SCHEDULING STATUS:
S3

PROPRIETARY NAME AND DOSAGE FORM:
BIO-NAPROXEN 250 mg Tablets
BIO-NAPROXEN 500 mg Tablets

COMPOSITION:
Each BIO-NAPROXEN 250 mg tablet contains 250 mg of Naproxen as active ingredient.
Contains sugar: Lactose 78,40 mg.
Each BIO-NAPROXEN 500 mg tablet contains 500 mg of Naproxen as active ingredient.
Contains sugar: Lactose 156,80 mg
The following inactive ingredients are also included:
Lactose, pregelatinised starch, sodium starch glycolate, quinoline yellow lake 19248, polysorbate 80, povidone, purified talc, magnesium stearate, purified water.

PHARMACOLOGICAL CLASSIFICATION:
3.1 Antirheumatics (anti-inflammatory agent)

PHARMACOLOGICAL ACTION:
Naproxen is a non-steroidal anti-inflammatory agent (NSAID) with analgesic and antipyretic properties. Naproxen is readily absorbed from the gastrointestinal tract, with peak plasma levels being reached 2 to 4 hours after ingestion. Naproxen is extensively plasma protein bound, with a plasma half-life of 12 to 15 hours.
Approximately 95 % of a dose is excreted in the urine as Naproxen and 6-O-desmethyl naproxen. Naproxen crosses the placenta and is excreted in breast milk.
Naproxen is an inhibitor of cyclo-oxygenase, responsible for the biosynthesis of prostaglandins. It also alters platelet function to prolong bleeding time. Naproxen inhibits leucocyte migration.

INDICATIONS:
Treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. BIO-NAPROXEN may also be used in the treatment of acute gout, mild to moderate pain, associated with primary dysmenorrhoea, bursitis and acute tendonitis.

CONTRAINDICATIONS:
- Hypersensitivity or allergic reactions to medicines containing naproxen or naproxen sodium, aspirin or other non-steroidal anti-inflammatory agents.
- Patients in whom aspirin or other non-steroidal anti-inflammatory / analgesic medicines induce the syndrome of asthma, rhinitis, nasal polyps or urticaria. These reactions have the potential of being fatal. Severe anaphylactic-like reactions to naproxen have been reported in such patients.
- BIO-NAPROXEN should not be used in pregnant women or mothers breastfeeding their infants.
- Heart failure.
- History of gastrointestinal perforation, ulceration or bleeding (PUBs) related to previous NSAIDs.
- Active or history of recurrent ulcer/haemorrhage/perforations.
- Porphyria.
- *Children:* BIO-NAPROXEN is not recommended for use in children under the age of 16 years.
- Severe renal function impairment: BIO-NAPROXEN is not recommended in patients with baseline creatinine clearance of less than 20 ml/minute because accumulation of naproxen metabolites has been seen in such patients (see WARNINGS and SPECIAL PRECAUTIONS)

WARNINGS and SPECIAL PRECAUTIONS:
BIO-NAPROXEN should be used with special care in patients with gastrointestinal bleeding, with a history of bronchospasm (asthma), with impaired renal or liver function and elderly patients or patients with cardiovascular disease.
Cardiovascular events:
Caution is required in patients with a history of hypertension and/or heart failure as fluid retention and oedema have been reported in association with BIO-NAPROXEN therapy. In view of BIO-NAPROXEN's inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.
Caution is required in patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) and should only be treated after careful consideration.
Elderly patients:
The elderly have an increased frequency of adverse reactions to NSAIDs including BIO-NAPROXEN, especially gastrointestinal perforation, ulceration and bleeding (PUBs) which may be fatal.
Elderly or debilitated patients may be at a greater risk of experiencing undesirable effects than younger patients. In elderly patients the clearance is reduced. Use of the lowest possible dose is recommended.
Gastrointestinal ulceration, bleeding and perforation (see CONTRAINDICATIONS):
Gastrointestinal mucosal injury may occur. Serious gastrointestinal toxicity, such as gastrointestinal irritation, bleeding, ulceration and perforation can occur at any time, with or without warning signs, in patients treated with NSAIDs including BIO-NAPROXEN therapy.
BIO-NAPROXEN should be given with caution to patients with a history of gastrointestinal disease (e.g. ulcerative colitis, Crohn's disease, hiatus hernia, gastro-oesophageal reflux disease, angiodysplasia) as the condition may be exacerbated. The risk of gastrointestinal perforation, ulceration or bleeding (PUBs) is higher with increasing dose and duration of BIO-NAPROXEN treatment, in patients with a history of ulcers, and the elderly.
When gastrointestinal bleeding or ulceration occurs in patients receiving BIO-NAPROXEN, treatment with BIO-NAPROXEN should be stopped.
Haematological:
BIO-NAPROXEN decreases platelet aggregation and prolongs bleeding time. This effect should be brought into consideration when bleeding times are determined. Patients who suffer from coagulation disorders or are receiving medicine therapy that interferes with haemostasis should be carefully monitored if BIO-NAPROXEN is administered.
Patients at high risk of bleeding, and those on full anticoagulation therapy, may be at increased risk of bleeding if given BIO-NAPROXEN concurrently.
As it causes an increased bleeding tendency it should be given with caution to patients receiving coumarin anti-coagulants such as warfarin, and to patients with bleeding disorders and cardiovascular disease. BIO-NAPROXEN may interfere with some tests for 17-ketogenic steroids.
Anaphylactic (anaphylactoid) reactions:
Hypersensitivity reactions may occur in susceptible individuals. Anaphylactic (anaphylactoid) reactions may occur in patients with or without a history of hypersensitivity or previous exposure to aspirin, or other non-steroidal anti-inflammatory medicines or BIO-NAPROXEN.
Because of the possibility of cross-sensitivity due to structural relationships which exist among non-steroidal, anti-inflammatory medicines, acute allergic reactions are more likely to occur in patients who have exhibited previous allergic reactions to these compounds.
Patients who have exhibited aspirin hypersensitivity in the past (usually as the angioedema/asthma syndrome) may exhibit the same phenomenon with BIO-NAPROXEN. Bronchospasm may be precipitated in such patients and in patients suffering from, or with a history of bronchial asthma or allergic disease (see CONTRAINDICATIONS).
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported. BIO-NAPROXEN should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.
Renal effects:
There have been reports of impaired renal function, renal failure, acute interstitial nephritis, haematuria, proteinuria, renal papillary necrosis and occasionally nephrotic syndrome associated with naproxen-containing products.
BIO-NAPROXEN should be used with caution in patients with impaired renal function or a history of kidney disease, especially if long-term usage is considered as BIO-NAPROXEN is an inhibitor of prostaglandin synthesis.
Caution should be taken in patients with conditions leading to a reduction in blood volume and/or renal blood flow where renal prostaglandins play a supportive role in the maintenance of renal perfusion. In these patients administration of BIO-NAPROXEN may lead to a dose-dependent reduction in renal prostaglandin formation and may cause overt renal decompensation or failure. Patients with the greatest risk of developing this reaction are those with impaired renal function, hypovolaemia, heart failure, liver dysfunction, salt depletion, those taking diuretics and the elderly. Discontinuation of BIO-NAPROXEN is generally followed by recovery to the pre-treatment state.
BIO-NAPROXEN should be used with great caution in these patients and the close monitoring of serum creatinine and/or creatinine clearance is recommended. BIO-NAPROXEN is not recommended in patients with baseline creatinine clearance of less than 20 ml/min because accumulation of Naproxen metabolites has been seen in these patients (see CONTRAINDICATIONS).
Haemodialysis does not decrease the plasma concentration of BIO-NAPROXEN due to the high degree of its protein binding.
Hepatic effects:
Elevations of one or more liver function tests may occur. Hepatic abnormalities could be the result of hypersensitivity rather than direct toxicity. Severe hepatic reactions, including jaundice and hepatitis (some cases of hepatitis have been fatal) have been reported. Cross-reactivity has been reported.
Antipyretic effects:
The antipyretic and anti-inflammatory activities of BIO-NAPROXEN may reduce fever and inflammation and therefore diminish their utility as diagnostic signs.
Corticosteroids:
If the corticosteroid dosage is reduced or eliminated during BIO-NAPROXEN therapy, the corticosteroid dosage must be reduced gradually and the patient must be monitored closely for any evidence of adverse effects, including adrenal insufficiency and worsening of symptoms of arthritis.
Ocular effects:
Cases of adverse ocular disorders including papillitis, retrobulbar optic neuritis and papilloedema have been reported in users of NSAIDs including BIO-NAPROXEN, although a cause-and-effect relationship cannot be established; accordingly, patients who develop visual disturbances during treatment with BIO-NAPROXEN should have an ophthalmological examination.
Pregnancy:
Regular use of NSAIDs such as BIO-NAPROXEN during the third trimester of pregnancy, may result in premature closure of the foetal ductus arteriosus in utero, and possibly, in persistent pulmonary hypertension of the new-born. The onset of labour may be delayed and its duration increased.
Combination with other NSAIDs:
The concurrent use of BIO-NAPROXEN and other NSAIDs is not recommended, due to the cumulative risks of inducing serious NSAID-related adverse events.
Other:
BIO-NAPROXEN contains lactose and should not be administered to patients with rare hereditary problems, or a history of lactose intolerance, Lapp lactose deficiency or glucose-galactose malabsorption.
Driving and operating machinery:
Some patients may experience drowsiness, dizziness, vertigo, insomnia or depression with the use of BIO-NAPROXEN. If patients experience any of these or similar undesirable effects, they should exercise caution in carrying out activities that require alertness.

INTERACTIONS:
Antacids or cholestyramine: the concurrent administration with BIO-NAPROXEN can delay the absorption of BIO-NAPROXEN, but does not affect the extent thereof.
Food: concomitant administration can delay the absorption of BIO-NAPROXEN but does not affect the extent thereof.
Probenecid: during concurrent administration caution is advised as it increases BIO-NAPROXEN plasma levels and extends its half-life considerably.
Methotrexate: during concurrent administration caution is advised since BIO-NAPROXEN has been reported to reduce the clearance of methotrexate, and thus possibly enhances its toxicity.
Furosemide: BIO-NAPROXEN may inhibit the natriuretic effect of furosemide. The effect of furosemide is diminished on concomitant administration of BIO-NAPROXEN.
Lithium: inhibition of renal lithium clearance leading to increases in plasma lithium concentrations has been reported.
Cardiac glycosides: increased plasma concentrations of digoxin have been reported.
ACE inhibitors, cyclosporin or diuretics: concomitant administration may increase the risk of nephrotoxicity.
ACE inhibitors and potassium-sparing diuretics: concomitant administration may increase the risk of hyperkalaemia.
Antihypertensive agents: the antihypertensive effect of agents such as ACE inhibitors, beta-blockers and diuretics may be reduced.
Quinolones: convulsions may occur.
Phenytoin and sulphonylurea antidiabetics: the effects may be enhanced.
Thyroid function tests: BIO-NAPROXEN may interfere with thyroid function tests by lowering serum thyroid hormone concentrations.
Adrenal function tests: it is advised that BIO-NAPROXEN therapy should be temporarily discontinued 48 hours before these tests are performed.
BIO-NAPROXEN may artifactually interfere with some tests for 17-ketogenic steroids. BIO-NAPROXEN may similarly interfere with some urinary assays of 5-hydroxyindoleacetic acid (5-HIAA).
NSAIDS: use of two or more NSAIDs concomitantly could result in an increase in side effects.
Corticosteroids: increased risk of gastrointestinal perforation, ulceration or bleeding (PUBs).
Anti-coagulants: BIO-NAPROXEN may enhance the effects of anti-coagulants such as warfarin.
Anti-platelet medicines and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding.
Aspirin: Plasma concentrations of BIO-NAPROXEN are significantly decreased by concomitant administration of therapeutic doses of aspirin.
Thiazide diuretics, beta-adrenergic antagonists, prazosin and captopril:
BIO-NAPROXEN may reduce the diuretic, natriuretic and anti-hypertensive effects of these medicines, due to the inhibition of synthesis of renal prostaglandins.

PREGNANCY AND LACTATION:
The safety and efficacy of BIO-NAPROXEN in pregnancy and lactation has not yet been established.
BIO-NAPROXEN should not be used during pregnancy. Use during the third trimester of pregnancy may cause uterine inertia and/or premature closure of the ductus arteriosus.
BIO-NAPROXEN crosses the placenta and has been found in the milk of lactating mothers.

DOSAGE AND DIRECTIONS FOR USE:
BIO-NAPROXEN should not be used in children under the age of 16 years.
Adults:
Rheumatoid arthritis, osteo-arthritis and ankylosing spondylitis: 250 to 375 mg twice daily with food.
Acute gout: An initial dose of 750 mg with meals, followed by 250 mg every 8 hours until the attack has subsided.
Mild to moderate pain associated with primary dysmenorrhoea, bursitis and acute tendonitis: An initial dose of 500 mg followed by 250 mg every 6 to 8 hours with food.
Use the lowest effective dose for the shortest possible duration of treatment.

SIDE EFFECTS:
Gastrointestinal system disorders
The most commonly observed adverse effects occurring with BIO-NAPROXEN are gastrointestinal in nature. Peptic ulcers, perforation or gastrointestinal bleeding, sometimes fatal. Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease, gastritis.
Frequency unknown: Colitis, oesophagitis, non-peptic gastrointestinal ulceration, abdominal discomfort.
Central nervous system disorders
Frequent: Dizziness, drowsiness, headache, light-headedness, vertigo
Frequency unknown: Malaise, nervousness, depression, insomnia, cognitive dysfunction, convulsions, dream abnormalities, myalgia, muscle weakness, headache, inability to concentrate.
Skin and subcutaneous tissue disorders
Frequent: Ecchymoses, itching (pruritus), purpura, skin eruptions, sweating
Frequency unknown: Bullous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis, skin rash, erythema multiforme, erythema nodosum, fixed drug eruption, lichen planus, pustular reaction, SLE, urticaria, alopecia, photosensitivity reactions, including cases of porphyria cutanea tarda or epidermolysis bullosa. If skin fragility, blistering or other symptoms suggestive of pseudoporphyria occur, treatment should be discontinued immediately and the patient closely monitored.
Ear and labyrinth disorders
Frequent: Hearing disturbances, tinnitus
Frequency unknown: Hearing impairment
Eye disorders
Frequent: Visual disturbances
Frequency unknown: Blurred vision and other ocular reactions, corneal opacity, papillitis, retrobulbar optic neuritis and papilloedema
Cardiac disorders
Frequent: Palpitations, oedema
Frequency unknown: Cardiac failure, hypertension, pulmonary oedema, vasculitis, angioneurotic oedema
Hepato-biliary disorders
Frequency unknown: Abnormalities of liver function tests, hepatitis (some cases of hepatitis have been fatal), jaundice
Respiratory, thoracic and mediastinal disorders
Frequent: Dyspnoea
Frequency unknown: Asthma, eosinophilic pneumonitis
Endocrine disorders
Frequency unknown: Pancreatitis
Immune system disorders
Less frequent: Hypersensitivity reactions including fever, asthma, rashes, hepatotoxicity, and aseptic meningitis may occur.
Frequency unknown: Skin rashes and angioedema, anaphylactoid reactions
Renal and urinary disorders
Frequency unknown: Impairment of renal function, haematuria, hyperkalaemia, interstitial nephritis, nephrotic syndrome, renal disease, reversible renal failure, renal papillary necrosis, raised serum creatinine and fluid retention may occur.
Blood and the lymphatic system disorders
Frequency unknown: Agranulocytosis, thrombocytopenia, leukopenia, granulocytopenia, neutropenia, eosinophilia, anaemias, including aplastic anaemia and haemolytic anaemia.
Infections and infestations
Frequency unknown: Pyrexia (chills and fever).

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
(See SIDE EFFECTS). Symptoms of overdosage may include dizziness, drowsiness, epigastric pain, abdominal discomfort, heartburn, indigestion, nausea, transient alterations in liver function, hypoprothrombinaemia, renal dysfunction, metabolic acidosis, apnoea, disorientation or vomiting. BIO-NAPROXEN may be absorbed rapidly and high blood levels could be reached quickly.
A few patients have experienced convulsions.
Treatment is supportive and symptomatic. Haemodialysis does not decrease the plasma concentration of naproxen due to the high degree of its protein binding.

IDENTIFICATION:
Bio-Naproxen 250 mg:
Yellow, round, biconvex tablet, breakline on one side, plain on the other side.
Bio-Naproxen 500 mg:
Yellow, capsule-shaped, biconvex tablet coded with 'NPX 500' on one side and breakline on reverse.

PRESENTATION:
BIO-NAPROXEN 250 mg and BIO-NAPROXEN 500 mg can be packed in the following containers:
White opaque, polypropylene securitainer containing 30, 100 and 250 tablets.
Screw cap white, opaque HDPE container containing 100 and 250 tablets.
Amber PVC/PVDC blister containing 56 or 140 tablets per carton.
White, opaque, polyethylene zip lock patient ready pack (for state use only), containing 56 tablets.
All pack sizes may not necessarily be marketed at one time.

STORAGE INSTRUCTIONS:
Store at or below 25 °C in a dry place. Protect from light.
Keep out of reach of children.

REGISTRATION NUMBER
BIO-NAPROXEN 250 mg: W/3.1/436
BIO-NAPROXEN 500 mg: W/3.1/437

NAME AND BUSINESS ADDRESS OF APPLICANT
Biotech Laboratories (Pty) Ltd
Ground Floor, Block K West, Central Park,
400 16th Road, Randjespark, Midrand, 1685
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SKEDULERINGSTATUS:
S3

EIENDOMSNAAM EN DOSEERVORM:
BIO-NAPROXEN 250 mg Tablette
BIO-NAPROXEN 500 mg Tablette

SAMESTELLING:
Elke BIO-NAPROXEN 250 mg tablet bevat 250 mg Naproksen as aktiewe bestanddeel.
Bevat suiker: Laktose 78,40 mg.
Elke BIO-NAPROXEN 500 mg tablet bevat 500 mg Naproksen as aktiewe bestanddeel.
Bevat suiker: Laktose 156,80 mg.
Die onaktiewe bestanddele is as volg:
Laktose, pregegelatiniseerde stysel, natriumstyselglikolaat, quinoline yellow lake 19248, polysorbaat 80, povidoon, gesuiwerde talk, magnesiumstearaat, gesuiwerde water.

FARMAKOLOGIESE KLASSIFIKASIE:
3.1 Anti-rumatiekmiddels (anti-inflammatoriese middels)

FARMAKOLOGIESE WERKING:
Naproksen is 'n nie-steroïdale anti-inflammatoriese geneesmiddel (NSAIG) met pynstillende en koorswerende eienskappe. Naproksen word geredelik vanuit die gastro-intestinale kanaal geabsorbeer, met piekplasmavlakke wat 2 tot 4 ure na inname bereik word. Naproksen is omvattend plasmaproteïengebonde, met 'n plasma-halfleeftyd van 12 tot 15 ure. Ongeveer 95 % van 'n dosis word in die uriene uitgeskei as naprokseen en 6-O-desmetielnaprokseen.
Naprokseen kruis die plasenta on word in borsmelk uitgeskei.
Naprokseen is 'n onderdrukker van siklo-oksigenase wat vir die biosintese van prostaglandiene verantwoordelik is. Naprokseen verleng bloedingstyd deur die bloedplaatjiefunksie te verander. Naprokseen onderdruk leukosietmigrasie.

INDIKASIES:
Behandeling van rumatoïede artritis, osteo-artritis en ankiloserende spondilitis. BIO-NAPROXEN kan ook gebruik word vir die behandeling van akute jig, lig tot matige pyn, wat verband hou met primêre dismenoree, bursitis en akute tendonitis.

KONTRAINDIKASIES:
- Hipersensitiwiteits- of allergiese reaksies teenoor medisynes wat naproksen of natriumnaproksen, aspirien, of ander nie-steroïedale anti-inflammatoriese middels bevat.
- Pasiënte by wie aspirien of ander nie-steroïedale anti-inflammatoriese middels / analgetiese medisynes 'n sindroom van asma, rinitis, nasale poliepe or urtikarie veroorsaak. Hierdie reaksies het die potensiaal om noodlottig te wees. Ernstige anafilaktiese-agtige reaksies teenoor naproksen is aangemeld in hierdie pasiënte.
- BIO-NAPROXEN moet nie gebruik word in swanger of borsvoedende vrouens nie.
- Hartversaking.
- Geskiedenis van gastro-intestinale perforasie, ulserasie of bloeding (PUBs) wat verband hou met vorige gebruik van NSAIGs.
- Aktiewe, of 'n geskiedenis van herhalende ulkus/bloeding/perforasies.
- Porfirie.
- *Kinders:* BIO-NAPROXEN word nie anbeveel vir gebruik in kinders onder die ouderdom van 16 jaar nie.
- Ernstige nierfunksie inkorting: BIO-NAPROXEN word nie aanbeveel vir gebruik in pasiënte met 'n basislyn kreatinienopruiming van minder as 20 ml / minuut nie, aangesien 'n opeenhoping van naproksen-metaboliete waargeneem is in hierdie pasiënte (sien WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS).

WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS:
BIO-NAPROXEN moet met omsigtigheid gebruik word in pasiënte met gastro-intestinale bloeding, met 'n geskiedenis van brongospasma (asma), met ingekorte nier- of lewerfunksie, en bejaarde pasiënte of pasiënte met kardiovaskulêre siekte.
Kardiovaskulêre gebeurtenisse:
Omsigtigheid word vereis in pasiënte met 'n geskiedenis van hipertensie en/of hartversaking aangesien vloeistofretensie en edeem aangemeld is wat verband hou met BIO-NAPROXEN behandeling. In die lig van BIO-NAPROXEN se inherente potensiaal om vloeistofretensie te veroorsaak, kan hartversaking veroorsaak word in sommige verswakte pasiënte.
Omsigtigheid word vereis in pasiënte met beduidende risikofaktore vir kardiovaskulêre gebeurtenisse (bv. hipertensie, hiperlipidemie, diabetes mellitus, rook) en moet slegs behandel word na deeglike oorweging.
Bejaarde pasiënte:
Die gereeldheid wat negatiewe reaksies teenoor NSAIGs, ingesluit BIO-NAPROXEN, voorkom is verhoog in bejaardes, veral gastro-intestinale perforasie, ulserasie en bloeding (PUBs), wat noodlottig kan wees.
Bejaarde of verswakte pasiënte loop 'n groter risiko tot negatiewe effekte as jonger pasiënte.
In bejaardes is die opruiming verminder. Die laagste moontlike dosis word aanbeveel.
Gastro-intestinale ulserasie, bloeding en perforasie (sien KONTRAINDIKASIES):
Gastro-mukosale besering mag voorkom. Ernstige gastro-intestinale toksisiteit, soos gastro-intestinale irritasie, bloeding, ulserasie en perforasie kan ter enige tyd voorkom, met of sonder waarskuwingstekens, in pasiënte wat behandel word met NSAIGs, wat BIO-NAPROXEN behandeling insluit.
BIO-NAPROXEN moet met omsigtigheid toegedien word aan pasiënte met 'n geskiedenis van gastro-intestinale siektes (bv. ulseratiewe kolitis, Crohn se siekte, diafragmabreuk, gastro-esofageale refluks siekte, angiodisplasie) aangesien die toestand vererger kan word.
Daar is 'n verhoogde risiko van gastro-intestinale perforasie, ulserasie of bloeding (PUBs), byverhoogde dosisse en duur van BIO-NAPROXEN behandeling, asook by pasiënte met 'n geskiedenis van ulkusse asook bejaardes.
Wanneer gastro-intestinale bloeding of ulserasie voorkom in pasiënte wat BIO-NAPROXEN ontvang, moet die behandeling met BIO-NAPROXEN gestaak word.
Hematologies:
BIO-NAPROXEN verminder plaatjieklomping en verleng bloedingstyd. Hierdie effek moet in ag geneem word wanneer bloedingstye bepaal word. Pasiënte wat aan bloedstollingafwykings ly, of wie medisinale behandeling ontvang wat inmeng met hemostase, moet noukeurig gemonitor word indien BIO-NAPROXEN toegedien word.
Pasiënte met 'n hoë risiko vir bloeding, asook diegene op volle antistolterapie, mag 'n hoër risiko hê op bloeding indien BIO-NAPROXEN gesamentlik gebruik word. Aangesien dit die neiging tot bloeding verhoog, moet dit met omsigtigheid
toegedien word aan pasiënte wie kumarien antistolmiddels soos warfarien ontvang, asook pasiënte met bloeding- en kardiovaskulêre siektes.
BIO-NAPROXEN kan sommige toetse vir 17-ketogeensteroïede belemmer.
Anafilaktiese (anafilaktoïede) reaksies:
Hipersensitiwiteitsreaksies kan by vatbare individue voorkom. Anafilaktiese (anafilaktoïede) reaksies kan voorkom in pasiënte met, of sonder, 'n geskiedenis van hipersensitiwiteit of vorige blootstelling aan aspirien, of 'n ander nie-steroïdale anti-inflammatoriese geneesmiddel of BIO-NAPROXEN.
As gevolg van die moontlikheid dat daar 'n kruissensitiwiteit bestaan tussen nie-steroïdale anti-inflammatoriese geneesmiddels, as gevolg van hulle stukturele verwantskap, is akute allergiese reaksies meer geneig om plaas te vind in pasiënte wat voorheen 'n allergiese reaksie getoon het tot hierdie verbindings.
Pasiënte wat voorheen 'n aspirien sensitiwiteit getoon het (gewoonlik as die angioedeem/asma simdroom) mag dieselfde reaksie toon tot BIO-NAPROXEN. Brongospasma kan ook vererger word by hierdie pasiënte asook in pasiënte wat ly aan, of met 'n geskiedenis van, brongiale asma or allergiese siekte (sien KONTRAINDIKASIES).
Ernstige vel-reaksies, sommige noodlottig, ingesluit eksfoliatiewe dermatitis, Stevens-Johnson sindroom en toksiese epidermale nekrolise is aangemeld. BIO-NAPROXEN moet gestaak word by die eerste verskyning van veluitslag, mukosale letsels of enige ander teken van hipersensitiwiteit.
Renale effekte:
Daar is verslae van ingekorte nierfunksie, nierversaking, akute interstisiële nefritis, hematurie, proteienurie, renale papilêre nekrose en soms ook nefrotiese sindroom verbonde aan naproksen-bevattende produkte.
BIO-NAPROXEN moet met omsigtigheid gebruik word in pasiënte met ingekorte nierfunksie of wie 'n geskiedenis van niersiekte het, veral indien lang-termyn gebruik oorweeg word, aangesien BIO-NAPROXEN 'n inhibeerder is van prostaglandien-sintese.
Sorg moet geneem word met pasiënte wat toestande het wat lei tot 'n verlaging in bloedvolume en/of renale bloedvloei waarin prostaglandiene 'n ondersteunende rol speel in die instandhouding van renale perfusie. In hierdie pasiënte kan die toediening van BIO-NAPROXEN lei tot 'n dosisafhanklike afname in renale prostaglandienvorming en kan duidelike nierdekompensasie of –versaking veroorsaak. Pasiënte wat die grootste risiko loop om hierdie reaksie te ontwikkel is diegene met ingekorte nierfunksie, hipovolemie, hartversaking, lewerdisfunksie, souttekort, diegene wie diuretikum neem asook bejaardes. Staking van BIO-NAPROXEN word gewoonlik gevolg deur die herstel na die voorbehandelingstoestand.
BIO-NAPROXEN moet met groot omsigtigheid gebruik word in hierdie pasiënte en noukeurige monitering van serum kreatinien en/of kreatinien opruiming word aanbeveel. BIO-NAPROXEN is nie aanbeveel in pasiënte met basislyn kreatinien opruiming van minder as 20 ml/min nie, aangesien die ophoping van naproksen matoboliete waargeneem is in hierdie pasiënte (sien KONTRAINDIKASIES).
Hemodialise verlaag nie die plasma konsentrasie van BIO-NAPROXEN nie, as gevolg van die hoë graad van proteienbinding.
Hepatiese effekte:
Verhoging van een of meer lewerfunksietoetse mag voorkom. Hepatiese abnormaliteite mag as gevolg van hipersensitiwiteit, eerder as toksisiteit wees. Erge hepatiese reaksies, insluitend geelsug en hepatitis (sommige gevalle van hepatitis was noodlottig) is aangemeld. Kruis-reaktiwiteit is aangemeld.
Antipiretiese effekte:
Die antipiretiese en anti-inflammatoriese aktiwiteit van BIO-NAPROXEN kan koors en inflammasie verlaag, en dus die gebruik van hierdie simptome in diagnose belemmer.
Kortikosteroïede:
Indien die kortikosteroïed dosis verminder of gestaak moet word gedurende BIO-NAPROXEN behandeling, moet die kortikosteroïed dosis geleidelik verminder word en die pasient noukeurig gemonitor word vir enige tekens van ongunstige effekte, insluitend adrenale ontoereikendheid en die verergering van artritis simptome.
Okkulêre effekte:
Gevalle van ongunstige okkulêre ongesteldhede, insluitend papillitis, retrobulbêre optiese neuritis en papiledeem is aangemeld by gebruikers van NSAIGs, insluitend BIO-NAPROXEN, alhoewel die oorsaak-en-gevolg verwantskap nie vasgestel kan word nie; gevolglik moet pasiënte wie visuele afwykings ontwikkel gedurende behandeling met BIO-NAPROXEN, 'n oftalmologiese ondersoek ondergaan.
Swangerskap:
Die gereelde gebruik van NSAIGs, soos BIO-NAPROXEN gedurende die derde trimester van swangerskap, kan die premature sluiting van die fetale ductus arteriosus in utero veroorsaak, en moontlik ook die aanhoudende pulmonale hipertensie by die pasgeborene. Die aanvang van kraam mag vertraag word en die duur daarvan verhoog word.
Kombinasie met ander NSAIGs:
Die gelyktydige gebruik van BIO-NAPROXEN en ander NSAIGs word nie aanbeveel nie, as gevolg van die bykomende risiko tot die indusering van ernstige NSAIG-verwante newe effekte.
Ander:
BIO-NAPROXEN bevat laktose en moet nie toegedien word aan pasiënte met seldsame oorerflike probleme, of 'n geskiedenis van, laktose onverdraagsaamheid, erge laktase tekort of glukose-galaktose wanabsorpsie nie.
Bestuur en hantering van masjinerie:
Sommige pasiënte mag lomerigheid, duiseligheid, vertigo, slapeloosheid of depressie ervaar met die gebruik van BIO-NAPROXEN. Indien pasiënte enige van hierdie, of soortgelyke, ongunstige newe effekte ervaar, moet aktiwiteite wat paraatheid vereis, met versigtigheid uitgevoer word.

INTERAKSIES:
Teensuurmiddels of cholestiramien: die gelyktydige toediening van BIO-NAPROXEN kan die absorpsie van BIO-NAPROXEN vertraag, maar dit beïnvloed nie die omvang daarvan nie.
Voedsel: gelyktydige inname van die absorpsie van BIO-NAPROXEN vertraag, maar beïnvloed nie die omvang daarvan nie.
Probenesied: tydens gelyktydige toediening word omsigtigheid aanbeveel aangesien dit die plasmavlakke en halflewe van BIO-NAPROXEN aansienlik verhoog.
Metotreksaat: gedurende gelyktydige toediening word omsigtigheid aanbeveel aangesien dit aangemeld is dat BIO-NAPROXEN die opruiming van metotreksaat verlaag, en dus die middel se toksisiteit verhoog.
Furosemied: BIO-NAPROXEN kan die natriuretiese effek van furosemied inhibeer. Die effek van furosemied is verminder met die gelyktydige toediening van BIO-NAPROXEN.
Litium: inhibisie van renale litium-opruiming wat lei tot 'n verhoging in litium plasmakonsentrasies was aangemeld.
Hartglikosiede: verhoogde plasmakonsentrasies van digoksien is aangemeld.
AOE remmers, siklosporien of diuretika: gelyktydige toediening kan die risiko vir nefrotoksisiteit verhoog.
AOE remmers en kalium-besparende diuretika: gelyktydige toediening mag die risiko van hiperkalemie verhoog.
Antihipertensiewe middels: die antihipertensiewe effek van middels soos AOE remmers, beta-blokkeerders en diuretikum kan verlaag word.
Kinolone: konvulsies mag voorkom.
Fenitoïen en sulfonielureum anti-diabetiese middels: die effekte mag verhoog word.
Skildklier-funksie toetse: BIO-NAPROXEN kan skildklier-funksie toetse belemmer deur serum- tiroïedhormoon konsentrasies te verlaag.
Adrenale-funksie toetse: dit word aanbeveel dat BIO-NAPROXEN behandeling tydelik gestaak word vir 48 uur voordat hierdie toetse uitgevoer word. BIO-NAPROXEN kan kunsmatig inmeng met sommige toetse vir 17-ketogeensteroïede. BIO-NAPROXEN mag op soortgelyke wyse inmeng met sommige urinêre toetse vir 5-hidroksie-indoolasynsuur (5-HIAS).
NSAIGs: die gelyktydige gebruik van twee of meer NSAIGs kan 'n verhoging in newe effekte tot gevolg hê.
Kortikosteroïede: verhoogde risiko vir gastro-intestinale perforasie, ulserasie of bloeding (PUBs).
Antistolmiddels: BIO-NAPROXEN kan die uitwerking van antistolmiddels soos warfarien verhoog.
Antiplaatjiemedisynes en selektiewe serotonien heropname inhibeerders (SSHIs): verhoogde risiko van gastro-intestinale bloeding.
Aspirien: Plasmakonsentrasies van BIO-NAPROXEN word aansienlik verminder met die gelyktydige toediening van terapeutiese dosisse aspirien.
Thiasied-diuretika, beta-adrenergiese antagoniste, prasosien, en captopril: BIO-NAPROXEN kan die diuretiese, natriuretiese en anti-hipertensiewe uitwerking van hierdie medisynes verlaag, as gevolg van die inhibisie van die sintese van renale prostaglandiene.

SWANGERSKAP EN LAKTASIE:
Die veiligheid en effektiwiteit van BIO-NAPROXEN tydens swangerskap en laktasie is nie vasgestel nie.
BIO-NAPROXEN moet nie tydens swangerskap gebruik word nie. Die gebruik gedurende die derde trimester van swangerskap kan uteriene inersie en of premature sluiting van die ductus arteriosus veroorsaak.
BIO-NAPROXEN kruis die plasenta en is aangetref in die melk van borsvoedende moeders.

DOSIS EN GEBRUIKSAANWYSINGS:
BIO-NAPROXEN moet nie gebruik word in kinders onder die ouderdom van 16-jaar nie.
Volwassenes:
Rumatoïede artritis, osteo-artritis en ankiloserende spondilitis: 250 tot 375 mg twee maal per dag met voedsel.
Akute jig: 'n Aanvangsdosis van 750 mg met ete, gevolg deur 250 mg elke 8 ure totdat die aanval opklaar.
Lig tot matige pyn, wat verband hou met primêre dismenoree, bursitis en akute tendonitis: 'n Aanvanklike dosis van 500 mg gevolg deur 250 mg elke 6 tot 8 uur, met voedsel.
Gebruik die laagste effektiewe dosis, vir die kortste moontlike tydperk van behandeling.

NEWE EFFEKTE:
Gastro-intestinale afwykings
Die newe effekte wat mees dikwels voorkom met die gebruik van BIO-NAPROXEN is gastro-intestinaal van aard. Peptiese ulkusse, perforasie of gastro-intestinale bloeding, soms noodlottig. Naarheid, braking, diarree, winderigheid, hardlywigheid, dispepsie, abdominale pyn, melaena, hematemese, ulseratiewe stomatitis, verergering van kolitis en Crohn se siekte, gastritis.
Gebeurlikheid onbekend: Kolitis, esofagitis, nie-peptiese maagswere, abdominale ongemak. Sentralesenustelsel afwykings
Dikwels: Duiseligheid, lomerigheid, hoofpyn, lighoofdigheid, vertigo
Gebeurlikheid onbekend: Malaise, senuweeagtigheid, depressie, slapeloosheid, kognitiewe disfunksie, konvulsies, droom abnormaliteite, mialgie, spierswakheid, hoofpyn, onvermoë om te konsentreer.
Vel en subkutaneweefsel afwykings
Dikwels: Echymose, jeuk (pruritus), purpura, vel-erupsies, sweet
Gebeurlikheid onbekend: Bulluese reaksies, insluitende Stevens-Johnson sindroom en toksiese epidermale nekrolise, veluitslag, erythema multiforme, erythema nodosum, Bepaalde geneesmiddel erupsie, lichen planus, pustulêre reaksie, SLE, urtikarie, alopecia, fotosensitiwiteitsreaksies, insluitend gevalle van porfirie cutanea tarda of epidermolysis bullosa. Indien vel broosheid, blaasvorming of ander simptome, suggestief van pseudoporfirie, voorkom moet behandeling dadelik gestaak word en die pasient noukeurig gemonitor word.
Oor en labirint afwykings
Dikwels: Gehoor versteurings, tinnitus
Gebeurlikheid onbekend: Gehoorverlies
Oogafwykings
Dikwels: Visuele versteurings
Gebeurlikheid onbekend: Belemmerde sig en ander okulêre reaksies, korneale ondeursigtigheid, papillitis, retrobulbêre optiese neuritis en papiledeem.
Kardiale afwykings
Dikwels: Hartkloppings, edeem
Gebeurlikheid onbekend: Hartversaking, hipertensie, pulmonêre edeem, vaskulitis, angioneurotiese edeem
Hepato-billiêre afwykings
Gebeurlikheid onbekend: Abnormaliteite van lewerfunksie-toetse, hepatitis (sommige gevalle van hepatitis was noodlottig), geelsug
Respiratoriese-, torakale- en mediastinale afwykings
Dikwels: Asemnood
Gebeurlikheid onbekend: Asma, eosinofiliese pneumonitis
Endokriene afwykings
Gebeurlikheid onbekend: Pankreatitis
Imuunstelsel afwykings
Minder dikwels: Hipersensitiwiteitsreaksies insluitend koors, asma, veluitslag, hepatotoksisiteit, en aseptiese meningitis mag voorkom.
Gebeurlikheid onbekend: Veluitslag en angioedeem, anafilatoïede reaksies
Renale- en urinêre afwykings
Gebeurlikheid onbekend: Inkorting van nierfunksie, hematurie, hiperkalemie, interstisiële nefritis, nefrotiese sindroom, renale siekte, omkeerbare nierversaking, renale papillêre nekrose, verhoogde serum kreatinien en vloeistofretensie kan voorkom.
Bloed- en limfatiese stelsel afwykings
Gebeurlikheid onbekend: Agranulositose, trombositopenie, leukopenie, granulositopenie, neutropenie, eosinofilie, anemieë, insluitend aplastiese anemie en hemolitiese anemie.
Infeksies en infestasies
Gebeurlikheid onbekend: Pireksie (kouekoors en koors).

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:
(Sien NEWE EFFEKTE). Simptome van oordosering sluit duiseligheid, lomerigheid, epigastriese pyn, abdominale ongemak, sooibrand, slegte spysvertering, naarheid, verbygaande veranderinge in lewerfunksie, hipoprotrombinemie, nierdisfunksie, metaboliese asidose, apnee, disoriëntasie en braking in.
BIO-NAPROXEN mag vinnig absorbeer word en hoë bloedvlakke kan vinnig bereik word. 'n Paar pasiënte het konvulsies ervaar.
Behandeling is ondersteunend en simptomaties. Hemodialise verlaag nie die plasmakonsentrasie van naproksen nie as gevolg van die hoë graad van proteienbinding.

IDENTIFIKASIE:
Bio-Naproxen 250 mg:
Geel, ronde, bikonvekse tablet, met breeklyn aan een kant en gewoon aan die ander kant.
Bio-Naproxen 500 mg:
Geel, kapsuul-vorm, bikonvekse tablet gekodeer met 'NPX 500' aan die een kant en breek lyn op omgekeerde kant.

AANBIEDING:
BIO-NAPROXEN 250 mg en BIO-NAPROXEN 500 mg kan verpak word in die volgende houers:
Wit ondeursigtige, polipropileen veiligheidshouer bevattend 100 of 250 tablette.
Wit skroefprop, ondeursigtige HDPE houer bevattend 100 of 250 tablette.
Amberkleurige PVC/PVDC stulpstrook bevattend 14 tablette per stulpstrook en 56 of 140 tablette per buitenste karton.
Wit, ondeursigtige, poliëtileen toerits pasient-gereed pakkie (vir gebruik deur die staat alleenlik), bevattend 56 tablette.
Al die verpakkingsgroottes word nie noodwendig op een slag bemark nie.

BERGINGSINSTRUKSIES:
Bewaar teen of onder 25 °C op 'n droë plek. Beskerm teen lig.
Hou buite die gebruik van kinders.

REGISTRASIENOMMER:
BIO-NAPROXEN 250 mg: W/3.1/436
BIO-NAPROXEN 500 mg: W/3.1/437

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