NAPROSYN - naproxen tablet
Bryant Ranch Prepack

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naproxen250mg

Description
Naproxen is a proprionic acid derivative related to the arylacetic acid group of nonsteroidal anti-inflammatory drugs.

The chemical names for naproxen and naproxen sodium are (S)-6-methoxy-α-methyl-2-naphthaleneacetic acid and (S)-6-methoxy-α-methyl-2-naphthaleneacetic acid, sodium salt, respectively. Naproxen and naproxen sodium have the following structures, respectively:

Naproxen has a molecular weight of 230.26 and a molecular formula of C14H14O3. Naproxen sodium has a molecular weight of 252.23 and a molecular formula of C14H13NaO3.

Naproxen is an odorless, white to off-white crystalline substance. It is lipid-soluble, practically insoluble in water at low pH and freely soluble in water at high pH. The octanol/water partition coefficient of naproxen at pH 7.4 is 1.6 to 1.8. Naproxen sodium is a white to creamy white, crystalline solid, freely soluble in water at neutral pH.

NAPROSYN (naproxen tablets) is available as yellow tablets containing 250 mg of naproxen, pink tablets containing 375 mg of naproxen and yellow tablets containing 500 mg of naproxen for oral administration. The inactive ingredients are croscarmellose sodium, iron oxides,povidone and magnesium stearate.

EC-NAPROSYN (naproxen delayed-release tablets) is available as enteric-coatedwhite tablets containing 375 mg of naproxen and 500 mg of naproxen for oral administration. The inactive ingredients are croscarmellose sodium, povidone and magnesium stearate. The enteric coating dispersion contains methacrylic acid copolymer, talc, triethyl citrate, sodium hydroxide and purified water. The dissolution of this enteric-coated naproxen tablet is pH dependent with rapid dissolution above pH 6. There is no dissolution below pH 4.

ANAPROX (naproxen sodium tablets) is available as blue tablets containing 275 mg of naproxen sodium and ANAPROX DS (naproxen sodium tablets) for oral administration. The inactive ingredients are croscarmellose sodium, povidone and magnesium stearate. The enteric coating dispersion contains methacrylic acid copolymer, talc, triethyl citrate, sodium hydroxide and purified water.

CLINICAL PHARMACOLOGY

Naproxen is a nonsteroidal anti-inflammatory drug (NSAID) with analgesic and antipyretic properties. The sodium salt of naproxen has been developed as a more rapidly absorbed formulation of naproxen for use as an analgesic. The mechanism of action of the naproxen anion, like that of other NSAIDs, is not completely understood

but maybe related to prostaglandin synthetase inhibition.

Naproxen and naproxen sodium are rapidly and completely absorbed from the gastrointestinal tract with an in vivo bioavailability of 95%. The different dosage forms of NAPROSYN are bioequivalent in terms of extent of absorption (AUC) and peak concentration (Cmax); however, the products do differ in their pattern of absorption.

These differences between naproxen products are related to both the chemical form of naproxen used and its formulation. Even with the observed differences in pattern of absorption, the elimination half-life of naproxen is unchanged across products ranging from 12 to 17 hours.

Steady-state levels of naproxen are reached in 4 to 5 days, and the degree of naproxen accumulation is consistent with this half-life.

This suggests that the differences in pattern of release play only a negligibie role in the attainment of steady-state plasma levels.

INDICATION AND USAGE

Carefully consider the potential benefits and risks of NAPROSYN, EC-NAPROSYN, ANAPROX, ANAPROX DS or NAPROSYN Suspension and other treatment options before deciding to use NAPROSYN, EC-NAPROSYN, ANAPROX, ANAPROX DS or NAPROSYN Suspension. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.

Naproxen as NAPROSYN, EC-NAPROSYN, ANAPROX, ANAPROX DS or NAPROSYN Suspension is indicated:

* For the relief of the signs and symptoms of rheumatoid arthritis
* For the relief of the signs and symptoms of osteoarthritis
* For the relief of the signs and symptoms of ankylosing spondylitis
* For the relief of the signs and symptoms of juvenile arthritis

Naproxen as NAPROSYN Suspension is recommended for juvenile rheumatoid arthritis in order to obtain the maximum dosage flexibility based on the patient's weight.

Naproxen as NAPROSYN, ANAPROX, ANAPROX DS and NAPROSYN Suspension is also indicated:

* For relief of the signs and symptoms of tendonitis
* For relief of the signs and symptoms of bursitis
* For relief of the signs and symptoms of acute gout
* For the management of pain
* For the management of primary dysmenorrhea

EC-NAPROSYN is not recommended for initial treatment of acute pain because the absorption of naproxen is delayed compared

to absorption from other naproxen-containing products.

CONTRADICTIONS

NAPROSYN, EC-NAPROSYN, ANAPROX, ANAPROX DS and NAPROSYN Suspension are contraindicated in patients with known hypersensitivity to naproxen and naproxen sodium.

NAPROSYN, EC-NAPROSYN, ANAPROX, ANAPROX DS and NAPROSYN Suspension 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

NAPROSYN, EC-NAPROSYN, ANAPROX, ANAPROX DS and NAPROSYN Suspension are contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.

Adverse Reactions

Adverse reactions reported in controlled clinical trials in 960 patients treated for rheumatoid arthritis or osteoarthritis are listed below. In general, reactions in patients treated chronically were reported 2 to 10 times more frequently than they were in short-term studies in the 962 patients treated for mild to moderate pain or for dysmenorrhea. The most frequent complaints reported related to the gastrointestinal tract.

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 (see CLINICAL PHARMACOLOGY).

In controlled clinical trials with about 80 pediatric patients and in well-monitored, open-label studies with about 400 pediatric patients with juvenile arthritis treated with naproxen, the incidence of rash and prolonged bleeding times were increased, the incidence of gastrointestinal and central nervous system reactions were about the same, and the incidence of other reactions were lower in pediatric patients than in adults.

In patients taking naproxen in clinical trials, the most frequently reported adverse experiences in approximately 1% to 10% of patients are:

Gastrointestinal (GI) Experiences, including: heartburn1, abdominal pain1, nausea1, constipation1, diarrhea, dyspepsia, stomatitis

Central Nervous System: headache1, dizziness1, drowsiness1, lightheadedness, vertigo

OVERDOSAGE

Significant naproxen overdosage may be characterized by lethargy, dizziness, drowsiness, epigastric pain, abdominal discomfort, heartburn, indigestion, nausea, transient alterations in liver function, hypoprothrombinemia, renal dysfunction, metabolic acidosis, apnea, disorientation or vomiting. Gastrointestinal bleeding can occur. Hypertension, acute renal failure, respiratory depression, and coma may occur, but are rare. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following an overdose. Because naproxen sodium may be rapidly absorbed, high and early blood levels should be anticipated. A few patients have experienced convulsions, but it is not clear whether or not these were drug-related. It is not known what dose of the drug would be life threatening. The oral LD50 of the drug is 543 mg/kg in rats, 1234 mg/kg in mice, 4110 mg/kg in hamsters, and greater than 1000 mg/kg in dogs.

Dosage and Administration

Carefully consider the potential benefits and risks of NAPROSYN, EC-NAPROSYN, ANAPROX, ANAPROX DS and NAPROSYN Suspension and other treatment options before deciding to use NAPROSYN, EC-NAPROSYN, ANAPROX, ANAPROX DS and NAPROSYN Suspension. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.

After observing the response to initial therapy with NAPROSYN, EC-NAPROSYN, ANAPROX, ANAPROX DS or NAPROSYN Suspension, the dose and frequency should be adjusted to suit an individual patient's needs.

Different dose strengths and formulations (ie, tablets, suspension) of the drug are not necessarily bioequivalent. This difference should be taken into consideration when changing formulation.

Although NAPROSYN, NAPROSYN Suspension, EC-NAPROSYN, ANAPROX and ANAPROX DS all circulate in the plasma as naproxen, they have pharmacokinetic differences that may affect onset of action. Onset of pain relief can begin within 30 minutes in patients taking naproxen sodium and within 1 hour in patients taking naproxen. Because EC-NAPROSYN dissolves in the small intestine rather than in the stomach, the absorption of the drug is delayed compared to the other naproxen formulations.

The recommended strategy for initiating therapy is to choose a formulation and a starting dose likely to be effective for the patient and then adjust the dosage based on observation of benefit and/or adverse events. A lower dose should be considered in patients with renal or hepatic impairment or in elderly patients.

Studies indicate that although total plasma concentration of naproxen is unchanged, the unbound plasma fraction of naproxen is increased in the elderly. Caution is advised when high doses are required and some adjustment of dosage may be required in elderly

patients. As with other drugs used in the elderly, it is prudent to use the lowest effective dose.
Naproxen-containing products are not recommended
for use in patients with moderate to severe renal impairment
Rheumatoid Arthritis, Osteoarthritis and Ankylosing Spondylitis:
NAPROSYN 250 mg or 375 mg or 500 mg twice daily
275 mg (naproxen 250 mg with 25 mg sodium) twice daily
ANAPROX DS 550 mg (naproxen 500 mg with 50 mg sodium) twice daily
NAPROSYN Suspension 250 mg (10 mL/2 tsp) or 375 mg (15 mL/3 tsp or 500 mg) or (20 mL/4 tsp) twice daily
EC-NAPROSYN 375 mg or 500 mg twice daily.
To maintain the integrity of the enteric coating,
the EC-NAPROSYN tablet should not be broken, crushed or chewed during
ingestion. NAPROSYN Suspension should be shaken gently before use.
During long-term administration, the dose of naproxen
may be adjusted up or down depending on the clinical response of the
patient. A lower daily dose may suffice for long-term administration.
The morning and evening doses do not have to be equal in size and
the administration of the drug more frequently than twice daily is not necessary.
In patients who tolerate lower
doses well, the dose may be increased to naproxen 1500 mg/day for
limited periods of up to 6 months when a higher level of anti-inflammatory/analgesic
activity is required. When treating such patients with naproxen 1500
mg/day, the physician should observe sufficient increased clinical
benefits to offset the potential increased risk. The morning
and evening doses do not have to be equal in size and administration
of the drug more frequently than twice daily does not generally make
a difference in response .
The use of NAPROSYN Suspension is recommended for
juvenile arthritis in children 2 years or older because it allows
for more flexible dose titration based on the child's weight. In pediatric
patients, doses of 5 mg/kg/day produced plasma levels of naproxen
similar to those seen in adults taking 500 mg of naproxen.
The recommended total daily dose
of naproxen is approximately 10 mg/kg given in 2 divided doses (ie,
5 mg/kg given twice a day). A measuring cup marked in 1/2 teaspoon
and 2.5 milliliter increments is provided with the NAPROSYN Suspension.
The following table may be used as a guide for dosing of NAPROSYN
Suspension:

Patient's Weight	Dose	Administered as
13 kg (29 lb)	62.5 mg bid	2.5 mL (1/2 tsp) twice daily
25 kg (55 lb)	125 mg bid	5.0 mL (1 tsp) twice daily
38 kg (84 lb)	187.5 mg bid	7.5 mL (1 1/2 tsp) twice daily

The recommended starting dose is 550 mg of naproxen
sodium as ANAPROX/ANAPROX DS followed by 550 mg every 12 hours or
275 mg every 6 to 8 hours as required. The initial total daily dose
should not exceed 1375 mg of naproxen sodium. Thereafter, the total
daily dose should not exceed 1100 mg of naproxen sodium. Because the
sodium salt of naproxen is more rapidly absorbed, ANAPROX/ANAPROX
DS is recommended for the management of acute painful conditions when
prompt onset of pain relief is desired. NAPROSYN may also be used
but EC-NAPROSYN is not recommended for initial treatment of acute
pain because absorption of naproxen is delayed compared to other naproxen-containing

products.
The recommended starting dose is 750 mg of NAPROSYN followed by 250 mg every 8 hours until the attack has subsided. ANAPROX may also be used at a starting dose of 825 mg followed by 275 mg every 8 hours. EC-NAPROSYN is not recommended because of the delay in absorption (see CLINICAL PHARMACOLOGY, INDICATIONS AND USAGE).).

How Supplied

NAPROSYN Tablets: 250 mg: round, yellow, biconvex, engraved with NPR LE 250 on one side and scored on the other. Packaged in light-resistant bottles of 100.

100's (bottle):
NDC 0004-6313-01.

375 mg: pink, biconvex oval, engraved with NPR LE 375 on one side. Packaged in light-resistant bottles of 100.

100's
(bottle): NDC 0004-6314-01.

500 mg: yellow, capsule-shaped, engraved with NPR LE 500 on one side and scored on the other. Packaged in light-resistant bottles of 100.

100's (bottle): NDC 0004-6316-01.

Store at 15° to 30°C (59° to 86°F) in well-closed containers; dispense in light-resistant containers.

NAPROSYN Suspension: 125 mg/5 mL (contains 39 mg sodium, about 1.5 mEq/teaspoon): Available in 1 pint (473 mL) light-resistant bottles (NDC 0004-0028-28).

Store at 15° to 30°C (59° to 86°F); avoid excessive heat, above 40°C (104°F). Dispense in light-resistant containers. Shake gently before use.

EC-NAPROSYN Delayed-Release Tablets: 375 mg: white, oval biconvex coated tablets imprinted with NPR-EC 375 on one side. Packaged in light-resistant bottles of 100.

100's (bottle): NDC 0004-6415-01.

500 mg: white, oblong coated tablets, imprinted with NPR-EC 500 on one side. Packaged in light-resistant bottles of 100.

100's (bottle): NDC 0004-6416-01.

Store at 15° to 30°C (59° to 86°F) in well-closed containers; dispense in light-resistant containers.

ANAPROX Tablets: Naproxen sodium 275 mg: light blue, oval-shaped, engraved with NPS-275 on one side. Packaged in bottles of 100.

100's (bottle): NDC 0004-6202-01.

Store at 15° to 30°C (59° to 86°F) in well-closed containers.

ANAPROX DS Tablets: Naproxen sodium 550 mg: dark blue, oblong-shaped, engraved with NPS 550 on one side and scored on both sides. Packaged in bottles of 100.

100's (bottle): NDC 0004-6203-01.

Store at 15° to 30°C (59° to 86°F) in well-closed containers.

Revised: September 2007

Medication Guide Approval

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Medication Guide Revised: July 2008

Distributed by:

Roche Laboratories Inc.

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Nutley, NJ 07110–1199

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NAPROSYN

naproxen tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:63629-3202(NDC:53746-188)
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
NAPROXEN (UNII: 57Y76R9ATQ) (NAPROXEN - UNII:57Y76R9ATQ)	NAPROXEN	250 mg

Inactive Ingredients	
Ingredient Name	**Strength**
MAGNESIUM STEARATE (UNII: 70097M6I30)	
CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)	

Product Characteristics			
Color	white (whitecolor)	**Score**	no score
Shape	ROUND (roundnoscore)	**Size**	4mm
Flavor		**Imprint Code**	IP188;250
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:63629-3202-1	30 in 1 BOTTLE		
2	NDC:63629-3202-2	60 in 1 BOTTLE		
3	NDC:63629-3202-3	20 in 1 BOTTLE		
4	NDC:63629-3202-4	120 in 1 BOTTLE		
5	NDC:63629-3202-5	10 in 1 BOTTLE		
6	NDC:63629-3202-6	90 in 1 BOTTLE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA075927	09/01/2009	

Labeler - Bryant Ranch Prepack (171714327)

Registrant - Bryant Ranch Prepack (171714327)

Establishment

Name	Address	ID/FEI	Business Operations
Bryant Ranch Prepack		171714327	repack(63629-3202)

Revised: 11/2009 Bryant Ranch Prepack