

Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product

ALBIC FORTE 20 TABLET (Esomeprazole 20 mg Tab)

2. Qualitative and quantitative composition

Each enteric-coated tablet contains Esomeprazole 20 mg (as Esomeprazole Magnesium Trihydrate)

Excipients of known effect: Propylene Glycol

For the full list of excipients, see section 6.1

3. Pharmaceutical form

Yellowish, oval biconvex enteric coated tablet with both sides plain.

4. Clinical particulars

4.1 Therapeutic indications

Albic 20 (Esomeprazole) is indicated for the treatment of

- Risk Reduction of NSAID-associated gastric ulcer& duodenal ulcer
- Treatment of Gastro esophageal reflux disease (GERD)
- Healing of Erosive Esophagitis
- Peptic Ulcer disease (PUD)
- H. Pylori eradication (Triple therapy)
- Zollinger-Ellision Syndrome

4.2 Posology and method of administration

DOSAGE AND ADMINISTRATION

Indications	Dose and Frequency
Healing of erosive esophagitis	20 mg or 40 mg once daily
Symptomatic GERD	20 mg once daily
Risk reduction of NSAID associated gastric ulcer	20 mg or 40 mg once daily
Duodenal ulcer associated gastric ulcer, Gastro esophageal reflux disease(GERD) with erosive esophagitis	20 to 40 mg per day

4.3 Contraindications

Esomeprazole is contraindicated in those who have known hypersensitivity to any other components of the formulation or to substituted benzimidazoles.

4.4 Special warnings and precautions for use

Proton pump inhibitors may mask the symptoms of gastric cancer, particular care is required in those presenting with alarm feature, (bleeding, recurrent vomiting, dysphagia), in such cases gastric malignancy should be ruled out before treatment.

4.5 Interaction with other medicinal products and other forms of interaction

Gastric acid suppression during treatment with esomeprazole and other PPIs might decrease or increase the absorption of medicinal products with a gastric pH dependent absorption. As with other medicinal products that decrease intragastric acidity, the absorption of medicinal products such as ketoconazole, itraconazole and erlotinib can decrease and the absorption of digoxin can increase during treatment with esomeprazole. Concomitant treatment with omeprazole (20 mg daily) and digoxin in healthy subjects increased the bioavailability of digoxin by 10% (up to 30% in two out of ten subjects). Digoxin toxicity has been rarely reported. However, caution should be exercised when esomeprazole is given at high doses in elderly patients. Therapeutic drug monitoring of digoxin should then be reinforced.

Protease inhibitors

Omeprazole has been reported to interact with some protease inhibitors. The clinical importance and the mechanisms behind these reported interactions are not always known.

Increased gastric pH during omeprazole treatment may change the absorption of the protease inhibitors. Other possible interaction mechanisms are via inhibition of CYP 2C19.

For atazanavir and nelfinavir, decreased serum levels have been reported when given together with omeprazole and concomitant administration is not recommended. Co-administration of omeprazole (40 mg once daily) with atazanavir 300 mg/ritonavir 100 mg to healthy volunteers resulted in a substantial reduction in atazanavir exposure (approximately 75% decrease in AUC, C_{max} and C_{min}). Increasing the atazanavir dose to 400 mg did not compensate for the impact of omeprazole on atazanavir exposure. The co-administration of omeprazole (20 mg qd) with atazanavir 400 mg/ritonavir 100 mg to healthy volunteers resulted in a decrease of approximately 30% in the atazanavir exposure as compared with the exposure observed with atazanavir 300 mg/ritonavir 100 mg qd without omeprazole 20 mg qd. Co-administration of omeprazole (40 mg qd) reduced mean nelfinavir AUC, C_{max} and C_{min} by 36-39 % and mean AUC, C_{max} and C_{min} for the pharmacologically active metabolite M8 was reduced by 75-92%. Due to the similar pharmacodynamic effects and pharmacokinetic properties of omeprazole and esomeprazole, concomitant administration with esomeprazole and atazanavir is not recommended (see section 4.4) and concomitant administration with esomeprazole and nelfinavir is contraindicated (see section 4.3).

For saquinavir (with concomitant ritonavir), increased serum levels (80-100%) have been reported during concomitant omeprazole treatment (40 mg qd). Treatment with omeprazole

20 mg qd had no effect on the exposure of darunavir (with concomitant ritonavir) and amprenavir (with concomitant ritonavir). Treatment with esomeprazole 20 mg qd had no effect on the exposure of amprenavir (with and without concomitant ritonavir). Treatment with omeprazole 40 mg qd had no effect on the exposure of lopinavir (with concomitant ritonavir).

Methotrexate

When given together with PPIs, methotrexate levels have been reported to increase in some patients. In high- dose methotrexate administration a temporary withdrawal of esomeprazole may need to be considered.

Tacrolimus

Concomitant administration of esomeprazole has been reported to increase the serum levels of tacrolimus. A reinforced monitoring of tacrolimus concentrations as well as renal function (creatinine clearance) should be performed, and dosage of tacrolimus adjusted if needed.

Medicinal products metabolised by CYP2C19

Esomeprazole inhibits CYP2C19, the major esomeprazole-metabolising enzyme. Thus, when esomeprazole is combined with medicinal products metabolised by CYP2C19, such as diazepam, citalopram, imipramine, clomipramine, phenytoin etc., the plasma concentrations of these medicinal products may be increased and a dose reduction could be needed. This should be considered especially when prescribing esomeprazole for on-demand therapy.

Diazepam

Concomitant administration of 30 mg esomeprazole resulted in a 45% decrease in clearance of the CYP2C19 substrate diazepam.

Phenytoin

Concomitant administration of 40 mg esomeprazole resulted in a 13% increase in trough plasma levels of phenytoin in epileptic patients. It is recommended to monitor the plasma concentrations of phenytoin when treatment with esomeprazole is introduced or withdrawn.

Voriconazole

Omeprazole (40 mg once daily) increased voriconazole (a CYP2C19 substrate) C_{max} and AUC_{0-12h} by 15% and 41%, respectively.

Warfarin

Concomitant administration of 40 mg esomeprazole to warfarin-treated patients in a clinical trial showed that coagulation times were within the accepted range. However, post-marketing, a few isolated cases of elevated INR of clinical significance have been reported during concomitant treatment. Monitoring is recommended when initiating and ending concomitant esomeprazole treatment during treatment with warfarin or other coumarine derivatives.

Cilostazol

Omeprazole as well as esomeprazole act as inhibitors of CYP2C19. Omeprazole, given in doses of 40 mg to healthy subjects in a cross-over study,

increased C_{max} and AUC for cilostazol by 18% and 26% respectively, and one of its active metabolites by 29% and 69% respectively.

Cisapride

In healthy volunteers, concomitant administration of 40 mg esomeprazole resulted in a 32% increase in area under the plasma concentration-time curve (AUC) and a 31% prolongation of elimination half-life ($t_{1/2}$) but no significant increase in peak plasma levels of cisapride. The slightly prolonged QT_c interval observed after administration of cisapride alone, was not further prolonged when cisapride was given in combination with esomeprazole (see also section 4.4).

Clopidogrel

Results from studies in healthy subjects have shown a pharmacokinetic (PK)/pharmacodynamic (PD) interaction between clopidogrel (300 mg loading dose/75 mg daily maintenance dose) and esomeprazole (40mg p.o.daily) resulting in decreased exposure to the active metabolite of clopidogrel by an average of 40% and resulting in decreased maximum inhibition of (ADP induced) platelet aggregation by an average of 14%.

When clopidogrel was given together with a fixed dose combination of esomeprazole 20 mg

+ ASA 81 mg compared to clopidogrel alone in a study in healthy subjects there was a decreased exposure by almost 40% of the active metabolite of clopidogrel. However, the maximum levels of inhibition of (ADP induced) platelet aggregation in these subjects were the same in the clopidogrel and the clopidogrel + the combined (esomeprazole + ASA) product groups.

Inconsistent data on the clinical implications of a PK/PD interaction of esomeprazole in terms of major cardiovascular events have been reported from both observational and clinical studies. As a precaution concomitant use of clopidogrel should be discouraged.

In a crossover clinical study, clopidogrel (300 mg loading dose followed by 75 mg/day) alone and with omeprazole (80 mg at the same time as clopidogrel) were administered for 5 days. The exposure to the active metabolite of clopidogrel was decreased by 46% (Day 1) and 42% (Day 5) when clopidogrel and omeprazole were administered together. Mean inhibition of platelet aggregation (IPA) was diminished by 47% (24 hours) and 30% (Day 5) when clopidogrel and omeprazole were administered together. In another study it was shown that administering clopidogrel and omeprazole at different times did not prevent their interaction that is likely to be driven by the inhibitory effect of omeprazole on CYP2C19. Inconsistent data on the clinical implications of this PK/PD interaction in terms of major cardiovascular events have been reported from observational and clinical studies.

4.6 Pregnancy and Lactation

There are no adequate and well-controlled studies in pregnant women. Esomeprazole should be used during pregnancy only if clearly needed. Esomeprazole is likely to be excreted in human milk; a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

Esomeprazole has minor influence on the ability to drive and use machines. Adverse reactions such as dizziness (uncommon) and blurred vision (rare) has been reported (see section 4.8). If affected patients should not drive or use machines.

4.8 Undesirable effects

In general, Esomeprazole is well tolerated in both short and long-term use. Common side effects reported with Esomeprazole include headache, diarrhea, abdominal pain, flatulence, nausea and constipation.

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via the relevant national regulatory authority pharmacovigilance.

4.9 Overdose

There is very limited experience to date with deliberate overdose.

Symptoms

The symptoms described in connection with 280 mg were gastrointestinal symptoms and weakness. Single doses of 80 mg esomeprazole were uneventful.

Management

No specific antidote is known. Esomeprazole is extensively plasma protein bound and is therefore not readily dialyzable. As in any case of overdose, treatment should be symptomatic and general supportive measures should be utilized.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs for acid related disorders, proton pump inhibitors ATC code: A02BC05

Esomeprazole is the *S*-isomer of omeprazole. and reduces gastric acid secretion through a specific targeted mechanism of action. It is a specific inhibitor of the acid pump in the parietal cell. Both the *R*- and *S*-isomer of omeprazole have similar pharmacodynamic activity.

Mechanism of action

Esomeprazole is a weak base and is concentrated and converted to the active form in the highly acidic environment of the secretory canaliculi of the parietal cell, where it inhibits the enzyme $H^+K^+-ATPase$ – the acid pump and inhibits both basal and stimulated acid secretion.

5.2 Pharmacokinetic properties

Absorption

Absorption of esomeprazole is rapid, with peak plasma levels occurring approximately 1-2 hours after dose. The absolute bioavailability is 64 % after a single dose of 40 mg and increases to 89 % after repeated once-daily administration. For 20 mg esomeprazole the corresponding values are 50 % and 68 %, respectively.

Food intake both delays and decreases the absorption of esomeprazole although this has no significant influence on the effect of esomeprazole on intragastric acidity.

Distribution

The apparent volume of distribution at steady state in healthy subjects is approximately 0.22 l/kg body weight. Esomeprazole is 97 % plasma protein bound.

Biotransformation

Esomeprazole is completely metabolized by the cytochrome P450 system (CYP). The major part of the metabolism of esomeprazole is dependent on the polymorphic CYP2C19, responsible for the formation of the hydroxy- and desmethyl metabolites of esomeprazole. The remaining part is dependent on another specific isoform, CYP3A4, responsible for the formation of esomeprazole sulphone, the main metabolite in plasma.

Elimination

The parameters below reflect mainly the pharmacokinetics in individuals with a functional CYP2C19 enzyme, extensive metabolizers.

Total plasma clearance is about 17 l/h after a single dose and about 9 l/h after repeated administration. The plasma elimination half-life is about 1.3 hours after repeated once-daily dosing. Esomeprazole is completely eliminated from plasma between doses with no tendency for accumulation during once-daily administration.

The major metabolites of esomeprazole have no effect on gastric acid secretion. Almost 80% of an oral dose of esomeprazole is excreted as metabolites in the urine, the remainder in the faeces. Less than 1% of the parent drug is found in urine.

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 and development. Adverse reactions not observed in clinical studies, but seen in animals at exposure levels similar to clinical exposure levels and with possible relevance to clinical use were as follows:

No new or unexpected toxicity findings were observed in juvenile rats and dogs, after administration of esomeprazole for up to 3 months, as compared to adult animals.

Carcinogenicity studies in the rat with the racemic mixture have shown gastric ECL-cell hyperplasia and carcinoids. These gastric effects in the rat are the result of sustained, pronounced hypergastrinemia secondary to reduced production of gastric acid and are observed after long-term treatment in the rat with inhibitors of gastric acid secretion.

No new or unexpected toxicity findings were observed in juvenile rats and dogs, after administration of esomeprazole for up to 3 months, as compared to adult animal.

6. Pharmaceutical Particulars

6.1 List of Excipients

Name

Microcrystalline Cellulose (Avicel PH 102)
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Sodium Starch Glycolate (Type A)

Magnesium Stearate

Hypromellose (HPMC - 2910), 15cps

Purified Talc

Methanol

Dichloromethane (Methylene Chloride)

Methacrylic Acid-Ethyl Acrylate Copolymer 1:1 (Kollicoat MAE 100P)
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Propylene Glycol

Egg Yellow Color

Titanium Dioxide

Purified Water

6.2 Incompatibilities

The product is stable for the mentioned shelf life. So it can be assured that there is no incompatibility with active and excipients.

6.3 Shelf-Life

Two (2) years from the date of manufacturing when it is kept in original pack. Best use, immediately after opening the blister.

6.4 Special Precautions for storage

Store below 30°C. Protect from direct sunlight and heat.

Keep out of children's reach. To be issued strictly on a medical prescription.

6.5 Nature and Content of container

Blister pack:

Alu – Alu blister pack of 10 tablets

6.6 Special precautions for disposal and other handling

No special requirements

7. Marketing Authorization Holder

Name: Aliction Limited

Address : Kangemi Plaza ,9244-00100, Nairobi, Kenya

8. Marketing Authorization Number

H2022/CTD10591/22478

9. Date of first authorization/renewal of the authorization

31/10/2023

10. Date of revision of the text

31/10/2023