported. Rare cases of cholestatic or mixed hepatocellular and cholestatic injury with jaundice have been reported, with reversal of the abnormalities after discontinuation.

The following effects have also been rarely reported, thrombocytopenic purpura, fatal thrombocytopenia, leucopenia, agranulocytosis, anaemia, exfoliative dermatitis, vasculitis, arthralgia, myalgia, gynaecomastia, impotence, hyperuricaemia, fever, nausea and reversible mental confusion.

Rare episodes of hypersensitivity reactions (eg, bronchospasm, laryngeal oedema, rash, pruritus and eosinophilia), serum sickness and anaphylaxis have been reported.

Very rarely headache and diarrhoea have been reported.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms
There is little experience of overdose in humans. Tested at very high doses in animals, nizatidine has been shown to be relatively non-toxic. Animal studies suggest that cholinergic-type effects, including lacrimation, salivation, emesis, miosis and diarrhoea, may occur following very large oral doses.

Treatment
Symptomatic and supportive therapy is recommended. Activated charcoal, emesis or lavage may reduce nizatidine absorption. The ability of haemodialysis to remove nizatidine from the body has not been conclusively demonstrated. However, this method is not expected to be efficient, since nizatidine has a large volume of distribution.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs for peptic ulcer and gastro-oesophageal reflux disease (GORD), H2-receptor antagonists, ATC code: A02BA04

Mechanism of action

Nizatidine is a potent, selective, competitive and fully reversible histamine H2-receptor antagonist. Nizatidine significantly decreased basal and stimulated gastric acid and pepsin concentration, in addition to the volume of gastric secretion.

Pharmacodynamic effects

In various clinical trials, nizatidine, administered as either a single daily dose (at bedtime) or in two divided doses (morning and evening), significantly inhibited gastric acid secretion, and ulcer pain was usually rapidly abolished.

Nizatidine has no significant effect on the serum concentrations of gastrin, gonadotrophins, prolactin, growth hormone, antidiuretic hormone, cortisol, testosterone, 5-alpha-dihydrotestosterone or oestradiol.

Nizatidine has no antiandrogenic action.

5.2 Pharmacokinetic properties

Bioavailability of orally administered nizatidine is not significantly influenced by food intake, anticholinergic agents or antacids.

Absorption
Absorption of nizatidine after oral administration is rapid and peak plasma concentrations (700-1800ng/ml after 150mg; 1400-3600ng/ml after 300mg dose) are usually achieved within two hours of administration (range 0.5-3 hours). Oral bioavailability exceeds 70%, and the elimination half-life is approximately 1.6 hours.

Distribution

Approximately 35 percent of nizatidine is bound to plasma protein. Warfarin, diazepam, paracetamol, propantheline, Phenobarbitone and propranolol did not affect plasma protein binding of nizatidine *in vitro.*

Biotransformation
Minor (6%) first pass hepatic metabolism occurs, but nizatidine is principally excreted via the kidneys, about 60% as unchanged drug, renal clearance is about 500ml/min. Metabolites include desmethyl nizatidine (7%), sulphoxide (6%) and N-oxide (5%). Desmethyl nizatidine is an active metabolite of limited potency.

Elimination
More than 90% of an oral dose of nizatidine (including metabolites) is excreted in the urine within 12 hours.

5.3 Preclinical safety data

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Crosscarmellose sodium,
Povidone,
Maize starch,
Dimeticone,
Talc.

Capsule shell
Quinoline Yellow (E104)
Erythrosine (E127)
Titanium Dioxide (E171)
Yellow Iron oxide (E172)
Gelatin

Printing ink
Shellac
Black iron oxide (E172)
Potassium hydroxide
Propylene glycol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Transparent PVC/PVdC/aluminium foil blisters.
28 and 30 capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

Relonchem Limited,
Cheshire House,
Gorsey Lane,
Widnes,
Cheshire,
WA8 0RP.

8 MARKETING AUTHORISATION NUMBER(S)

PL 20395/0303

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12/11/2008

10 DATE OF REVISION OF THE TEXT

05/06/2025