SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE PRODUCT

Ulcerex® **(Cimetidine) Injection**

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ulcerex® Injection
Each 2ml contains:
Cimetidine USP.....200mg

3. PHARMACEUTICAL FORM

Injection

Appearance: Clear colorless to slightly colored solution.

4. CLINICAL PARTICULARS

4.1. THERAPEUTIC INDICATIONS:

The treatment of benign gastric and duodenal ulcers, reflux oesophagitis, Zollinger-Ellison syndrome, and in other conditions associated with gastric hypersecretory states, such as systemic mastocytosis and multiple endocrine adenomas. It is also indicated at reduced dosage for duodenal ulcer recurrence in selected patients.

4.2. POSOLOGY AND METHOD OF ADMINISTRATION

Posology:
The total daily use by any route should not exceed 2.4g.
Adults: The dose with intravenous or intramuscular injections, is normally 200mg. Injections may be repeated at 4 or 6 hourly intervals. The 200mg injection for intravenous use should be diluted in 0.9% Normal Saline (or other compatible solution) to a total volume of 20mL and given very slowly, at least over 2 minutes. The dose by intravenous infusion is usually 50 to 100mg/hour for 2 hours and repeated at 4 to 6 hourly intervals. The maximum infusion rate should not usually exceed 150mg/hour or 2mg/kg body mass/hour. Intravenous infusion is preferred in patients where cardiovascular impairment is present. Cimetidine injection has been shown to be compatible with Dextrose (5 and 10%), and Normal Saline (0.9%) solutions for intravenous infusion and the resultant solution is stable for 1 week at normal room temperature.
Paediatric population: Cimetidine therapy not recommended for children.
Method of administration:
For intramuscular injection or slow intravenous injection or intravenous infusion.

4.3. CONTRAINDICATIONS:

Cimetidine is not recommended for minor digestive complaints. It is also not recommended for patients with impaired renal function.

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE:

General: Rare instances of cardiac arrhythmias and hypotension have been reported following the rapid administration of cimetidine hydrochloride injection by intravenous bolus. Symptomatic response to cimetidine therapy does not preclude the presence of a gastric malignancy. There have been rare reports of transient healing of gastric ulcers despite subsequently documented malignancy. Reversible confusional states have been observed on occasion, predominantly, but not exclusively, in severely ill patients. Advancing age (50 or more years) and pre-existing liver and/or renal disease appear to be contributing factors. In some patients these confusional states have been mild and have not required discontinuation of cimetidine therapy. In cases where discontinuation was judged necessary, the condition usually cleared within 3 to 4 days of drug withdrawal.
Before giving cimetidine to patients with gastric ulcers the possibility of malignancy should be excluded since cimetidine may mask symptoms and delay diagnosis. It should be given in reduced dosage to patients with impaired renal function. For further details of administration in renal failure, intravenous injections of cimetidine should be given slowly and intravenous infusion is recommended in patients with cardiovascular impairment.

4.5. INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORM OF INTERACTIONS:

Cimetidine has been reported to reduce the hepatic metabolism of warfarin-type anticoagulants, phenytoin, propranolol, chlordiazepoxide, diazepam and theophylline, thereby delaying elimination and increasing blood levels of these medicines. Dosages of the medicines mentioned above and other similarly metabolized medicines may require adjustment when starting or stopping concomitantly administered Cimetidine to maintain safe, optimum therapeutic blood levels.

4.6. FERTILITY, PREGNANCY AND LACTATION:

Fertility: Not known.
Pregnancy: The use of cimetidine should be avoided during pregnancy unless essential.
Breast-feeding: The use of cimetidine should be avoided during breast-feeding unless essential.

4.7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:

Not known.

4.8. UNDESIRABLE EFFECTS:

Adverse reactions to cimetidine are generally infrequent and are usually reversible following a reduction of dosage or withdrawal of therapy. The commonest side-effects reported have been diarrhoea, 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. Cimetidine has a weak anti-androgenic effect and gynecomastia and impotence have also occasionally occurred in men receiving relatively high doses for conditions such as the Zollinger-Ellison syndrome.

4.9. OVERDOSE:

Reported acute ingestions orally of up to 20g have been associated with transient adverse effects similar to those encountered in normal clinical experience. The usual measures to remove unabsorbed material from the gastrointestinal tract, clinical monitoring and supportive therapy, should be employed. There have been reports of severe CNS symptoms, including unresponsiveness, following ingestion of between 20 and 40g of cimetidine, and extremely rare reports following concomitant use of multiple CNS-active medications and ingestion of cimetidine at doses less than 20g. Elderly, terminally ill dehydrated patient with organic brain syndrome receiving concomitant antipsychotic agents and cimetidine 4800mg intravenously over a 24-hour period experienced mental deterioration with reversal on cimetidine discontinuation. There have been two deaths in adults who were reported to have ingested over 40g orally on a single occasion.

5. PHARMACOLOGICAL PROPERTIES

5.1. PHARMACODYNAMIC PROPERTIES:

Pharmacotherapeutic group: H2-receptor antagonists, **ATC code:** A02BA01
Cimetidine is a histamine H2-receptor antagonist which rapidly inhibits both basal and stimulated gastric secretion of acid and reduces pepsin output. It is a reversible, competitive antagonist, and is used as an anti-ulcer drug. It is highly selective in its action, is virtually without effect on H1 receptors, or indeed on receptors for other autocoids or drugs. Despite the widespread distribution of H2-receptors in the body, Cimetidine interferes remarkably little with physiological functions other than gastric secretion, implying that the extragastric H2-receptors are of minor physiological importance. However, H2 blockers like Cimetidine do inhibit those effects on the cardiovascular and other systems that are elicited through the corresponding receptors by exogenous or endogenous histamine. Cimetidine inhibits gastric acid secretion elicited by histamine or other H2 agonists in a dose-dependent, competitive manner; the degree of inhibition parallels the plasma concentration of the drug over a wide range. In addition, the H2 blockers inhibit gastric secretion elicited by muscarinic agonists or by gastrin, although this effect is not always complete. This breadth of inhibitory effect is not due to non-specific actions at the receptors for these other secretagogues. Rather, this effect, which is non-competitive and indirect, appears to indicate either that these two classes of secretagogues utilize histamine as the final common mediator or, more probably, that ongoing histaminergic stimulation of the parietal cell is important for amplification of the stimuli provided by ACh or gastrin when they act on their own discrete receptors. Receptors for all three secretagogues are present on the parietal cell. The ability of H2 blockers to suppress responses to all three physiological secretagogues makes them potent inhibitors of all phases of gastric acid secretion. Thus, these drugs will inhibit basal (fasting) secretion and nocturnal secretion and also that stimulated by food, sham feeding, fundic distension, insulin, or caffeine. The H2 blockers reduce both the volume of gastric juice secreted and its hydrogen ion concentration. Output of pepsin, which is secreted by the chief cells of the gastric glands (mainly under cholinergic control), generally falls in parallel with the reduction in volume of the gastric juice. Secretion of intrinsic factor is also reduced, but it is normally secreted in great excess, and absorption of vitamin B12 is usually adequate even during long-term therapy with H2 blockers. Concentrations of gastrin in plasma are not significantly altered under fasting conditions; however, the normal prandial elevation of gastrin concentration may be augmented, apparently as a consequence of a reduction in the negative feedback that is normally provided by acid

SUMMARY OF PRODUCT CHARACTERISTICS

Mechanism of action: Cimetidine is a histamine H2-receptor antagonist. Its main action is to inhibit gastric acid secretion. It also inhibits competitively the other actions of histamine mediated by H2-receptors. The decrease in gastric acid secretion occurs regardless of the nature of the physiological stimulus to secretion, i.e. basal or unstimulated secretion, is reduced. Both the volume of secretion and the concentration of acid in the secretion are reduced.

5.2. PHARMACOKINETICS:
Absorption: Cimetidine is rapidly and virtually completely absorbed from the gastrointestinal tract. Absorption is little impaired by food or by antacids. Peak plasma concentrations are obtained about an hour after administration on an empty stomach, and about 2 hours after administration with food.
Distribution: The duration of action is reported to be prolonged by administration with food. Peak concentrations in plasma are attained in about 1 to 2 hours.
Metabolism: Hepatic first-pass metabolism results in bioavailability of about 60% for Cimetidine.
Elimination: The elimination half-life is about 2-3 hours. Cimetidine is eliminated primarily by the kidneys, and 60% or more may appear in the urine unchanged; much of the rest is oxidation products. Small amounts are recovered in the stools. Cimetidine crosses the placental barrier and is excreted in milk. It does not readily cross the blood-brain barrier.

5.3. PRECLINICAL SAFETY DATA:
Not available.

6. PHARMACEUTICAL PARTICULARS

6.1. LIST OF EXCIPIENTS:
- Phenol
- Propylene glycol
- Hydrochloric Acid
- Sodium Hydroxide

6.2. INCOMPATIBILITIES:
Not applicable.

6.3. SHELF LIFE:
See expiry on the pack.

6.4. SPECIAL PRECAUTIONS FOR STORAGE:
Avoid exposure to heat, light and freezing. Store between 15 to 30°C. Improper storage may deteriorate the medicine.
Keep out of reach of children.
Injection should not be used if container is leaking, solution is cloudy or it contains undissolved particle(s).

6.5. NATURE AND CONTENTS OF CONTAINER:
3ml amber colored glass ampoule USP Type I, pack size is 5 x 2ml ampoules.

6.6. SPECIAL PRECAUTIONS FOR DISPOSAL OF A USED PRODUCT:
Nothing stated.

6.7. DRUG PRODUCT SPECIFICATIONS:
BP Specs.

7. MARKETING AUTHORISATION HOLDER

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, Off Hub River Road, S.I.T.E., Karachi-Pakistan
www.samipharmapk.com
Mfg. Lic. No. 000072

8. MARKETING AUTHORISATION NUMBER(S)
012527

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
12th May, 1991

10. DATE OF REVISION OF THE TEXT

السی ریکس انجکشن
(سائمیٹڈین)

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں

صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں

بچوں کی پہنچ سے دور رکھیں

دوا کو گرمی، روشنی اور منجمد ہونے سے محفوظ ۱۵ سے ۳۰ ڈگری سینٹی گریڈ

کے درمیان میں رکھیں ورنہ دوا خراب ہو جائیگی

انجکشن کے لیک ہونے، دھندلا ہونے یا اس میں کوئی غیر حل پذیر

شے نظر آنے کی صورت میں ہرگز استعمال نہ کریں