SUMMARY OF PRODUCT CHARACTERISTICS
NAPROMED (Naproxen 500 mg / Esomeprazole 20 mg Modified-Release Tablets)

1. NAME OF THE MEDICINAL PRODUCT

NAPROMED (Naproxen 500 mg / Esomeprazole Magnesium 20 mg Modified-Release Tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each modified-release tablet contains naproxen 500 mg and esomeprazole magnesium equivalent to esomeprazole 20 mg.

Excipients with known effect:

Contains lactose and propylene glycol. For warnings, see section 4.4.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Modified-release tablet.

White, capsule-shaped, film-coated tablet, scored on one side and plain on the other. The score line is not intended to divide the tablet; the tablet must be swallowed whole.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

NAPROMED is indicated in adults for the symptomatic treatment of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis, in patients who are at risk for developing NSAID-associated gastric and/or duodenal ulcers and where treatment with lower doses of naproxen or of other NSAIDs is not considered sufficient.

4.2 Posology and method of administration

The recommended dose is one tablet (naproxen 500 mg / esomeprazole 20 mg) twice daily. The lowest effective dose should be used for the shortest duration necessary to control symptoms. Treatment should be reviewed periodically. If treatment with naproxen alone is discontinued, the need for continued PPI therapy should be re-evaluated.

Renal impairment

NAPROMED should be used with caution in patients with mild to moderate renal impairment with regular monitoring. NAPROMED is contraindicated in patients with severe renal impairment (creatinine clearance <30 ml/min) — see section 4.3. When the total daily naproxen dose of 1,000 mg is not considered appropriate, alternative treatment with a lower naproxen dose as non-fixed combination should be used.

Hepatic impairment

NAPROMED should be used with caution in patients with mild to moderate hepatic impairment with close monitoring. NAPROMED is contraindicated in patients with severe hepatic impairment — see section 4.3.

Elderly

Elderly patients are at increased risk of serious adverse reactions. If treatment is considered necessary, the lowest effective dose should be used with regular monitoring for GI bleeding.

Paediatric population

Safety and efficacy in children and adolescents below 18 years of age have not been established. Not recommended.

Method of administration

For oral use. Tablets should be swallowed whole with water; do not split, chew or crush. Should be taken at least 30 minutes before meals.

4.3 Contraindications

- Hypersensitivity to naproxen, esomeprazole, any other substituted benzimidazole or to any of the excipients listed in section 6.1.
- History of asthma, urticaria or allergic-type reactions induced by acetylsalicylic acid or other NSAIDs.

- Third trimester of pregnancy.
- Severe hepatic impairment.
- Severe heart failure.
- Severe renal impairment (creatinine clearance <30 ml/min).
- Active peptic ulceration or gastrointestinal bleeding.
- Concomitant use with atazanavir or nelfinavir (due to the esomeprazole component).

4.4 Special warnings and precautions for use

Gastrointestinal effects (naproxen)

GI bleeding, ulceration or perforation — which can be fatal — has been reported with all NSAIDs at any time during treatment, with or without warning symptoms or previous GI history. Risk is higher with increasing NSAID doses, in patients with a history of ulcer (particularly complicated), and in the elderly. Concomitant use of protective agents (e.g. misoprostol or PPIs) should be considered in patients at risk.

Cardiovascular and cerebrovascular effects

Appropriate monitoring and advice are required for patients with hypertension and/or mild to moderate congestive heart failure. Clinical trial data suggest that use of naproxen, particularly at high dose and in long-term treatment, may be associated with a small increased risk of arterial thrombotic events. Naproxen may be associated with a lower cardiovascular thrombotic risk than selective COX-2 inhibitors and some other NSAIDs.

Renal effects

Renal impairment may be precipitated by NSAID use. Patients at greatest risk are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics and the elderly. NAPROMED is contraindicated in patients with a baseline creatinine clearance less than 30 ml/min.

Acute tubulointerstitial nephritis (TIN)

Acute TIN has been observed with esomeprazole and naproxen-containing products and may occur at any time during NAPROMED therapy. Acute TIN can progress to renal failure. If TIN is suspected, NAPROMED should be discontinued and appropriate measures taken.

Esomeprazole-related warnings

Gastric/oesophageal malignancy: Symptomatic response to NAPROMED does not preclude the possibility of malignancy; exclude malignancy before commencing treatment. Hypomagnesaemia: Severe hypomagnesaemia has been reported with PPIs taken for at least 3 months, most commonly >1 year. Monitor magnesium before and during treatment in patients on prolonged therapy or taking PPIs with digoxin or magnesium-lowering drugs. Clostridium difficile: Acid-suppressing therapy may increase the risk of GI infections. Bone fractures: PPIs — especially at high doses for >1 year — may modestly increase the risk of hip, wrist and spine fractures. Interference with CgA testing: Stop NAPROMED for at least 5 days before CgA measurement.

Haematological effects (naproxen)

Patients with coagulation disorders or on anticoagulant therapy should be closely monitored.

Pregnancy

NAPROMED should not be initiated during pregnancy. See section 4.6 and the contraindication for the third trimester.

Lactose and propylene glycol

This product contains lactose and propylene glycol. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. Propylene glycol may cause irritation.

4.5 Interaction with other medicinal products and other forms of interaction

Anticoagulants and antiplatelet agents:

Concomitant use increases the risk of bleeding.

Other NSAIDs and corticosteroids:

Increased frequency of gastrointestinal undesirable effects.

Antihypertensives and diuretics:

NSAIDs may reduce the effect of these agents. ACE inhibitors, ARBs or diuretics combined with NSAIDs increase the risk of acute renal failure, especially in the elderly.

Lithium:

NSAIDs may increase plasma concentrations of lithium; frequent monitoring is required.

Methotrexate:

Caution if NSAIDs and methotrexate are administered within 24 hours of each other. Temporary withdrawal of NAPROMED is recommended with high-dose methotrexate.

Ciclosporin:

NSAIDs may increase nephrotoxicity; monitor renal function.

SSRIs:

Increased risk of gastrointestinal bleeding with concomitant NSAIDs.

Quinolone antibiotics:

Increased risk of convulsions.

Atazanavir and nelfinavir (contraindicated):

Esomeprazole significantly reduces plasma concentrations of these HIV protease inhibitors.

CYP2C19 substrates (e.g. clopidogrel):

Esomeprazole inhibits CYP2C19 and may increase exposure to CYP2C19 substrates. Caution with clopidogrel.

Tacrolimus:

Esomeprazole may increase tacrolimus levels; monitor.

4.6 Fertility, pregnancy and lactation

Pregnancy

NAPROMED should not be used during the first two trimesters of pregnancy unless clearly necessary; the dose should be kept as low and duration as short as possible. NAPROMED is contraindicated during the third trimester of pregnancy. Exposure during the third trimester can cause foetal cardiopulmonary toxicity (premature closure of ductus arteriosus), renal dysfunction and prolonged bleeding time. For esomeprazole, no clinical data are available on exposed pregnancies.

Breast-feeding

Naproxen passes into breast milk in small amounts and should not be administered during breast-feeding. Limited data on esomeprazole in breast milk; NAPROMED is not recommended during breast-feeding.

Fertility

Use of NSAIDs including naproxen may impair female fertility and is not recommended in women attempting to conceive.

4.7 Effects on ability to drive and use machines

Undesirable effects such as dizziness, drowsiness, somnolence and fatigue may occur. Patients should not drive or operate machinery if affected.

4.8 Undesirable effects

The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding — sometimes fatal — may occur. Common adverse reactions include nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain. Oedema, hypertension and cardiac failure have been reported with NSAID treatment. Hypersensitivity reactions (anaphylaxis, angioedema, bronchospasm), rash, tinnitus, dizziness, headache and visual disturbances may occur. PPI-class effects include headache, diarrhoea, nausea, abdominal pain and constipation.

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 the National Regulatory Authority.

4.9 Overdose

Naproxen: Overdose may cause vomiting, GI haemorrhage, diarrhoea, dizziness, tinnitus or convulsions. In the event of significant poisoning, acute renal failure and liver damage are possible. Treatment is symptomatic. Esomeprazole: Maximum established exposure has not exceeded 60 mg twice daily or 160 mg once daily without serious adverse effects. Esomeprazole is extensively protein-bound and is not dialysable. Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroidal; propionic acid derivatives. ATC code: M01AE52.

NAPROMED is a sequential-delivery modified-release tablet combining an immediate-release esomeprazole magnesium layer and an enteric-coated delayed-release naproxen core. Esomeprazole is released in the stomach prior to dissolution of naproxen in the small intestine; the enteric coating prevents naproxen release at pH <5, protecting against local gastric toxicity. After 9 days of twice-daily dosing in healthy volunteers, intragastric pH above 4 was maintained for a mean of 17.1 hours. Naproxen is a propionic acid NSAID that inhibits prostaglandin synthesis by blocking both COX-1 and COX-2, providing anti-inflammatory, analgesic and antipyretic effects. Esomeprazole is an S-isomer of omeprazole — a PPI that suppresses gastric acid by specific inhibition of the H^+/K^+-ATPase enzyme (proton pump).

5.2 Pharmacokinetic properties

Naproxen: Well absorbed after oral administration. Bioavailability is similar to gastro-resistant tablets. At steady state, proportional increases in plasma levels occur at usual naproxen doses; at >500 mg/day, less than proportional increase occurs due to saturation of plasma protein binding. Protein binding >99%, mainly to albumin. Volume of distribution approximately 0.12–0.17 L/kg. Biotransformation produces glucuronide and hydroxylated metabolites. Terminal half-life 12–17 hours. Approximately 95% eliminated in urine (mainly as conjugates). Esomeprazole: Absorption begins after the pellets leave the stomach. Peak plasma levels approximately 3.5 hours after a 20 mg dose. AUC increases with repeated administration due to saturation of first-pass CYP2C19 metabolism. Protein binding approximately 97%. Terminal half-life 1–2 hours.

5.3 Preclinical safety data

Non-clinical data for naproxen reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and reproductive toxicity. Esomeprazole: Non-clinical data reveal no special hazard. Combined studies showed no additional toxicological concerns beyond those of the individual components.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core: Lactose monohydrate, maize starch, microcrystalline cellulose, povidone K-30, crospovidone, purified talc, magnesium stearate, colloidal silicon dioxide (Aerosil). Film coat: Hydroxypropyl methylcellulose (HPMC), titanium dioxide (E171), propylene glycol, purified talc, Colour coat EC 4S white (film-coat mixture).

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. Keep out of the reach and sight of children.

6.5 Nature and contents of container

10 tablets packed in one ALU-ALU blister; 3 such blisters packed in a printed carton with package insert. Pack size: 30 tablets.

6.6 Special precautions for disposal and other handling

No special requirements. Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

PROMED PHARMACEUTICALS LTD

P.O. Box 22953-00100, Nairobi, Kenya.

8. MARKETING AUTHORISATION NUMBER (PPB REGISTRATION NUMBER)

H2026/CTD12245/26847

9. DATE OF FIRST AUTHORISATION / RENEWAL OF AUTHORISATION

16.03.2026

10. DATE OF REVISION OF THE TEXT

16.03.2026