NAPROXEN

Indications/Uses

Listed in Dosage.

Dosage/Direction for Use

Adult : PO Rheumatoid arthritis; Osteoarthritis; Ankylosing spondylitis As conventional tab/gastro-resistant tab/oral susp: 500-1,000 mg daily as a single or in 2 divided doses. As effervescent tab: Initial: 250 mg twice daily, may be adjusted to 500-1,000 mg daily in 2 divided doses. As extended-release tab: 750-1,000 mg once daily, may be adjusted according to clinical response. Max: 1,000 mg/day. As delayed-release tab: 375 mg or 500 mg twice daily, may be adjusted according to clinical response. Use lowest effective dose for the shortest possible duration based on individual patient treatment goals. Acute musculoskeletal disorders; Mild to moderate pain; Dysmenorrhoea As conventional tab/gastro-resistant tab/oral susp: Initial: 500 mg, then 250 mg 6-8 hourly as necessary. Max: 1,250 mg/1st day then 1,000 mg thereafter. As extended-release tab: Initial: 1,000 mg once daily, may be adjusted to 1,500 mg once daily for a short period. Max: 1,000 mg/day. Acute gout As conventional tab/effervescent tab: Initially, 750 mg followed by 250 mg 8 hourly until the attack subsides. As extended-release tab: Initially, 1,000-1,500 mg followed by 1,000 mg once daily until the attack subsides.

Dosage Details

Oral

Acute musculoskeletal disorders, Dysmenorrhoea, Mild to moderate pain

Adult: As conventional tab/gastro-resistant tab/oral susp: Initially, 500 mg followed by 250 mg 6-8 hourly as necessary. Max: 1,250 mg on the 1st day then 1,000 mg thereafter. As extended-release tab: Initially, 1,000 mg once daily, may be adjusted to 1,500 mg once daily for a short period. Max: 1,000 mg daily.

Elderly: Lowest effective dose for the shortest possible duration.

Oral

Juvenile idiopathic arthritis

Child: >5 years 10 mg/kg daily in 2 divided doses 12 hourly. Max: 1,000 mg daily.

Oral

Ankylosing spondylitis, Osteoarthritis, Rheumatoid arthritis

Adult: As conventional tab/gastro-resistant tab/oral susp: 500-1,000 mg daily as a single or in 2 divided doses. As effervescent tab: Initially, 250 mg twice daily, may be adjusted to 500-1,000 mg daily in 2 divided doses. As extended-release tab: 750-1,000 mg once daily, may be adjusted according to clinical response. Max: 1,000 mg daily. As delayed-release tab: 375 mg or 500 mg twice daily, may be adjusted according to clinical response. Use lowest effective dose for the shortest possible duration based on individual patient treatment goals.

Elderly: Lowest effective dose for the shortest possible duration.

Oral

Acute gout

Adult: As conventional tab/effervescent tab: Initially, 750 mg followed by 250 mg 8 hourly until the attack subsides. As extended-release tab: Initially, 1,000-1,500 mg followed by 1,000 mg once daily until the attack subsides.

Elderly: Lowest effective dose for the shortest possible duration.

Special Patient Group

Patient with severe night time pain or morning stiffness, pain as predominant symptom in osteoarthritis, and who are switched to naproxen from high dose of another anti-rheumatic drug: As conventional tab/gastro-resistant tab/oral susp: Loading dose of 750 mg or 1,000 mg daily.

Renal Impairment

CrCl <30 mL/min or on dialysis: Contraindicated.

Hepatic Impairment

Severe: Contraindicated.

Administration

Should be taken with food.

Contraindications

Hypersensitivity. Patient with active or history of recurrent peptic ulcer, history of gastrointestinal bleeding or perforation related to previous NSAID therapy, chronic dyspepsia, severe heart failure, history of asthma, bronchospasm, nasal polyps, rhinitis, angioedema, or urticaria associated with aspirin or NSAID therapy. Treatment of peri-operative pain in the setting of CABG surgery. Renal (CrCl <30 mL/min) and severe hepatic impairment. Pregnancy (3rd trimester).

Special Precautions

Patient with or a history of bronchial asthma, inflammatory bowel disease (e.g. Crohn's disease, ulcerative colitis), mild to moderate heart failure, fluid retention, ischaemic heart disease, peripheral arterial disease, cerebrovascular disease, coagulation disorders, risk factors for CV events (e.g. hyperlipidaemia, diabetes mellitus, smoking), cirrhosis, chronic alcoholic liver disease, dehydration, hypovolaemia. Debilitated patients. Mild to moderate renal and hepatic impairment. Elderly. Pregnancy (1st-2nd trimester) and lactation.

Adverse Reactions

Significant: Aggrevated asthma, bronchospasm, hypertension, hyperkalaemia, fluid retention, anaemia, increased ALT/AST.

Blood and lymphatic system disorders: Haemolysis, purpura, agranulocytosis, leucopenia, neutropenia, thrombocytopenia.

Cardiac disorders: Palpitation.

Ear and labyrinth disorders: Tinnitus, hearing disturbances.

Eye disorders: Visual disturbances, corneal opacity.

Gastrointestinal disorders: Nausea, vomiting, constipation, abdominal pain, heartburn, diarrhoea, flatulence, dyspepsia, stomatitis.

General disorders and administration site conditions: Fatigue, malaise, pyrexia, diaphoresis.

Hepatobiliary disorders: Jaundice, abnormal liver function.

Musculoskeletal and connective tissue disorders: Myalgia, muscle weakness.

Nervous system disorders: Headache, vertigo, paraesthesia.

Psychiatric disorders: Insomnia, depression, confusion, hallucination, disorientation, dream abnormality.

Renal and urinary disorders: Cystitis.

Respiratory, thoracic and mediastinal disorders: Dyspnoea, asthma, eosinophilic pneumonitis, pulmonary oedema.

Skin and subcutaneous tissue disorders: Pruritus, urticaria, rash, ecchymoses, alopecia, photosensitivity reaction.

Vascular disorders: Vasculitis.

Potentially Fatal: Gastrointestinal obstruction, inflammation, bleeding, ulceration or perforation, CV thrombotic events including MI and stroke, anaphylactic reactions. Rarely, fulminant hepatitis, hepatic necrosis, hepatic failure, angioedema, Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis.

Patient Counseling Information

This drug may cause dizziness, drowsiness or blurred vision, if affected, do not drive or operate machinery.

MonitoringParameters

Monitor CBC, chemistry profile, renal and liver function. Blood pressure should be monitored during initiation of treatment and throughout the course of therapy.

Overdosage

Symptoms: Headache, nausea, vomiting, epigastric pain, indigestion, heartburn, gastrointestinal bleeding, lethargy, hypoprothrombinaemia, apnoea, metabolic acidosis. Rarely, diarrhoea, disorientation, excitation, drowsiness, dizziness, tinnitus, fainting, convulsions, hypertension, respiratory depression, coma, acute renal and liver damage. Management: Symptomatic and supportive treatment. Consider activated charcoal, emesis, osmotic cathartic, or gastric lavage within 1-4 hours of ingestion. Ensure good urine output. Administer IV diazepam for frequent or prolonged convulsions.

Drug Interactions

May increase the risk of bleeding with other NSAIDs or salicylates (e.g. aspirin), anticoagulants (e.g. warfarin), corticosteroids, SSRI. May decrease efficacy of antihypertensive agents (e.g. ß-blockers, ACE inhibitors, angiotensin II receptor antagonists). Increased risk of nephrotoxicity of ciclosporin and tacrolimus. May increase risk of haematological toxicity with zidovudine. Reduced natriuretic effects of diuretics (e.g. furosemide, thiazide diuretics). Increased plasma concentration and prolonged half-life with probenecid. May increase serum levels of lithium, digoxin, and methotrexate. May decrease the effects of mifepristone. Increased risk of myelosuppression, renal and gastrointestinal toxicity of pemetrexed. Delayed absorption rate with antacid, colestyramine, and sucralfate.

Food Interaction

Decreased rate of absorption with food.

Lab Interference

May result to false-positive aldosterone/renin ratio (ARR). May interfere with 5-hydroxyindoleacetic acid (5-HIAA) urinary assays. May cause a falsely elevated urinary 17-ketogenic steroid concentrations by interfering with the m-dinitrobenzene reagent in Porter-Silber test.

Action

Description: Naproxen, a propionic acid derivative, is a prototypical NSAID which reversibly inhibits the cyclooxygenase-1 and -2 (COX-1 and -2) enzymes, thus resulting in decreased formation of prostaglandin precursors. It has anti-inflammatory, analgesic and antipyretic activity, and can inhibit platelet aggregation.

Onset: Analgesic: 30-60 minutes.

Duration: Analgesic: <12 hours.

Pharmacokinetics:

Absorption: Readily absorbed from the gastrointestinal tract. Decreased absorption rate with food. Bioavailability: 95%. Time to peak plasma concentration: Conventional tab: Approx 1-2 hours (naproxen Na); Approx 2-4 hours (naproxen); Delayed-release tab: 4-6 hours (empty stomach); 12 hours (with food); 1-4 hours (oral susp).

Distribution: Diffuses into synovial fluid. Crosses placenta and distributed into breast milk (small amounts). Volume of distribution: 0.16 L/kg. Plasma protein binding: >99% mainly to albumin.

Metabolism: Extensively metabolised in the liver by CYP1A2 and CYP2C9 isoenzymes to inactive 6-O-desmethylnaproxen which undergoes further metabolism to its respective acylglucuronide conjugate metabolites.

Excretion: Mainly via urine (approx 95%) as unchanged drug and metabolites; faeces (<5%). Elimination half-life: Approx 12-17 hours.

Chemical Structure

Click on icon to see table/diagram/image

Storage

Store between 15-30°C. Protect from light and heat.

MIMS Class

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

ATC Classification

M01AE02 - naproxen ; Belongs to the class of propionic acid derivatives of non-steroidal antiinflammatory and antirheumatic products.