ESPLUS IT

(Enteric coated Esomeprazole Magnesium and Sustained Release Itopride HCL Capsules)

Summary of Product Characteristics (SmPC)

1. Name of the medicinal product:

ESPLUS IT (Enteric coated Esomeprazole Magnesium and Sustained Release Itopride HCL Capsules)

2. Qualitative and quantitative composition

Each capsule contains 40 mg Esomeprazole Magnesium Trihydrate USP equivalent to Esomeprazole (as enteric coated pellets) and 150 mg Itopride Hydrochloride (as sustained release pellets).

Excipients of Known effects:

"For the full list of excipients see section 6.1"

3. PHARMACEUTICAL FORM

Capsule

Green cap/green body size '0' hard gelatin capsules containing white and off white pellets.

4.CLINICAL PARTICULARS

4.1 Therapeutic indications

ESPLUS IT CAPSULES is a combination medicine of Esomeprazole & Itopride, where Esomeprazole is a proton pump inhibitor and Itopride is a gastroprokinetic agent used to treat acidity, gastro-oesophageal reflux disease (GERD), stomach ulcers (peptic ulcers, gastric ulcers due to H pylori), heartburn symptoms and Zollinger Ellison syndrome.

4.2 Posology and method of administration

Take ESPLUS IT CAPSULES 30-60 minutes before taking food/meal.

Swallow ESPLUS IT CAPSULES as a whole with a glass of water; do not chew, or crush the capsule. Depending on your medical condition, your doctor will decide how long you need to take ESPLUS IT CAPSULES.

Patients with kidney problems

Dose adjustment may be needed. Consult your doctor before taking ESPLUS IT CAPSULES if you have kidney impairment or any concerns regarding this.

Patients with liver problems

Dose adjustment may be needed. Consult your doctor before taking ESPLUS IT CAPSULES if you have a liver impairment or any concerns regarding this.

Method of administration

Oral

4.3 Contraindications

Hypersensitivity to esomeprazole magnesium trihydrate and/or Itopride HCl , or to any of the excipients used n this formulation.

4.4 Special warnings and precautions for use

Talk to your doctor if

- You are allergic to the active ingredient esomeprazole or any other medicine.
- You have unexplained weight loss, frequent vomiting, difficulty in swallowing and blood vomiting.
- You are undergoing long-term treatment with this medicine.
- You are undergoing treatment for a bacterial infection caused by H. pylori and are using an antibiotic called Clarithromycin.
- You develop stomach infections after using ESPLUS IT CAPSULES.
- You have a vitamin B12 deficiency. The use of ESPLUS IT CAPSULES can result in very low levels of Vitamin B12 during prolonged therapy.
- You have a magnesium deficiency. It can result in very low levels of magnesium characterized by weakness, fits and irregular heartbeats.
- You are an elderly patient on long-term therapy. It increases the risk of fracture of the hip, wrist and spine bones.
- You have a skin disorder, subacute cutaneous lupus erythematosus, characterised by a rash on the areas of the skin exposed to the Sun.
- You are using anti-HIV medicines like Atazanavir or Nelfinavir.

4.5 Interaction with other medicinal products and other forms of interaction

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

- ESPLUS IT CAPSULES may affect the way other medicines work and other medicines may affect how ESPLUS IT CAPSULES works if taken at the same time.
- Always inform your doctor about all the medications you are taking, which includes all prescribed or non-prescribed herbal medicines, dietary supplements as well as other treatments if you are taking.
- Especially if you are taking medicines for heart-related disorders like digoxin, brain-related diseases, anti-epileptic medicines like phenytoin, anti-fungal medicines, antipsychotic medicines, etc.
- ESPLUS IT CAPSULES can decrease the effect of Anti-HIV medicines if taken along.
- The blood-thinning action of Warfarin is increased when used together with ESPLUS IT CAPSULES and there is a risk of bleeding.
- Other medicines such as cisapride (used for constipation), clopidogrel (Blood-thinner), and tacrolimus (immunosuppressants) should be used cautiously with ESPLUS IT CAPSULES.

4.6 Fertility, pregnancy and lactation

Pregnancy: ESPLUS IT CAPSULES can be used during pregnancy. However, it should be used only under the recommendation of a doctor after assessing if this medicine is beneficial and will not harm the unborn child.

Breastfeeding: ESPLUS IT CAPSULES should not be used by lactating mothers as it is not known if this medicine is passed into the breastmilk and can have undesirable effects on the nursing infant.

4.7 Effects on ability to drive and use machines

None stated

4.8 Undesirable effects

COMMON: Headache**,** Dizziness and shaking of hands**,** Diarrhoea, stomach pain, constipation, flatulence, nausea, vomiting**,** Easy bruising**,** Increased milk production**,** Excessive development of breasts in male, Yellowing of skin and eyes**,** Skin rash, redness, and itching
UNCOMMON: Swelling of the feet and ankles**,** Difficulty in falling asleep**,** Tingling or pricking feeling in nerves**,** Excessive sleepiness**,** Head spinning sensation (vertigo)**,** Dry mouth**,** Hip, wrist, or spine fractures (if used in high dose and long duration)
RARE: Signs of reduced white blood cells (weakness, or more chances of infections)**,** Weakness, cramps
Feeling agitated, confused, or depressed, Taste changes, Eyesight problems like blurred vision, Suddenly feeling of wheezing or breathlessness, Inflammation inside the mouth, Thrush (fungal infection of the gut), Hair loss, Joint or muscle pains, Generally feeling unwell and lacking energy, Increased sweating.

Stop taking ESPLUS IT CAPSULES and consult your doctor immediately if you experience any of the following side effects:
Low magnesium levels (signs include extreme tiredness, involuntary muscle contractions, disorientation, fits, dizziness or increased heart rate)
Severe allergic reaction (signs include sudden wheezing, swelling of your lips, tongue and throat or body, rash, fainting, or trouble swallowing)
Steven-johnson syndrome or toxic epidermal necrolysis (signs include reddening of the skin with blisters or peeling, severe blisters and bleeding in the lips, eyes, mouth, nose, genitals)
Signs of liver problems (such as yellow skin, dark urine, or tiredness)

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 Pharmacovigilance
Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org/

4.9 Overdose

There are no known symptoms of overdose in man.
If you or anyone else accidentally take too much of **ESPLUS IT CAPSULES,** consult your doctor immediately or visit the nearby hospital.

5.PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ESOMEPRAZOLE MAGNESIUM

ESPLUS IT

(Enteric coated Esomeprazole Magnesium and Sustained Release Itopride HCL Capsules)

Summary of Product Characteristics (SmPC)

Pharmacotherapeutic group: Drugs for acid related disorders, proton pump inhibitors.
ATC Code: A02BC05
Mechanism of action: 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.

ITOPRIDE HCl
Pharmacotherapeutic group: Drugs for functional gastrointestinal disorders, propulsives.
ATC Code: A03FA07
Mechanism of action
Itopride activates the gastrointestinal propulsive motility by dopamine D2 receptors antagonistic action and acetylcholine esterase inhibitory action. Itopride activates acetylcholine release and inhibits its degradation. In addition, itopride has an antiemetic action which is based on interaction with dopamine D2 receptors in chemoreceptor zone. Itopride accelerates stomach emptying in humans and does not influence plasma concentrations of gastrin.

5.2 Pharmacokinetic properties
ESOMEPRAZOLE MAGNESIUM
Absorption
Esomeprazole is acid labile and is administered orally as enteric-coated granules.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.
Metabolism
Esomeprazole is completely metabolised 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 metabolisers. 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 compound is found in urine.

Linearity/non-linearity

The pharmacokinetics of esomeprazole has been studied in doses up to 40 mg b.i.d. The area under the plasma concentration-time curve increases with repeated administration of esomeprazole. This increase is dose-dependent and results in a more than dose proportional increase in AUC after repeated administration. This time- and dose-dependency is due to a decrease of first pass metabolism and systemic clearance probably caused by an inhibition of the CYP2C19 enzyme by esomeprazole and/or its sulphone metabolite.

Special patient populations

Poor metabolisers

Approximately 2.9±1.5% of the population lack a functional CYP2C19 enzyme and are called poor metabolisers. In these individuals the metabolism of esomeprazole is probably mainly catalysed by CYP3A4. After repeated once-daily administration of 40 mg esomeprazole, the mean area under the plasma concentration-time curve was approximately 100% higher in poor metabolisers than in subjects having a functional CYP2C19 enzyme (extensive metabolisers). Mean peak plasma concentrations were increased by about 60%. These findings have no implications for the posology of esomeprazole.

Gender

Following a single dose of 40 mg esomeprazole the mean area under the plasma concentration-time curve is approximately 30% higher in females than in males. No gender difference is seen after repeated once-daily administration. These findings have no implications for the posology of esomeprazole.

Hepatic impairment

The metabolism of esomeprazole in patients with mild to moderate liver dysfunction may be impaired. The metabolic rate is decreased in patients with severe liver dysfunction resulting in a doubling of the area under the plasma concentration-time curve of esomeprazole. Therefore, a maximum of 20 mg should not be exceeded in patients with severe dysfunction.

Esomeprazole or its major metabolites do not show any tendency to accumulate with once-daily dosing.

Renal impairment

No studies have been performed in patients with decreased renal function. Since the kidney is responsible for the excretion of the metabolites of esomeprazole but not for the elimination of the parent compound, the metabolism of esomeprazole is not expected to be changed in patients with impaired renal function.

Elderly

The metabolism of esomeprazole is not significantly changed in elderly subjects (71-80 years of age).

Paediatric population

Adolescents 12-18 years: Following repeated dose administration of 20 mg and 40 mg esomeprazole, the total exposure (AUC) and the time to reach maximum plasma concentration (tmax) in 12 to18 year-olds was similar to that in adults for both esomeprazole doses.

ITOPRIDE HCl

Absorption: On oral administration, Itopride is rapidly and extensively absorbed and peak serum concentrations are achieved within 35 minutes after oral dosing. Food does not affect its absorption.

Metabolism: Itopride is metabolized in the liver by N-oxidation to inactive metabolites by the enzyme
flavin-containing monooxygenase (FMO). Biotransformation of itopride does not involve the cytochrome P450 enzyme system, thus, it is devoid of drug interaction potential with cytochrome P450 enzyme inhibitors.

Excretion: The half-life of Itopride is about 6 hours. It is excreted mainly by the kidneys as metabolites and unchanged drug. Food did not significantly affect the absorption of Itopride.

5.3 Preclinical safety data

ESOMEPRAZOLE MAGNESIUM

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 Health clinical studies, but seen in animals at exposure levels similar to clinical exposure levels and with possible relevance to clinical use were as follows: 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 hypergastrinaemia secondary to reduced production of gastric acid and are observed after long-term treatment in the rat with inhibitors of gastric acid secretion.

ITOPRIDE HCl

Preclinical safety studies were carried out only at exposures considered sufficiently in excess of therapeutic human doses indicating little relevance to clinical use. In addition humans are less sensitive to hormonal effects observed in animals. High doses of itopride (30 mg/kg/day) caused hyperprolactinaemia and secondary reversible hyperplasia of uterine mucosa in rats, but not in dogs (dose up to 100 mg/kg/day) or primates (dose up to 300 mg/kg/day). In a 3-month toxicity study in dogs, prostate atrophy was observed after oral doses of 30 mg/kg/day, but not after 6-month oral administration of higher doses (100 mg/kg/day) in rats, nor more higher doses (300 mg/kg/day) in primates. Long-term studies of carcinogenic potential in animals have

not been carried out. No clastogenic or mutagenic effects of itopride were found in a series of in vitro and in vivo tests. Fertility studies in female rats receiving doses of 30 mg/kg/day and higher, showed hyperprolactinaemia and secondary prolongation of oestral cycle. Prolonged precoital interval was observed at doses 300 mg/kg/day. No side effect on copulation or fertility were observed.

6.PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Green Cap/Green Body Size '0' Hard Gelatin Capsules

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 30°C. Protect from light and moisture.

6.5 Nature and contents of container

10 capsules are packed in ALU-ALU blister, such 3 blisters packed in one carton with insert coded with batch number, manufacturing date and expiry date packed in an inner carton.

6.6 Special precautions for disposal and other handling

Not applicable

7. Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
NATIONAL PHARMACY LTD.
P.O. Box 17843-00500,
Nairobi, Kenya

Manufacturer:
ZAIN PHARMA LIMITED
Plot No: 209/13741, Colchester Park,
Go-Down No.1, 2, 3, Off Mombasa Road,
Behind Nice And Lovely House,
P.O. Box: 100167-00101, Nairobi, Kenya

8. Marketing Authorization Number:

H2025/CTD12243/26497

9. Date of First <Registration> / Renewal of The <Registration>

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November 2025

10. Date of Revision of the Text:

November 2025