Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Momendol 220 mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Naproxen 200 mg (as Naproxen sodium 220 mg)

Excipient with known effect: 41,8 mg lactose

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

White, round, biconvex.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Momendol is indicated in adults and adolescents above 16 years for short-term symptomatic treatment of mild to moderate pain such as joint and muscle pain, headache, toothache and menstrual pain. Momendol may also be useful in the relief of fever.

4.2 Posology and method of administration

Posology
Adults and adolescents over age 16: 1 film-coated tablet every 8-12 hours.
On the first day, if needed, a better effect may be obtained by starting with 2 film-coated tablets followed by 1 film-coated tablet after 8-12 hours.
Do not exceed 3 film-coated tablets in 24 hours.

Elderly/Renal impairment

In elderly and in patients with mild to moderate renal impairment dosages should not exceed 2 film-coated tablets in 24 hours (see sections 4.3 and 4.4).

Paediatric population

Momendol is contraindicated in children aged 12 years. (see section 4.3).

Method of administration
Momendol should be administered preferably after meal. Swallow film-coated whole tablets with some water. Do not take for more than 7 days for pain and 3 days for the treatment of fever. Patients should be advised to consult their physician if pain or fever persist or worsen.

4.3 Contraindications

Hypersensitivity to the active substance, or to any of the excipients listed in section 6.1 or other chemically-related substances.

Naproxen is contraindicated in patients suffering from allergic manifestations such as asthma, urticaria, rhinitis, nasal polyps, angioedema, anaphylactic or anaphylactoid reactions induced by acetylsalicylic acid, analgesics, NSAIDs and/or anti-rheumatic medicinal products due to possible cross-sensitivity. Naproxen is contraindicated in patients with gastro-intestinal bleeding or perforation related to previous NSAIDs therapy , active or history of recurrent peptic ulcer/haemorrhage, chronic inflammatory bowel diseases (ulcerative colitis, Crohn's disease), severe liver impairment, severe heart failure, severe renal impairment (creatinine clearance <30 ml/min) angioedema, during intensive care with diuretics and in subjects with current bleeding and at hemorrhagic risk under treatment with anticoagulants. Third trimester of pregnancy and lactation(see section 4.6, *)*.Contra-indicated in children under 12 years.

4.4 Special warnings and precautions for use

Undesirable effects may be minimised by using the minimum effective dose for the shortest duration necessary to control symptoms (see GI and cardiovascular risks below). 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 (1000 mg daily) may be associated with a lower risk, some risk cannot be excluded. There are insufficient data regarding the effects of low dose naproxen (600 mg/die) to draw firm conclusions on possible thrombotic risks.
There is a strong relationship between dose and severe gastrointestinal adverse events. Therefore the lowest effective dose should always be used.

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.
Urine output and renal function should be closely monitored, particularly in the elderly, in patients with chronic congestive heart failure or chronic renal failure and in patients on diuretic treatment, following major surgery having involved hypovolemia. In severe heart failure, worsening of the condition may occur.

Adopt special caution in patients with past or present signs of allergy, since the product may cause bronchospasm, asthma or other allergic manifestations and in patients with a previous gastrointestinal disease or hepatic impairment. If vision disorders occur Momendol should be discontinued. 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 NSAIDSs (see section 4.8). Patients appear to be at highest risk of these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment. Momendol should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity. Naproxen as any other NSAID may mask symptoms of underlying infectious disease.

In isolated cases an exacerbation of infective inflammations (e.g. development of necrotizing fasciitis) has been described in temporal connection with the use of NSAIDs. 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. The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (See section 4.3), and in the elderly. These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk (see below and 4.5).

Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment. 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). When GI bleeding or ulceration occurs in patients receiving Momendol, the treatment should be withdrawn. 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 use of Momendol with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided. In elderly patients, compromised renal, hepatic and cardiac function are more likely and this group of patients is more exposed to the risk of undesirable effects

of NSAIDs especially gastrointestinal bleeding and perforation which may be fatal. Prolonged use of NSAIDs in the elderly is not recommended. Naproxen inhibits platelet aggregation and can prolong bleeding time. Patients who have coagulation disorders or are receiving drug therapy that interferes with haemostasis should be carefully observed when Momendol is administered. Caution should be taken in daily consumers of high doses of alcohol, due to risk of stomach bleeding. In case of pain from gastro-intestinal origin the use of the product should be avoided. This medicinal product contains lactose: patients with rare hereditary problems of galactose intolerance, the lace lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Not recommended combinations:
Naproxen administration with other NSAIDs or corticosteroids is not recommended due to the increased risk of ulcers and gastrointestinal bleeding (see section 4.4).
Naproxen may enhance the effect of anticoagulants such as of cumarinic-like anticoagulants (e.g. warfarin, dicumarol) because it prolongs protrombin time and reduces platelet aggregation increasing the risk of gastrointestinal bleeding (see section 4.4).
The combination of naproxen and lithium should be avoided; when it is necessary, monitoring of lithium plasma levels should be reinforced and dosage should be adjusted.

Combinations to be administered with precaution:
Due to the high binding of naproxen with plasma proteins, treatment with hydantoic or sulphamidic drugs should be used with caution. Special care should be used also in patients under treatment with cyclosporin, tacrolimus, sulfonyluria, loop diuretics, methotrexate, beta-blocking agents, ACE inhibitors, probenecid, thiazide diuretics and digoxin. Naproxen can alter bleeding time (may prolong bleeding time until 4 days after discontinuation of therapy), creatinine clearance (may decrease), BUN, serum creatinine and potassium concentrations (may increase), liver function test (may have elevation of transaminases). Naproxen may falsely increase urinary 17-ketosteroid values; may interfere with urinary assays for 5-hydroxy-indoleacetic acid.

Before testing adrenal function Naproxen therapy should be discontinued for at least 72 hours.

4.6 Fertility, pregnancy and lactation

Pregnancy

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/fœtal development. Data from epidemiological studies raise concern about an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The risk is believed to increase with dose and duration of therapy.
In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period. During the first and second trimester of pregnancy, naproxen should not be given unless clearly necessary. If naproxen is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:
- Cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction which may progress to renal failure with olig-hydroamniosis;

the mother and the neonate, at the end of pregnancy, to:
- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses.

- inhibition of uterine contractions resulting in delayed and prolonged labour.

Consequently, Naproxen is contraindicated during the third trimester of pregnancy.(see section 4.3)

Lactation:
Since NSAIDs are excreted in breast milk, as a precautionary measure, their use is contraindicated during breast-feeding (see section 4.3).

Fertility
There is some evidence that drugs which inhibit cyclo-oxygenase / prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment.

4.7 Effects on ability to drive and use machines

Momendol does not normally affect the capacity to drive and use other machinery. However, caution is recommended to those who perform a job requiring vigilance, should, in the course of therapy, they notice sleepiness, dizziness, depression.

4.8 Undesirable effects

The following adverse events have been reported with NSAIDs and with naproxen The most commonly observed adverse events are gastrointestinal in nature.
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).

Undesirable effects are reported below according to the MedDRA classification and System Organ Class
The following rate values have been used: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1000 to < 1/100); rare (≥ 1/10000 to < 1/1000); very rare (< 1/10000), not known (cannot be estimated from the available data).

Blood and lymphatic system disorders - *Very rare:* aplastic or hemolytic anemia, trombocytopenia, granulocytopenia.

Immune system disorders - *Uncommon:* allergic reaction (including facial oedema and angioedema)

Psychiatric system disorders - *Uncommon:* sleep disturbances, excitation

Nervous system disorders - *Common*: headache, somnolence, dizziness. *Very rare:* meningitis-like reaction.

Eye disorders - *Uncommon:* visual disturbances.

Ear and labyrinth disorders - *Uncommon:* tinnitus, hearing disorders.

Cardiac disorders – *Very rare:* tachycardia, oedema, hypertension and cardiac failure have been reported in association with NSAID treatment

Vascular disorders - *Uncommon:* bruise

Respiratory, thoracic and mediastinal disorders - *Very rare:* dyspnea, asthma.

Gastrointestinal disorders – *Common*: nausea, dyspepsia, vomiting, pyrosis, gastralgia, flatulence. *Uncommon:* diarrhoea, constipation. *Rare*: peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (see section 4.4) haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4) *Very rare:* colitis, stomatitis.
Less frequently, gastritis has been observed

Hepatobiliary disorders - *Very rare:* jaundice, hepatitis, impaired liver function

Skin and subcutaneous tissue disorders - *Uncommon:* skin rash/pruritus. *Very rare:* photosensitivity, alopecia, bullous disorder including Stevens-Johnson syndrome and toxic epidermal necrolysis

Renal and urinary disorders - *Uncommon:* kidney function abnormal.

General disorders and administration site conditions - *Uncommon:* chills, oedema (including peripheral oedema).

Investigations - *Very rare:* blood pressure increased.

As with other NSAIDs, allergic reactions of anaphylactic or anaphylactoid nature may occur in patients with or without a previous exposure to this class of medicinal products. The typical symptoms of an anaphylactic reaction include: severe and sudden hypotension, acceleration or slowing down of the heart beat, unusual fatigue or weakness, anxiety, agitation, loss of consciousness, difficult breathing or swallowing, pruritus, urticaria with or without angioedema, skin reddening, nausea, vomiting, cramp-like abdominal pain, diarrhoea.

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
HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517, E-mail:medsafety@hpra.ie: Website: www.hpra.ie.

4.9 Overdose

Symptoms
Overdose signs include numbness, heartburn, diarrhoea, nausea, vomiting, drowsiness, hypernatremia, metabolic acidosis, convulsions.

Management
In case of incidental or voluntary ingestion/administration of an overdose of the medicinal product, the physician should adopt the usual requested remedies for these cases. Emptying of the stomach and normal supportive measures are recommended. The prompt administration of an adequate amount of active carbon can reduce medicinal absorption.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antiinflammatory and antirheumatic products, non-steroids, propionic acid derivatives, ATC-code: M01AE02

Naproxen has an analgesic, anti-inflammatory and antipyretic activity. The analgesic activity is of the non narcotic type. Naproxen also inhibits platelet functions. All these properties are believed to result from a reduction of prostaglandin synthesis by inhibition of the cyclooxygenase enzymatic pathway. In addition, naproxen stabilizes the lysosomal membrane and possesses antibradykinin and anticomplement effects.

5.2 Pharmacokinetic properties

In man naproxen sodium is absorbed following oral administration and reaches therapeutic blood levels around 1 hour after administration. It has a half-life of about 16 hours. The steady-state level is reached after 4-5 doses. Over 99% of naproxen sodium is reversibly bound to plasma proteins. 95% of the administered dose is excreted through the urine, in part unaltered and in part as 6-o-desmethylnaproxen, in the free or conjugated form.

5.3 Preclinical safety data

Toxicological tests on different animal species with different routes of administration have shown that acute toxicity of naproxen is low. In chronic toxicity studies naproxen showed toxicity profile typical of NSAIDs, i.e. gastrointestinal toxicity and, at high doses, renal damage. No teratogenic effects have been shown with naproxen and there was no indication of a carcinogenic potential in a two-year study in the rat. Mutagenicity tests with naproxen showed negative results. Due to prostaglandin synthesis inhibition, naproxen given during the last period of pregnancy can cause delay in parturition and fetotoxic effects.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Lactose monohydrate
Maize starch
Cellulose microcrystalline
Povidone (K25)
Sodium starch glycollate
Sillica colloidal anhydrous
Magnesium stearate

Tablet film-coating:

Hypromellose
Macrogol 400
Titanium dioxide (E171)
Talc

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years.

6.4 Special precautions for storage

Store in original container and original package to protect from light and moisture.

6.5 Nature and contents of container

Aluminium/PVC blisters containing 12 film-coated tablets.

Each lithographed cardboard box contains 12 or 24 film-coated tablets (1-2 blisters of 12 film-coated tablets each).

Not all pack-sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Aziende Chimiche Riunite Angelini Francesco A.C.R.A.F. S.p.A.
Viale Amelia 70
00181 Rome
Italy

8 MARKETING AUTHORISATION NUMBER

PA 959/2/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16 May 2003
Date of last renewal: 7 March 2007

10 DATE OF REVISION OF THE TEXT

August 2016