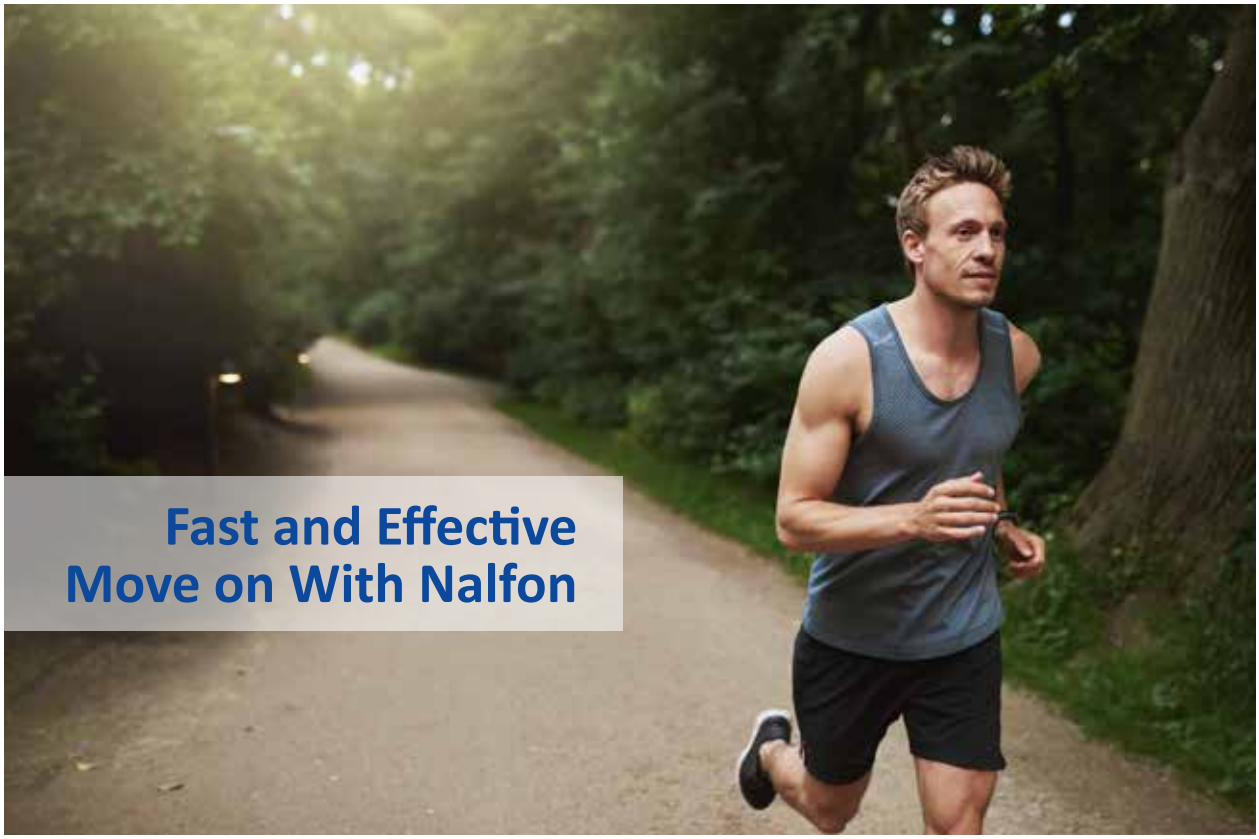
NALFON®
(fenoprofen calcium)

400mg Capsules

600mg Tablets

PROVIDES A BALANCED NSAID OPTION



Cardiovascular Thrombotic Events

- Nonsteroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use (see WARNINGS and PRECAUTIONS).
- Nalfon capsules and tablets are contraindicated in the setting of coronary artery bypass graft (CABG) surgery (see CONTRAINDICATIONS and WARNINGS).

Gastrointestinal Risk

- NSAIDs cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration and perforation of stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events (see WARNINGS).

Xspire Pharma

WraSer™ PHARMACEUTICALS

NALFON provides an NSAID with a predictable patient prescription Co-pay

- Exceptional prescription drug formulary access nationwide without patient restrictions.
- Predictable Co-pays with WraSer Direct™. • Eligible patients to PAY AS LITTLE AS $0.
- Instant Co-pay coupon available with no activation required.

$0 Co-Pay on Insured Covered Claims*

NALFON®
(fenoprofen calcium)
600mg Tablets

BIN# **017290** Group# **X6879**

PCN# **55101202** ID# **100100101**

Commercially covered on Express Scripts, Optum, United Healthcare, Anthem, Cigna and more.

**As long as coupon maximums are not exceeded.*

Xspire Pharma WraSer™ PHARMACEUTICALS

NALFON®
(fenoprofen calcium)

400mg Capsules

600mg Tablets

PROVIDES A BALANCED NSAID OPTION

Selectivity for Cyclooxygenase (COX) Enzymes of Various NSAIDs

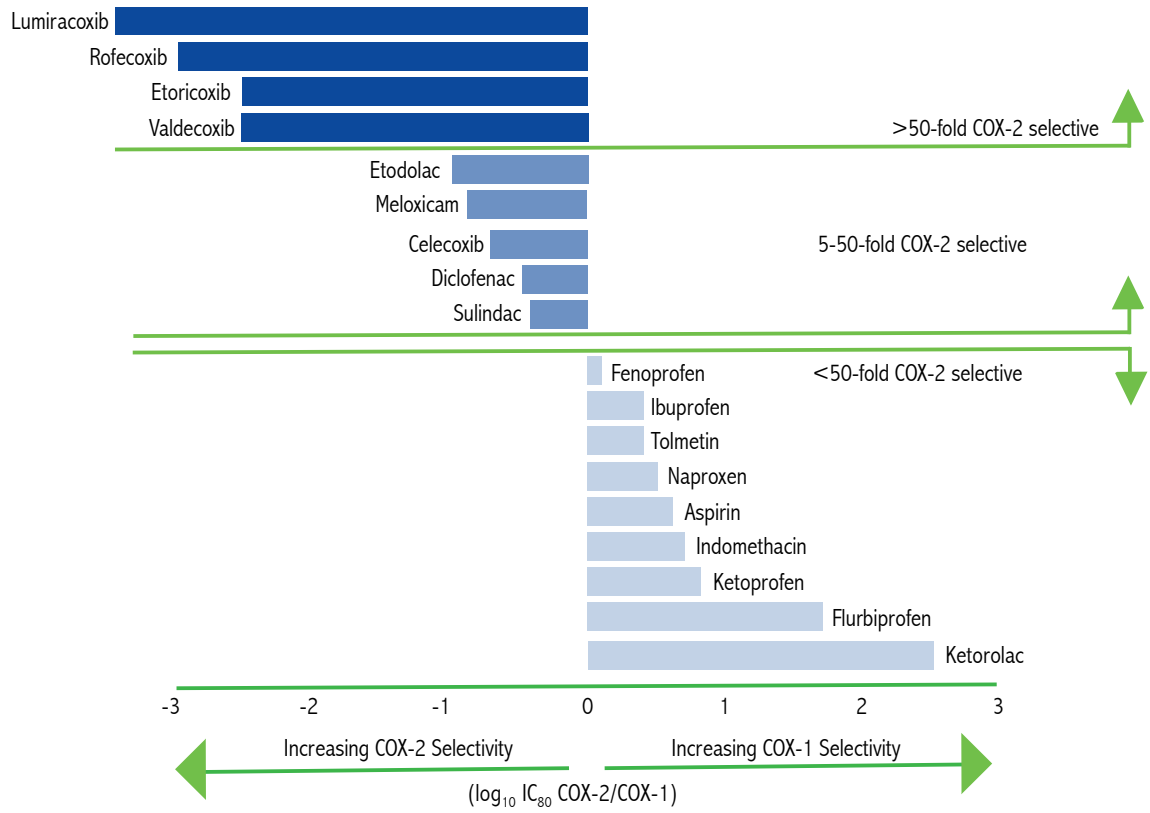


Figure 2. In vitro selectivity for cyclooxygenase (COX) enzymes of various nonsteroidal antiinflammatory drugs. $1C_{80}$ = drug concentration that inhibits 80% of the COX enzyme. (Adapted from reference below).

NALFON safety data includes over 40 years of clinician use with a single ingredient

- Over 6,700 patients participated in clinical studies of NALFON; 188 were observed for 1 year. Based on clinical trials, LESS THAN 2% of patients discontinued use of NALFON due to gastro-intestinal adverse events (AEs).
- NALFON has less suppression of collage-induced platelet aggregation with single doses of NALFON than there is with Aspirin.

NALFON®
(fenoprofen calcium)

400mg Capsules

600mg Tablets

PROVIDES A BALANCED NSAID OPTION

NALFON provides fast and effective pain relief

- NALFON begins to relieve pain and reduce inflammation in as little as 15 to 30 minutes and for a minimum of 8 hours.
- NALFON is 99% bound to blood proteins for greater Cox-2 inhibition.
- In patients with osteoarthritis, NALFON reduces tenderness as a response to pressure and reductions in night pain, stiffness, swelling, and overall disease activity. NALFON relieves pain with motion and at rest, and increases range of motion in involved joints.
- NALFON is available in two strengths to meet individual patient needs:

NALFON 400 mg Capsules

NALFON 600 mg Tablets

Recommended Dosing

Carefully consider the potential benefits and risks of Nalfon and other treatment options before deciding to use Nalfon. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.

NALFON is indicated:

- For relief of mild to moderate pain in adults.
- For relief of the signs and symptoms of rheumatoid arthritis.
- For relief of the signs and symptoms of osteoarthritis.

After observing the response to initial therapy with Nalfon, the dose and frequency should be adjusted to suit an individual patient's needs.

- The dose should be tailored to the needs of the patient and may be increased or decreased depending on the severity of the symptoms.
- Total daily dosage should not exceed 3,200 mg.
- Nalfon may be administered with meals and/or milk to reduce the potential for stomach upset.
- The smallest dose that yields acceptable control should be employed.

NALFON® Capsules

200mg/400mg and 600mg

Rx Only

Cardiovascular Risk

• Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk (see **WARNINGS).**

• Nalfon® is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery (see **WARNINGS).**

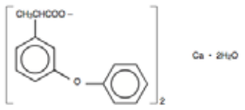
Gastrointestinal Risk

• NSAIDs cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events (see WARNINGS).

DESCRIPTION

Nalfon capsules, USP is a nonsteroidal, anti-inflammatory, antiarthritic drug. Nalfon capsules contain Nalfon as the dihydrate in an amount equivalent to 200 mg (0.826 mmol) or 400 mg (1.65 mmol) of fenoprofen. The 200 mg capsules contain cellulose, gelatin, iron oxides, silicone, titanium dioxide and other inactive ingredients. The 400 mg capsules contain crospovidone, FD&C Blue 1, FD&C Red 40, gelatin, iron oxide yellow, magnesium stearate, sodium lauryl sulfate, talc, and titanium dioxide. Chemically, Nalfon is an arylacetic acid derivative. The 600 mg USP is a white crystalline powder, soluble in alcohol (95%) to the extent of approximately 15 mg/mL at 25°C, slightly soluble in water and insoluble in benzene. The pKa of fenoprofen calcium is 4.5 at 25°C. Film-coated fenoprofen calcium tablets for oral administration are available containing fenoprofen calcium as the dihydrate equivalent to 600 mg of fenoprofen and the following inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80, pregelatinized starch, sodium lauryl sulfate, titanium dioxide and FD&C Yellow No. 6 Aluminum Lake.

The structural formula is as follows:



Nalfon is a white crystalline powder that has the structural formula C30H-26CaO6•2H2O representing a molecular weight of 558.65. At 25°C, it dissolves to a 15 mg/mL solution in alcohol (95%). It is slightly soluble in water and insoluble in benzene.
The pKa of Nalfon is a 4.5 at 25°C.

CLINICAL PHARMACOLOGY

Nalfon is a nonsteroidal, anti-inflammatory, antiarthritic drug that also possesses analgesic and antipyretic activities. Its exact mode of action is unknown, but it is thought that prostaglandin synthetase inhibition is involved.

Results in humans demonstrate that fenoprofen has both anti-inflammatory and analgesic actions. The emergence and degree of erythemic response were measured in adult male volunteers exposed to ultraviolet irradiation. The effects of Nalfon, aspirin, and indomethacin were each compared with those of a placebo. All 3 drugs demonstrated antierythemic activity.

In all patients with rheumatoid arthritis, the anti-inflammatory action of Nalfon has been evidenced by relief of pain, increase in grip strength, and reductions in joint swelling, duration of morning stiffness, and disease activity (as assessed by both the investigator and the patient). The anti-inflammatory action of Nalfon has also been evidenced by increased mobility (i.e., a decrease in the number of joints having limited motion).

The use of Nalfon in combination with gold salts or corticosteroids has been studied in patients with rheumatoid arthritis. The studies, however, were inadequate in demonstrating whether further improvement is obtained by adding Nalfon to maintenance therapy with gold salts or steroids. Whether or not Nalfon used in conjunction with partially effective doses of a corticosteroid has a “steroid-sparing” effect is unknown.

In patients with osteoarthritis, the anti-inflammatory and analgesic effects of Nalfon have been demonstrated by reduction in tenderness as a response to pressure and reductions in night pain, stiffness, swelling, and overall disease activity (as assessed by both the patient and the investigator). These effects have also been demonstrated by relief of pain with motion and at rest and increased range of motion in involved joints.

In patients with rheumatoid arthritis and osteoarthritis, clinical studies have shown Nalfon to be comparable to aspirin in controlling the aforementioned measures of disease activity, but mild gastrointestinal reactions (nausea, dyspepsia) and tinnitus occurred less frequently in patients treated with Nalfon than in aspirin-treated patients. It is not known whether Nalfon causes less peptic ulceration than does aspirin.

In patients with pain, the analgesic action of Nalfon has produced a reduction in pain intensity, an increase in pain relief, improvement in total analgesia scores, and a sustained analgesic effect.

Under fasting conditions, Nalfon is rapidly absorbed, and peak plasma levels of 50 µg/mL are achieved within 2 hours after oral administration of 600 mg doses. Good dose proportionality was observed between 200 mg and 600 mg doses in fasting male volunteers. The plasma half-life is approximately 3 hours. About 90% of a single oral dose is eliminated within 24 hours as fenoprofen glucuronide and 4’-hydroxyfenoprofen glucuronide, the major urinary metabolites of fenoprofen. Fenoprofen is highly bound (99%) to albumin.

The concomitant administration of antacid (containing both aluminum and magnesium hydroxide) does not interfere with absorption of Nalfon.
There is less suppression of collagen-induced platelet aggregation with single doses of Nalfon than there is with aspirin.

INDICATIONS AND USAGE

Carefully consider the potential benefits and risks of Nalfon and other treatment options before deciding to use Nalfon. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals (see **WARNINGS).**

Nalfon is indicated:

- For relief of mild to moderate pain in adults.
- For relief of the signs and symptoms of rheumatoid arthritis.
- For relief of the signs and symptoms of osteoarthritis.

CONTRAINDICATIONS

Nalfon is contraindicated in patients who have shown hypersensitivity to Nalfon.

Nalfon should not be given to patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylactic-like reactions to NSAIDs have been reported in such patients (see **WARNINGS – Anaphylactoid Reactions, and PRECAUTIONS – Preexisting Asthma).**

Nalfon is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery (see WARNINGS).

Nalfon is contraindicated in patients with a history of significantly impaired renal function (see WARNINGS – Advanced Renal Disease).

WARNINGS

CARDIOVASCULAR EFFECTS

Cardiovascular Thrombotic Events

Clinical trials of several COX-2 selective and nonselective NSAIDs of up to three years duration have shown an increased risk of serious cardiovascular (CV) thrombotic events, myocardial infarction, and stroke, which can be fatal. All NSAIDs, both COX-2 selective and nonselective, may give a similar risk. Patients with known CV disease or risk factors for CV disease may be at greater risk. To minimize the potential risk for an adverse CV event in patients treated with an NSAID, the lowest effective dose should be used for the shortest duration possible. Physicians and patients should remain alert for the development of such events, even in the absence of previous CV symptoms. Patients should be informed about the signs and/or symptoms of serious CV events and the steps to take if they occur.

There is no consistent evidence that concurrent use of aspirin mitigates the increased risk of serious CV thrombotic events associated with NSAID use. The concurrent use of aspirin and an NSAID does increase the risk of serious GI events (see **WARNINGS - Gastrointestinal Effects).**

Two large, controlled, clinical trials of a COX-2 selective NSAID for the treatment of pain in the first 10-14 days following CABG surgery found an increased incidence of myocardial infarction and stroke (see CONTRAINDICATIONS).

Hypertension

NSAIDs, including Nalfon, can lead to onset of new hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of CV events. Patients taking thiazides or loop diuretics may have impaired response to these therapies when taking NSAIDs. NSAIDs, including Nalfon, should be used with caution in patients with hypertension. Blood pressure should be monitored closely during the initiation of NSAID treatment and throughout the course of therapy.

Congestive Heart Failure and Edema

Fluid retention and edema have been observed in some patients taking NSAIDs. Nalfon should be used with caution in patients with fluid retention, compromised cardiac function or heart failure. The possibility of renal involvement should be considered.

Gastrointestinal Effects – Risk of Ulceration, Bleeding, and Perforation

NSAIDs, including Nalfon, can cause serious gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the stomach, small intestine, or large intestine, which can be fatal. These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with NSAIDs. Only one in five patients, who develop a serious upper GI adverse event on NSAID therapy, is symptomatic. Upper GI ulcers, gross bleeding, or perforation caused by NSAIDs 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 with longer duration of use, increasing the likelihood of developing a serious GI event at some time during the course of therapy. However, even short-term therapy is not without risk.

NSAIDs should be prescribed with extreme caution in those with a prior history of ulcer disease or gastrointestinal bleeding. Patients with a prior history of peptic ulcer disease and/or gastrointestinal bleeding who use NSAIDs have a greater than 10-fold increased risk for developing a GI bleed compared to patients with neither of these risk factors. Other factors that increase the risk for GI bleeding in patients treated with NSAIDs include concomitant use of oral corticosteroids or anticoagulants, longer duration of NSAID therapy, smoking, use of alcohol, older age, and poor general health status. 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 in patients treated with an NSAID, the lowest effective dose should be used for the shortest possible duration. Patients and physicians should remain alert for signs and symptoms of GI ulceration and bleeding during NSAID therapy and promptly initiate additional evaluation and treatment if a serious GI adverse event is suspected. This should include discontinuation of the NSAID until a serious GI adverse event is ruled out. For high risk patients, alternate therapies that do not involve NSAIDs should be considered.

Renal Effects

Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of a nonsteroidal anti-inflammatory drug may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decomposition. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors, and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pretreatment state.

Advanced Renal Disease

No information is available from controlled clinical studies regarding the use of Nalfon in patients with advanced renal disease. Therefore, treatment with Nalfon is not recommended in patients with advanced renal disease. (see **CONTRAINDICATIONS).**

Anaphylactoid Reactions

As with other NSAIDs, anaphylactoid reactions may occur in patients without known prior exposure to Nalfon. Nalfon should not be given to patients with the aspirin 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 aspirin or other NSAIDs (see CONTRAINDICATIONS and PRECAUTIONS - Preexisting Asthma). Emergency help should be sought in cases where an anaphylactoid reaction occurs.

Skin Reactions

NSAIDs, including Nalfon, can cause serious skin adverse events such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. These serious events may occur without warning. Patients should be informed about the signs and symptoms of serious skin manifestations and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

Pregnancy

Starting at 30-weeks gestation, Nalfon and other NSAIDs should be avoided by pregnant women as premature closure of the ductus arteriosus in the fetus may occur.

Ocular

Studies to date have not shown changes in the eyes attributable to the administration of Nalfon. However, adverse ocular effects have been observed with other anti-inflammatory drugs. Eye examinations, therefore, should be performed if visual disturbances occur in patients taking Nalfon.

Central Nervous System (CNS)

Caution should be exercised by patients whose activities require alertness if they experience CNS side effects while taking Nalfon.

Hearing

Since the safety of Nalfon has not been established in patients with impaired hearing, these patients should have periodic tests of auditory function during prolonged therapy with Nalfon.

PRECAUTIONS

General

Nalfon cannot be expected to substitute for corticosteroids or to treat corticosteroid insufficiency. Abrupt discontinuation of corticosteroids may lead to disease exacerbation. Patients on prolonged corticosteroid therapy should have their therapy tapered slowly if a decision is made to discontinue corticosteroids.

The pharmacological activity of Nalfon in reducing inflammation may diminish the utility of these diagnostic signs in detecting complications of presumed noninfectious, painful conditions.

Hepatic Effects

Borderline elevations of one or more liver tests may occur in up to 15% of patients taking NSAIDs including Nalfon. These laboratory abnormalities may progress, may remain unchanged, or may be transient with continuing therapy. Notable elevations of ALT or AST (approximately three or more times the upper limit of normal) have been reported in approximately 1% of patients in clinical trials with NSAIDs. In addition, rare cases of severe hepatic reactions, including jaundice and fatal fulminant hepatitis, liver necrosis and hepatic failure, some of them with fatal outcomes, have been reported.

A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of a more severe hepatic reaction while on therapy with Nalfon. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur, (e.g., eosinophilia, rash, etc.), Nalfon should be discontinued.

Hematological Effects

Anemia is sometimes seen in patients receiving NSAIDs, including Nalfon. This may be due to fluid retention, occult or gross GI blood loss, or an incompletely described effect upon erythropoiesis. Patients on long-term treatment with NSAIDs, including Nalfon, should have their hemoglobin or hematocrit checked if they exhibit any signs or symptoms of anemia. NSAIDs inhibit platelet aggregation and have been shown to prolong bleeding time in some patients. Unlike aspirin, their effect on platelet function is quantitatively less, of shorter duration, and reversible. Patients receiving Nalfon who may be adversely affected by alterations in platelet function, such as those with coagulation disorders or patients receiving anticoagulants, should be carefully monitored.

Preexisting Asthma

Patients with asthma may have aspirin-sensitive asthma. The use of aspirin in patients with aspirin-sensitive asthma has been associated with severe bronchospasm which can be fatal. Since cross reactivity, including bronchospasm, between aspirin and other nonsteroidal anti-inflammatory drugs has been reported in such aspirin-sensitive patients, Nalfon should not be administered to patients with this form of aspirin sensitivity and should be used with caution in patients with preexisting asthma.

Information for Patients

Patients should be informed of the following information before initiating therapy with an NSAID and periodically during the course of ongoing therapy. Patients should also be encouraged to read the NSAID Medication Guide that accompanies each prescription dispensed.

1. Nalfon, like other NSAIDs, may cause serious CV side effects, such as myocardial infarction (MI) or stroke, which may result in hospitalization and even death. Although serious CV events can occur without warning symptoms, patients should be alert for the signs and symptoms of chest pain, shortness of breath, weakness, slurring of speech, and should ask for medical advice when observing any indicative sign or symptoms. Patients should be apprised of the importance of this follow-up (see **WARNINGS - Cardiovascular Effects).**
2. Nalfon, like other NSAIDs, can cause GI discomfort and, rarely, serious GI side effects, such as ulcers and bleeding, which may result in hospitalization and even death. Although serious GI tract ulcerations and bleeding can occur without warning symptoms, patients should be alert for the signs and symptoms of ulcerations and bleeding, and should ask for medical advice when observing any indicative signs or symptoms including epigastric pain, dyspepsia, melena, and hematemesis. Patients should be apprised of the importance of this follow-up (see **WARNINGS - Gastrointestinal Effects – Risk of Ulceration, Bleeding, and Perforation).**
3. Nalfon, like other NSAIDs, can cause serious skin side effects such as exfoliative dermatitis, SJS, and TEN, which may result in hospitalization and even death. Although serious skin reactions may occur without warning, patients should be alert for the signs and symptoms of skin rash and blisters, fever, or other signs of hypersensitivity such as itching, and should ask for medical advice when observing any indicative signs or symptoms. Patients should be advised to stop the drug immediately if they develop any type of rash and contact their physicians as soon as possible.
4. Patients should promptly report signs or symptoms of unexplained weight gain or edema to their physicians.
5. Patients should be informed of the warning signs and symptoms of hepatotoxicity (e.g., nausea, fatigue, lethargy, pruritus, jaundice, right upper quadrant tenderness, and “flu-like” symptoms). If these occur, patients should be instructed to stop therapy and seek immediate medical therapy.
6. Patients should be informed of the signs of an anaphylactoid reaction (e.g. difficulty breathing, swelling of the face or throat). If these occur, patients should be instructed to seek immediate emergency help (see **WARNINGS).**
7. Starting at 30-weeks gestation, Nalfon and other NSAIDs should be avoided by pregnant women as premature closure of the ductus arteriosus in the fetus may occur.

Laboratory Tests

Because serious GI tract ulcerations and bleeding can occur without warning symptoms, physicians should monitor for signs or symptoms of GI bleeding. Patients on long-term treatment with NSAIDs should have their CBC and a chemistry profile checked periodically. If clinical signs and symptoms consistent with liver or renal disease develop, systemic manifestations occur (e.g., eosinophilia, rash, etc.) or abnormal liver tests persist or worsen, Nalfon should be discontinued.

Drug Interactions

ACE-inhibitors

Reports suggest that NSAIDs may diminish the antihypertensive effect of ACE-inhibitors. This interaction should be given consideration in patients taking NSAIDs concomitantly with ACE-inhibitors.

Aspirin

The coadministration of aspirin decreases the biologic half-life of fenoprofen because of an increase in metabolic clearance that results in a greater amount of hydroxylated fenoprofen in the urine. Although the mechanism of interaction between fenoprofen and aspirin is not totally known, enzyme induction and displacement of fenoprofen from plasma albumin binding sites are possibilities. As with other NSAIDs, concomitant administration of Nalfon and aspirin is not generally recommended because of the potential of increased adverse effects.

Diuretics

Clinical studies, as well as postmarketing observations, have shown that Nalfon can reduce the natriuretic effect of furosemide and thiazides in some patients. This response has been attributed to inhibition of renal prostaglandin synthesis. During concomitant therapy with NSAIDs, the patient should be observed closely for signs of renal failure (see WARNINGS - Renal Effects), as well as to assure diuretic efficacy.

Lithium

NSAIDs have produced an elevation of plasma lithium levels and a reduction in

renal lithium clearance. The mean minimum lithium concentration increased 15% and the renal clearance was decreased by approximately 20%. These effects have been attributed to inhibition of renal prostaglandin synthesis by the NSAID. Thus, when NSAIDs and lithium are administered concurrently, subjects should be observed carefully for signs of lithium toxicity.

Methotrexate
NSAIDs have been reported to competitively inhibit methotrexate accumulation in rabbit kidney slices. This may indicate that they could enhance the toxicity of methotrexate. Caution should be used when NSAIDs are administered concomitantly with methotrexate.

Warfarin
The effects of warfarin and NSAIDs on GI bleeding are synergistic, such that users of both drugs together have a risk of serious GI bleeding higher than users of either drug alone.

Phenobarbital
Chronic administration of phenobarbital, a known enzyme inducer, may be associated with a decrease in the plasma half-life of fenoprofen. When phenobarbital is added to or withdrawn from treatment, dosage adjustment of Nalfon may be required.

Plasma Protein Binding
In vitro studies have shown that fenoprofen, because of its affinity for albumin, may displace from their binding sites other drugs that are also albumin bound, and this may lead to drug interactions. Theoretically, fenoprofen could likewise be displaced. Patients receiving hydantoins, sulfonamides, or sulfonylureas should be observed for increased activity of these drugs and, therefore, signs of toxicity from these drugs.

Drug/Laboratory Test Interactions
Amerlex-M kit assay values of total and free triiodothyronine in patients receiving Nalfon have been reported as falsely elevated on the basis of a chemical cross-reaction that directly interferes with the assay. Thyroid-stimulating hormone, total thyroxine, and thyrotropin-releasing hormone response are not affected.

Carcinogenesis, Mutagenesis, and Impairment of Fertility
Long-term studies in animals have not been conducted to evaluate the carcinogenic potential of fenoprofen. Studies have not been conducted to determine the effect of fenoprofen on mutagenicity or fertility.

Pregnancy

Teratogenic Effects. Pregnancy Category C Prior to 30-Weeks Gestation; Category D starting at 30-Weeks Gestation.
Starting at 30-weeks gestation, Nalfon and other NSAIDs should be avoided by pregnant women as premature closure of the ductus arteriosus in the fetus may occur. Nalfon can cause fetal harm when administered to a pregnant woman starting at 30-weeks gestation. If this drug is used during this time period in pregnancy, the patient should be apprised of the potential hazard to a fetus. There are no adequate and well-controlled studies in pregnant women. Prior to 30-weeks gestation, Nalfon should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Reproductive studies conducted in rats and rabbits have not demonstrated evidence of developmental abnormalities when given daily oral doses of 50 or 100 mg/kg Nalfon, respectively (0.15 and 0.6 times the maximum human daily dose of 3200 mg based on body surface area comparisons). However, animal reproduction studies are not always predictive of human response.

Nonteratogenic Effects
Because of the known effects of nonsteroidal anti-inflammatory drugs on the fetal cardiovascular system (closure of ductus arteriosus), use during pregnancy (particularly late pregnancy) should be avoided.

Labor and Delivery
The effects of Nalfon on labor and delivery in pregnant women are unknown. In rat studies, maternal exposure to NSAIDs, as with other drugs known to inhibit prostaglandin synthesis, increased the incidence of dystocia, delayed parturition, and decreased pup survival.

Nursing Mothers
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Nalfon, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use
Safety and effectiveness in pediatric patients under the age of 18 have not been established.

Geriatric Use
As with any NSAIDs, caution should be exercised in treating the elderly (65 years and older).

ADVERSE REACTIONS

During clinical studies for rheumatoid arthritis, osteoarthritis, or mild to moderate pain and studies of pharmacokinetics, complaints were compiled from a checklist of potential adverse reactions, and the following data emerged. These encompass observations in 6,786 patients, including 188 observed for at least 52 weeks.
For comparison, data are also presented from complaints received from the 266 patients who received placebo in these same trials. During short-term studies for analgesia, the incidence of adverse reactions was markedly lower than that seen in longer-term studies.

Adverse Drug Reactions Reported in ≥1% of Patients During Clinical Trials

Digestive System—During clinical trials with Nalfon, the most common adverse reactions were gastrointestinal in nature and occurred in 20.8% of patients receiving Nalfon as compared to 16.9% of patients receiving placebo. In descending order of frequency, these reactions included dyspepsia (10.3% Nalfon vs. 2.3% placebo), nausea (7.7% vs. 7.1%), constipation (7% vs. 1.5%), vomiting (2.6% vs. 1.9%), abdominal pain (2% vs. 1.1%), and diarrhea (1.8% vs. 4.1%). The drug was discontinued because of adverse gastrointestinal reactions in less than 2% of patients during premarketing studies.

Nervous System—The most frequent adverse neurologic reactions were headache (8.7% vs. 7.5%) and somnolence (8.5% vs. 6.4%). Dizziness (6.5% vs. 5.6%), tremor (2.2% vs. 0.4%), and confusion (1.4% vs. none) were noted less frequently. Nalfon was discontinued in less than 0.5% of patients because of these side effects during premarketing studies.

Skin and Appendages—Increased sweating (4.6% vs. 0.4%), pruritus (4.2% vs. 0.8%), and rash (3.7% vs. 0.4%) were reported. Nalfon was discontinued in about 1% of patients because of an adverse effect related to the skin during premarketing studies.

Special Senses—Tinnitus (4.5% vs. 0.4%), blurred vision (2.2% vs. none), and decreased hearing (1.6% vs. none) were reported. Nalfon was discontinued in less than 0.5% of patients because of adverse effects related to the special senses during premarketing studies.

Cardiovascular—Palpitations (2.5% vs. 0.4%). Nalfon was discontinued in about 0.5% of patients because of adverse cardiovascular reactions during premarketing studies.

Miscellaneous—Nervousness (5.7% vs. 1.5%), asthenia (5.4% vs. 0.4%), peripheral edema (5.0% vs. 0.4%), dyspnea (2.8% vs. none), fatigue (1.7% vs. 1.5%), upper respiratory infection (1.5% vs. 5.6%), and nasopharyngitis (1.2% vs. none).

Adverse Drug Reactions Reported in <1% of Patients During Clinical Trials

Digestive System—Gastritis, peptic ulcer with/without perforation, gastro- intestinal hemorrhage, anorexia, flatulence, dry mouth, blood in the stool. Increases in alkaline phosphatase, LDH, SGOT, jaundice, cholestatic hepatitis, aphthous ulcerations of the buccal mucosa, metallic taste, and pancreatitis (see PRECAUTIONS).

Cardiovascular—Atrial fibrillation, pulmonary edema, electrocardiographic changes, and supraventricular tachycardia.

Genitourinary Tract—Renal failure, dysuria, cystitis, hematuria, oliguria, azotemia, anuria, interstitial nephritis, nephrosis, and papillary necrosis (see WARNINGS).

Hypersensitivity—Angioedema (angioneurotic edema).

Hematologic—Purpura, bruising, hemorrhage, thrombocytopenia, hemolytic anemia, aplastic anemia, agranulocytosis, and pancytopenia.

Nervous System—Depression, disorientation, seizures, and trigeminal neuralgia.

Special Senses—Burning tongue, diplopia, and optic neuritis.

Skin and Appendages—Exfoliative dermatitis, toxic epidermal necrolysis, Stevens-Johnson syndrome, and alopecia.

Miscellaneous—Anaphylaxis, urticaria, malaise, insomnia, tachycardia, personality change, lymphadenopathy, mastodynia, and fever.

OVERDOSAGE

Signs and Symptoms—Symptoms of overdose appear within several hours and generally involve the gastrointestinal and central nervous systems. They include dyspepsia, nausea, vomiting, abdominal pain, dizziness, headache, ataxia, tinnitus, tremor, drowsiness, and confusion. Hyperpyrexia, tachycardia, hypotension, and acute renal failure may occur rarely following overdose. Respiratory depression and metabolic acidosis have also been reported following overdose with certain NSAIDs.

Treatment—To obtain up-to-date information about the treatment of overdose, a good resource is your certified Regional Poison Control Center. Telephone numbers of certified poison control centers are listed in the Physicians' Desk Reference (PDR). In managing overdosage, consider the possibility of multiple drug overdoses, interaction among drugs, and unusual drug kinetics in your patient.

Protect the patient's airway and support ventilation and perfusion. Meticulously monitor and maintain, within acceptable limits, the patient's vital signs, blood gases, serum electrolytes, etc. Absorption of drugs from the gastrointestinal tract may be decreased by giving activated charcoal, which, in many cases, is more effective than lavage; consider charcoal instead of or in addition to gastric emptying. Repeated doses of charcoal over time may hasten elimination of some drugs that have been absorbed. Safeguard the patient's airway when employing gastric emptying or charcoal.

Alkalinization of the urine, forced diuresis, peritoneal dialysis, hemodialysis, and charcoal hemoperfusion do not enhance systemic drug elimination.

DOSAGE AND ADMINISTRATION

Carefully consider the potential benefits and risks of Nalfon and other treatment options before deciding to use Nalfon. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals (see WARNINGS).

After observing the response to initial therapy with Nalfon, the dose and frequency should be adjusted to suit an individual patient's needs.
Analgesia
For the treatment of mild to moderate pain, the recommended dosage is 200 mg given orally every 4 to 6 hours, as needed.

Rheumatoid Arthritis and Osteoarthritis
For the relief of signs and symptoms of rheumatoid arthritis or osteoarthritis the recommended dose is 400 to 600 mg given orally, 3 or 4 times a day. The dose should be tailored to the needs of the patient and may be increased or decreased depending on the severity of the symptoms. Dosage adjustments may be made after initiation of drug therapy or during exacerbations of the disease. Total daily dosage should not exceed 3,200 mg.

Nalfon may be administered with meals or with milk. Although the total amount absorbed is not affected, peak blood levels are delayed and diminished.

Patients with rheumatoid arthritis generally seem to require larger doses of Nalfon than do those with osteoarthritis. The smallest dose that yields acceptable control should be employed.

Although improvement may be seen in a few days in many patients, an additional 2 to 3 weeks may be required to gauge the full benefits of therapy.

HOW SUPPLIED

Nalfon (Nalfon capsules, USP) are available in:

The **200 mg*** capsule is opaque yellow No. 97 cap and opaque white body, imprinted with "RX681" on the cap and body.

NDC 15014-0600-10 Bottles of 100

The **400 mg*** capsule is opaque green cap and opaque blue body, imprinted with

"NALFON 400 mg" on the cap and "EP 123" on the body.

NDC 15014-0400-90 Bottles of 90

*** Equivalent to fenoprofen.**

Preserve in well-closed containers.

Store at 20° - 25° C (68° - 77° F). (See USP Controlled Room Temperature).

ATTENTION DISPENSER: Accompanying Medication Guide must be dispensed with this product.

Nalfon capsules
generic name: Nalfon

Medication Guide
For
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)
(See the end of this Medication Guide for a list of prescription NSAID medicines.)

What is the most important information I should know about medicines called Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)?

NSAID medicines may increase the chance of a heart attack or stroke that can lead to death. This chance increases:
- with longer use of NSAID medicines
- in people who have heart disease

NSAID medicines should never be used right before or after a heart surgery called a "coronary artery bypass graft (CABG)."

NSAID medicines can cause ulcers and bleeding in the stomach and intestines at any time during treatment. Ulcers and bleeding:
- can happen without warning symptoms
- may cause death

The chance of a person getting an ulcer or bleeding increases with:
- taking medicines called "corticosteroids" and "anticoagulants"
- longer use
- smoking
- drinking alcohol
- older age
- having poor health

NSAID medicines should only be used:
- exactly as prescribed
- at the lowest dose possible for your treatment
- for the shortest time needed

What are Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)?
NSAID medicines are used to treat pain and redness, swelling, and heat (inflammation) from medical conditions such as:
- different types of arthritis
- menstrual cramps and other types of short-term pain

Who should not take a Non-Steroidal Anti-Inflammatory Drug (NSAID)? Do not take an NSAID medicine:
- if you had an asthma attack, hives, or other allergic reaction with aspirin or any other NSAID medicine
- for pain right before or after heart bypass surgery

Tell your healthcare provider:
- about all of your medical conditions.
- about all of the medicines you take. NSAIDs and some other medicines can interact with each other and cause serious side effects. **Keep a list of your medicines to show to your healthcare provider and pharmacist.**
- if you are pregnant, N**SAID medicines should not be used by pregnant women late in their pregnancy.**
- if you are breastfeeding, **talk to your doctor.**

What are the possible side effects of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)?

Serious side effects include:	**Other side effects include:**
• heart attack	• stomach pain
• stroke	• constipation
• high blood pressure	• diarrhea
• heart failure from body swelling (fluid retention)	• gas
• kidney problems including kidney failure	• heartburn
• bleeding and ulcers in the stomach and intestine	• nausea
• low red blood cells (anemia)	• vomiting
• life-threatening skin reactions	• dizziness
• life-threatening allergic reactions	
• liver problems including liver failure	
• asthma attacks in people who have asthma	

Get emergency help right away if you have any of the following symptoms:
- shortness of breath or trouble breathing
- chest pain
- weakness in one part or side of your body
- slurred speech
- swelling of the face or throat

Stop your NSAID medicine and call your healthcare provider right away if you have any of the following symptoms:
- nausea
- more tired or weaker than usual
- itching
- your skin or eyes look yellow
- stomach pain
- flu-like symptoms
- vomit blood
- there is blood in your bowel movement or it is black and sticky like tar
- unusual weight gain
- skin rash or blisters with fever
- swelling of the arms and legs, hands and feet

These are not all the side effects with NSAID medicines. Talk to your healthcare provider or pharmacist for more information about NSAID medicines.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Other information about Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)
- Aspirin is an NSAID medicine but it does not increase the chance of a heart attack. Aspirin can cause bleeding in the brain, stomach, and intestines. Aspirin can also cause ulcers in the stomach and intestines.
- Some of these NSAID medicines are sold in lower doses without a prescription (over-the-counter). Talk to your healthcare provider before using over-the-counter NSAIDs for more than 10 days.

NSAID medicines that need a prescription

Generic Name	**Trade Name**
Celecoxib	Celebrex
Diclofenac	Cataflam, Voltaren, Arthrotec (combined with misoprostol)
Diflunisal	Dolobid
Etodolac	Lodine, Lodine XL
Fenoprofen	Nalfon, Nalfon 200
Flurbiprofen	Ansaid
Ibuprofen	Motrin, Tab-Profen, Vicoprofen* (combined with hydrocodone), Combunox (combined with oxycodone)
Indomethacin	Indocin, Indocin SR, Indo-Lemmon, Indomethagan
Ketoprofen	Oruvail
Ketorolac	Toradol
Mefenamic Acid	Ponstel
Meloxicam	Mobic
Nabumetone	Relafen
Naproxen	Naprosyn, Anaprox, Anaprox DS, EC-Naproxyn, Naprelan, Naprapac (copackaged with lansoprazole)
Oxaprozin	Daypro
Piroxicam	Feldene
Sulindac	Clinoril
Tolmetin	Tolectin, Tolectin DS, Tolectin 600

* Vicoprofen contains the same dose of ibuprofen as over-the-counter (OTC) NSAIDs, and is usually used for less than 10 days to treat pain. The OTC NSAID label warns that long term continuous use may increase the risk of heart attack or stroke.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised 06/2009.

Manufactured for:
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