Regd. Office & Factory : Plot No. 33, Sector II, The Vasai Taluka Industrial Co-op. Estate Ltd. Gauraipada, Vasai (E), Dist. Thane - 401 208. INDIA.
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Brand Name : AGOCIM-400 **Generic Name :** Cimetidine Tablets BP 400 mg	2021
Module 1 Administrative Information and Product Information **1.5** Product Information	**Confidential**

1.5 PRODUCT INFORMATION

1.5.1 Prescribing information (Summary of products characteristics)

SUMMARY PRODUCT CHARACTERISTICS

1. Name of drug product:

AGOCIM -400 (Cimetidine Tablets BP 400 mg)

2. Qualitative and Quantitative Composition:

Each film coated tablet contains: Cimetidine BP 400 mg

3. Pharmaceutical form:

Green coloured elongated film coated tablets having a break line on one side of each tablet.

4. Clinical particulars:

4.1 Therapeutic Indications:

histamine H_2 receptor antagonist that inhibits stomach acid production. It is mainly used in the treatment of heartburn and peptic ulcers

The development of longer-acting H_2 receptor antagonists with fewer drug interactions and adverse effects, such as ranitidine and famotidine, decreased the use of cimetidine, and though it is still used, cimetidine is no longer among the more widely used of the H_2 receptor antagonists

Cimetidine was developed in 1971 and came into commercial use in 1977 Cimetidine was approved in the United Kingdom in 1976, and was approved in the United States by the Food and Drug Administration for prescriptions in 1979.

4.2 Posology and Method of Administration:

Benign gastric ulcer:400 mg twice at breakfast bedtime .
Acute duodenal ulcer: 800 mg a bed time.

Prophylaxis of recurrent duodenal ulcer maintain dose of 400 mg at bedtime
Peptic oesophagitis : 0.8-1.6 mg daily-1.6 mg daily.
Persistent dyspeptic symptoms: 200 mg 4 time daily. Max. period of treatment should be 4 weeks 800-1600 mg/ day depending on severity of symptoms, has to be given in 4 divided dose. Maintain 400 mg at bedtime

Method of administration : Oral.

4.3 Contraindications:

- Cimetidine affects the metabolism of methadone, sometimes resulting in higher blood levels and a higher incidence of side effects, and may interact with the antimalarial medication hydroxychloroquine.
- Cimetidine can also interact with a number of psychoactive medications, including tricyclic antidepressants and selective serotonin reuptake inhibitors, causing increased blood levels of these drugs and the potential of subsequent toxicity.
- Following administration of cimetidine, the elimination half-life and area-under-curve of zolmitriptan and its active metabolites were roughly doubled.
- Cimetidine is a potent inhibitor of tubular creatinine secretion. Creatinine is a metabolic byproduct of creatine breakdown. Accumulation of creatinine is associated with uremia, but the symptoms of creatinine accumulation are unknown, as they are hard to separate from other nitrogenous waste buildups.
- Like several other medications (e.g. erythromycin), cimetidine interferes with the body's metabolization of sildenafil, causing its strength and duration to increase (therefore also its side effects to be more likely and prominent).Clinically significant drug interactions with the CYP1A2 substrate theophylline, the CYP2C9 substrate tolbutamide, the CYP2D6 substrate desipramine, and the CYP3A4 substrate triazolam have all been demonstrated with cimetidine, and interactions with other substrates of these enzymes are likely as well.
- Cimetidine has been shown clinically to reduce the clearance of mirtazapine, imipramine, timolol, nebivolol, sparteine, loratadine, nortriptyline, gabapentin, and desipramine in humans.
- Cimetidine inhibits the renal excretion of metformin and procainamide, resulting in increased circulating levels of these drugs.
- Interactions of potential clinical importance with cimetidine include warfarin, theophylline, phenytoin, carbamazepine, pethidine and other opioid analgesics, tricyclic antidepressants, lidocaine, terfenadine, amiodarone, flecainide, quinidine, fluorouracil, and benzodiazepines
- Cimetidine may decrease the effects of CYP2D6 substrates that are prodrugs, such as codeine, tramadol, and tamoxifen.
- Cimetidine reduces the absorption of ketoconazole and itraconazole (which require a low pH).
- Cimetidine has a theoretical but unproven benefit in paracetamol toxicity. This is because N-acetyl-p-benzoquinone imine (NAPQI), a metabolite of paracetamol (acetaminophen) that is responsible for its hepatotoxicity, is

formed from it by the cytochrome P450 system (specifically, CYP1A2, CYP2E1, and CYP3A4).

4.4 Special Warnings and Precautions for Use :

Exclude presence of gastric malignancy. Pregnancy, lactation, Impaired renal function

4.5 Pregnancy and Lactation:

Exclude presence of gastric malignancy. Pregnancy, lactation, Impaired renal function

4.6 Overdose:

Cimetidine appears to be very safe in overdose, producing no symptoms even with massive overdoses

5. Pharmacological properties:

5.1 Pharmacodynamic properties:

Histamine H_2 receptor antagonism

The mechanism of action of cimetidine as an antacid is as a histamine H_2 receptor antagonist. It has been found to bind to the H_2 receptor with a K_d of 42 nM.

Cytochrome P450 inhibition[edit]

Cimetidine is a potent inhibitor of certain cytochrome P450 (CYP) enzymes including CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4 drug appears to primarily inhibit CYP1A2, CYP2D6, and CYP3A4, of which it is described as a moderate inhibitor.This is notable since these three CYP isoenzymes are involved in CYP-mediated drug biotransformations; however, CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4 are also involved in the oxidative metabolism of many commonly used drugs.As a result, cimetidine has the potential for a large number of pharmacokinetic interactions.

Cimetidine is reported to be a competitive and reversible inhibitor of several CYP enzymes,alhough mechanism-based (suicide) irreversible inhibition has also been identified for cimetidine's inhibition of CYP2D6− t reversibly inhibits CYP enzymes by binding directly with the complexed heme-iron of the active site via one of its imidazole ring nitrogen atoms, thereby blocking the oxidation of other drugs.

5.2 Pharmacokinetic Properties:

Cimetidine is rapidly absorbed regardless of route of administration The oral bioavailability of cimetidine is 60 to 70%. The onset of action of cimetidine when taken orally is 30 minutes, and peak levels occur within 1 to 3 hours—Cimetidine is widely distributed throughout all tissues. It is able to cross the blood–brain barrier and can produce effects in the central nervous system (e.g., headaches, dizziness, somnolence). The volume of distribution of cimetidine is 0.8 L/kg in adults and 1.2 to 2.1 L/kg in children. Its plasma protein binding is 13 to 25% and is said to be without pharmacological significance. Cimetidine undergoes relatively little metabolism, with 56 to 85% excreted unchanged. It is metabolized in the liver into cimetidine sulfoxide, hydroxycimetidine, and guanyl urea cimetidine. The major metabolite of cimetidine is the sulfoxide, which accounts for about 30% of excreted material.Cimetidine is rapidly eliminated, with an elimination half-life of 123 minutes, or about 2 hours. It has been said to have a duration of action of 4 to 8 hours. The medication is mainly eliminated in urine.

6. Pharmaceutical particulars:

6.1 List of Excipients:

Lactose	BP
Microcrystalline cellulose	BP
Maize starch	BP
Methyl Paraben sodium	BP
Propyl Paraben sodium	BP
Purified talc	BP
Sodium Starch Glycolate	BP
Magnesium stearate	BP
Colloidal silicon dioxide	BP
Sodium Lauryl sulphate	BP
Cross Carmellose sodium	BP
Polacrilin potassium	USP
Polyplasdone XL-10	USP
Iso Propyl alcohol	BP
Colour instacoat sol Green IC-S-798 INH	

6.2 Incompatibilities:
None Reported

6.3 Shelf-Life:
36 months from the date of manufacture.

6.4 Special Precautions for Storage:
Store in a cool, dry and dark place. Protect from light.

6.5 Nature and Contents of Container:
10 tablets packed in one blister. Such 10 blister packed in unit printed duplex board carton along with its package insert. Such cartons packed in export worthy shipper.

1000 tablets packed in one jar. Such jar packed in export worthy shipper.

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6.6 Special precautions for disposal:
None reported.

7. Registrant:
AGOG PHARMA LTD.
Plot No. 33, Sector II,
The Vasai Taluka Industrial
Co-Op. Estate Ltd., Gauraipada,
Vasai (E), Dist. Thane, India.

8. Manufacturer:
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9. Date of revision of the text :