

**NAPROXEN 250MG ENTERIC-COATED TABLETS  
PL 00289/0699**

**UKPAR**

**TABLE OF CONTENTS**

Lay Summary	Page 2
Scientific discussion	Page 3
Steps taken for assessment	Page 10
Steps taken after authorisation – summary	Page 11
Summary of Product Characteristics	Page 12
Product Information Leaflet	Page 27
Labelling	Page 29

**NAPROXEN 250MG ENTERIC-COATED TABLETS  
PL 00289/0699**

**LAY SUMMARY**

The MHRA granted Teva UK Limited a Marketing Authorisation (licence) for the medicinal product Naproxen 250mg Enteric-Coated Tablets on 12<sup>th</sup> September 2007. This product, to be available by prescription only (POM), contains naproxen and is used for the treatment of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, juvenile rheumatoid arthritis, acute gout, short term problems with the joints such as sprains and strains, to relieve stiffness and pain in the back and to relieve period pains..

The active ingredient naproxen is part of a group of medicines called non-steroidal anti-inflammatory drugs, which cause a reduction in the levels of prostaglandins, substances believed to be responsible for causing pain and inflammation.

This application is a duplicate of a previously granted application for Naproxen Enteric-Coated Tablets 250mg (PL 00289/0129), also granted to Teva UK Limited on 16<sup>th</sup> March 1990.

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Naproxen 250mg Enteric-Coated Tablets outweigh the risks, hence a Marketing Authorisation has been granted.

**NAPROXEN 250MG ENTERIC-COATED TABLETS  
PL 00289/0699**

**SCIENTIFIC DISCUSSION**

**TABLE OF CONTENTS**

Introduction	Page 4
Pharmaceutical assessment	Page 5
Preclinical assessment	Page 8
Clinical assessment	Page 9
Overall conclusions and risk benefit assessment	Page 10

## **INTRODUCTION**

The UK granted a marketing authorisation for the medicinal product Naproxen 250mg Enteric-Coated Tablets (PL 00289/0699) to Teva UK Limited on 12<sup>th</sup> September 2007. The product is available as a prescription-only medicine (POM).

The application was submitted as a simple abridged application according to Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC, cross-referring to Naproxen Enteric-Coated Tablets 250mg (PL 00289/0129), approved on 16<sup>th</sup> March 1990 to the marketing authorisation holder Teva UK Limited.

No new data were submitted nor were they necessary for this simple application, as the data are identical to that of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no PAR was generated for it.

The active ingredient naproxen acts as a non-steroidal anti-inflammatory, reducing the levels of prostaglandins. Naproxen 250mg Enteric-Coated Tablets is indicated for the the treatment of juvenile rheumatoid arthritis, rheumatoid arthritis, ankylosing spondylitis, osteoarthritis, acute gout, and acute musculoskeletal disorders (for example sprains and strains, tenosynovitis, fibrositis, lumbosacral pain, direct trauma, and cervical spondylitis), and dysmenorrhoea.

## **PHARMACEUTICAL ASSESSMENT**

**LICENCE NO:** PL 00289/0699

**PROPRIETARY NAME:** Naproxen 250mg Enteric-Coated Tablets

**ACTIVE(S):** Naproxen

**COMPANY NAME:** Teva UK Limited

**E.C. ARTICLE:** Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC

**LEGAL STATUS:** POM

### **1. INTRODUCTION**

This is a simple, piggy back application for Naproxen 250mg Enteric-Coated Tablets submitted under Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC. The proposed MA holder is Teva UK Limited, Brampton Road, Hampden Park, Eastbourne, East Sussex, BN22 9AG.

The application cross-refers to Naproxen Enteric-Coated Tablets 250mg (PL 00289/0129), approved on 16<sup>th</sup> March 1990 to the marketing authorisation holder Teva UK Limited. The current application is considered valid.

### **2. MARKETING AUTHORISATION APPLICATION FORM**

#### **2.1 Name(s)**

The proposed name of the product is Naproxen 250mg Enteric-Coated Tablets. The product has been named in-line with current requirements.

#### **2.2 Strength, pharmaceutical form, route of administration, container and pack sizes**

The product contains naproxen, equivalent to 250mg. It is to be stored in a polyvinylidene chloride/polyvinylchloride/aluminium blister. The proposed shelf-life (3 years) and storage conditions (store in original packaging, do not store above 25 degrees) are consistent with the details registered for the cross-reference product.

#### **2.3 Legal status**

On approval, the products will be available as prescription-only medicines (POM).

#### **2.4 Marketing authorisation holder/Contact Persons/Company**

Teva UK Limited, Brampton Road, Hampden Park, Eastbourne, East Sussex, BN22 9AG.

The QP responsible for pharmacovigilance is stated and his CV is included.

#### **2.5 Manufacturers**

The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of GMP compliance has been provided.

#### **2.6 Qualitative and quantitative composition**

The proposed composition is consistent with the details registered for the cross-reference product.

## **2.7 Manufacturing process**

The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

## **2.8 Finished product/shelf-life specification**

The proposed finished product specification is in-line with the details registered for the cross-reference product.

## **2.9 Drug substance specification**

The proposed drug substance specification is consistent with the details registered for the cross-reference product.

## **2.10 TSE Compliance**

With the exception of lactose monohydrate, no materials of animal or human origin are included in the product. This is consistent with the cross reference product.

Lactose monohydrate is sourced from milk that is fit for human consumption and no animal materials, with the exception of bovine rennet, have been used in its manufacture.

## **3. EXPERT REPORTS**

The applicant has included detailed expert reports in Module 2 of the application. Signed declarations and copies of the experts' CVs are enclosed in Module 1.4 for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

## **4. PRODUCT NAME & APPEARANCE**

See 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

## **5. SUMMARY OF PRODUCT CHARACTERISTICS**

The proposed summary is consistent with the details registered for the cross-reference product.

## **6. PATIENT INFORMATION LEAFLET/CARTON**

### PIL

The patient information leaflet has been prepared in-line with the details registered for the cross-reference product.

### Carton and blister

The applicant has provided the proposed wording for the packaging. No mock-ups have been provided as the applicant is not currently planning to market the product in the UK. Confirmation has been provided that mock-ups of the packaging will be provided before any marketing of the product takes place in the UK.

## **7. CONCLUSIONS**

The data submitted with the application are acceptable. A Marketing Authorisation should be granted.

## **PRECLINICAL ASSESSMENT**

No new preclinical data have been supplied with this application and none are required for an application of this type.

## **CLINICAL ASSESSMENT**

As this is a duplicate application, no new clinical data have been supplied and none are required.



## **OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT**

### **QUALITY**

The data are consistent with those previously assessed for the cross-reference product and as such have been judged to be satisfactory.

### **PRECLINICAL**

No new preclinical data were submitted and none are required for an application of this type.

### **EFFICACY**

This application is identical to a previously granted application for Naproxen Enteric-Coated Tablets 250mg (PL 00289/0129).

No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory and consistent with that for the cross-reference product.

### **RISK BENEFIT ASSESSMENT**

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-reference product. Extensive clinical experience with naproxen is considered to have demonstrated the therapeutic value of the compound. The risk:benefit is, therefore, considered to be positive.

**NAPROXEN 250MG ENTERIC-COATED TABLETS  
PL 00289/0699**

**STEPS TAKEN FOR ASSESMENT**

1	The MHRA received the marketing authorisation application on 13/05/2004.
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 27/05/2004.
3	Following assessment of the application the MHRA requested further information on 29/06/2004 and 16/09/2005.
4	The applicant responded to the MHRA's requests, providing further information on 15/09/2005 and 05/09/2007
5	The application was determined on 12/09/2007

**NAPROXEN 250MG ENTERIC-COATED TABLETS  
PL 00289/0699**

**STEPS TAKEN AFTER ASSESSMENT**

<b>Date submitted</b>	<b>Application type</b>	<b>Scope</b>	<b>Outcome</b>

# NAPROXEN 250MG ENTERIC-COATED TABLETS

## PL 00289/0699

### SUMMARY OF PRODUCT CHARACTERISTICS

**1. NAME OF THE MEDICINAL PRODUCT**

Naproxen 250 mg Enteric Coated Tablets

**2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each tablet contains 250 mg of naproxen. For excipients, see 6.1.

**3. PHARMACEUTICAL FORM**

Tablet

White, round, biconvex enteric coated tablets, overprinted in black 3N3.

**4. CLINICAL PARTICULARS**

**4.1. Therapeutic indications**

Naproxen is indicated for the treatment of juvenile rheumatoid arthritis, rheumatoid arthritis, ankylosing spondylitis, osteoarthritis, acute gout, and acute musculoskeletal disorders (for example sprains and strains, tenosynovitis, fibrositis, lumbosacral pain, direct trauma, and cervical spondylitis), and dysmenorrhoea.

**4.2. Posology and method of administration**

Undesirable effects may be minimized by using the lowest effective dose for the shortest duration of time to control symptoms (see section 4.4).

For oral administration.

To be taken preferably with or after food.

Adults

Rheumatoid arthritis, osteoarthritis and ankylosing spondylitis:

Normally, 500 mg to 1 g per day in two doses at 12 hour intervals.

Acute gout:

750 mg immediately, then 250 mg every 8 hours until the attack has passed.

Acute musculoskeletal disorders and dysmenorrhoea:

500 mg initially, then 250 mg every 6 – 8 hours as needed. The maximum daily dose (after the first day) is 1250 mg.

Children

(Children over 5 years of age)

Juvenile rheumatoid arthritis:

Normally, dosage is 10 mg/kg bodyweight daily taken in 2 doses at 12 hour intervals.

The Elderly

The lowest effective dose should be used, as the elderly are at an increased risk of the serious consequences of adverse reactions. When high doses are required caution should be exercised. In patients where impaired renal function may be expected a reduced dosage should be considered.

The patient should be monitored for GI bleeding for 4 weeks following initiation of NSAID therapy.

**4.3. Contraindications**

Naproxen is contra-indicated in patients with a history of, or active peptic ulceration and active gastrointestinal bleeding.

Naproxen is contra-indicated for patients with known hypersensitivity to naproxen, naproxen sodium formulations or any of the excipients.

Naproxen should not be given to patients in whom aspirin or other non-steroidal anti-inflammatory/analgesic drugs induce the syndrome of asthma, rhinitis or urticaria.

Severe heart failure.

#### **4.4. Special warnings and precautions for use**

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2, and GI and cardiovascular risks below).

##### *Cardiovascular and cerebrovascular effects*

Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

Clinical trial 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 (for example myocardial infarction or stroke). Although data suggest that the use of naproxen (1000mg daily) may be associated with a lower risk, some risk cannot be excluded.

Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with naproxen after careful consideration. Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemias, diabetes mellitus, smoking).

##### *Gastrointestinal effects*

Although naproxen is usually well tolerated, there have been reported incidences of gastro-intestinal bleeding. Therefore, patients with a history of gastro-intestinal disease receiving naproxen should be closely monitored.

Serious gastro-intestinal adverse reactions, may occur at any time in patients on therapy with non-steroidal anti-inflammatory drugs. The duration of therapy does not seem to change the risk of occurrence. Studies to date have not identified any subset of patients not at risk of developing peptic ulcer and bleeding. However, elderly and debilitated patients tolerate gastro-intestinal ulceration or bleeding less well than others. Most of the serious gastro-intestinal events associated with non-steroidal anti-inflammatory drugs occurred in this patient population.

The anti-inflammatory and antipyretic activities of Naproxen may reduce inflammation and fever, thereby diminishing their utility as diagnostic signs.

In patients with a history of bronchial asthma or allergic disease, administration of naproxen may elicit bronchospasm.

Naproxen decreases platelet aggregation and prolongs bleeding time.

The use of NSAIDs may result in a deterioration of renal function.

In patients with impaired renal function, or cardiac impairment, naproxen should be used with great caution and serum creatinine and/or creatinine clearance should be monitored. When the baseline creatinine clearance is less than 20 ml/min naproxen is not recommended.

When renal blood flow is compromised, patients should have renal function assessed before and during naproxen therapy. A reduction in daily dosage should be considered to avoid the possibility of excessive accumulation of naproxen metabolites in these patients.

When liver function is impaired, the plasma concentration of unbound naproxen is increased, the significance of this is unknown but caution is advised when high doses are required.

#### *Haematological*

Patients who have coagulation disorders or patients who are receiving drug therapy that interferes with haemostasis should be carefully observed if naproxen-containing products are administered.

Patients at high risk of bleeding or those on full anti-coagulation therapy (e.g. dicoumarol derivatives) can be at increased risk of bleeding if given naproxen-containing products.

#### *Anaphylactic (anaphylactoid) reactions*

In susceptible individuals hypersensitivity reactions may occur. Anaphylactic (anaphylactoid) reactions may occur both in patients with and without a history of hypersensitivity or exposure to aspirin, other non-steroidal anti-inflammatory drugs or naproxen-containing products. They may also occur in individuals with a history of angioedema, bronchospastic reactivity (e.g. asthma), rhinitis and nasal polyps.

Anaphylactoid reactions, like anaphylaxis, may have a fatal outcome.

#### *Steroids*

If steroid dosage is eliminated or reduced during therapy, the steroid dosage should be reduced slowly and the patients must be observed closely for any evidence of adverse effects, including adrenal insufficiency and exacerbation of symptoms of arthritis.

#### *Ocular effects*

Studies have not shown any changes in the eye attributable to naproxen administration. Rarely, adverse ocular disorders including papillitis, retrobulbar optic neuritis and papilledema, have been reported in users of NSAIDs including naproxen, although a cause-and-effect relationship cannot be established; accordingly, patients who develop visual disturbances during treatment with naproxen-containing products should have an ophthalmological examination.

#### *Combination with other NSAIDs*

The combination of naproxen-containing products and other NSAIDs is not recommended, because of the cumulative risks of inducing serious NSAID-related adverse events.

### **4.5. Interactions with other medicinal products and other forms of interaction**

Concomitant administration of antacid, cholestyramine or food may delay the absorption of naproxen but does not affect its extent.

Care should be taken in patients treated with any of the following drugs as interactions have been reported in some patients.

Anti-hypertensives: reduced anti-hypertensive effect.

Naproxen and other non-steroidal anti-inflammatory drugs may increase the risk of renal impairment associated with the use of ACE-inhibitors.

Diuretics: reduced diuretic effect. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.

Lithium: Decreased elimination of lithium.

Methotrexate: Decreased elimination of methotrexate.

Ciclosporin: Increased risk of nephrotoxicity.

Mifepristone: NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

Other analgesics: Avoid concomitant use of two or more NSAIDs. See section 4.4 Special Warnings and Special Precautions for use.

Corticosteroids: Increased risk of GI bleeding. See section 4.4 Special Warnings and Special Precautions for use.

Anti-coagulants: Enhanced anticoagulant effect. See section 4.4 Special Warnings and Special Precautions for use.

Quinolone antibiotics: Animal data indicate that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions.

Naproxen is highly bound to plasma proteins and if anti-coagulants, hydantoins or highly protein-bound sulphonamides are given simultaneously, overdosage of these drugs may result.

Co-administration of probenecid inhibits the renal tubule secretion of naproxen, so raising its plasma concentration and prolonging its half-life.

It is suggested that naproxen is withdrawn 48 hours before adrenal function tests as it may interfere with some tests for 17-ketogenic steroids. Naproxen may interfere with some assays of urinary 5-hydroxy-indoleacetic acid.

#### **4.6. Pregnancy and lactation**

Whilst no teratogenic effects have been demonstrated in animal toxicology studies, the use of naproxen during pregnancy should if possible be avoided. Congenital abnormalities have been reported in association with naproxen administration in man; however, these are low in frequency and do not appear to follow any discernible pattern. In view of the known effects of NSAIDs on the foetal cardiovascular system (a closure of ductus arteriosus), use in late pregnancy should be avoided. In the limited studies so far available, naproxen appears in the breast milk in very low concentrations and is unlikely to adversely affect the breast-fed infant. However, the use of naproxen should be avoided in patients who are breast-feeding.

#### **4.7. Effects on ability to drive and use machines**

Dizziness, drowsiness, vertigo, insomnia, depression or visual disturbances are possible undesirable effects after taking NSAIDs. If affected, patients should not drive or operate machinery.

#### **4.8. Undesirable effects**

Gastro-intestinal: the most commonly-observed adverse events are gastrointestinal in nature. Nausea, vomiting, diarrhoea, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis and gastrointestinal haemorrhage have been reported following administration. Less frequently, gastritis, duodenal ulcer, gastric ulcer, gastrointestinal perforation and colitis have been observed.

Hypersensitivity: Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of (a) non-specific allergic reactions and anaphylaxis (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritis, urticaria, purpura, angioedema and, less commonly, bullous dermatoses (including epidermal necrolysis, erythema multiforme and Stevens-Johnson Syndrome).

Cardiovascular: Oedema, hypertension, cardiac failure and vasculitis have been reported in association with NSAID treatment. Clinical trial and epidemiological data suggest that use of some NSAIDs (particularly at high doses and in long term treatment) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

Eosinophilic pneumonitis and aseptic meningitis have also been reported.

Other adverse events reported less commonly include:

Renal: Nephrotoxicity in various forms, including glomerular nephritis, interstitial nephritis, nephrotic syndrome, haematuria and renal failure.

Hepatic: Abnormal liver function, hepatitis and jaundice.

Neurological and special senses: Visual disturbances, optic neuritis, headaches, paraesthesia, depression, confusion, hallucinations, tinnitus, hearing impairment, vertigo, dizziness, convulsions, insomnia, inability to concentrate, cognitive dysfunction, malaise, fatigue and drowsiness.

Haematological: Thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia, hyperkalaemia and haemolytic anaemia.

Dermatological: Photosensitivity, alopecia.

#### **4.9. Overdose**

Human experiences of overdosage with naproxen may result in drowsiness, heartburn, indigestion, nausea or vomiting. The stomach may be emptied by inducing emesis or aspiration and lavage. Activated charcoal may reduce the absorption of naproxen. (See section 5.2 Pharmacokinetic properties). Further treatment is symptomatic.

Haemodialysis does not decrease the plasma concentration of naproxen because of the high degree of protein binding. However, haemodialysis may still be appropriate for a patient with renal failure who has taken naproxen.

Correction of severe electrolyte abnormalities should be considered.

### **5. PHARMACOLOGICAL PROPERTIES**

#### **5.1. Pharmacodynamic properties**

Naproxen is a propionic acid derivative. It acts as an anti-inflammatory agent, analgesic and has anti-pyretic activity in man. By its action on cyclo-oxygenase it inhibits prostaglandin synthesis. However, the exact mechanism of its anti-inflammatory action is not known.

ATC Code: M01A E02 (anti-inflammatory and antirheumatic products, non-steroids, propionic acid derivatives).

#### **5.2. Pharmacokinetic properties**

Animal studies suggest that prompt administration of activated charcoal would reduce the absorption of naproxen.

Following oral administration, naproxen is fully absorbed from the gastro-intestinal tract. Depending on food in-take, peak plasma concentrations are reached 2 to 4 hours after ingestion. More than 99% is bound to plasma proteins. The plasma half-life is between 12 and 15 hours. Excretion in urine accounts for approximately 95% of the dose. Naproxen crosses the placental barrier and is excreted in breast milk.

When naproxen is administered in the enteric-coated form, the peak plasma levels are delayed when compared with the standard tablets. However, the mean areas under the plasma concentration time curves, and hence bioavailability, are equivalent. The tablets do not disintegrate until they reach the small intestine, where dissolution is rapid and complete. This delay in absorption makes Naproxen EC of value for patients in whom gastric dissolution is undesirable.

#### **5.3. Preclinical safety data**

Preclinical information has not been included because the safety profile of naproxen has been established after many years of clinical use. Please refer to section 4.

### **6. PHARMACEUTICAL PARTICULARS**

#### **6.1. List of excipients**

Tablet Contains:  
Lactose Monohydrate,  
Maize Starch,



Polyvidone,  
Sodium Starch Glycolate (type A),  
Magnesium Stearate (E572).

Coating contains:

Lactose Monohydrate:  
Hydroxypropyl methylcellulose (E464),  
Colloidal silicon dioxide,  
Polyethylene glycol,  
Polyvinyl acetate phthalate,  
Purified stearic acid (E570),  
Purified talc (E553(b)),  
Sodium alginate (E401),  
Sodium bicarbonate (E500),  
Triethyl citrate,  
Titanium Dioxide (E171).

Printing Ink:  
Shellac  
Black iron oxide (E172)  
Propylene glycol (E1520)

**6.2. Incompatibilities**

Not Applicable

**6.3. Shelf life**

36 months

**6.4. Special precautions for storage**

Do not store above 25°C. Store in the original package.

**6.5. Nature and contents of container**

Blister strips in packs of 10, 28, 56 or 100 tablets

**6.6 Special precautions for disposal**

Not applicable

**7. MARKETING AUTHORISATION HOLDER**

TEVA UK Limited  
Eastbourne  
BN22 9AG.

Trading Address:  
Leeds LS27 OJG  
England

**8. MARKETING AUTHORISATION NUMBER**

PL 00289/0699

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

12/09/2007

**10 DATE OF REVISION OF THE TEXT**

12/09/2007

# **NAPROXEN 250MG ENTERIC-COATED TABLETS**

## **PL 00289/0699**

### **Patient Information Leaflet**

### **Naproxen 250mg Enteric Coated Tablets**

Please read this leaflet carefully before you take these tablets. It briefly outlines the most important things you need to know. If you want to know more about this medicine, or you are not sure about anything, ask your doctor or your pharmacist.

The name of your medicine is Naproxen 250 mg Enteric Coated Tablets

#### WHAT IS NAPROXEN ?

Naproxen enteric coated tablets contain 250 mg of naproxen. The other ingredients are lactose, maize starch, povidone, sodium starch glycolate and magnesium stearate. In addition, the coating contains colloidal silicon dioxide, polyvinyl acetate phthalate, polyethylene glycol, stearic acid, hydroxypropyl methylcellulose, sodium alginate, sodium bicarbonate, purified talc, triethyl citrate and the colour titanium dioxide (E171). The printing ink contains shellac, black iron oxide and propylene glycol..

The tablet is coated with an enteric coat. This coat allows the tablet to pass undissolved, through the stomach into the small intestine, where naproxen is released.

The product is available in packs sizes<sup>1</sup> of 10, 28, 56 and 100 tablets.  
See outer packaging or the pharmacy label for contents i.e. the number of tablets.

Naproxen is a non-steroidal anti-inflammatory drug.

The Marketing Authorisation holder and company responsible for manufacture is TEVA UK Limited, Eastbourne, BN22 9AG.

#### WHAT IS YOUR MEDICINE USED FOR ?

Naproxen enteric coated tablets are used to treat rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, juvenile rheumatoid arthritis, acute gout, short term problems with the joints such as sprains and strains, to relieve stiffness and pain in the back and to relieve period pains. Ask your doctor or pharmacist if you need additional information.

#### BEFORE YOU TAKE YOUR MEDICINE

Are you sensitive to any of the ingredients in the medicine (listed above)?

Are you pregnant or breast-feeding ?

Are you allergic to aspirin, naproxen, or any other non-steroidal anti-inflammatory drugs, e.g. diclofenac? (You may have had asthma; an itchy runny nose; rashes or swelling of the skin as a result of taking the drug).

Are you currently suffering from or do you have a history of peptic ulcers, or any other disease affecting the digestive tract ?

Do you suffer from high blood pressure ?

---

<sup>1</sup> Only marketed pack sizes will be included on the printed version of this PIL.

Do you suffer from any kidney, heart or liver problems ?

Do you suffer from asthma or allergic diseases causing difficulties in breathing ?

Do you have a blood clotting disorder or are you taking an anticoagulant which reduces the clotting of the blood e.g. heparin, warfarin ?

Are you taking aspirin or any other non-steroidal anti-inflammatory drug ?

Are you taking ciclosporin, a medicine used following organ transplants ?

Are you taking any corticosteroids e.g. hydrocortisone or prednisolone ?

Are you taking any quinolone antibiotics e.g. ciprofloxacin, norfloxacin or levofloxacin, or sulphonamides e.g. co-trimoxazole ?

Are you taking lithium, a drug used in the treatment of depression ?

Are you taking methotrexate, a treatment for leukaemia ?

Are you taking probenecid, a drug used to treat gout ?

Are you taking a diuretic ('water tablet'), an antihypertensive which reduces your blood pressure, or a drug that stimulates your heart ?

Are you taking phenytoin, a medicine used to treat epilepsy ?

Have you taken mifepristone to terminate a pregnancy in the last 8 - 12 days ?

**If the answer to any of these questions is YES, do not take naproxen before talking to your doctor or pharmacist.**

Medicines such as naproxen may be associated with a small increased risk of heart attack ("myocardial infarction") or stroke. Any risk is more likely with high doses and prolonged treatment. Do not exceed the recommended dose or duration of treatment.

If you have heart problems, previous stroke or think that you might be at risk of these conditions (for example if you have high blood pressure, diabetes or high cholesterol or are a smoker) you should discuss your treatment with your doctor or pharmacist.

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

If you are to undergo adrenal function tests your doctor may tell you to temporarily stop taking naproxen in case it interferes with these tests.

Your tablets may cause dizziness, drowsiness, vertigo, loss of concentration, insomnia (difficulty sleeping), depression or visual disturbances.

Do not drive or operate machinery if you experience these effects.

## TAKING YOUR MEDICINE

Your doctor has decided the dose which is suited to you. Always follow your doctor's instructions and those which are on the pharmacy label. If you do not understand these instructions, or you are in any doubt, ask your doctor or pharmacist.

The tablets should be swallowed whole with a drink of water and not chewed. Take with or after food. The usual dosage instructions are given below.

### *Adults*

Rheumatoid arthritis,  
osteoarthritis  
and ankylosing spondylitis:

250 - 500 mg twice a day at 12 hour intervals.

Acute musculoskeletal disorders and  
period pains

500 mg initially, then 250 mg every 6 – 8  
hours as needed. The maximum daily dose (after the  
first day) is 1250 mg.

Acute gout:

750 mg immediately, then 250 mg every 8 hours  
until the attack has passed.

### *The Elderly*

The usual adult dose. If you have kidney problems your doctor may recommend a reduction in dosage.

To reduce the possibility of side effects if you are elderly, you should use the minimum dose for the shortest possible duration. Your doctor may monitor you for bleeding in the stomach.

### *Children over 5 years of age*

Juvenile rheumatoid arthritis:

10 mg/kg bodyweight per day taken in 2 doses  
at 12 hour intervals.

These tablets are not recommended for use in any other indication in children under 16 years of age.

You should continue to take these tablets for as long as your doctor tells you to. If you forget to take a tablet, take one as soon as you remember, unless it is nearly time to take the next one. Do not take a double dose to make up for the missed dose. Take the remaining doses at the correct time.

If you see another doctor or go into hospital, let him or the staff know what medicines you are taking.

If you (or someone else) swallows a lot of the tablets all together, or if you think a child has accidentally swallowed any of the tablets, contact your nearest hospital casualty department or your doctor immediately.

## AFTER TAKING YOUR MEDICINE

Naproxen, like many other medicines may cause side effects in some people. If you experience any of the following, stop taking the tablets and tell your doctor immediately:

- Nausea, vomiting (possibly containing blood), diarrhoea (occasionally with blood and mucus), dark tarry stools
- Blood in the urine
- Abdominal pain, indigestion, inflammation or ulceration of the stomach and occasionally bleeding in the stomach
- Inflammation or ulceration of the mouth e.g. mouth ulcers or cold sores
- Allergic reactions, asthma, wheezing, breathlessness, difficulty breathing
- Stevens-Johnson syndrome (severe blisters and bleeding in the mucous membranes of the lips, eyes, mouth, nasal passage, and genitals)
- Rashes, itching, nettle rash, a bruise like rash, swelling of the voice box and other areas or a skin reaction causing blistering and flaking of the skin
- Jaundice (yellowing of the skin or whites of the eyes)
- Convulsions.

Other side effects may include:

Cardiovascular: inflammation of the blood vessels, accumulation of fluid throughout the body which may result in swollen ankles. Medicines such as Naproxen may be associated with a small increased risk of heart attack (“myocardial infarction”) or stroke.

Kidney: rarely kidney disease.

Liver: abnormal liver function tests or occasionally liver disease.

Nervous system: visual disturbances, headaches, pin-and-needles or numbness, depression, confusion, hallucinations, dizziness and vertigo, insomnia, ringing in the ears, hearing problems, tiredness, drowsiness, inability to concentrate, mental slowing, a general feeling of being unwell or fever with a dislike of light.

Blood: unusual tiredness or weakness, unusual bleeding or unexplained bruising, blood disorders which may be characterised by fever or chills, sore throat, ulcers in your mouth or throat.

Skin: sensitivity to light.

Hair: hair loss (alopecia).

If you have these or any other side-effects whilst taking Naproxen tell your doctor or pharmacist.

## STORING YOUR MEDICINE

Do not use this medicine after the expiry date shown on the outside packaging. These tablets should be stored in the package or container supplied. Do not store above 25°C. Do not transfer them to another container. Keep them in a secure place where children cannot get at them. This medicine is for you ONLY, do not give it to anyone else. Unless your doctor

tells you to, do not keep these tablets for longer than you need. Return all unused medicines to your pharmacist for safe disposal.

#### FURTHER INFORMATION

This leaflet only gives a brief outline of some of the more important points about naproxen. If you want to know more about these tablets or their effects, please ask your doctor or pharmacist.

Revised: August 2007

**NAPROXEN 250MG ENTERIC-COATED TABLETS  
PL 00289/0699**

**LABELLING**

**CARTON/LABEL BRANDED TEXT**

Naproxen 250 mg Enteric Coated Tablets

For oral administration

x tablets

Each tablet contains 250 mg of naproxen.  
Also includes lactose.

Dosage: Use as directed by the physician.  
These tablets should be swallowed whole.

Please read the enclosed leaflet.

**KEEP OUT OF THE REACH AND SIGHT OF CHILDREN**

Do not store above 25°C. Store in the original package.

PL 0289/0699

MA Holder:           TEVA UK Limited  
                              Eastbourne, BN22 9AG England.

**POM**

Distributed By:       Distributor Logo  
                              Distributor Address

Batch No:  
Date of Manf:  
Use Before:

(x = number of tablets)



**BLISTER FOIL**

Naproxen 250 mg Enteric Coated Tablets

MA Holder: TEVA UK Ltd.

Logo

The foil will be overprinted with the batch number and the use before date

N.B: For calendar packs, the foil will also be printed with the days of the week