Cimetidine Tablets 200mg

SUMMARY OF PRODUCT CHARACTERISTICS

This summary of product characteristics focuses on uses of the medicine covered by WHO's Prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information from stringent regulatory authorities (term to be revised).
The medicine may be authorized for additional or different uses by national medicines regulatory authorities.

1. NAME OF THE MEDICINAL PRODUCT

Cimetidine Tablets 200mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains: Cimetidine 200mg

3. PHARMACEUTICAL FORM

Cimetidine is a histamine H2 receptor impedance agent, which is mainly used to inhibit gastric acid secretion. It can significantly inhibit basal and nocturnal gastric acid secretion, inhibit gastric acid secretion caused by histamine, peptide gastrin, insulin and food stimulation, and reduce its acidity. It can prevent and protect corrosive gastritis caused by chemical stimulation, and has obvious curative effect on stress gastric ulcer and upper gastrointestinal bleeding.

Its chemical formula is 1-methyl-2-cyano-3 - [2 - [(5-methylimidazol-4-yl) methyl] thio] ethyl] guanidine. Its molecular formula is $C_{10}H_{16}N_6S$, and its molecular weight is 252.34.

Group: H2 receptor blocker for tablet 200 mg in 1 tablet.

4. CLINICAL PARTICULARS

Therapeutic indications

Treatment and maintenance therapy of active duodenal ulcer.

Treatment of benign gastric ulcers.

Treatment of reflux oesophagitis.

Treatment of pathological hypersecretory conditions (Zollinger-Ellison Syndrome).

DOSAGE AND ADMINISTRATION :

Cimetidine should be administered preferably with meals or at bed time. Doses should be adjusted to individual patient needs & should continue as long as clinically indicated.

As directed by the physician.

Active duodenal ulcer: 200 mg thrice daily for 4-6 weeks.

Maintenance therapy for duodenal ulcer: 400 mg once or twice daily for 6 months.

Active benign gastric ulcer : 300 mg four times a day.

Reflux oesophagitis : 400 mg ti.d. for 4-6 weeks.

Pathological hypersecretory conditions (such as Zollinger-Ellison syndrome): 300 mg four times a day or as directed by the physician.

CLINICAL PHARMACOLOGY :

Cimetidine competitively inhibits the action of histamine at the H? receptor antagonist.

Antisecretory Activity

Acid Secretion : Nocturnal: Cimetidine 800 mg orally at bed time reduces mean houriy H^+activity by greater than 85% over an eight hour period in duodenal ulcer Patients, with no effect on daytime acid secretion.

Pepsin : Oral Cimetidine 300 mg reduced total pepsin output as a result of the decrease in volume of gastric juice.

Intrinsic Factor : Intrinsic factor secretion was studied with betazole as a stimulant oral cimetidine 300mg. inhibited the rise in intrinsic factor concentration produced by betazole, but some intrinsic factor was secreted at all times.

PHARMACOKINETICS :

Cimetidine is rapidly absorbed after oral administration and peak levels occur in 45-90 minutes. The half life is approximately 2 hours. The principal route of excretion is through urine. Following a single oral dose, 48% of the drug is recovered from the urine after 24 hours as the parent compound.

Excipients

This medicinal product contains Maize Starch、Low-Substituted Hydroxypropyl Cellulose、Sodium Starch Glycolate、Magnesium Stearate

Interaction with other medicinal products and other forms of interaction

1. Combined with acid making drugs, it can synergistically relieve pain in duodenal ulcer, but the absorption of cimetidine may be reduced, so it is generally not recommended. If it must be used with acid making drugs, they should be taken at least 1 hour apart.

2. Taking metoclopramide (metoclopramide) together with this product can reduce the blood concentration of this product, and the dose of this product should be increased appropriately.

3. Since sucralfate can play its role only after gastric acid hydrolysis, this product inhibits gastric acid secretion. The combination of the two may reduce the efficacy of sucralfate.

4. This product inhibits the oxidative metabolic pathway catalyzed by cytochrome P450 and can reduce liver blood flow. Therefore, when combined with other drugs, this product can reduce the metabolism of other drugs and enhance their pharmacological activity or toxicity. These include:

(1) Combined with benzodiazepines for a long time, intrahepatic metabolism can be inhibited, resulting in the increase of blood drug concentration of the latter, aggravating sedation and other central nervous inhibition, and developing into respiratory and circulatory failure. However, lorazepam, oxazepam and temazepam did not seem to be affected.

(2) When combined with warfarin and other coumarin anticoagulants, prothrombin time can be

further prolonged. Therefore, it is necessary to pay close attention to the changes of the disease and adjust the dosage of anticoagulants.

(3) When combined with phenytoin sodium or other hydantoins, the blood concentration of the latter may increase, resulting in phenytoin sodium poisoning. If it must be used, the blood concentration of phenytoin sodium should be measured after 5 days in order to adjust the dose, and pay attention to regular recheck of peripheral blood.

(4) When combined with propranolol, metoprolol and metronidazole, the blood concentration may increase.

(5) When combined with xanthine drugs such as theophylline, caffeine and aminophylline, liver metabolism decreases, which can lead to delayed clearance, increased blood drug concentration and possible toxic reaction.

(6) This product can increase the absolute bioavailability of verapamil (verapamil) from 26.3% ± 16.8% to 49.3% ± 23.6%. Due to the rare but serious side effects of verapamil, attention should be paid.

(7) This product can inhibit quinidine metabolism. When patients take digoxin and quinidine at the same time, this product should not be used again. Because quinidine can replace digoxin from its binding site, the blood concentrations of quinidine and digoxin increased. At this time, the blood drug concentration should be monitored.

(8) When combined with other intrahepatic metabolic drugs, such as lidocaine and tricyclic antidepressants, they should be used with caution.

5. When combined with opioids, it has been reported that adverse reactions such as respiratory depression, mental confusion and loss of orientation can occur in patients with chronic renal failure. The dosage of opioids should be reduced for such patients.

6. Because this product increases the pH value of gastric juice, when combined with tetracycline, it can reduce the dissolution rate, absorption and function of tetracycline (but the liver drug enzyme inhibition of this product may increase the blood concentration of tetracycline); If combined with aspirin, the opposite result appears, which can enhance the effect of aspirin.

7. Combined with ketoconazole can interfere with the absorption of the latter and reduce its antifungal activity, but taking some acidic drinks can avoid the above changes.

8. The combination of this product and captopril may cause mental symptoms.

9. Because this product has the muscle nerve blocking effect similar to aminoglycoside antibiotics, this effect is not antagonized by neostigmine, but only by calcium chloride. Therefore, when combined with aminoglycosides, it may lead to respiratory depression or respiratory arrest.

Fertility, pregnancy and breastfeeding

Medication for pregnant and lactating women

This product can pass through the placental barrier and enter milk. It is forbidden for pregnant and lactating women.

Medication for children

Not recommended for children under 16.

Geriatric medication

Reduce the dosage.

Effects on ability to drive and use machines

There is no information on the effect on the ability to drive or use machines. The patient'sclinical status should be considered when assessing ability to drive or operate machinery.

Undesirable effects

Generally speaking, adverse reactions of this product are not common, and usually disappear after continued medication or withdrawal.

1. The more common adverse reactions are diarrhea, fatigue, dizziness, drowsiness, headache and rash.

2. This product has mild anti androgen effect. When the dosage is large (more than 1.6g per day), it can cause male breast development, female galactorrhea, decreased sexual desire, impotence, decreased sperm count, etc., which will disappear after stopping the drug.

3. This product can pass through the blood cerebrospinal fluid barrier and has certain neurotoxicity. Mental disorders are occasionally seen. Anxiety, depression, anxiety, delirium, hallucination and disorientation are common in elderly and seriously ill patients. Generally, the symptoms disappear 3-4 days after drug withdrawal. When treating the gastrointestinal complications of alcoholics, tremor delirium can appear, which is similar to abstinence syndrome;

4. rare adverse reactions include allergic reaction, fever, arthralgia, myalgia, interstitial nephritis, urinary retention, liver toxicity, and pancreatitis.

5. Very few people have leukopenia and agranulocytosis. These people have other serious diseases and receive drugs and treatments known to reduce blood cells. Thrombocytopenia and aplastic anemia are rarely reported. Occasionally, plasma creatinine or serum transaminase increased. Very rare hepatitis.

6. Reports of bradycardia, tachycardia, heart block, and allergic vasculitis are extremely rare when using H2 receptor blockers. All these reactions usually disappear after withdrawal.

Overdose

Common are shortness of breath or dyspnea, and tachycardia.

Treatment: first, clear the drugs that have not been absorbed in the gastrointestinal tract, and give

clinical monitoring and support therapy. In case of respiratory failure, give artificial respiration

immediately, and in case of tachycardia β- Receptor blockers.

5. PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic group: H2 receptor blocker, CAS NO.: 51481-61-9

Mechanism of action

Animal pharmacology and toxicology: in vitro studies have shown that this product is a specific competitive H2 receptor antagonist with catecholamine β- Receptors, histamine H1 receptors or muscarinic receptors had no significant interaction. The efficacy of this product for human and experimental animals is very similar according to the dose administered, more specifically the blood concentration reached. In all species animal studies, the blood drug concentration of about 2mol / l can inhibit the maximum gastric acid secretion by 50%. For rats, dogs and mice, the median lethal dose of oral administration is about 2 ~ 3G / kg and that of intravenous administration is 100 ~ 150mg / kg. In the chronic toxicity experiment on dogs, some animals show signs of liver and kidney damage after administration of 504mg / kg. For rats and dogs, this product shows anti androgen effect. After 12 months of administration of 150 ~ 950mg / kg drug, the prostate of male rats in each dose group decreased, and the testis and seminal vesicle gland in the high dose group decreased. The weight of prostate was reduced 12 months after the drug with a dose level of 41 ~ 504mg / kg was given to dogs. The study found that this product has no obvious effect on fertility. For the toxicological study of rats for 24 months, the dose levels were 150378 and 950mg / kg / day (about 4 ~ 24 times the recommended dose for human body). Compared with the control group, the incidence of benign Leydig cell tumor in the drug treatment group was higher and statistically significant. Tumors occurred in both

the control group and the treatment group, and the difference became obvious only in the elderly rats. For intravenous administration studies in dogs, tachycardia and hypotension were observed at a dose level of 25 mg / kg. Tachycardia occurred at an oral dose of 336 mg / kg. Propranolol can prevent or reverse the acceleration of heart rate. For humans, rats and dogs, the pharmacokinetics of this product and its absorption, metabolism and excretion are basically similar. Human pharmacology: effect on basal (non irritating) gastric acid secretion: a double-blind, placebo-controlled study was conducted in patients with duodenal ulcer. A single dose of cimetidine can significantly and continuously reduce basal gastric acid secretion during daytime, fasting and night, which is related to the dose. The degree of inhibition is related to the blood drug level. When the blood drug level exceeds 0.5mg/l, the degree of inhibition can usually reach more than 80%. At different doses, the duration of this level is also different. After a single dose of 200mg, the effect disappears after 4 ~ 5 hours, and at 300mg, the effect disappears after 7 ~ 8 hours. However, 400mg still has an effect after 8 hours. The effect of cimetidine is not only because it can significantly reduce the concentration of gastric acid, but also reduce the secretion of gastric juice. When the effective plasma concentration is reached, the pH level of gastric acid is usually above 5.0, which indicates that pepsin will be inactivated for most of the time during the treatment. Effect on stimulating gastric acid secretion, cimetidine is known to be a powerful inhibitor of gastric acid secretion caused by histamine, pentagastrin, insulin, food or caffeine stimulation in normal people and patients with duodenal ulcer. When the blood drug concentration was 0.5mg/l, the gastric acid secretion was inhibited by 50% or more, and when the blood drug concentration was more than 1.0mg/l, the gastric acid inhibition was up to 80 ~ 90%. The choice of administration time related to the experimental meal affects the pattern of blood drug level. The data show that administration at meal can properly control gastric acid secretion. The study showed that the daily doses of 800mg and 1g reduced the 24-hour gastric acidity by 70% and 72% respectively. In these studies, the effect of cimetidine on pepsin concentration was different, but the total pepsin secretion decreased as a result of the decrease of gastric juice. As mentioned above, when the pH exceeds 5, all secreted pepsins are inactive during this period. This product significantly inhibits the increase of internal factor concentration caused by histamine stimulation, but does not affect the basic level of internal factor. In the study of detecting serum gastrin, as expected, the increase caused by irritants (food, etc.) can be observed. In these studies, when gastric pH was controlled in both placebo and cimetidine groups, there was no significant difference in gastrin levels between the two groups. However, if intragastric pH was not controlled, gastrin levels were higher in the cimetidine group. This appears to be due to the high intragastric pH level caused by cimetidine. Cimetidine had no effect on gastric emptying rate and lower esophageal sphincter (LOS) pressure.

Pharmacokinetic properties

After oral administration, about 60% ~ 70% of the drug is rapidly absorbed by the intestine, and the

peak time of plasma concentration (Tmax) is 45 ~ 90 minutes. Oral bioavailability (f) is about 70%. The absorption of this product by young people is often better than that of the elderly. Plasma protein binding rate is low. The average peak concentration (Cmax) of 300mg was 1.44 μ G / ml can inhibit basal gastric acid secretion by 50% for 4 ~ 5 hours. This product is widely distributed in the whole body (except the brain), metabolized in the liver and excreted mainly through the kidney. After 24 hours, about 48% of the oral dose was discharged from the kidney in its original form; 10% is excreted from feces. This product can be removed by hemodialysis. When the renal function is normal, the half-life (T1 / 2) is 2 hours, the creatinine clearance rate is 20 ~ 50ml / min, the half-life (T1 / 2) is 2.9 hours, when it is < 20ml / min, it is 3.7 hours, and when the renal function is incomplete, it is 5 hours. This product can be transported through placenta and discharged from milk.

Pharmacology and Toxicology

1. Pharmacology

It mainly acts on H2 receptor on gastric parietal cells and plays a competitive role in inhibiting histamine. It can inhibit the secretion of basic gastric acid and gastric acid stimulated by food, histamine, pentagastrin, caffeine and insulin.

2. Toxicology

Acute toxicity: the oral LD50 of mice is 3190 ~ 3280mg / kg, and that of rats is 5840 ~ 7500mg / kg. Subacute and chronic toxicity tests in rats and dogs showed that this product had mild anti androgen effect, resulting in the reduction of the weight of prostate and seminal vesicle and the secretion of milk, but disappeared after stopping the drug. No mutagenic, carcinogenic, teratogenic effects, dependence and drug resistance.

6. PHARMACEUTICAL PARTICULARS

List of excipients：

Maize Starch、Low-Substituted Hydroxypropyl Cellulose、Sodium Starch Glycolate、Magnesium Stearate

Incompatibilities

Not applicable

Shelf life

36 months, at least 5/6th of the shelf life must remain at the time of shipment.

The supplier will provide manufacturer’s stability test data substantiating the claimed shelf life in the offered package

Special precautions for storage

It should be Store in a cool, dry and dark place.Keep out of the reach of children.

Nature and contents of container

This product is white tablet.

Each uncoated caplet contains:Cimetidine B.P. 200 mg

Pack size: Packs of 1000's caplets in HOPE Bottles or 10 Blister strips of 10 caplets in a unit carton or Blister strip of 20 caplets in a unit carton.One small box containing a leaflet showing the summary Instructions for the product

7. SUPPLIER

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