SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Naproxen Apofri 250 mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 250 mg naproxen

Excipient with known effect: Lactose monohydrate 17 mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablets

Round, yellow, flat tablet with bevelled edge. Diameter 10 mm and embossed with “250” on one side and with a score line on the other side. The score line is not intended for breaking the tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Rheumatoid arthritis. Juvenile rheumatoid arthritis. Osteoarthritis. Ankylosing spondylitis. Dysmenorrhoea without organic cause. Acute attacks of migraine. Acute pain of mild to moderate intensity.

4.2 Posology and method of administration

Posology

Treatment should be initiated at the lowest expected effective dose, enabling later adjustment in response to therapy and possible adverse reactions. During long-term treatment, a low maintenance dose is desired. The risk of adverse events can be minimized by using the lowest effective dose for the shortest duration needed to control the symptoms (see section 4.4).

Rheumatic diseases and acute mild to moderate pain.
Adults: 250–500 mg in the morning and evening, to a maximum of 1000 mg/day. Patients with pronounced morning stiffness and/or night pain should take 500 mg at bedtime. For patients on a 1000 mg maintenance dose, the recommended intake is 500 mg in the morning and in the evening. Some patients can, however, take 750–1000 mg once a day. The single 1000 mg dose is recommended to take it in the evening.

Acute attacks of migraine:
750 mg, initially and then 250 mg as needed. The maximum daily dose is 1250 mg. It is substantial that Naproxen Apofri is taken at the first sign of the migraine attack.

Dysmenorrhoea:

250–500 mg as needed to a maximum of 1250 mg/day. Begin treatment at the first sign of menstrual pain.

Paediatric population
The score line is not intended for division of the tablet into equal doses, and, therefore, Naproxen Apofri 250 mg tablet should not be used in children under 50 kg. For this patient population other products are recommended. Children over 50 kg should be given the adult dose. Naproxen Apofri is not recommended for children under 12 years experiencing acute pain.

Elderly patients
A lower dose is recommended (see section 4.4). Naproxen Apofri 250 mg can, despite its score line, not be divided into two equal doses, which makes a titrating of Naproxen Apofri 250 mg to doses less than 250 mg impossible.

Impaired renal function:
Naproxen should be administered at the lowest effective dose for patients with mild renal impairment, and renal function must be carefully monitored. If possible, naproxen should be avoided in patients with moderate renal impairment and is contraindicated in severe renal impairment (see sections 4.3 and 4.4). Naproxen Apofri 250 mg can, despite its score line, not be divided into two equal doses, which makes a titrating of Naproxen Apofri 250 mg to doses less than 250 mg impossible.

Impaired hepatic function:
Naproxen should be used with caution in patients with severe hepatic impairment (see section 4.4). If possible, naproxen should be avoided in patients with severe hepatic impairment and is contraindicated to cirrhotic liver disease (see section 4.3). Naproxen Apofri 250 mg can, despite its score line, not be divided into two equal doses, which makes a titrating of Naproxen Apofri 250 mg to doses less than 250 mg impossible.

Route of administration:
Naproxen Apofri: oral administration

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Due to cross-reaction, Naproxen Apofri must not be administered to patients who have exhibited symptoms of asthma, rhinitis or urticaria when taking acetylsalicylic acid or other nonsteroidal anti-inflammatory drugs (NSAID). Conditions with increased haemorrhagic tendencies. History of gastrointestinal bleeding or perforation related to previous NSAID therapy. Active or prior repeated occurrence of peptic ulcer/bleeding (two or more distrinct episodes of proven ulceration or bleeding). Liver cirrhosis. Severe heart failure and severe renal disease (glomerulus filtration < 30 ml/min.). Third trimester of pregnancy.

4.4 Special warnings and precautions for use

Concurrent use of Naproxen Apofri and other NSAIDs, including selective cyclooxygenase-2 (COX 2) inhibitors should be avoided.
The risk of undesirable effects can be minimised by using the lowest effective dose for the shortest possible time needed to control the symptoms (see section 4.2 and the effects on the gastrointestinal tract and heart/blood vessels below).

Caution should be taken when treating patients with history of asthma, gastrointestinal, disorders, SLE, haematological disorders, coagulation disorders, or inflammatory bowel diseases.

When treating patients with mild to moderate heart failure, kidney or liver disease the risk for fluid retention and impaired renal function must be observed, especially when they are on concurrent diuretic therapy. Naproxen should be avoided if possible in patients with moderate to severe renal impairment or severe hepatic impairment. Caution should be exercised when initiating treatment with naproxen in patients with considerable dehydration. As with other NSAIDs, long-term treatment with naproxen has caused papillary renal necrosis and other pathological renal changes. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of NSAIDs may cause a dose-dependent reduction of prostaglandin synthesis and, secondarily, reduce renal blood flow, which may induce renal decompensation. The patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those treated with diuretics and ACE inhibitors, and the elderly. Discontinuation of NSAID therapy usually provides recovery to the state that existed before treatment began. Naproxen may increase the risk of renal dysfunction associated with treatment with ACE inhibitors.

Elderly patients have an increased risk of undesired effects when treated with NSAIDs, such as gastrointestinal haemorrhage and perforation, which may be fatal. One study suggests that the amount of free naproxen in serum increases in elderly even though the total serum concentration is unchanged. The consequences, (gastrointestinal bleeding and/or perforation) often becomes more serious and may occur at any time during treatment without warning symptoms and without any history of such disorders. It is also more likely that elderly patients have impaired renal, cardiac or hepatic function.

Gastrointestinal bleeding, ulceration or perforation, which can be fatal, has been reported with all sorts of NSAIDs and has occurred regardless of treatment duration, with or without warning symptoms or a previous history of serious gastrointestinal events.

The risk of gastrointestinal haemorrhage, ulceration or perforation is higher at elevated doses of NSAIDs in patients with a history of gastric ulcers, particularly when complicated by haemorrhage or perforation (see section 4.3, Contraindications) and in elderly patients. Patients with identified risk factors should commence treatment on lowest possible dose. Treatment with mucosa-protective preparations (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, as well as for patients treated with low-dose acetylsalicylic acid or other medicines that may increase the risk of undesirable gastrointestinal effects (see below and section 4.5).

Patients, particularly elderly, with a history of adverse gastrointestinal effects should be advised to be alert of any unusual abdominal symptoms (especially gastrointestinal bleeding), especially in early treatment and to contact health care if it occur.

Caution is needed in patients who are concomitantly treated with medicinal products, which may increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin reuptake inhibitors or products that counteract the platelet aggregation such as acetylsalicylic acid (see section 4.5).

When gastro-intestinal bleeding or ulceration occurs in patients who are receiving naproxen, the treatment should be discontinued.

NSAIDs should be used with caution in patients with a history of gastro-intestinal diseases (e.g. ulcerative colitis, Crohn's disease) as these conditions may worsen (see section 4.8).

Pending further clinical documentation, Naproxen Apofri is not recommended in children under 5 years of age.

Naproxen may reduce fertility (temporarily and during ongoing use) and is not recommended for women who wish to become pregnant. Discontinuation of naproxen should be considered for women with problems conceiving or who are undergoing fertility investigation.

Naproxen may affect tests for 17-ketogenic steroids and 5-HIAA in urine and should be temporarily withdrawn 48 hours before sampling.

Serious skin reactions, of which some fatal, including exfoliative dermatitis, Stevens-Johnson's syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported very rarely in connection with the use of NSAIDs (see section 4.8). The risk for this type of reactions is increased in the beginning of the treatment: in the majority of the cases the reaction started within the first month of treatment. Treatment with naproxen must be discontinued with the first symptoms of a skin rash, mucosal lesions or any other signs of hypersensitivity. If the patient has developed SJS, or TEN or DRESS with the use of naproxen, treatment with Naproxen Apofri must not be restarted and should be permanently discontinued.

In rare cases, serious skin and soft tissue infections may originate from chickenpox. To date, a contributing role of NSAIDs in the worsening of these infections cannot be ruled out. The recommendation is therefore to avoid use of Naproxen Apofri in patients having chickenpox.

Adequate monitoring and information is required to patients with a history of hypertension and/or mild to moderate heart failure, since fluid retention and oedema have been reported in connection to NSAID treatment.

Clinical trials and epidemiological data suggest that use of coxibs and some NSAIDs, (particularly at high doses and in long-term treatment), may be associated with a small increased risk of arterial thrombotic events (e.g. myocardial infarction or stroke). Data indicate that use of naproxen (1000 mg daily) have a lower risk then described above, even if a small risk cannot be ruled out.

Caution should be exercised in patients with a history of uncontrolled hypertension, heart failure, established ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease prior treatment with naproxen. Similar consideration should be given prior initiation of long-term treatment in patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidemia, diabetes mellitus, smoking).

Patients with any of the following rare, heritable conditions should not use this drug: galactose intolerance, total lactase deficiency or glucose-galactose malabsorption.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

The following combinations should be avoided with Naproxen Apofri:

Warfarin
NSAIDs inhibit thrombocyte aggregation and damage the mucosal lining of the gastrointestinal tract, which would increase the risk of gastrointestinal bleeding in patients taking anticoagulants. Recent epidemiological studies indicate that the risk of bleeding gastrointestinal ulcers is especially high during concomitant use of NSAIDs and warfarin. Concomitant use should therefore be avoided. It has recently been shown that this interaction also may have a metabolic component, in that NSAIDs and warfarin are metabolised by the same enzyme, CYP2C9. NSAIDs inhibit the metabolism of anticoagulants *in vitro*. The interaction potential is greatest for phenylbutazone followed by diclofenac and ibuprofen. Other drugs have not been investigated (see section 4.4).

Methotrexate, high dose
Organic acids such as NSAIDs may reduce the clearance of methotrexate as a result of tubular secretion of methotrexate being inhibited, and some metabolic interaction. During *high-dose methotrexate treatment*, concomitant prescription of NSAIDs should therefore always be avoided.

Ticlopidine
NSAIDs should not be combined with ticlopidine, due to additive inhibition of thrombocyte function.

NSAIDs and ASA
Naproxen in combination with other NSAIDs is not recommended due to an increased cumulative risk of serious NSAID-related adverse events.

The following combinations of Naproxen Apofri may require dose adjustment or special monitoring of the patient:

Methotrexate, low dose
Caution should be exercised if both a NSAID and methotrexate are given within 24 hours, as the plasma level of methotrexate may increase and cause toxicity. The risk of a potential interaction between NSAID and methotrexate must therefore be considered even for low doses of methotrexate. Patients with impaired renal function may be a risk group for this interaction. Renal function should therefore be monitored during combination therapy.

Lithium
Naproxen decreases the renal clearance of lithium. This cause up to a 40 %increase of the lithium concentration in serum. Because of lithium’s very low therapeutic index, the combination of lithium and NSAIDs should be avoided unless frequent monitoring of serum lithium can be implemented, and a reduction can be made to the lithium dose.

Cyclosporin

The risk of nephrotoxic effect caused by ciclosporin is increased by the co-administration of certain NSAIDs, due to the reduced synthesis of prostacyclin in the kidneys. Renal function must therefore be carefully monitored during concomitant treatment.
Probenecid
Probenecid prolongs the half-life of naproxen.

Tacrolimus
Concomitant administration of NSAIDs with tacrolimus may increase the risk of nephrotoxicity due to decreased synthesis of prostacyclin in the kidneys. Renal function must therefore be carefully monitored during concomitant treatment.

NSAIDs may reduce the effect of diuretics and antihypertensive medicinal products.

Loop diuretics, thiazides
NSAIDs (propionic acid derivatives) have been shown to counteract the diuretic effect of furosemide and bumetanide (loop diuretics), possibly through inhibition of prostaglandin synthesis. NSAIDs may also reduce the antihypertensive effect of thiazide derivatives. Diuretics can increase the nephrotoxicity caused by NSAIDs.

Beta blockers
NSAIDs counteract the antihypertensive effect of beta-blockers. It is however mainly indomethacin that has been studied.

ACE inhibitors and Angiotensin II antagonists
There is an increased risk of usually reversible acute renal failure in patients with renal impairment (e.g. dehydrated patients and/or elderly) when ACE inhibitors or angiotensin II receptor antagonists are combined with NSAIDs, including selective cyclooxygenase-2 inhibitors. The combination should therefore be used with caution in patients with impaired renal function, especially the elderly. Patients should be adequately hydrated, and monitoring of renal function should be considered after initiation of concomitant treatment and at regular intervals throughout treatment (see section 4.4)

Corticosteroids
Concomitant treatment increases the risk of gastrointestinal ulceration or bleeding (see section 4.4).

Aggregation Inhibitors, Platelet
Concomitant treatment increases the risk of gastrointestinal ulceration or bleeding (see Section 4.4).

Clopidogrel
Experimental studies have found that clopidrogrel increases naproxen-induced gastrointestinal blood loss (see section 4.4). This is likely to apply to all NSAIDs.

Selective serotonin re-uptake inhibitors (SSRI)
Both SSRIs and NSAIDs pose an increased risk of bleeding, e.g. from the gastrointestinal tract. This risk is increased during combination therapy. The mechanism may be associated with a decreased uptake of serotonin in the thrombocytes.

The clinical significance of the following combination with Naproxen Apofri is yet to be determined:

Antacids, cholestyramine or food may delay the absorption of naproxen without decreasing the amount absorbed.

Acetylsalicylic acid
Clinical pharmacodynamic data suggest that concomitant naproxen usage for more than one day consecutively may inhibit the effects of low-dose acetylsalicylic acid on platelet activity. This inhibition may persist for up to several days after discontinuing naproxen treatment. The clinical relevance of this interaction is not known.

4.6 Pregnancy, breast-feeding and fertility

Pregnancy
Inhibition of prostaglandin synthesis may negatively affect the pregnancy and/or embryonic/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation after use of prostaglandin-synthesis inhibitors in the early stages of the pregnancy. The absolute risk of cardiovascular malformations was increased from less than 1 % to approximately 1.5%. It is assumed that the risk increases with the dose and the duration of the treatment. The administration of prostaglandin synthesis inhibitors in animals resulted in an increased pre- and post-implantation loss and embryo-foetal lethality. In addition, an increased incidence of various malformations, including cardiovascular ones, have been reported in animals who received a prostaglandin synthesis inhibitor during the period of organogenesis. From the 20th week of pregnancy onward, Naproxen Apofri use may cause oligohydramnios resulting from foetal renal dysfunction. This may occur shortly after treatment initiation and is usually reversible upon discontinuation. In addition, there have been reports of ductus arteriosus constriction following treatment in the second trimester, most of which resolved after treatment cessation. Therefore, during the first and second trimesters of pregnancy, Naproxen Apofri should not be given unless clearly necessary. If Naproxen Apofri is used by a woman planning to become pregnant or taken during the first and second trimester, the dose should be as low, and the treatment period as short as possible. Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to Naproxen Apofri for several days from gestational week 20 onward. Naproxen Apofri should be discontinued if oligohydramnios or ductus arteriosus constriction are found.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors can expose the foetus to:
- Cardiopulmonary toxicity (premature constriction/closure of the ductus arteriosus and pulmonary hypertension).
- Renal dysfunction, which may develop into renal failure with oligohydramnios (see above).

and at the end of pregnancy expose the mother and neonate to:
- Prolonged bleeding time.
- Inhibition of the contraction of the uterus resulting in a delayed or prolonged delivery.

Based on the above, Naproxen Apofri is contraindicated during the third trimester of pregnancy.

Breast-feeding

Naproxen is excreted into human milk, but the risk of affecting the infant is considered unlikely at therapeutic doses.

Fertility
The use of naproxen, as with all drugs that inhibit cyclooxygenase/prostaglandin synthesis, may impair fertility and is not recommended for women who wish to become pregnant. For women who have difficulty conceiving or are undergoing investigation of infertility, withdrawal of Naproxen Apofri should be considered (see section 4.4).

4.7 Effects on ability to drive and use machines

During treatment with naproxen, undesirable effects such as visual disturbances and dizziness may occur. This should be considered in cases when sharpened attentiveness is required, for example in operating motor vehicles.

4.8 Undesirable effects

The undesirable effects are mainly linked to the pharmacological effect of naproxen on prostaglandin synthesis. Undesirable gastrointestinal effects such as dyspepsia, abdominal pain and nausea are the most frequently reported undesirable effects.
The undesirable effects are compiled in accordance with MedDRA System Organ Class and frequency. The following frequency categories have been used:
Very common (≥1/10), Common (≥ 1/100, <1/10), Uncommon (≥1/1 000, <1/100), Rare (≥1/10 000, <1/1 000) and not known (cannot be estimated from the available data).

System Organ Class	**Frequency**	**Undesirable effects**
Blood and lymphatic system disorders	Rare	Thrombocytopaenia, granulocytopaenia, leukopenia, aplastic and haemolytic anaemia, agranulocytosis
Metabolism	Rare	Hyperkalemia
Psychiatric disorders	Uncommon	Difficulty falling asleep, difficulty concentrating
	Rare	Cognitive disturbances, depression, nightmares, minor anxiety, myalgia
Central and peripheral nervous system disorders	Rare	Aseptic meningitis
Eyes	Common	Visual disturbances
Ear and labyrinth disorders	Common	Tinnitus
	Uncommon	Hearing impairment
Vascular disorders	Common	Fluid retention, palpitations, oedema
	Rare	Vasculitis, congestive heart failure, hypertension, pulmonary oedema
Respiratory, thoracic and mediastinal disorders	Uncommon	Asthma, dyspnoea
	Rare	Eosinophilic pneumonitis

Gastrointestinal disorders	Common	Dyspepsia, abdominal pain, nausea, diarrhoea, constipation, heartburn, stomatitis
	Uncommon	Gastrointestinal bleeding, gastric ulcers, ulcerative stomatitis, gastritis
	Rare	Colitis, perforation, vomiting, melaena, esophagitis, pancreatitis, haematemesis, flatulence, exacerbation of ulcerative colitis, exacerbation of Crohn's disease
Hepatobiliary disorders	Uncommon	Abnormal liver function
	Rare	Toxic hepatitis (in isolated cases fatal)
Renal and urinary disorders	Uncommon	Abnormal kidney function
	Rare	Haematuria
Skin and subcutaneous tissue disorders	Common	Exanthema, skin erosions
	Uncommon	Urticaria, photosensitivity including pseudoporphyria
	Rare	Severe mucocutaneous skin reactions such as Stevens-Johnson Syndrome, angioneurotic oedema, erythema multiforme, toxic epidermal necrolysis
	Not known	Drug reaction with eosinophilia and systemic symptoms (DRESS) (see section 4.4) Fixed drug eruption
General disorders and/or administration-site conditions	Common	Drowsiness, dizziness, headache, thirst and sweating
	Uncommon	Hair loss, fever
	Rare	Anaphylaxis, seizures, muscle weakness

At signs of pseudoporphyria, treatment should be discontinued, and the patient monitored.
Elevated liver function test results have occasionally been reported for non-steroidal anti-inflammatory drugs.
In rare cases, severe skin and soft tissue infections appear in association with chickenpox.

Sodium retention has not been reported in metabolic studies, but it is possible that patients with suspected or verified heart failure are at greater risk when treated with Naproxen Apofri.

Naproxen inhibits thrombocyte aggregation and prolongs bleeding time.

Gastroduodenal ulcers, perforation or gastrointestinal bleeding can be fatal, especially in the elderly (see section 4.4).

Clinical trials and epidemiological data indicate that use of certain NSAIDs, (particularly in high doses and during long-term treatment), may lead to a small, increased risk of arterial thrombotic events (e.g. cardiac infarct or stroke, see section 4.4).

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 reporting system listed in Appendix V.*

4.9 Overdose

Toxicity: 1 g to a 7-year-old resulted in no symptoms. 12.5 and 25 g resulted in moderate intoxication in adults who received gastric lavage. Adults have however developed kidney problems following 3.75 to 5 g, while one other adult developed moderate intoxication after 6.25 g. Also, 12.5 g to an adult caused severe intoxication.

Symptoms: Nausea, vomiting, abdominal pain. Headache, dizziness, lethargy, tinnitus. Tachycardia, palpitations. At high doses, disorientation, hyperkinesia, aggressiveness, possibly seizures. Kidney disorders, metabolic acidosis. Hypoprothrombinaemia Possibly hypokalaemia, leukocytosis.

Treatment: If justifiable, gastric lavage, charcoal. Antacids as required. Correction of acid-base and electrolyte imbalance. Ensure good diuresis. In the case of seizures, administer diazepam. Use general symptomatic treatment.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Non-steroidal anti-inflammatory drugs. NSAID.
ATC code: M01AE02

Naproxen Apofri belongs to the group of non-steroidal antiinflammatory/antirheumatic drugs (NSAID). Naproxen is a propionic acid derivative with the chemical name (S)-2-(6-methoxy-2-naphthyl) propionic acid. Naproxen has also analgesic and antipyretic properties.

Naproxen inhibits prostaglandin synthesis. Naproxen affects hypercontractility in the uterus and reduces elevated basal tone associated with dysmenorrhoea. Naproxen prolongs bleeding time and inhibits platelet aggregation.

Naproxen suppresses renal prostacyclin synthesis. This effect has no essential significance in patients with normal renal function. In patients with chronic renal insufficiency, cardiac insufficiency or hepatic insufficiency, as well as in patients with conditions of changes in plasma volume, the suppressed prostacyclin synthesis can lead to acute renal insufficiency, fluid retention and heart failure. See 4.3 Contraindications and 4.4 Special warnings and precautions.

5.2 Pharmacokinetic properties

Absorption
Naproxen is rapidly and completely absorbed regardless of pharmaceutical form.
The maximal plasma concentration is reached after approximately 2 hours. Steady state is reached after 4 to 5 doses. The absorption is not affected by simultaneous intake of antacids food.

Distribution and metabolism
Over 99% is bound to serum albumin at a therapeutic dose. The volume of distribution is small, approximately 0.1 l/kg body weight. Approximately 30% of naproxen is metabolised into 6-O-desmethylnaproxen, which is not pharmacologically active.

Elimination
The plasma half-life is 10 to 17 hours. Naproxen is mainly excreted via the urine, and only in small amounts (1–2%) in faeces. Mainly intact naproxen is found in the blood in humans.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional animal studies of genotoxicity, carcinogenicity, embryo-foetal toxicity and fertility in addition to what is stated in the Summary of product characteristics.

Naproxen acid has been studied *in vitro* and *in vivo* for mutagenicity, but no relevant evidence of a mutagenic potential was observed. No carcinogenic effects from naproxen have been detected in studies on rats.

Naproxen (20 mg/kg/day) showed no teratogenic effects in studies on rats and rabbits.

The main findings in animal toxicity studies using high oral repeated doses were gastrointestinal irritation and kidney damage, both of which were attributed to inhibition of prostaglandin synthesis. Oral administration in peri- and postnatal studies of naproxen (2, 10 and 20 mg/kg/day) given to pregnant rats during the third trimester of pregnancy resulted in difficult delivery. This is a known effect for this class of compounds.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydroxypropylcellulose
Cellulose, microcrystalline
Magnesium trisilicate
Croscarmellose sodium
Silica, colloidal anhydrous
Lactose monohydrate
Magnesium stearate
Iron oxide yellow (E172)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

4 years.

6.4 Special precautions for storage

No special storage conditions.

6.5 Nature and contents of container

Al/PVC blisters containing 10, 20, 30, 40, 50, 100, 105, 200, 300, 400 and 500 tablets.

Not all pack sizes may be marketed.

6.6 Special instructions for destruction and other handling

No special requirements.

7 MARKET AUTHORISATION HOLDER

[To be completed nationally]

8 MARKETING AUTHORISATION NUMBER(S).

[To be completed nationally]

9 DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

[To be completed nationally]

10 DATE OF REVISION OF THE TEXT

31 Oct 2024