SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Feminax® Ultra 250mg Gastro-Resistant Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 250 mg of Naproxen. For full list of excipients, see 6.1.

3 PHARMACEUTICAL FORM

Gastro-Resistant Tablet
White, round, biconvex enteric-coated tablets, overprinted in black 3N3.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Indicated for the treatment of primary dysmenorrhoea in women aged 15 to 50 years.

4.2 Posology and method of administration

For oral administration.

To be taken preferably with or after food swallowed whole with water.

Adolescents (post puberty) and adult females between the ages of 15 and 50:

On the first day 2 tablets (500 mg) should be taken initially and then one tablet (250 mg) after 6 to 8 hours if needed.

On the second and third day, if needed, one tablet (250mg) should be taken every 6 to 8 hours. Not more than 3 tablets to be taken per day. The maximum duration of continuous treatment in any one cycle (period) is 3 days.

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 in patients with a history of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.

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.

Naproxen should not be given to patients with 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 warnings on GI and cardiovascular risks below).

Cardiovascular and cerebrovascular effects
Caution (discussion with doctor or pharmacist) is required prior to starting treatment in patients with a history of hypertension and/or heart failure as fluid retention, hypertension 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 infaction or stroke). Although data suggest that the use of naproxen (1000mg daily) may be associated with a lower risk, some risk cannot be excluded. There are insufficient data regarding the effects of low dose naproxen 250mg – 750mg daily to draw firm conclusions on possible thrombotic risks.

Gastrointestinal effects
GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at anytime during treatment, with or without warning symptoms or a previous history of serious GI events.

Although naproxen is usually well tolerated, there have been reported incidences of gastro-intestinal bleeding. Therefore, patients with a history of gastro-

intestinal disease should not take naproxen without being closely monitored by their doctor.

Patients with a history of GI toxicity should report any unusual abdominal symptoms. Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as aspirin (see section 4.5).

If GI bleeding or ulceration occurs in patients receiving the product, the treatment should be withdrawn.

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.

NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as their condition may be exacerbated (see section 4.8).

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.

Patients with impaired renal function, or cardiac impairment should only use naproxen with great caution and under their doctor's supervision who will monitor serum creatinine and/or creatinine clearance. 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.

Patients with impaired liver function should only take naproxen under the supervision of their doctor. 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.

Serious skin reactions, some of them fatal, including Exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see section 4.8). The product should be discontinued at the first appearance of skin rash, mucosal lesion, or any other sign of hypersensitivity.

Steroids
Patients taking steroids should not take naproxen except under the supervision of their doctor. 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 including ibuprofen, cyclooxygenase-2 selective inhibitors or aspirin is not recommended, because of the cumulative risks of inducing serious NSAID-related adverse events.

This product should not be taken, except on the advice of a doctor, by women who first experience period pain more than a year after starting menstruation.

This medicine contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

The label will include:

Read the enclosed leaflet before taking this product. Do not take if you - have or have ever had a stomach ulcer, perforation or bleeding - are allergic to naproxen or any other ingredient of the product, aspirin, ibuprofen or other related painkillers - are taking other NSAID painkillers, or aspirin Speak to a pharmacist or your doctor before taking this product if - you have asthma, liver, heart, kidney or bowel problems - there is a chance you may be pregnant If symptoms persist or worsen, consult your doctor.

4.5 Interaction with other medicinal products and other forms of interaction

Naproxen should not be taken with other medication except on the advice of a doctor, pharmacist or nurse.

Concomitant administration of antacid, colestyramine 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.

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

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 ulceration or bleeding. See section 4.4 Special Warnings and Special Precautions for use.

Anti-coagulants: NSAIDs may enhance the effects of anti-coagulants, such as warfarin. See section 4.4 Special Warnings and Special Precautions for use.

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding (see section 4.4)

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 Fertility, Pregnancy and lactation

Naproxen should not be used during pregnancy or lactation except on the advice of a doctor.

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.

Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (See section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis exacerbation of colitis and Crohn's disease (See section 4.4 - Special warnings and precautions for use) have been reported following administration. Less frequently, gastritis has 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, and cardiac failure, have been reported in association with NSAID treatment.

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) (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.

Bullous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis (very rare).

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 intake, 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 Glycollate (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 (E904),
Soya lecithin (E322),
Antifoam agent,
Black iron oxide (E172).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Do not store above 25ºC. Store in the original package.

6.5 Nature and contents of container

Blister strips in packs of 3, 6, 8 or 9 tablets.

6.6 Special precautions for disposal

Not applicable

7 MARKETING AUTHORISATION HOLDER

Bayer plc

400 South Oak Way

Reading

RG2 6AD

8 MARKETING AUTHORISATION NUMBER(S)

PL 00010/0631

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

04/02/2013

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18/10/2018