Product Monograph

Including Patient Medication Information

[Pr] PEDIAPHARM NAPROXEN SUSPENSION

Naproxen oral suspension U.S.P.

For oral use

25 mg/mL of naproxen

Non-Steroidal Anti-Inflammatory Drug (NSAID)

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Date of Authorization:
2025-10-17

Control Number: 298245

Recent Major Label Changes

4.2. Recommended Dose and Dosage Adjustment	[2025-10]

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Certain sections or subsections that are not applicable at the time of the preparation of the most recent authorized product monograph are not listed.

Part 1: Healthcare Professional Information

1. Indications

PEDIAPHARM NAPROXEN SUSPENSION (naproxen) is indicated for:

- The treatment of the signs and symptoms of osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, and juvenile rheumatoid arthritis.
- The relief of minor aches and pains in muscles, bones and joints, mild to moderate pain accompanied by inflammation in musculoskeletal injuries (sprains and strains) and primary dysmenorrhea.

For patients with an increased risk of developing cardiovascular and/or gastrointestinal adverse events, other management strategies that do NOT include the use of NSAIDs should be considered first. See 2. Contraindications and 7. Warnings and Precautions.

Use of PEDIAPHARM NAPROXEN SUSPENSION should be limited to the lowest effective dose for the shortest possible duration of treatment in order to minimize the potential risk for cardiovascular or gastrointestinal adverse events. See 2. Contraindications and 7. Warnings and Precautions.

PEDIAPHARM NAPROXEN SUSPENSION, as a NSAID, does NOT treat clinical disease or prevent its progression.

PEDIAPHARM NAPROXEN SUSPENSION, as a NSAID, only relieves symptoms and decreases inflammation for as long as the patient continues to take it.

1.1. Pediatrics

Pediatrics (< 2 years of age): PEDIAPHARM NAPROXEN SUSPENSION should not be used in children under 2 years of age. The safety and efficacy in infants younger than 2 years of age has not been established.

1.2. Geriatrics

Geriatrics (> 65 years of age): Evidence from clinical studies and postmarket experience suggests that use in the geriatric population is associated with differences in safety (see 4. Dosage and Administration and 7.1.4 Geriatrics).

2. Contraindications

PEDIAPHARM NAPROXEN SUSPENSION is contraindicated in:

- the peri-operative setting of coronary artery bypass graft surgery (CABG). Although PEDIAPHARM NAPROXEN SUSPENSION has NOT been studied in this patient population, a selective COX-2 inhibitor NSAID studied in such a setting has led to an increased incidence of cardiovascular/thromboembolic events, deep surgical infections and sternal wound complications.
- the third trimester of pregnancy, because of risks of premature closure of the ductus arteriosus and prolonged parturition
- women who are breastfeeding, because of the potential for serious adverse reactions in nursing infants

- patients with severe uncontrolled heart failure
- patients with known hypersensitivity to naproxen or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6. Dosage Forms, Strengths, Composition, and Packaging.
- patients with a history of asthma, urticaria, or allergic-type reactions after taking Acetylsalicylic Acid (ASA) or other NSAIDs (i.e. complete or partial syndrome of ASA-intolerance - rhinosinusitis, urticaria/angioedema, nasal polyps, asthma). Fatal anaphylactoid reactions have occurred in such individuals. Individuals with the above medical problems are at risk of a severe reaction even if they have taken NSAIDs in the past without any adverse reaction. The potential for cross-reactivity between different NSAIDs must be kept in mind (see 7. Warnings and Precautions, Sensitivity/resistance, Anaphylactoid Reactions).
- patients with active gastric / duodenal / peptic ulcer, active GI bleeding
- patients with cerebrovascular bleeding or other bleeding disorders
- patients with inflammatory bowel disease
- patients with severe liver impairment or active liver disease
- patients with severe renal impairment (creatinine clearance <30 mL/min or 0.5 mL/sec) or deteriorating renal disease (individuals with lesser degrees of renal impairment are at risk of deterioration of their renal function when prescribed NSAIDs and must be monitored) (see7. Warnings and Precautions, Renal)
- patients with known hyperkalemia (see 7. Warnings and Precautions, Renal, Fluid and Electrolyte Balance)
- children less than 2 years of age

3. Serious Warnings and Precautions Box

Risk of Cardiovascular (CV) Adverse Events: Ischemic Heart Disease, Cerebrovascular Disease, Congestive Heart Failure (NYHA II-IV)

PEDIAPHARM NAPROXEN SUSPENSION is a non-steroidal anti-inflammatory drug (NSAID). Use of some NSAIDs is associated with an increased incidence of cardiovascular adverse events (such as myocardial infarction, stroke or thrombotic events) which can be fatal. The risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. See 7. Warnings and Precautions, Cardiovascular.

Caution should be exercised in prescribing PEDIAPHARM NAPROXEN SUSPENSION to any patient with ischemic heart disease (including but NOT limited to acute myocardial infarction, history of myocardial infarction and/or angina), cerebrovascular disease (including but NOT limited to stroke, cerebrovascular accident, transient ischemic attacks and/or amaurosis fugax) and/or congestive heart failure (NYHA II-IV).

Use of NSAIDs, such as PEDIAPHARM NAPROXEN SUSPENSION, can promote sodium retention in a dose-dependent manner, through a renal mechanism, which can result in increased blood pressure and/or exacerbation of congestive heart failure. See also 7. Warnings and Precautions, Renal, Fluid and Electrolyte Balance.

Randomized clinical trials with naproxen have not been designed to detect differences in cardiovascular events in a chronic setting. Therefore, caution should be exercised when prescribing PEDIAPHARM NAPROXEN SUSPENSION.

Risk of Gastrointestinal (GI) Adverse Events:
Use of NSAIDs, such as PEDIAPHARM NAPROXEN SUSPENSION, is associated with an increased incidence of gastrointestinal adverse events (such as ulceration, bleeding, perforation and obstruction of the upper and lower gastrointestinal tract). See 7. Warnings and Precautions, Gastrointestinal.

Risk in Pregnancy:
Caution should be exercised in prescribing PEDIAPHARM NAPROXEN SUSPENSION during the first and second trimesters of pregnancy. Use of NSAIDS at approximately 20 weeks of gestation or later may cause fetal renal dysfunction leading to oligohydramnios and neonatal renal impairment or failure (see 7. Warnings and Precautions, 7.1.1 Pregnancy. PEDIAPHARM NAPROXEN SUSPENSION is contraindicated for use during the third trimester because of risks of premature closure of the ductus arteriosus and uterine inertia (prolonged parturition). See 2. Contraindications.

4. Dosage and Administration

4.1. Dosing Considerations

Use of PEDIAPHARM NAPROXEN SUSPENSION should be limited to the lowest effective dose for the shortest possible duration of treatment (see 1. Indications). For all indications, treatment must be initiated with the lowest dose.

4.2. Recommended Dose and Dosage Adjustment

Adult:

Osteoarthritis/Rheumatoid Arthritis/Ankylosing Spondylitis
The usual total daily oral dosage for osteoarthritis, rheumatoid arthritis and ankylosing spondylitis is 250 mg twice per day. It may be increased gradually to 375 mg or 500 mg twice per day or decreased depending on the patient's response.

Table 1 – Recommended Dosage Chart: Osteoarthritis / Rheumatoid Arthritis / Ankylosing Spondylitis

	Dose Frequency	Total Daily Dose
Initial Dose:		
250 mg / 10 mL	Two times per day	500 mg
Dose Adjustment: May gradually increase dose (if necessary) to:		
375 mg / 15 mL	Two times per day	750 mg
OR		
500 mg / 20 mL	Two times per day	1000 mg
Dose Adjustment: Decrease dose depending on response. Use lowest effective dose.		

Studies have not shown any clinically significant benefit in using doses higher than 1000 mg/day. In patients who tolerate lower doses of naproxen well and who exhibit only a partial response to

1000 mg/day, the dose may be increased to 1500 mg/day for limited periods. The 1500 mg/kg dose has not been studied in clinical trials with PEDIAPHARM NAPROXEN SUSPENSION.

When treating such patients with naproxen 1500 mg/day, the physician should observe sufficient increased clinical benefit to offset the potential increased risk (see 8. Adverse Reactions).

In addition, patients on 1500 mg/day need to be followed closely for the development of any adverse events.

During long-term administration the dose of PEDIAPHARM NAPROXEN SUSPENSION may be adjusted up or down depending on the clinical response of the patient. A lower dose may suffice for long-term administration.

Analgesia/Musculoskeletal Injuries

The recommended oral dose is 750 mg/day divided into either two or three doses/day. This may be increased to 1000 mg/day if needed. The lowest effective dose should be used.

Table 2 – Recommended Dosage Chart: Analgesia / Musculoskeletal Injuries

	Dose Frequency	**Total Daily Dose**
Initial Dose:		
Option 1: 375 mg / 15 mL	Two times per day	750 mg
OR		
Option 2: 250 mg / 10 mL	Three times per day	750 mg
Dose Adjustment: May increase dose (if necessary) to:		
500 mg / 20 mL	Two times per day	1000 mg
Dose Adjustment: Decrease dose depending on response. Use lowest effective dose.		

Dysmenorrhea

The recommended starting dose is 500 mg, followed by 250 mg every 6 - 8 hours, as required. The total daily dose should not exceed 1250 mg on the first day of use and should not exceed 1000 mg on subsequent days of use. Alternatively, a dose of 500 mg given twice daily may be used.

Table 3 – Recommended Dosage Chart: Dysmenorrhea

	Dose Frequency	**Total Daily Dose**
Option 1:		
First dose: 500 mg / 20 mL **Followed by:** 250 mg / 10 mL	Once Every 6-8 hours, as required.	**First day:** 1000 to 1250 mg **Followed by:** 750 to 1000 mg
OR		
Option 2: 500 mg / 20 mL	Two times per day	1000 mg

Juvenile Rheumatoid Arthritis (2-16 years):

PEDIAPHARM NAPROXEN SUSPENSION is indicated for juvenile arthritis in children 2 years or older. It allows for flexible dose titration based on the child's weight. The recommended total daily dose is approximately 10 mg/kg in two divided doses at 12 hour intervals.

Do not exceed recommended dose, dose frequency or total daily dose. Administration of PEDIAPHARM NAPROXEN SUSPENSION more frequently than twice daily is not necessary. Clinical experience has shown that steroids can often be decreased and sometimes eliminated when PEDIAPHARM NAPROXEN SUSPENSION is administered.

The following dosing chart may be used as a guide:

Table 4 – Recommended Dosage Chart: Juvenile Rheumatoid Arthritis

Child's weight	Dose (Volume)*	Dose Frequency*	Total Daily Dose*
13 kg	65 mg / 2.6 mL	Two times per day	130 mg
15 kg	75 mg / 3 mL	Two times per day	150 mg
20 kg	100 mg / 4 mL	Two times per day	200 mg
25 kg	125 mg / 5 mL	Two times per day	250 mg
30 kg	150 mg / 6 mL	Two times per day	300 mg
40 kg	200 mg / 8 mL	Two times per day	400 mg
50 kg	250 mg / 10 mL	Two times per day	500 mg

*** Do not exceed recommended dose, dose frequency or total daily dose.**

Geriatrics (>65 years of age): In the elderly, frail and debilitated, the dosage should be reduced to the lowest level providing control of symptoms, and adjusted when necessary. See 7.1.4. Geriatrics.

Renal impairment: A lower dose should be considered in patients with mild and moderate renal impairment. PEDIAPHARM NAPROXEN SUSPENSION is contraindicated in severe renal impairment (creatinine clearance <30 mL/min or 0.5 mL/sec) or deteriorating renal disease (individuals with lesser degrees of renal impairment are at risk of deterioration of their renal function when prescribed NSAIDs and must be monitored). See 2. Contraindications.

Hepatic impairment: A lower dose should be considered in patients with mild and moderate hepatic impairment. PEDIAPHARM NAPROXEN SUSPENSION is contraindicated in severe liver impairment or active liver disease. See 2. Contraindications.

4.4. Administration

Bottles of PEDIAPHARM NAPROXEN SUSPENSION should be shaken gently before use.

4.5. Missed Dose

The missed dose should be taken as soon as remembered, and then the regular dosing schedule should be continued. Two doses of PEDIAPHARM NAPROXEN SUSPENSION should not be taken at the same time.

5. Overdose

For the most recent information in the management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

Symptoms and Signs

Significant overdosage may be characterized by drowsiness, dizziness, disorientation, heartburn, indigestion, epigastric pain, abdominal discomfort, nausea, vomiting, transient alterations in liver function, hypoprothrombinemia, renal dysfunction, metabolic acidosis and apnea. A few patients have experienced convulsions, but it is not clear whether or not these were naproxen related.

Gastrointestinal bleeding may occur. Hypertension, acute renal failure, respiratory depression and coma may occur after the ingestion of NSAIDs but are rare.

Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following an overdose.

Treatment

Patients should be managed by symptomatic and supportive care following NSAIDs overdose. There are no specific antidotes. Prevention of further absorption (e.g. activated charcoal) may be indicated in patients seen within 4 hours of ingestion with symptoms or following a large overdose. Forced diuresis, alkalinization of urine, hemodialysis, or hemoperfusion may not be useful due to high protein binding.

6. Dosage Forms, Strengths, Composition, and Packaging

Table 5 – Dosage Forms, Strengths, and Composition

Route of Administration	Dosage Form/ Strength/Composition	Non-Medicinal Ingredients
Oral	Suspension, 25 mg/mL	FD&C Yellow No. 6, fumaric acid, imitation orange flavour, imitation pineapple flavour, magnesium aluminum silicate, methylparaben, sodium chloride, sorbitol solution 70%, sucrose

Description

PEDIAPHARM NAPROXEN SUSPENSION is available as an oral suspension. Each 5 mL contains 125 mg of naproxen. Available in 474 mL polyethyleneterephthalate (PET) bottles.

7. Warnings and Precautions

See 3. Serious Warnings and Precautions Box.

General

Frail or debilitated patients may tolerate side effects less well and therefore special care should be taken in treating this population. **To minimize the potential risk for an adverse event, the lowest effective dose should be used for the shortest possible duration.** As with other NSAIDs, caution should be used in the treatment of elderly patients who are more likely to be suffering from impaired renal, hepatic or cardiac function. For high-risk patients, alternate therapies that do not involve NSAIDs should be considered.

PEDIAPHARM NAPROXEN SUSPENSION is NOT recommended for use with other NSAIDs, with the exception of low-dose ASA for cardiovascular prophylaxis, because of the absence of any evidence demonstrating synergistic benefits and the potential for additive adverse reactions. See 9.4 Drug-Drug Interactions, Acetylsalicylic acid (ASA) or other NSAIDs.

PEDIAPHARM NAPROXEN SUSPENSION (naproxen) should not be used concomitantly with the related drug naproxen sodium since they both circulate in plasma as the naproxen anion.

Carcinogenesis and Genotoxicity

There is no evidence from animal data that PEDIAPHARM NAPROXEN SUSPENSION is carcinogenic or mutagenic. See 16. Non-Clinical Toxicology.

Cardiovascular

PEDIAPHARM NAPROXEN SUSPENSION is a non-steroidal anti-inflammatory drug (NSAID). Use of some NSAIDs is associated with an increased incidence of cardiovascular adverse events (such as myocardial infarction, stroke or thrombotic events) which can be fatal. The risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.

Caution should be exercised in prescribing PEDIAPHARM NAPROXEN SUSPENSION to patients with risk factors for cardiovascular disease, cerebrovascular disease or renal disease, such as any of the following (NOT an exhaustive list)

- **Hypertension**
- **Dyslipidemia / Hyperlipidemia**
- **Diabetes Mellitus**
- **Congestive Heart Failure (NYHA I)**
- **Coronary Artery Disease (Atherosclerosis)**
- **Peripheral Arterial Disease**
- **Smoking**
- **Creatinine Clearance < 60 mL/min or 1 mL/sec**

Use of NSAIDs, such as PEDIAPHARM NAPROXEN SUSPENSION, can lead to new hypertension or can worsen pre-existing hypertension, either of which may increase the risk of cardiovascular events as described above. Thus, blood pressure should be monitored regularly. Consideration should be given to discontinuing PEDIAPHARM NAPROXEN SUSPENSION should hypertension either develop or worsen with its use.

Use of NSAIDs, such as PEDIAPHARM NAPROXEN SUSPENSION, can induce fluid retention and edema, and may exacerbate congestive heart failure, through a renally-mediated mechanism. See 7. Warnings and Precautions, Renal, Fluid and Electrolyte Balance.

For patients with a high-risk of developing an adverse CV event, other management strategies that do NOT include the use of NSAIDs should be considered first. **To minimize the potential risk for an adverse CV event, the lowest effective dose should be used for the shortest possible duration.**

Driving and Operating Machinery

There are no specific studies about effects on the ability to drive vehicles and to use machinery. Patients who experience visual disturbances or other central nervous system disturbances should refrain from these activities.

Endocrine and metabolism

Corticosteroids: PEDIAPHARM NAPROXEN SUSPENSION (naproxen) is NOT a substitute for

corticosteroids. It does NOT treat corticosteroid insufficiency. Abrupt discontinuation of corticosteroids may lead to exacerbation of corticosteroid-responsive illness. Patients on prolonged corticosteroid therapy should have their therapy tapered slowly if a decision is made to discontinue corticosteroids. See 9.4. Drug-Drug Interactions, Glucocorticoids.

Gastrointestinal

Serious GI toxicity (sometimes fatal), such as ulceration, inflammation, gastrointestinal bleeding, perforation and obstruction of the upper and lower gastrointestinal tract, can occur at any time, with or without warning symptoms, in patients treated with NSAIDs, such as PEDIAPHARM NAPROXEN SUSPENSION. Minor upper GI problems, such as dyspepsia, commonly occur at any time. Health care providers should remain alert for ulceration and bleeding in patients treated with PEDIAPHARM NAPROXEN SUSPENSION, even in the absence of previous GI tract symptoms. Most spontaneous reports of fatal GI events are in elderly or debilitated patients and therefore special care should be taken in treating this population. **To minimize the potential risk for an adverse GI event, the lowest effective dose should be used for the shortest possible duration.** For high-risk patients, alternate therapies that do not involve NSAIDs should be considered (see 7. Warnings and Precautions, 7.1.4. Geriatrics).

Patients should be informed about the signs and/or symptoms of serious GI toxicity and instructed to discontinue using PEDIAPHARM NAPROXEN SUSPENSION and seek emergency medical attention if they experience any such symptoms. The utility of periodic laboratory monitoring has NOT been demonstrated, nor has it been adequately assessed. Most patients who develop a serious upper GI adverse event on NSAID therapy have no symptoms. Upper GI ulcers, gross bleeding or perforation, caused by NSAIDs, appear to occur in approximately 1% of patients treated for 3-6 months, and in about 2-4% of patients treated for one year. These trends continue, thus increasing the likelihood of developing a serious GI event at some time during the course of therapy. Even short-term therapy has its risks.

Caution should be taken if prescribing PEDIAPHARM NAPROXEN SUSPENSION to patients with a prior history of peptic / duodenal ulcer disease or gastrointestinal bleeding as these individuals have a greater than 10-fold higher risk for developing a GI bleed when taking a NSAID than patients with neither of these risk factors. Other risk factors for GI ulceration and bleeding include the following: *Helicobacter pylori* infection, increased age, prolonged use of NSAID therapy, excess alcohol intake, smoking, poor general health status or concomitant therapy with any of the following:

- Anti-coagulants (e.g. warfarin)
- Anti-platelet agents (e.g. ASA, clopidogrel)
- Oral corticosteroids (e.g. prednisone)
- Selective Serotonin Reuptake Inhibitors (SSRIs) (e.g. citalopram, fluoxetine, paroxetine, sertraline)

Genitourinary

Some NSAIDs are associated with persistent urinary symptoms (bladder pain, dysuria, urinary frequency), hematuria or cystitis. The onset of these symptoms may occur at any time after the initiation of therapy with a NSAID. Should urinary symptoms occur, in the absence of an alternate explanation, treatment with PEDIAPHARM NAPROXEN SUSPENSION should be stopped to ascertain if symptoms disappear. This should be done before urological investigations or treatments are carried out.

Hematologic

NSAIDs inhibiting prostaglandin biosynthesis interfere with platelet function to varying degrees; patients who may be adversely affected by such an action, such as those on anti-coagulants or suffering from hemophilia or platelet disorders should be carefully observed when PEDIAPHARM NAPROXEN SUSPENSION is administered.

Anti-coagulants: Numerous studies have shown that the concomitant use of NSAIDs and anticoagulants increases the risk of bleeding. Concurrent therapy of PEDIAPHARM NAPROXEN SUSPENSION with warfarin requires close monitoring of the international normalized ratio (INR). Even with therapeutic INR monitoring, increased bleeding may occur. See 9.4. Drug-Drug Interactions, Anti-coagulants.

Anti-platelet Effects: NSAIDs inhibit platelet aggregation and have been shown to prolong bleeding time in some patients. Unlike acetylsalicylic acid (ASA), their effect on platelet function is quantitatively less, or of shorter duration, and is reversible.

PEDIAPHARM NAPROXEN SUSPENSION and other NSAIDs have no proven efficacy as anti-platelet agents and should NOT be used as a substitute for ASA or other anti-platelet agents for prophylaxis of cardiovascular thromboembolic diseases. Anti-platelet therapies (e.g. ASA) should NOT be discontinued. There is some evidence that use of NSAIDs with ASA can markedly attenuate the cardioprotective effects of ASA. See 9.4. Drug-Drug Interactions, Acetylsalicylic Acid or other NSAIDs.

Concomitant administration of PEDIAPHARM NAPROXEN SUSPENSION with low dose ASA increases the risk of GI ulceration and associated complications.

Blood dyscrasias: Blood dyscrasias (such as neutropenia, leukopenia, thrombocytopenia, aplastic anemia and agranulocytosis) associated with the use of NSAIDs are rare, but could occur with severe consequences.

Anemia is sometimes seen in patients receiving NSAIDs, including PEDIAPHARM NAPROXEN SUSPENSION. This may be due to fluid retention, GI blood loss, or an incompletely described effect upon erythropoiesis. Patients on long-term treatment with NSAIDs, including PEDIAPHARM NAPROXEN SUSPENSION, should have their hemoglobin or hematocrit checked if they exhibit any signs or symptoms of anemia or blood loss.

Hepatic/biliary/pancreatic

As with other NSAIDs, borderline elevations of one or more liver enzyme tests (AST, ALT, alkaline phosphatase) may occur in up to 15% of patients. These abnormalities may progress, may remain essentially unchanged, or may be transient with continued therapy.

Chronic alcoholic liver disease and probably also other forms of cirrhosis reduce the total plasma concentration of naproxen, but the plasma concentration of unbound naproxen is increased. The implication of this finding for naproxen dosing is unknown, but caution is advised when high doses are required. It is prudent to use the lowest effective dose.

A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver function test has occurred, should be evaluated for evidence of the development of a more severe hepatic reaction while on therapy with this drug. Severe hepatic reactions including jaundice and cases of fatal hepatitis, liver necrosis and hepatic failure, some of them with fatal outcomes, have been reported with NSAIDs.

Although such reactions are rare, if abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop (e.g. jaundice), or if systemic manifestations occur (e.g. eosinophilia, associated with rash, etc.), this drug should be discontinued.

If there is a need to prescribe this drug in the presence of impaired liver function, it must be done under strict observation.

Immune

Infection
PEDIAPHARM NAPROXEN SUSPENSION, in common with other NSAIDs, may mask signs and symptoms of an underlying infectious disease.

Aseptic Meningitis: Rarely, with some NSAIDs, the symptoms of aseptic meningitis (stiff neck, severe headaches, nausea and vomiting, fever or clouding of consciousness) have been observed. Patients with autoimmune disorders (systemic lupus erythematosus, mixed connective tissue diseases, etc.) seem to be pre-disposed. Therefore, in such patients, the health care provider must be vigilant to the development of this complication.

Monitoring and laboratory tests

Patients on long-term treatment with PEDIAPHARM NAPROXEN SUSPENSION should have their blood pressure monitored regularly and an ophthalmic examination should be carried out at periodic intervals. See 7. Warnings and Precautions, Cardiovascular and Ophthalmologic.

Hemoglobin, hematocrit, red blood cells (RBCs), white blood cells (WBCs), and platelets should be checked in patients on long-term treatment with PEDIAPHARM NAPROXEN SUSPENSION. Additionally, concurrent therapy with warfarin requires close monitoring of the international normalized ratio (INR). See 7.1 Warnings and Precautions, Hematologic.

Serum transaminase and bilirubin should be monitored regularly during PEDIAPHARM NAPROXEN SUSPENSION therapy. See 7.1 Warnings and Precautions, Hepatic/ biliary/pancreatic.

Serum creatinine, creatine clearance and serum urea should be checked in patients during PEDIAPHARM NAPROXEN SUSPENSION therapy. Electrolytes including serum potassium should be monitored periodically. See 7.1 Warnings and Precautions, Renal.

Monitoring of plasma lithium concentration is recommended when stopping or starting PEDIAPHARM NAPROXEN SUSPENSION therapy.

Pregnancy: If PEDIAPHARM NAPROXEN SUSPENSION is administered in the middle (approximately 20 weeks) to the end of the second trimester, it is recommended that pregnant women on PEDIAPHARM NAPROXEN SUSPENSION be closely monitored for amniotic fluid volume since PEDIAPHARM NAPROXEN SUSPENSION may result in reduction of amniotic fluid volume and even oligohydramnios (see 7.1.1. Pregnancy). PEDIAPHARM NAPROXEN SUSPENSION is contraindicated for use in the third trimester of pregnancy.

Neurologic

Some patients may experience drowsiness, dizziness, blurred vision, vertigo, tinnitus, hearing loss, insomnia or depression with the use of NSAIDs, such as PEDIAPHARM NAPROXEN SUSPENSION. If patients experience such adverse reaction(s), they should exercise caution in carrying out activities that

require alertness.

Ophthalmologic

Blurred and/or diminished vision has been reported with the use of NSAIDs. If such symptoms develop PEDIAPHARM NAPROXEN SUSPENSION should be discontinued and an ophthalmologic examination performed. Ophthalmologic examination should be carried out at periodic intervals in any patient receiving PEDIAPHARM NAPROXEN SUSPENSION for an extended period of time.

Perioperative considerations

See 2. Contraindications, Coronary Artery Bypass Graft Surgery.

Psychiatric

See 7.1 Warnings and Precautions, Neurologic.

Renal

Long term administration of NSAIDs to animals has resulted in renal papillary necrosis and other abnormal renal pathology. In humans, there have been reports of acute interstitial nephritis, hematuria, low grade proteinuria and occasionally nephrotic syndrome.

Renal insufficiency due to NSAID use is seen in patients with pre-renal conditions leading to reduction in renal blood flow or blood volume. Under these circumstances, renal prostaglandins help maintain renal perfusion and glomerular filtration rate (GFR). In these patients, administration of a NSAID may cause a reduction in prostaglandin synthesis leading to impaired renal function. Patients at greatest risk of this reaction are those with pre-existing renal insufficiency (GFR < 60 mL/min or 1 mL/s), dehydrated patients, patients on salt restricted diets, those with congestive heart failure, cirrhosis, liver dysfunction, taking angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, cyclosporin, diuretics, and those who are elderly. Serious or life-threatening renal failure has been reported in patients with normal or impaired renal function after short term therapy with NSAIDs. Even patients at risk who demonstrate the ability to tolerate a NSAID under stable conditions may decompensate during periods of added stress (e.g. dehydration due to gastroenteritis). Discontinuation of NSAIDs is usually followed by recovery to the pre-treatment state.

Caution should be used when initiating treatment with NSAIDs, such as PEDIAPHARM NAPROXEN SUSPENSION, in patients with considerable dehydration. Such patients should be rehydrated prior to initiation of therapy. Caution is also recommended in patients with pre-existing kidney disease.

Advanced Renal Disease: See 2. Contraindications.

Fluid and Electrolyte Balance: Use of NSAIDs, such as PEDIAPHARM NAPROXEN SUSPENSION, can promote sodium retention in a dose-dependent manner, which can lead to fluid retention and edema, and consequences of increased blood pressure and exacerbation of congestive heart failure. Thus, caution should be exercised in prescribing PEDIAPHARM NAPROXEN SUSPENSION in patients with a history of congestive heart failure, compromised cardiac function, hypertension, increased age or other conditions predisposing to fluid retention. See 7.1 Warnings and Precautions, Cardiovascular.

Use of NSAIDs, such as PEDIAPHARM NAPROXEN SUSPENSION, can increase the risk of hyperkalemia, especially in patients with diabetes mellitus, renal failure, increased age, or those receiving concomitant therapy with adrenergic blockers, angiotensin-converting enzyme inhibitors, angiotensin-II

receptor antagonists, cyclosporin, or some diuretics.

Electrolytes should be monitored periodically. See 2. Contraindications.

Naproxen formulated as a suspension (25 mg/mL) contains sodium chloride (20 mg/mL). This should be considered in patients whose overall intake of sodium must be restricted.

Reproductive health

- **Fertility**

  The use of PEDIAPHARM NAPROXEN SUSPENSION, as with any drug known to inhibit cyclooxygenase/ prostaglandin synthesis, may impair fertility and is not recommended in women attempting to conceive. Therefore, in women who have difficulties conceiving, or who are undergoing investigation of infertility, withdrawal of PEDIAPHARM NAPROXEN SUSPENSION should be considered.

Respiratory

ASA-induced asthma is an uncommon but very important indication of ASA and NSAID sensitivity. It occurs more frequently in patients with asthma who have nasal polyps.

Sensitivity/resistance

Anaphylactoid Reactions: As with NSAIDs in general, anaphylactoid reactions have occurred in patients without known prior exposure to PEDIAPHARM NAPROXEN SUSPENSION. In post-marketing experience, rare cases of anaphylactic/ anaphylactoid reactions and angioedema have been reported in patients receiving PEDIAPHARM NAPROXEN SUSPENSION. PEDIAPHARM NAPROXEN SUSPENSION should NOT be given to patients with the ASA-triad. This symptom complex typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking ASA or other NSAIDs. See 2. Contraindications.

ASA-Intolerance: PEDIAPHARM NAPROXEN SUSPENSION should NOT be given to patients with complete or partial syndrome of ASA-intolerance (rhinosinusitis, urticaria/angioedema, nasal polyps, asthma) in whom asthma, anaphylaxis, urticaria/angioedema, rhinitis or other allergic manifestations are precipitated by ASA or other NSAIDs. Fatal anaphylactoid reactions have occurred in such individuals. As well, individuals with the above medical problems are at risk of a severe reaction even if they have taken NSAIDs in the past without any adverse reaction. See 2. Contraindications.

Cross-sensitivity: Patients sensitive to one NSAID may be sensitive to any of the other NSAIDs as well.

Skin

Serious skin reactions: Use of some NSAIDs, such as Naproxen medicinal products, have been associated with rare post-market cases of serious, fatal or otherwise life-threatening skin reactions, including:

- Drug reaction with eosinophilia and systemic symptoms (DRESS)
- Stevens-Johnson syndrome (SJS)
- toxic epidermal necrolysis (TEN)
- exfoliative dermatitis
- erythema multiforme.

Patients appear to be at higher risk for these events early in the course of therapy, with the onset of cases usually occurring within the first month of treatment. These reactions may be reversible if the causative agent is discontinued and appropriate treatment instituted. Patients should be advised that they should discontinue their NSAID at the first appearance of a skin rash, mucosal lesions or any other sign of hypersensitivity, and contact their physician immediately for assessment and advice, including which therapies to discontinue.

DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, hematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection, and eosinophilia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident.

7.1. Special Populations

7.1.1. Pregnancy

PEDIAPHARM NAPROXEN SUSPENSION is CONTRAINDICATED for use during the third trimester of pregnancy because of risks of premature closure of the ductus arteriosus and the potential to prolong parturition. See 2. Contraindications and 16. Non-Clinical Toxicology. Caution is recommended in prescribing PEDIAPHARM NAPROXEN SUSPENSION during the first and second trimesters of pregnancy, particularly from the middle to end of the second trimester of pregnancy (onset at approximately 20 weeks) due to possible fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment or failure.

Published studies and postmarketing reports describe maternal NSAID use at approximately 20 weeks gestation or later in pregnancy associated with fetal renal dysfunction leading to oligohydramnios, and in some cases, neonatal renal impairment or failure. NSAIDs were shown to cause significant reduction in fetal urine production prior to reduction of amniotic fluid volume. There have also been a limited number of case reports of maternal NSAID use and neonatal renal dysfunction and renal impairment without oligohydramnios, some of which were irreversible, even after treatment discontinuation.

These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. Complications of prolonged oligohydramnios may for example, include limb contractures and delayed lung maturation. In some postmarketing cases of impaired neonatal renal function, invasive procedures such as exchange transfusion or dialysis were required.

If after careful consideration of the benefit-risk, NSAID treatment is considered necessary to be administered anywhere from the middle (onset at approximately 20 weeks) to the end of the second trimester of pregnancy, the use should be limited to the lowest effective dose and shortest duration possible. It is also recommended that ultrasound monitoring of amniotic fluid be considered if PEDIAPHARM NAPROXEN SUSPENSION treatment extends beyond 48 hours and that NSAIDs treatment be discontinued if oligohydramnios occurs, followed by appropriate medical follow up.

Inhibition of prostaglandin synthesis may adversely affect pregnancy and/or the embryo-foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation after use of a prostaglandin synthesis inhibitor in early pregnancy.

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.

PEDIAPHARM NAPROXEN SUSPENSION is not recommended in labour and delivery because, through their prostaglandin synthesis inhibitory effect, they may adversely affect fetal circulation and inhibit uterine contractions, thus increasing the risk of uterine hemorrhage.

7.1.2. Breastfeeding

PEDIAPHARM NAPROXEN SUSPENSION in breast-feeding women. See 2. Contraindications.

7.1.3. Pediatrics

Pediatrics (< 2 years of age): PEDIAPHARM NAPROXEN SUSPENSION should not be used in children under 2 years of age. The safety and efficacy in infants younger than 2 years of age has not been established. See 2. Contraindications.

7.1.4. Geriatrics

***Geriatrics (> 65 years of age)*:** Patients older than 65 years (referred to in this document as older or elderly) and frail or debilitated patients are more susceptible to a variety of adverse reactions from NSAIDs. The incidence of these adverse reactions increases with dose and duration of treatment. In addition, these patients are less tolerant to ulceration and bleeding. Most reports of fatal GI events are in this population. Older patients are also at risk of lower esophageal injury including ulceration and bleeding. For such patients, consideration should be given to a starting dose lower than the one usually recommended, with individual adjustment when necessary and under close supervision.

8. Adverse Reactions

8.1. Adverse Reaction Overview

The most common adverse reactions encountered with nonsteroidal anti-inflammatory drugs are gastrointestinal, of which peptic ulcer, with or without bleeding, is the most severe. Fatalities have occurred particularly in the elderly.

As with all drugs in this class, the frequency and severity of adverse events depends on several factors: the dose of the drug and duration of treatment; the age, the sex, physical condition of the patient; any concurrent medical diagnoses or individual risk factors.

8.2. Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. Therefore, the frequencies of adverse reactions observed in the clinical trials may not reflect frequencies observed in clinical practice and should not be compared to frequencies reported in clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

A clinical study found gastrointestinal reactions to be more frequent and more severe in rheumatoid arthritis patients taking daily doses of 1500 mg naproxen compared to those taking 750 mg naproxen.

Adverse reactions identified in controlled clinical trials in 960 patients with rheumatoid arthritis or osteoarthritis treated with naproxen, as standard tablets, are listed below. PEDIAPHARM NAPROXEN SUSPENSION was found to have similar bioavailability to the naproxen tablets.

Table 5 – Most Common Clinical Trial Adverse Drug Reactions (3%-9% and 1%-3%)

Body System	Incidence	Adverse Reaction
Gastrointestinal	3%-9%	Heartburn, constipation, abdominal pain, nausea
	1%-3%	Diarrhea, dyspepsia, stomatitis, diverticulitis, gastrointestinal bleeding
Central Nervous System	3%-9%	Headache, dizziness, drowsiness
	1%-3%	Light-headedness, vertigo, depression, fatigue. Occasionally patients had to discontinue treatment because of the severity of some of these complaints (headache and dizziness).
Dermatologic	3%-9%	Pruritus, ecchymoses, skin eruptions
	1%-3%	Sweating, purpura
Cardiovascular	3%-9%	Dyspnea, peripheral edema
	1%-3%	Palpitations
Special Senses	3%-9%	Tinnitus
	1%-3%	Hearing disturbances
General	1%-3%	Thirst

8.3. Less Common Clinical Trial Adverse Reactions

Less Common Clinical Trial Adverse Drug Reactions (<1%)

Gastrointestinal: Gastrointestinal bleeding, hematemesis, melena, peptic ulceration with or without bleeding and/or perforation, vomiting, ulcerative stomatitis.

Central Nervous System: Inability to concentrate, malaise, myalgia, insomnia and cognitive dysfunction (i.e. decreased attention span, loss of short-term memory, difficulty with calculations).

Dermatologic: Alopecia, urticaria, skin rash, erythema multiforme, Stevens-Johnson syndrome, epidermal necrolysis, photosensitive dermatitis, exfoliative dermatitis, erythema nodosum.

Hepatic: Abnormal liver function tests, jaundice, cholestasis and hepatitis.

Cardiovascular: Congestive heart failure and vasculitis.

Renal: Glomerular nephritis, hematuria, interstitial nephritis, nephrotic syndrome, nephropathy and tubular necrosis.

Hematologic: Eosinophilia, granulocytopenia, leukopenia, thrombocytopenia, agranulocytosis, aplastic anemia and hemolytic anemia.

Special Senses: Hearing impairment and visual disturbances.

Reproductive, female: Infertility

General:	Muscle weakness, anaphylactoid reactions, menstrual disorders, pyrexia (chills and fever), angioneurotic edema, hyperglycemia, hypoglycemia and eosinophilic pneumonitis.

8.5. Post-Market Adverse Reactions

The following additional adverse events have been reported with NSAIDs including naproxen and naproxen sodium:

Gastrointestinal:	Inflammation, bleeding (sometimes fatal, particularly in the elderly), ulceration, perforation and obstruction of the upper or lower gastrointestinal tract. Oesophagitis, gastritis, pancreatitis, stomatitis. Exacerbation of ulcerative colitis and Crohn's disease. Heartburn, dyspepsia, abdominal pain, nausea, vomiting, diarrhoea, flatulence, constipation, hematemesis, melaena.
Infections:	Aseptic meningitis
Blood and Lymphatic System Disorders:	Agranulocytosis, aplastic anemia, eosinophilia, hemolytic anaemia, leucopoenia, thrombocytopenia
Immune System Disorders:	Anaphylactoid reactions
Metabolic and Nutrition Disorders:	Hyperkalemia
Psychiatric Disorders:	Depression, dream abnormalities, insomnia
Nervous System Disorders:	Dizziness, drowsiness, headache, lightheadedness, retrobulbar optic neuritis convulsions, cognitive dysfunction, inability to concentrate
Eye Disorders:	Visual disturbances, corneal opacity, papillitis, papilledema
Ear and Labyrinth Disorders:	Hearing impairment, hearing disturbances, tinnitus, vertigo
Cardiac Disorders:	Palpitations, cardiac failure has been reported in association with NSAID treatment, congestive heart failure
Vascular Disorders:	Hypertension, vasculitis.
	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).
Respiratory, Thoracic and Mediastinal Disorders:	Dyspnoea, pulmonary edema, asthma, eosinophilic pneumonitis.
Hepatobiliary Disorders:	Hepatitis (some cases of hepatitis have been fatal), jaundice.
Skin and Subcutaneous Tissue Disorders:	Ecchymoses, itching (pruritus), purpura, skin eruptions, sweating, alopecia, epidermal necrolysis, very rarely toxic epidermal necrolysis, erythema multiforme, bullous reactions, including Stevens-Johnson syndrome, erythema nodosum, fixed drug eruption, lichen planus, pustular reaction, skin rashes, SLE, urticaria, photosensitivity reactions, including rare cases resembling porphyria cutanea tarda ("pseudoporphyria") or epidermolysis

	bullosa and angioneurotic edema. If skin fragility, blistering or other symptoms suggestive of pseudoporphyria occur, treatment should be discontinued and the patient monitored.
Musculoskeletal and Connective Tissue Disorders:	Myalgia, muscle weakness.
Renal and Urinary Disorders:	Hematuria, interstitial nephritis, nephrotic syndrome, renal disease, renal failure, renal papillary necrosis
Reproductive System and Breast Disorders:	Female infertility
General Disorders and Administration Site Conditions:	Edema, thirst, pyrexia (chills and fever), malaise
Investigations:	Abnormal liver function tests, raised serum creatinine

9. Drug Interactions

9.3. Drug-Behaviour Interactions

There are no specific studies about effects on the ability to drive vehicles and to use machinery. Patients who experience visual disturbances or other central nervous system disturbances should refrain from these activities.

Concurrent use of alcohol with an NSAID may increase the risk of gastrointestinal side effects, including ulceration and hemorrhage.

9.4. Drug-Drug Interactions

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Table 6 – Established or Potential Drug-Drug Interactions

Non-proprietary name(s) of the drug product(s)	Source of evidence	Effect	Clinical comment
Acetylsalicylic acid (ASA) or other NSAIDs	CT	• The concomitant use of PEDIAPHARM NAPROXEN SUSPENSION and other NSAIDs, (such as ASA and ibuprofen) does not produce any greater therapeutic effect than the use of NSAIDs alone. • The concomitant use of an NSAID and ASA (such as aspirin) was associated with a significantly increased incidence of GI adverse reactions as compared to use of the NSAID alone. The exception is the use of low dose ASA for cardiovascular protection, when another NSAID is being used for its analgesic/anti-inflammatory effect, keeping in mind that combination NSAID therapy is associated with additive adverse reactions. • Some NSAIDs (e.g. ibuprofen) may interfere with the anti-platelet effects of low dose ASA, possibly by competing with ASA for access to the active site of cyclooxygenase-1	• Because there may be an increased risk of CV events following discontinuation of naproxen due to the interference with the antiplatelet effect of ASA during the washout period, for patients taking low-dose ASA for cardioprotection who require intermittent analgesics, consider use of an NSAID that does not interfere with the antiplatelet effect of ASA, or non-NSAID analgesics where appropriate. • Concomitant use of PEDIAPHARM NAPROXEN SUSPENSION and analgesic doses of ASA or other NSAIDs is not recommended because of the increased risk of bleeding. See 7. Warnings and Precautions.

Non-proprietary name(s) of the drug product(s)	Source of evidence	Effect	Clinical comment
ACE Inhibitors, Angiotensin Receptor Blockers, and Beta-Blockers	T	• NSAIDs may diminish the anti-hypertensive effect of angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs) or beta-blockers (including propranolol). • In patients who are elderly, volume-depleted (including those on diuretic therapy), or have RI, co-administration of an NSAID with ACE inhibitors or ARBs may result in deterioration of renal function, including possible acute renal failure and hyperkalemia. These effects are usually reversible.	• Blood pressure and renal function (including electrolytes) should be monitored more closely in this situation, as occasionally there can be a substantial increase in blood pressure. See 7. Warnings and Precautions.
Albumin-Bound Drugs	T	• Naproxen is highly bound to plasma albumin; it thus has a theoretical potential for interaction with other albumin-bound drugs such as coumarin-type anticoagulants, warfarin, sulfonamide or sulphonylureas, hydantoins, other NSAIDs, and ASA.	• Patients should be under careful observation for adjustment of dose if required.
Antacids	N/A	• Concomitant administration of some antacids (magnesium oxide or aluminum hydroxide) and sucralfate can delay the absorption of naproxen.	• Concomitant administration is not recommended.
Anti-coagulants	CT	• Naproxen and anticoagulants such as warfarin have a synergistic effect on bleeding. • The concomitant use of naproxen and anticoagulants have an increased risk of serious bleeding compared to the use of either drug alone.	• Anticoagulation/INR should be monitored and warfarin dosage adjustments. See 7. Warnings and Precautions.

Non-proprietary name(s) of the drug product(s)	Source of evidence	Effect	Clinical comment
Anti-platelet Agents (including ASA)	CT	• There is an increased risk of bleeding, via inhibition of platelet function, when anti-platelet agents are combined with naproxen.	• Monitor patients for signs of bleeding. See 7. Warnings and Precautions.
Cyclosporin and Tacrolimus	T	• Inhibition of renal prostaglandin activity by NSAIDs may increase the nephrotoxic effect of cyclosporin or tacrolimus.	• Patients should be monitored for necessary dosage adjustment. • Monitor patients for signs of worsening renal function.
Cholestyramine	N/A	• Concomitant administration of cholestyramine can delay the absorption of naproxen.	• Concomitant administration is not recommended.
Digoxin	C	• The concomitant use of naproxen with digoxin has been reported to increase the serum concentration and prolong the half-life of digoxin which may result in digitalis toxicity.	• Monitor serum digoxin levels.
Diuretics	CT	• Clinical studies as well as post-marketing observations have shown that NSAIDs can reduce the effect of diuretics. • This effect has been attributed to the NSAID inhibition of renal prostaglandin synthesis.	• Observe patients for signs of worsening renal function, in addition to assuring diuretic efficacy including antihypertensive effects. See 7. Warnings and Precautions.
Glucocorticoids	CT	• The concomitant use of NSAIDs and oral glucocorticoids increases the risk of GI adverse events such as ulceration and bleeding, especially in older (> 65 years of age) patients.	• Monitor patients particularly those over 65 years of age for signs of bleeding. See 7. Warnings and Precautions.

Non-proprietary name(s) of the drug product(s)	Source of evidence	Effect	Clinical comment
Lithium	CT	• NSAIDs have produced elevations in plasma lithium levels and reductions in renal lithium clearance. The mean minimum lithium concentration increased 15%, and the renal clearance decreased by approximately 20%. This effect has been attributed to NSAID inhibition of renal prostaglandin synthesis.	• Monitor patients for plasma lithium concentrations when stopping or starting a NSAID.
Methotrexate	T	• Caution is advised in the concomitant administration of naproxen and methotrexate since naproxen and other non-steroidal anti-inflammatory agents have been reported to reduce the tubular secretion of methotrexate in an animal model, thereby possibly enhancing its toxicity.	• Monitor patients for methotrexate toxicity.
Pemetrexed	CT	• Concomitant use of PEDIAPHARM NAPROXEN SUSPENSION and pemetrexed may increase the risk of pemetrexed-associated myelosuppression, renal, and GI toxicity.	• In patients with renal impairment whose creatinine clearance ranges from 45 to 79 mL/min, monitor for myelosuppression, renal and GI toxicity.
Probenecid	CT	• Increases naproxen anion plasma levels and extends its plasma half-life significantly.	• Patients should be observed for adjustment of dose if required.
Selective Serotonin Reuptake Inhibitors (SSRIs)	C	• Serotonin release by platelets plays an important role in hemostasis. • Case-control and cohort epidemiological studies showed that concomitant use of drugs that interfere with serotonin reuptake and an NSAID may potentiate the risk of bleeding more than an NSAID alone.	• Monitor patients for signs of bleeding. See 7. Warnings and Precautions.

Non-proprietary name(s) of the drug product(s)	Source of evidence	Effect	Clinical comment
Quinolone antibacterials	C	• There have been isolated reports of convulsions which may have been due to concomitant use of quinolones and NSAIDs.	• Patients should be observed for adjustment of dose if required.

Legend: C = Case Study; CT = Clinical Trial; T = Theoretical; GI = Gastrointestinal; CV = Cardiovascular; INR = International normalized ratio; ASA = Acetylsalicylic acid; NSAID = Non-Steroidal Anti-Inflammatory Drug; ACE = Angiotensin converting enzyme; ARB = Angiotensin Receptor Blockers

9.5. Drug-Food Interactions

Concomitant administration of food can delay the absorption of naproxen, but does not affect its extent of absorption.

9.6. Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7. Drug-Laboratory Test Interactions

See 7. Warnings and Precautions, Monitoring and laboratory Tests.

10. Clinical Pharmacology

10.1. Mechanism of Action

PEDIAPHARM NAPROXEN SUSPENSION contains naproxen, a propionic acid derivative related to the the arylacetic acid group of NSAIDs.

Naproxen is a nonsteroidal anti-inflammatory drug (NSAID) with analgesic, anti-inflammatory and antipyretic properties. The mechanism of action of naproxen, like that of other NSAIDs, is not completely understood but may be related to prostaglandin synthetase inhibition.

10.2. Pharmacodynamics

Naproxen has been shown to possess anti-inflammatory and analgesic activity as assessed by a variety of animal test procedures.

Anti-inflammatory activity: In the rat paw edema assay, naproxen was more potent than phenylbutazone and acetylsalicylic acid, and slightly less potent than indomethacin.

In the rat granuloma assay, naproxen was more active than phenylbutazone and less active than indomethacin.

Analgesic activity: In a mouse analgesic assay using phenylquinone for pain induction, naproxen was more active than phenylbutazone and acetylsalicylic acid, and less active than indomethacin. Parallel comparative analgesic studies were done in rats with yeast induced paw edema.

In these assays, naproxen had a higher relative potency than phenylbutazone and acetylsalicylic acid, but lower relative potency when compared to indomethacin.

The comparative absorption, distribution, metabolism and excretion of naproxen was studied in several species, including man. Naproxen was found to be rapidly absorbed in all species and, once in the blood was eliminated with half-lives ranging from 2 to 35 hours. Estimated volumes of distribution indicated that a large fraction of the drug is held in the blood, much like salicylates are. Virtually all of the drug present in the blood of humans was determined to be unchanged naproxen, while the rat and the monkey showed minor amounts of transformation products. With the exception of the dog, all species excreted naproxen and its metabolic transformation products predominantly in the urine. In the dog the preferred route was fecal.

Studies by Tomlinson, et al. 1972 have shown that naproxen can inhibit the synthesis of prostaglandin E2 from arachidonic acid by bovine seminal vesicle microsomes. Naproxen therefore appears to act at least in part in a manner similar to other anti-inflammatory agents which block prostaglandin biosynthesis.

Human metabolic studies:
The plasma level response to oral naproxen doses ranging up to 900 mg twice daily was studied in normal subjects. Experiments with tritium labelled naproxen showed that there was no difference in the fraction of ingested drug excreted in the stools whether the dose was 250 mg or 900 mg, thus eliminating the possibility that this effect was a result of incomplete absorption. Accelerated renal clearance at high doses because of disproportionate increases in the amount of unbound drug appeared to be the most likely explanation for the plateau effect.

In patients treated with maintenance dialysis for terminal renal failure, serum level studies indicated that the metabolite 6-0-desmethyl naproxen is dialysed, whilst naproxen is not. No accumulation of naproxen was found although serum levels of the metabolite increased.

10.3. Pharmacokinetics

The average maximum plasma concentration (C_{max}) following the 375 mg and 500 mg standard immediate release tablets were 46.6 and 63.1 µg/mL, respectively. The T_{max}'s were 2.3 and 2.6 hr., respectively. At steady state (multiple dosing), fluctuation in plasma levels for C_{ave} was 85.3%. Concomitant administration of food can delay the absorption of naproxen, but does not affect its extent of absorption.

Absorption

Naproxen is rapidly and completely absorbed from the gastro-intestinal tract.

Distribution

After oral administration of naproxen, peak plasma levels of naproxen anion are attained in 2 to 4 hours, with steady state conditions normally achieved after 4-5 doses. Plasma naproxen levels and areas under plasma concentration vs. time curves increased linearly with dose increments up to 500 mg twice a day, but larger doses resulted in a plateau effect.

In children with rheumatic diseases aged between 5 to 16 years, naproxen reached peak plasma levels

2 to 4 hours following oral dosing and the mean plasma half-life was 11.5 to 14.1 hours. PEDIAPHARM NAPROXEN SUSPENSION was found to have similar bioavailability to the naproxen tablets in two single dose studies done in 24 healthy male volunteers. No clinically significant differences in tolerance were reported between the two dosage forms.

Metabolism

The mean biological half-life of the anion in humans is approximately 13 hours, and at therapeutic levels it is greater than 99% albumin bound.

Approximately 95% of the dose is excreted in the urine, primarily as naproxen, 6-0-desmethyl naproxen or their conjugates. The rate of excretion has been found to coincide closely with the rate of drug disappearance from the plasma. The drug does not induce metabolizing enzymes.

Elimination

Approximately 95% of the dose is excreted in the urine.

Special populations and conditions

- **Pediatrics**

  Pharmacokinetic studies of naproxen were not performed in children less than 2 years of age.

- **Geriatrics**

  Studies indicate that although total plasma concentration of naproxen is unchanged, the unbound plasma fraction of naproxen is increased in the elderly, although the unbound fraction is <1% of the total naproxen concentration. Unbound trough naproxen concentrations in elderly subjects have been reported to range from 0.12% to 0.19% of total naproxen concentration, compared with 0.05% to 0.075% in younger subjects.

- **Hepatic Insufficiency**

  Naproxen pharmacokinetics has not been determined in subjects with hepatic insufficiency.

  Chronic alcoholic liver disease and probably other diseases with decreased or abnormal plasma proteins (albumin) reduce the total plasma concentration of naproxen, but the plasma concentration of unbound naproxen is increased.

- **Renal Insufficiency**

  Given that naproxen and its metabolites are primarily excreted by the kidney, the potential exists for accumulation in the presence of renal insufficiency. Elimination of naproxen is decreased in patients with severe renal impairment. See 2. Contraindications.

11. Storage, Stability, and Disposal

Store at room temperature not exceeding 25°C, with protection from light. Store upright.

Keep out of reach and sight of children.

Part 2: Scientific Information

13. Pharmaceutical Information

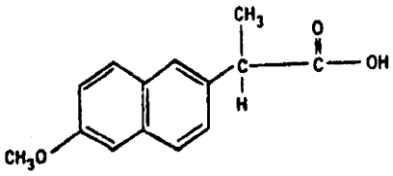
Drug Substance

Non-proprietary name of the drug substance(s): Naproxen

Chemical name: (+) 6 methoxy alpha methyl 2 naphthaleneacetic acid

Molecular formula and molecular mass: $C_{14}H_{14}O_3$; 230.27

Structural formula:



Physicochemical properties: Naproxen is an odorless white crystalline powder with a melting point of 152 – 158°C. It is highly lipid soluble, sparingly soluble in water at low pH and highly soluble in water at high pH.

Pharmaceutical standard: U.S.P

14. Clinical Trials

14.1. Clinical Trials by Indication

The clinical trial data on which the original indication was authorized is not available.

15. Microbiology

No microbiological information is required for this drug product.

16. Non-Clinical Toxicology

General toxicology

Acute Animal Toxicity

The oral LD_{50} values for naproxen are as follows:

Hamster	4110 mg/kg
Rats	543 mg/kg
Dogs	>1000 mg/kg
Mice	1234 mg/kg

Subacute and Chronic Oral Toxicity

In subacute and chronic oral studies with naproxen in a variety of species, the principal pathologic effect was gastrointestinal irritation and ulceration. The lesions seen were predominantly in the small intestine and ranged from hyperemia to perforation and peritonitis.

Nephropathy was seen occasionally in rats, mice and rabbits at high dose levels of naproxen, but not in rhesus monkeys or miniature pigs. In the affected species the pathologic changes occurred in the cortex and papilla. Some rats examined 14 days after single oral doses of 230 mg/kg or more of naproxen evidenced necrotic areas of cortical and papillary tissue. Tubular dilation (ectasia) occurred in rabbits dosed orally for 14 days with 200 mg/kg/day or more of naproxen. An examination of unfixed renal tissue from rabbits so treated was conducted and revealed the presence of diffraction patterns similar to that of crystalline naproxen. This suggests that the ectasia observed was physical response to deposition of excreted naproxen within the tubules.

In mice given oral doses of 120 mg/kg/day or more of naproxen for 6 months, the kidneys were characterized by a low but non dosage related incidence of cortical sclerosis and papillary tip necrosis. Chronic administration of high doses of naproxen to mice appears to be associated with exacerbation of spontaneous murine nephropathy.

A wide variation in susceptibility to gastrointestinal lesions from administration of naproxen was evident in the various species tested. For example, 30 mg/kg/day was tolerated well by rats for 90 days, but the same dose was ulcerogenic when administered for 6 months. Rhesus monkeys and miniature swine exhibited no significant pathology when dosed with naproxen at 45 mg/kg/day for 30 days. This dose of naproxen was also tolerated by miniature swine without obvious evidence of adverse effects when administered daily for 1 year. In rhesus monkeys doses as high as 120 mg/kg/day administered b.i.d. for 6 months produced no clinical or histopathological evidence of gastrointestinal irritation although occult blood in the feces occurred more frequently in these animals as compared to controls. In rabbits the maximum tolerated repeated oral dose is 200 mg/kg/day. Mice tolerated oral daily doses of 240 mg/kg/day for 6 months. In both rabbits and mice, gastrointestinal and renal toxicity was reported at these dose levels. In dogs, on the other hand, 5.0 mg/kg/day approaches the maximum tolerated dose. This peculiar canine susceptibility to gastrointestinal effects of non-steroidal anti-inflammatory agents has also been shown with indomethacin and ibuprofen.

In dogs, naproxen exhibits a considerably longer plasma half-life than it does in rats, guinea pigs, miniature swine, monkeys and man. The same observation has been made with ibuprofen in dogs compared to rats and man. In addition, in the species listed, only the dog excretes significant amounts of administered naproxen in the feces (50%). In the rat, guinea pigs, miniature swine, monkeys and man, 86 94% of the administered drug is excreted in the urine. The suggested enterohepatic circulation of naproxen in the dog (as judged by the fecal excretion) may be a major factor in the susceptibility of the dog to gastrointestinal irritation by this compound.

Pathologic changes in the spleen and mesenteric lymph nodes as well as peritoneal inflammation and adhesions were considered to be clearly secondary to the effects of high doses of naproxen on the gastrointestinal tract. Moderate weight loss of the male secondary sex glands occurred in some studies in naproxen treated rats and dogs. Histopathologically the affected glands in some instances exhibited atrophic and/or hypoplastic changes characterized by decreased secretory material. A possible estrogenic action of naproxen as a causative factor seems highly unlikely since in standard bioassay procedures the drug exhibited no estrogenic activity. Nevertheless, daily doses of naproxen as high as 30 mg/kg administered for 60 days before mating had no effect on fertility and reproductive performance of male rats. These results reflect the physiological integrity of the entire male reproductive apparatus after administration of naproxen throughout the spermatogenic cycle.

Effect on Induced Infections in Rabbits

To determine whether treatment with naproxen affects the ability of animals to respond to bacterial infection, rabbits were inoculated subcutaneously with Diplococcus pneumoniae. For 21 days before bacterial challenge and during a 2-week post-challenge period, the animals were dosed daily by gavage with 2, 10 or 20 mg/kg of naproxen. Clinical condition, morbidity, mortality, gross and histopathologic changes were evaluated. There were no apparent effects of naproxen in altering the response of the animals to bacterial challenge.

Genotoxicity

Mutagenicity was not seen in Salmonella typhimurium (5 cell lines), Sachharomyces cerevisisae (1 cell line), and mouse lymphoma tests.

Carcinogenicity

Naproxen was administered with food to Sprague-Dawley rats for 24 months at doses of 8, 16 and 24 mg/kg/day. Naproxen was not carcinogenic in rats.

Reproductive and developmental toxicology

Daily oral administration of 15, 30 or 60 mg/kg of naproxen to female rabbits from 2 weeks before mating until day 20 of pregnancy did not affect fertility, gestation or the numbers of live fetuses.

In a peri- and post-natal study in rats, oral doses of naproxen up to 20 mg/kg administered daily during the last part of pregnancy through weaning did not result in adverse effects in viability of pups, lactation index, sex ratio or weight gain of offspring. However, there was a slight increase in gestation length at the 10 and 20 mg/kg dose levels; and, at the 10 mg/kg dose level, there was a significant increase in stillbirths.

Naproxen at daily oral doses of 12, 36 or 108 mg/kg to female mice from 2 weeks before mating until weaning of the pups did not cause changes in length of gestation, number of live pups born, average pup weight at 0, 4, 7, 14 or 21 days, or sex distribution. The fertility index, gestation index and 4 day viability index were similar for mice from the control and treated groups. The 21 day survival and lactation indexes were decreased for mice from the group fed 108 mg/kg/day of naproxen but not for mice given 12 or 36 mg/kg/day. Most of this change was due to maternal mortality in the high dose group.

Recent evidence suggests that inhibition of prostaglandin synthesis by non-steroidal anti-inflammatory compounds may be related to decreased uterine contractibility. Thus, the onset of labor in a rat model system can be delayed with naproxen administration without causing maternal or fetal deaths in excess of that seen in controls. Since it has been shown that Naproxen inhibits prostaglandin synthesis in vitro, it has been suggested that the effects of naproxen on uterine contractility are mediated through that mechanism.

Maternal and fetal deaths seen in naproxen treated rats were, therefore, apparently related to dystocia rather than to a direct toxic effect of the compound. Naproxen is not unique in this regard since comparable results were obtained in the rat with other commonly used non-steroidal anti-inflammatory agents.

In teratology studies, no skeletal or visceral anomalies or pathologic changes were induced in the fetuses of pregnant rats and rabbits treated during organogenesis with daily oral doses of naproxen up to 20 mg/kg. In these studies there were also no significant differences from controls in the number of live fetuses, resorptions, fetal weights or ano-genital distances.

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr] PEDIAPHARM NAPROXEN SUSPENSION

Naproxen oral suspension U.S.P.

This Patient Medication Information is written for the person who will be taking **PEDIAPHARM NAPROXEN SUSPENSION**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This Patient Medication Information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about **PEDIAPHARM NAPROXEN SUSPENSION**, talk to a healthcare professional.

Serious warnings and precautions box

Heart and blood vessel problems:

- PEDIAPHARM NAPROXEN SUSPENSION can cause heart and blood vessel problems like heart attacks, stroke, blood clots, high blood pressure and heart failure. These can lead to death.
- The risk of having heart problems is higher if you take PEDIAPHARM NAPROXEN SUSPENSION for long periods of time and/or at higher doses and/or in people who have heart disease.
- Tell your healthcare professional if you have or had heart problems, high blood pressure or diabetes.

Stomach and intestine (gastrointestinal) problems:

- PEDIAPHARM NAPROXEN SUSPENSION can cause stomach and intestine problems like ulcers, inflammation, bleeding, holes/perforation, blockage or pain.

Talk to your healthcare professional about any medical conditions you have and drugs you are taking.

Pregnancy:

- **DO NOT** take PEDIAPHARM NAPROXEN SUSPENSION if you are pregnant and in a later stage of pregnancy (28 weeks or later).
- If you are pregnant and in an earlier stage of pregnancy (less than 28 weeks) only take PEDIAPHARM NAPROXEN SUSPENSION if you are told to do so by your healthcare professional.
- Medicines like PEDIAPHARM NAPROXEN SUSPENSION may cause harm to you and your baby. Your healthcare professional will need to closely monitor your health and that of your baby (including your amniotic fluid levels) if they prescribe PEDIAPHARM NAPROXEN SUSPENSION during this time.
- Tell your healthcare professional right away if you become pregnant, think you may be pregnant or want to get pregnant during your treatment with PEDIAPHARM NAPROXEN SUSPENSION.

What PEDIAPHARM NAPROXEN SUSPENSION is used for:

Your healthcare professional has prescribed PEDIAPHARM NAPROXEN SUSPENSION for you for one or more of the following medical conditions:

- Treat the signs and symptoms of arthritis disorders such as:
  - osteoarthritis
  - rheumatoid arthritis
  - ankylosing spondylitis
  - juvenile rheumatoid arthritis
- Help relieve:
  - minor aches and pains in muscles, bones and joints
  - mild to moderate pain with inflammation in sprains and strains and period cramps (primary dysmenorrhea)

How PEDIAPHARM NAPROXEN SUSPENSION works:

- PEDIAPHARM NAPROXEN SUSPENSION (naproxen) belongs to a group of medicines called non-steroidal anti-inflammatory drug (NSAIDs). It can reduce the chemicals produced by your body which cause pain and swelling.
- PEDIAPHARM NAPROXEN SUSPENSION only treats the symptoms and relieves pain and inflammation as long as you take it. PEDIAPHARM NAPROXEN SUSPENSION does not cure the illness or stop it from getting worse.

The ingredients in PEDIAPHARM NAPROXEN SUSPENSION are:

Medicinal ingredient: naproxen

Non-medicinal ingredients: FD&C Yellow No. 6, fumaric acid, imitation orange flavour, imitation pineapple flavour, magnesium aluminum silicate, methylparaben, sodium chloride, sorbitol solution 70%, sucrose.

PEDIAPHARM NAPROXEN SUSPENSION comes in the following dosage form:

Suspension: 25 mg/mL

Do not use PEDIAPHARM NAPROXEN SUSPENSION if you:

- have heart bypass surgery (planning to have or recently had).
- have severe, uncontrolled heart failure.
- are bleeding in the brain or have other bleeding disorders.
- are pregnant and in a later stage of pregnancy (28 weeks or later).
- are currently breastfeeding (or planning to breastfeed).
- are allergic to naproxen or any of the other ingredients in this medicine or the container.
- have a history of asthma, hives, growths in your nose, sinus swelling or symptoms of an allergic reaction after taking acetylsalicylic acid (ASA) or other NSAIDs.
- have active stomach or intestine ulcers.
- have active bleeding from the stomach or gut.
- have inflammatory bowel disease (Crohn’s Disease or Ulcerative Colitis).
- have liver disease (active or severe).
- have kidney disease (severe or worsening).
- have high potassium in the blood.

Patients who took a drug in the same class as PEDIAPHARM NAPROXEN SUSPENSION after a type of heart surgery (coronary artery bypass grafting (CABG)) were more likely to have heart attacks, strokes, blood clots in the leg(s) or lung(s), and infections or other complications than those who did NOT take that drug.

PEDIAPHARM NAPROXEN SUSPENSION should NOT be used in patients under 2 years of age since the safety and effectiveness have NOT been established.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take PEDIAPHARM NAPROXEN SUSPENSION. Talk about any health conditions or problems you may have, including if you:

- have high blood pressure, high cholesterol or diabetes
- have or had heart attacks, chest pain, heart disease, stroke or heart failure
- are on a low sugar diet
- have atherosclerosis (hardening of the arteries)
- have poor blood flow to your extremities (like your hands and feet)
- smoke or used to smoke
- drink a lot of alcohol
- have a stomach infection
- have liver or kidney problems, urine problems or are dehydrated
- have a history of ulcer or bleeding from the stomach or gut (small or large intestine)
- have previous bleeding in the brain
- have other bleeding or blood problems
- have family history of allergy to NSAIDs, such as acetylsalicylic acid (ASA), celecoxib, diclofenac, diflunisal, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, mefenamic acid, meloxicam, nabumetone, naproxen, oxaprozin, piroxicam, rofecoxib, sulindac, tenoxicam, tiaprofenic acid, tolmetin, or valdecoxib (NOT a complete list)
- have family history of asthma, nasal polyps, long-term swelling of the sinus (chronic sinusitis) or hives
- are pregnant, planning on becoming or become pregnant while taking PEDIAPHARM NAPROXEN SUSPENSION
- have immune system problems

Other warnings you should know about:

Tell any doctor, dentist, pharmacist or healthcare professional that you see that you are taking this medicine. This is especially important if you are planning to have heart surgery.

Do NOT drink alcoholic beverages while taking PEDIAPHARM NAPROXEN SUSPENSION as you will be more likely to develop stomach problems.

Serious Side Effects: PEDIAPHARM NAPROXEN SUSPENSION can cause serious side effects, including:

- **Blood and Bleeding Problems:**
  - PEDIAPHARM NAPROXEN SUSPENSION can cause blood problems, bleeding problems and prolonged bleeding.
  - Taking PEDIAPHARM NAPROXEN SUSPENSION with the following drugs can increase the risk of bleeding:

    - Anticoagulants (prevent blood clots), corticosteroids (anti-inflammatory) or antidepressants like selective serotonin reuptake inhibitors (SSRIs).

- **Serious Skin Reactions:**
  - In rare cases, serious or life-threatening allergic skin reactions have been reported with the use of PEDIAPHARM NAPROXEN SUSPENSION and other NSAIDs. These skin problems most often happen during the first month of treatment. Tell your healthcare professional immediately if you develop chills, fever, muscle aches or pains, or other flu-like symptoms, especially if they occur with a skin rash. These symptoms may be the first signs of a serious allergic reaction to this medication.
  - PEDIAPHARM NAPROXEN SUSPENSION might cause you to become more sensitive to sunlight. Sunlight or sunlamps may cause sunburn, skin blisters, skin rash, redness, itching or discolouration, or vision changes. If you have a reaction from the sun, talk to your healthcare professional.

Check-ups and Testing: You will have regular visits with your healthcare professional during treatment with PEDIAPHARM NAPROXEN SUSPENSION to monitor your health. They will:
- Check your blood pressure.
- Check your eyes. PEDIAPHARM NAPROXEN SUSPENSION can cause blurred or reduced vision.
- Do blood and urine tests to check your liver, kidney and blood health.

Driving and Using Machines: PEDIAPHARM NAPROXEN SUSPENSION may cause eye or nervous system problems. This includes tiredness, trouble sleeping, blurred vision, spinning or dizziness (vertigo), hearing problems or depression. Be careful about driving or doing activities that require you to be alert.

If you become drowsy, dizzy or light-headed after taking PEDIAPHARM NAPROXEN SUSPENSION, do NOT drive or operate machinery.

Fertility in Women: PEDIAPHARM NAPROXEN SUSPENSION may affect your fertility. This means that it may be difficult for you to have a child. If you have trouble having a child, you might need to stop taking PEDIAPHARM NAPROXEN SUSPENSION. Talk to your healthcare professional if you have questions about this.

Adults (65 years or older): Side effects like gastrointestinal problems may happen more often. Your healthcare professional might have you start with a lower dose of PEDIAPHARM NAPROXEN SUSPENSION. They will monitor your health during and after treatment.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with PEDIAPHARM NAPROXEN SUSPENSION:

- Acetylsalicylic Acid (ASA) or other NSAIDs, used to treat pain, fever and inflammation, like celecoxib, diclofenac, ibuprofen, indomethacin, ketorolac, meloxicam, naproxen
- Antacids, used to treat symptoms of excess stomach acid
- Medicines used to treat depression (antidepressants) like citalopram, fluoxetine, paroxetine, sertraline, and lithium
- Medicines used to treat high blood pressure like:
  - ACE (angiotensin converting enzyme) inhibitors (e.g. enalapril, ramipril, lisinopril, perindopril, propranolol)
  - ARBs (angiotensin II receptor blockers) (e.g. candesartan, irbesartan, losartan, valsartan)
- Medicines used as blood thinners or to prevent blood clots, like warfarin, ASA, clopidogrel

- Medicines used to lower extra fluid levels (diuretics), like furosemide, hydrochlorothiazide
- Medicines used to lower the risk of organ rejection, like tacrolimus and cyclosporin
- Medicines used to treat diabetes, like sulphonylurea or other oral hypoglycemics
- Medicines used to treat bacteria infections (antibiotics) like quinolone or sulphonamide
- Corticosteroids (including glucocorticoids such as prednisone) used as an anti-inflammatory
- Cholestyramine, used to lower cholesterol levels
- Digoxin, used to treat heart disorders
- Hydantoin, used to treat seizures
- Medicines used to treat different cancers, like methotrexate and pemetrexed
- Oral birth control, used to prevent pregnancy
- Probenecid, used to prevent gout
- Alcohol

Your healthcare professional may prescribe low dose ASA (acetylsalicylic acid) as a blood thinner to reduce your risk of having a heart attack or stroke while you are taking PEDIAPHARM NAPROXEN SUSPENSION. Take only the amount of ASA prescribed by your healthcare professional. You are more likely to upset or damage your stomach if you take both PEDIAPHARM NAPROXEN SUSPENSION and ASA than if you took PEDIAPHARM NAPROXEN SUSPENSION alone.

How to take PEDIAPHARM NAPROXEN SUSPENSION:

- PEDIAPHARM NAPROXEN SUSPENSION is intended for use in patients older than 2 years of age for the shortest possible duration. **Do NOT use in patients under 2 years of age since safety and effectiveness have NOT been established.**
- Take PEDIAPHARM NAPROXEN SUSPENSION only as directed by your healthcare professional. **Do NOT take more of it, do NOT take it more often and do NOT take it for a longer period of time than your healthcare professional recommended. If possible, you should take the lowest dose of this medication for the shortest time period.** Taking too much PEDIAPHARM NAPROXEN SUSPENSION may increase your chances of unwanted and sometimes dangerous side effects, especially if you are elderly, have other diseases or take other medications.
- If you will be using PEDIAPHARM NAPROXEN SUSPENSION for more than 7 days, see your healthcare professional regularly to discuss whether this medicine is working for you and if it is causing you any unwanted effects.
- **This medication has been prescribed specifically for you. Do NOT give it to anyone else. It may harm them, even if their symptoms seem to be similar to yours.**

Usual dose:

18 years or older:

Indication	Starting Dose	Dose Frequency
Osteoarthritis/ Rheumatoid Arthritis/ Ankylosing Spondylitis	10 mL	Twice a day

Indication	Starting Dose	Dose Frequency
Pain relief for minor aches and pains in muscles, bones and joints/Relief of pain and inflammation in sprains and strains	15 mL	Twice a day
	OR	
	10 mL	Three times a day
Painful menstruation	First dose only: 20 mL Following dose(s): 10 mL	Once Every 6-8 hours, as needed
	OR	
	20 mL	Twice a day

Do not increase the starting dose unless directed by your healthcare professional.

Juvenile Rheumatoid Arthritis (2-16 years):

The recommended total daily dose in children aged 2 and up is approximately 5 mg/kg, every 12 hours. See the following dosing guide:

Child's weight	Dose (25 mg per mL)	Dose Frequency
13 kg (29 lbs.)	2.6 mL	Twice a day (12 hours apart)
15 kg (33 lbs.)	3 mL	
20 kg (44 lbs.)	4 mL	
25 kg (55 lbs.)	5 mL	
30 kg (66 lbs.)	6 mL	
40 kg (88 lbs.)	8 mL	
50 kg (110 lbs.)	10 mL	

Overdose:

If you think you, or a person you are caring for, have taken too much PEDIAPHARM NAPROXEN SUSPENSION, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Missed dose:

- If you miss a dose of PEDIAPHARM NAPROXEN SUSPENSION take it as soon as possible. Take your next dose at the usual time.
- If it is close to the time of your next dose, skip the missed dose. Take your next dose at the usual time.
- Do not take two doses at the same time to make up for a forgotten dose.

Possible side effects from using PEDIAPHARM NAPROXEN SUSPENSION:

These are not all the possible side effects you may have when taking PEDIAPHARM NAPROXEN SUSPENSION. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

- nausea, vomiting, diarrhea, constipation, stomach upset/abdominal pain, heartburn, indigestion, feeling gassy
- headache, dizziness, light-headedness
- feeling of burning/prickliness/numbing
- confusion, hard to concentrate or think, short-term memory loss, nervousness
- bruises
- skin rash
- taste disorder, thirst, dry mouth
- muscle pain
- mouth sores
- hair loss
- increased sweating
- problems with your period (women)

Serious side effects and what to do about them

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
Common			
Gastrointestinal (GI) problems (bleeding, blockage, holes, ulcers or inflammation in your GI tract): blood in vomit, black tarry stool or bloody stool, dizziness, stomach pain, bloating, loss of appetite, weight loss, nausea, vomiting, constipation or diarrhea, chills or fever			✓
Hypertension (high blood pressure): fatigue, dizziness or fainting, chest pain		✓	
Uncommon			
Allergic reaction: difficulty swallowing or breathing, feeling sick to your stomach and throwing up, skin rash, hives, itching, swelling of the face, lips, tongue or throat			✓
Aseptic meningitis (inflammation of the protective lining of the brain that is not caused by infection): headaches, stiff neck, nausea, vomiting, fever or clouding of consciousness		✓	

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
Blood problems (low white and/or red blood cell or platelet count): feeling tired or weak, pale skin, bruising or bleeding for longer than usual if you hurt yourself, fever, chills		✓	
Congestive heart failure (heart does not pump blood as well as it should): shortness of breath, fatigue, weakness, swelling of the ankles, legs and feet, cough, fluid retention, lack of appetite, nausea, rapid or irregular heartbeat, reduced ability to exercise		✓	
Cystitis (bladder infection): increased need to urinate, pain in the pelvis or lower back, frequent urination during the night, cloudy urine that may contain blood, burning or pain urinating		✓	
Depression (sad mood that will not go away): difficulty sleeping or sleeping too much, changes in appetite or weight, reduced sex drive and thoughts of death or suicide		✓	
Kidney disorder/problems (including kidney failure): nausea, vomiting, fever, swelling of extremities, fatigue, thirst, dry skin, irritability, dark urine, increased or decreased urine output, blood in the urine, rash, weight gain (from retaining fluid), loss of appetite, mental status changes (drowsiness, confusion, coma)			✓
Liver problems (including hepatitis, liver failure, cholestasis): yellowing of your skin or eyes (jaundice), right upper stomach area pain or swelling, nausea or vomiting, unusual dark urine, unusual tiredness		✓	
Lung problems, asthma: increased shortness of breath, wheezing, difficulty breathing, cough or chest tightness, irregular heartbeat			✓

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
Myocardial infarction (heart attack): pressure or squeezing pain between the shoulder blades, in the chest, jaw, left arm or upper abdomen, shortness of breath, dizziness, fatigue, light-headedness, clammy skin, sweating, indigestion, anxiety, feeling faint and possible irregular heartbeat			✓
Stroke (bleeding or blood clot in the brain): sudden numbness, weakness or tingling of the face, arm, or leg, particularly on one side of the body, sudden headache, blurry vision, difficulty swallowing or speaking, lethargy, dizziness, fainting, vomiting, trouble understanding, trouble with walking and loss of balance			✓
Tinnitus (hearing problems): includes ringing, buzzing, clicking or hissing in ears, loss of hearing		✓	
Vertigo (a sense of severe spinning dizziness, light-headedness)		✓	
Rare			
Serious skin reactions: fever, severe rash, swollen lymph glands, flu-like feeling, blisters and peeling skin that may start in and around the mouth, nose, eyes and genitals and spread to other areas of the body, swelling of face and/or legs, yellow skin or eyes, shortness of breath, dry cough, chest pain or discomfort, feeling thirsty, urinating less often, less urine or dark urine, hives, red or dry itchy skin, purple or red spots on skin			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting side effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store at room temperature not exceeding 25°C. Protect from light. Store upright.

Do NOT keep outdated medicine or medicine no longer needed. Any outdated or unused medicine should be returned to your pharmacist.

Keep out of reach and sight of children.

If you want more information about PEDIAPHARM NAPROXEN SUSPENSION:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes the Patient Medication Information by visiting the Health Canada Drug Product Database website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website http://www.medexus.com; or by calling 1-877-633-3987.

This leaflet was prepared by Medexus Pharmaceuticals Inc.

Date of Authorization: 2025-10-27