

**NAPROXEN- naproxen tablet**  
**NuCare Pharmaceuticals, Inc.**

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CAREFULLY CONSIDER THE POTENTIAL BENEFITS AND RISKS OF NAPROXEN AND OTHER TREATMENT OPTIONS BEFORE DECIDING TO USE NAPROXEN TABLETS. USE THE LOWEST EFFECTIVE DOSE FOR THE SHORTEST DURATION CONSISTENT WITH INDIVIDUAL PATIENT TREATMENT GOALS (SEE WARNINGS: GASTROINTESTINAL BLEEDING, ULCERATION, AND PERFORATION).

**NAPROXEN TABLETS ARE 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 TABLETS ARE 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

**NAPROXEN TABLETS**

**500 MG:** WHITE TO OFF-WHITE, CAPSULE-SHAPED TABLETS WITH “140” DEBOSSSED ON ONE SIDE AND SCORED ON

OTHER SIDE.

NDC 68071-4006-1 Bottles of 10

NDC 68071-4006-7 Bottles of 14

NDC 68071-4006-5 Bottles of 15

NDC 68071-4006-2 Bottles of 20

NDC 68071-4006-3 Bottles of 30

NDC 68071-4006-4 Bottles of 40

NDC 68071-4006-6 Bottles of 60

NDC 68071-4006-9 Bottles of 90

STORE AT 20°-25°C (68°-77°F) EXCURSIONS PERMITTED TO 15°-30°C (59°-86°F) IN WELL-CLOSED CONTAINERS

[SEE USP CONTROLLED ROOM TEMPERATURE]. DISPENSE IN LIGHT-RESISTANT CONTAINERS.

**RX ONLY**

**CARDIOVASCULAR THROMBOTIC EVENTS**

CLINICAL TRIALS OF SEVERAL COX-2 SELECTIVE AND NON-SELECTIVE 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. BASED ON AVAILABLE DATA, IT IS UNCLEAR THAT THE RISK FOR CV THROMBOTIC EVENTS IS SIMILAR FOR ALL NSAIDS. THE RELATIVE INCREASE IN SERIOUS CV THROMBOTIC EVENTS OVER BASELINE CONFERRED BY NSAID USE APPEARS TO BE SIMILAR IN THOSE WITH AND WITHOUT KNOWN CV DISEASE OR RISK FACTORS FOR CV DISEASE. HOWEVER, PATIENTS WITH KNOWN CV DISEASE OR RISK FACTORS HAD A HIGHER ABSOLUTE INCIDENCE OF EXCESS SERIOUS CV THROMBOTIC EVENTS, DUE TO THEIR INCREASED BASELINE RATE. SOME OBSERVATIONAL STUDIES FOUND THAT THIS INCREASED RISK OF SERIOUS CV THROMBOTIC EVENTS BEGAN AS EARLY AS THE FIRST WEEKS OF TREATMENT. THE INCREASE IN CV THROMBOTIC RISK HAS BEEN OBSERVED MOST CONSISTENTLY AT HIGHER DOSES.

TO MINIMIZE THE POTENTIAL RISK FOR AN ADVERSE CV EVENT IN NSAID-TREATED PATIENTS, USE THE LOWEST EFFECTIVE DOSE FOR THE SHORTEST DURATION POSSIBLE. PHYSICIANS AND PATIENTS SHOULD REMAIN ALERT FOR THE DEVELOPMENT OF SUCH EVENTS, THROUGHOUT THE ENTIRE TREATMENT COURSE, EVEN IN THE ABSENCE OF PREVIOUS CV SYMPTOMS. PATIENTS SHOULD BE INFORMED ABOUT THE 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, SUCH AS NAPROXEN, INCREASES THE RISK OF SERIOUS GASTROINTESTINAL (GI) EVENTS (SEE WARNINGS; GASTROINTESTINAL BLEEDING, ULCERATION, AND PERFORATION).

#### STATUS POST CORONARY ARTERY BYPASS GRAFT (CABG) SURGERY

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. NSAIDS ARE CONTRAINDICATED IN THE SETTING OF CABG (SEE CONTRAINDICATIONS).

#### POST-MI PATIENTS

OBSERVATIONAL STUDIES CONDUCTED IN THE DANISH NATIONAL REGISTRY HAVE DEMONSTRATED THAT PATIENTS TREATED WITH NSAIDS IN THE POST-MI PERIOD WERE AT INCREASED RISK OF REINFARCTION, CV-RELATED DEATH, AND ALL CAUSE MORTALITY BEGINNING IN THE FIRST WEEK OF TREATMENT. IN THIS SAME COHORT, THE INCIDENCE OF DEATH IN THE FIRST YEAR POST-MI WAS 20 PER 100 PERSON YEARS IN NSAID-TREATED PATIENTS COMPARED TO 12 PER 100 PERSON YEARS IN NON-NSAID EXPOSED PATIENTS. ALTHOUGH THE ABSOLUTE RATE OF DEATH DECLINED SOMEWHAT

AFTER THE FIRST YEAR POST-MI, THE INCREASED RELATIVE RISK OF DEATH IN NSAID USERS PERSISTED OVER AT LEAST THE NEXT FOUR YEARS OF FOLLOW-UP.

AVOID THE USE OF NAPROXEN IN PATIENTS WITH A RECENT MI UNLESS THE BENEFITS ARE EXPECTED TO OUTWEIGH THE RISK OF RECURRENT CV THROMBOTIC EVENTS. IF NAPROXEN IS USED IN PATIENTS WITH A RECENT MI, MONITOR PATIENTS FOR SIGNS OF CARDIAC ISCHEMIA.

#### **GASTROINTESTINAL BLEEDING, ULCERATION, AND PERFORATION**

NSAIDS, INCLUDING NAPROXEN CAUSE SERIOUS GASTROINTESTINAL (GI) ADVERSE

EVENTS INCLUDING INFLAMMATION, BLEEDING, ULCERATION, AND PERFORATION OF THE ESOPHAGUS, 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 OCCURRED IN APPROXIMATELY 1% OF PATIENTS TREATED FOR 3-6 MONTHS, AND IN ABOUT 2%-

4% OF PATIENTS TREATED FOR ONE YEAR. HOWEVER, EVEN SHORT-TERM NSAID THERAPY IS NOT WITHOUT RISK. RISK FACTORS FOR GI BLEEDING, ULCERATION, AND PERFORATION PATIENTS WITH A PRIOR HISTORY OF PEPTIC ULCER DISEASE AND/OR GI BLEEDING WHO USED NSAIDS HAD A GREATER

THAN 10-FOLD INCREASED RISK FOR DEVELOPING A GI BLEED COMPARED TO PATIENTS WITHOUT THESE RISK FACTORS. OTHER FACTORS THAT INCREASE THE RISK OF GI BLEEDING IN PATIENTS TREATED WITH NSAIDS INCLUDE LONGER DURATION OF NSAID THERAPY; CONCOMITANT USE OF ORAL CORTICOSTEROIDS, ASPIRIN, ANTICOAGULANTS, OR SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS); SMOKING; USE OF ALCOHOL; OLDER AGE; AND POOR GENERAL HEALTH STATUS. MOST POSTMARKETING REPORTS OF FATAL GI EVENTS OCCURRED IN ELDERLY OR DEBILITATED PATIENTS.

ADDITIONALLY, PATIENTS WITH ADVANCED LIVER DISEASE AND/OR COAGULOPATHY ARE AT INCREASED RISK FOR GI BLEEDING.

#### **STRATEGIES TO MINIMIZE THE GI RISKS IN NSAID-TREATED PATIENTS:**

- USE THE LOWEST EFFECTIVE DOSAGE FOR THE SHORTEST POSSIBLE DURATION.
- AVOID ADMINISTRATION OF MORE THAN ONE NSAID AT A TIME.
- AVOID USE IN PATIENTS AT HIGHER RISK UNLESS BENEFITS ARE EXPECTED TO OUTWEIGH THE INCREASED RISK OF
- BLEEDING. FOR SUCH PATIENTS, AS WELL AS THOSE WITH ACTIVE GI BLEEDING, CONSIDER ALTERNATE THERAPIES OTHER THAN NSAIDS.
- REMAIN ALERT FOR SIGNS AND SYMPTOMS OF GI ULCERATION AND BLEEDING DURING NSAID THERAPY.
- IF A SERIOUS GI ADVERSE EVENT IS SUSPECTED, PROMPTLY INITIATE EVALUATION AND TREATMENT, AND DISCONTINUE NAPROXEN UNTIL A SERIOUS GI ADVERSE EVENT IS RULED OUT.
- IN THE SETTING OF CONCOMITANT USE OF LOW-DOSE ASPIRIN FOR CARDIAC PROPHYLAXIS, MONITOR PATIENTS MORE CLOSELY FOR EVIDENCE OF GI BLEEDING (SEE PRECAUTIONS; DRUG INTERACTIONS).

#### **HEPATOTOXICITY**

ELEVATIONS OF ALT OR AST (THREE OR MORE TIMES THE UPPER LIMIT OF NORMAL [ULN]) HAVE BEEN REPORTED IN APPROXIMATELY 1% OF PATIENTS IN CLINICAL TRIALS. IN ADDITION, RARE, SOMETIMES FATAL, CASES OF SEVERE HEPATIC INJURY, INCLUDING FULMINANT HEPATITIS, LIVER NECROSIS AND HEPATIC FAILURE HAVE BEEN REPORTED.

ELEVATIONS OF ALT OR AST (LESS THAN THREE TIMES ULN) MAY OCCUR IN UP TO 15% OF PATIENTS TAKING NSAIDS INCLUDING NAPROXEN.

INFORM PATIENTS OF THE WARNING SIGNS AND SYMPTOMS OF HEPATOTOXICITY (E.G., NAUSEA, FATIGUE, LETHARGY, DIARRHEA, PRURITUS, JAUNDICE, RIGHT UPPER QUADRANT TENDERNESS, AND "FLULIKE" SYMPTOMS). IF CLINICAL SIGNS AND

SYMPTOMS CONSISTENT WITH LIVER DISEASE DEVELOP, OR IF SYSTEMIC MANIFESTATIONS OCCUR (E.G., EOSINOPHILIA, RASH, ETC.), DISCONTINUE NAPROXEN IMMEDIATELY, AND PERFORM A CLINICAL EVALUATION OF THE PATIENT.

## **HYPERTENSION**

NSAIDS, INCLUDING NAPROXEN, 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 ANGIOTENSIN CONVERTING ENZYME (ACE) INHIBITORS, THIAZIDES OR LOOP DIURETICS MAY HAVE IMPAIRED RESPONSE TO THESE THERAPIES WHEN TAKING NSAIDS (SEE PRECAUTIONS; DRUG INTERACTIONS).

MONITOR BLOOD PRESSURE (BP) DURING THE INITIATION OF NSAID TREATMENT AND THROUGHOUT THE COURSE OF THERAPY.

## **HEART FAILURE AND EDEMA**

THE COXIB AND TRADITIONAL NSAID TRIALISTS' COLLABORATION META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS DEMONSTRATED AN APPROXIMATELY TWO-FOLD INCREASE IN HOSPITALIZATION FOR HEART FAILURE IN COX-2 SELECTIVE-TREATED PATIENTS AND NONSELECTIVE NSAID-TREATED PATIENTS COMPARED TO PLACEBO-TREATED PATIENTS. IN A DANISH NATIONAL REGISTRY STUDY OF PATIENTS WITH HEART FAILURE, NSAID USE INCREASED THE RISK OF MI, HOSPITALIZATION FOR HEART FAILURE, AND DEATH. ADDITIONALLY, FLUID RETENTION AND EDEMA HAVE BEEN OBSERVED IN SOME PATIENTS TREATED WITH NSAIDS. USE OF NAPROXEN MAY BLUNT THE CV EFFECTS OF SEVERAL THERAPEUTIC AGENTS USED TO TREAT THESE MEDICAL CONDITIONS (E.G., DIURETICS, ACE INHIBITORS, OR ANGIOTENSIN RECEPTOR BLOCKERS [ARBS]) (SEE PRECAUTIONS; DRUG INTERACTIONS).

AVOID THE USE OF NAPROXEN IN PATIENTS WITH SEVERE HEART FAILURE UNLESS THE BENEFITS ARE EXPECTED TO OUTWEIGH THE RISK OF WORSENING HEART FAILURE. IF NAPROXEN IS USED IN PATIENTS WITH SEVERE HEART FAILURE, MONITOR PATIENTS FOR SIGNS OF WORSENING HEART FAILURE.

## **RENAL TOXICITY AND HYPERKALEMIA**

### RENAL TOXICITY

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 AN NSAID MAY CAUSE A DOSEDEPENDENT REDUCTION IN PROSTAGLANDIN FORMATION AND, SECONDARILY, IN RENAL BLOOD FLOW, WHICH MAY PRECIPITATE OVERT RENAL DECOMPENSATION. PATIENTS AT GREATEST RISK OF THIS REACTION ARE THOSE WITH IMPAIRED

RENAL FUNCTION, HYPOVOLEMIA, HEART FAILURE, LIVER DYSFUNCTION, SALT DEPLETION, THOSE TAKING DIURETICS AND ACE INHIBITORS OR ARBS, AND THE ELDERLY. DISCONTINUATION OF NSAID THERAPY IS USUALLY FOLLOWED BY RECOVERY TO THE PRETREATMENT STATE. NO INFORMATION IS AVAILABLE FROM CONTROLLED CLINICAL STUDIES REGARDING THE USE OF NAPROXEN IN PATIENTS WITH ADVANCED RENAL DISEASE. THE RENAL EFFECTS OF NAPROXEN MAY HASTEN THE PROGRESSION OF RENAL DYSFUNCTION IN PATIENTS WITH PREEXISTING RENAL DISEASE.

CORRECT VOLUME STATUS IN DEHYDRATED OR HYPOVOLEMIC PATIENTS PRIOR TO

INITIATING NAPROXEN. MONITOR RENAL FUNCTION IN PATIENTS WITH RENAL OR HEPATIC IMPAIRMENT, HEART FAILURE, DEHYDRATION, OR HYPOVOLEMIA DURING USE OF NAPROXEN (SEE PRECAUTIONS; DRUG INTERACTIONS). AVOID THE USE OF NAPROXEN IN PATIENTS WITH ADVANCED RENAL DISEASE UNLESS THE BENEFITS ARE EXPECTED TO OUTWEIGH THE RISK OF WORSENING RENAL FUNCTION. IF NAPROXEN IS USED IN PATIENTS WITH ADVANCED RENAL DISEASE, MONITOR PATIENTS FOR SIGNS OF

WORSENING RENAL FUNCTION.

### **HYPERKALEMIA**

INCREASES IN SERUM POTASSIUM CONCENTRATION, INCLUDING HYPERKALEMIA, HAVE BEEN REPORTED WITH USE OF NSAIDS, EVEN IN SOME PATIENTS WITHOUT RENAL IMPAIRMENT. IN PATIENTS WITH NORMAL RENAL FUNCTION, THESE EFFECTS HAVE BEEN ATTRIBUTED TO A HYPORENINEMIC HYPOALDOSTERONISM STATE.

### **ANAPHYLACTOID REACTIONS**

NAPROXEN HAS BEEN ASSOCIATED WITH ANAPHYLACTIC REACTIONS IN PATIENTS WITH AND WITHOUT KNOWN HYPERSENSITIVITY TO NAPROXEN AND IN PATIENTS WITH ASPIRIN-SENSITIVE ASTHMA (SEE

CONTRAINDICATIONS, WARNINGS; EXACERBATION OF ASTHMA RELATED TO ASPIRIN SENSITIVITY).

### **EXACERBATION OF ASTHMA RELATED TO ASPIRIN SENSITIVITY**

A SUBPOPULATION OF PATIENTS WITH ASTHMA MAY HAVE ASPIRIN-SENSITIVE ASTHMA WHICH MAY INCLUDE CHRONIC RHINOSINUSITIS COMPLICATED BY NASAL POLYPS; SEVERE, POTENTIALLY FATAL BRONCHOSPASM; AND/OR INTOLERANCE TO ASPIRIN AND OTHER NSAIDS. BECAUSE CROSS-REACTIVITY BETWEEN ASPIRIN AND OTHER NSAIDS HAS BEEN REPORTED IN SUCH ASPIRIN-SENSITIVE PATIENTS, NAPROXEN TABLETS ARE CONTRAINDICATED IN PATIENTS WITH THIS FORM OF ASPIRIN SENSITIVITY (SEE CONTRAINDICATIONS). WHEN NAPROXEN TABLETS ARE USED IN PATIENTS WITH PREEXISTING ASTHMA (WITHOUT KNOWN ASPIRIN SENSITIVITY), MONITOR PATIENTS FOR CHANGES IN THE SIGNS AND SYMPTOMS OF ASTHMA.

### **SERIOUS SKIN REACTIONS**

NSAIDS, INCLUDING NAPROXEN, 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 TO DISCONTINUE THE USE OF NAPROXEN AT THE FIRST APPEARANCE OF SKIN RASH OR ANY OTHER SIGN OF HYPERSENSITIVITY. NAPROXEN TABLETS ARE CONTRAINDICATED IN PATIENTS WITH PREVIOUS

SERIOUS SKIN REACTIONS TO NSAIDS (SEE CONTRAINDICATIONS).

### **PREMATURE CLOSURE OF FETAL DUCTUS ARTERIOSUS**

NAPROXEN MAY CAUSE PREMATURE CLOSURE OF THE FETAL DUCTUS ARTERIOSUS. AVOID USE OF NSAIDS, INCLUDING NAPROXEN, IN PREGNANT WOMEN STARTING AT 30 WEEKS OF GESTATION (THIRD TRIMESTER) (SEE PRECAUTIONS; PREGNANCY).

### **HEMATOLOGIC TOXICITY**

ANEMIA HAS OCCURRED IN NSAID-TREATED PATIENTS. THIS MAY BE DUE TO OCCULT

OR GROSS BLOOD LOSS, FLUID RETENTION, OR AN INCOMPLETELY DESCRIBED EFFECT ON ERYTHROPOIESIS. IF A PATIENT TREATED WITH NAPROXEN HAS ANY SIGNS OR SYMPTOMS OF ANEMIA, MONITOR HEMOGLOBIN OR HEMATOCRIT.

NSAIDS, INCLUDING NAPROXEN, MAY INCREASE THE RISK OF BLEEDING EVENTS. COMORBID CONDITIONS SUCH AS COAGULATION DISORDERS, OR CONCOMITANT USE OF WARFARIN AND OTHER ANTICOAGULANTS, ANTIPLATELET AGENTS (E.G., ASPIRIN), SEROTONIN REUPTAKE INHIBITORS (SSRIS) AND SEROTONIN NOREPINEPHRINE REUPTAKE INHIBITORS (SNRIS) MAY INCREASE THIS RISK. MONITOR THESE PATIENTS FOR SIGNS OF BLEEDING (SEE PRECAUTIONS; DRUG INTERACTIONS).

CAREFULLY CONSIDER THE POTENTIAL BENEFITS AND RISKS OF NAPROXEN AND OTHER TREATMENT OPTIONS BEFORE DECIDING TO USE NAPROXEN TABLETS. USE THE LOWEST EFFECTIVE DOSE FOR THE SHORTEST DURATION CONSISTENT WITH INDIVIDUAL PATIENT TREATMENT GOALS (SEE WARNINGS; GASTROINTESTINAL BLEEDING, ULCERATION, AND PERFORATION).

AFTER OBSERVING THE RESPONSE TO INITIAL THERAPY WITH NAPROXEN TABLETS, THE DOSE AND FREQUENCY SHOULD BE ADJUSTED TO SUIT AN INDIVIDUAL PATIENT'S NEEDS.

DIFFERENT DOSE STRENGTHS AND FORMULATIONS (I.E., TABLETS, SUSPENSION) OF THE DRUG ARE NOT NECESSARILY BIOEQUIVALENT. THIS DIFFERENCE SHOULD BE TAKEN INTO CONSIDERATION WHEN CHANGING FORMULATION.

ALTHOUGH NAPROXEN TABLETS, NAPROXEN SUSPENSION, NAPROXEN DELAYED-RELEASED TABLETS, AND NAPROXEN SODIUM TABLETS ALL CIRCULATE IN THE PLASMA AS NAPROXEN, THEY HAVE PHARMACOKINETIC DIFFERENCES THAT MAY AFFECT ONSET OF ACTION. ONSET OF PAIN RELIEF CAN BEGIN WITHIN 1 HOUR IN PATIENTS TAKING NAPROXEN. 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 (SEE WARNINGS; HEPATOTOXICITY, AND RENAL TOXICITY AND HYPERKALEMIA, AND PRECAUTIONS; GERIATRIC USE).

### **GERIATRIC 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.

### **PATIENTS WITH MODERATE TO SEVERE RENAL IMPAIRMENT**

NAPROXEN-CONTAINING PRODUCTS ARE NOT RECOMMENDED FOR USE IN PATIENTS WITH MODERATE TO SEVERE AND SEVERE RENAL IMPAIRMENT (CREATININE CLEARANCE < 30 ML/MIN) (SEE WARNINGS: RENAL EFFECTS).

### **RHEUMATOID ARTHRITIS, OSTEOARTHRITIS AND ANKYLOSING SPONDYLITIS**

THE RECOMMENDED DOSE IS 250 MG, 375 MG, OR 500 MG TWICE DAILY. 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 (SEE CLINICAL PHARMACOLOGY).

### **JUVENILE ARTHRITIS**

NAPROXEN TABLETS MAY NOT ALLOW FOR THE FLEXIBLE DOSE TITRATION NEEDED IN PEDIATRIC PATIENTS WITH JUVENILE ARTHRITIS. A LIQUID FORMULATION MAY BE MORE APPROPRIATE. 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 (SEE CLINICAL PHARMACOLOGY). THE RECOMMENDED TOTAL DAILY DOSE OF NAPROXEN IS APPROXIMATELY 10 MG/KG GIVEN IN 2 DIVIDED DOSES. ONE-HALF OF THE 250 MG TABLET WILL BE NEEDED FOR DOSING LOWER-WEIGHT CHILDREN. DOSING WITH NAPROXEN TABLETS IS NOT APPROPRIATE FOR CHILDREN WEIGHING LESS THAN 25 KILOGRAMS. THE RECOMMENDED TOTAL DAILY DOSE OF NAPROXEN IS APPROXIMATELY 10 MG/KG GIVEN IN 2 DIVIDED DOSES (I.E., 5 MG/KG GIVEN TWICE A DAY). NAPROXEN TABLETS ARE NOT WELL SUITED TO THIS DOSAGE SO USE OF NAPROXEN ORAL SUSPENSION IS RECOMMENDED FOR THIS INDICATION.

### **MANAGEMENT OF PAIN, PRIMARY DYSMENORRHEA, AND ACUTE TENDONITIS AND BURSITIS**

BECAUSE THE SODIUM SALT OF NAPROXEN IS MORE RAPIDLY ABSORBED, NAPROXEN SODIUM IS RECOMMENDED FOR THE MANAGEMENT OF ACUTE PAINFUL CONDITIONS WHEN PROMPT ONSET OF PAIN RELIEF IS DESIRED. NAPROXEN MAY ALSO BE USED. THE RECOMMENDED STARTING DOSE OF NAPROXEN IS 500 MG, FOLLOWED BY 500 MG EVERY 12 HOURS OR 250 MG EVERY 6 TO 8 HOURS AS REQUIRED. THE INITIAL TOTAL DAILY DOSE SHOULD NOT EXCEED 1250 MG OF NAPROXEN.

### **ACUTE GOUT**

THE RECOMMENDED STARTING DOSE IS 750 MG OF NAPROXEN FOLLOWED BY 250 MG EVERY 8 HOURS UNTIL THE ATTACK HAS SUBSIDED.

NDC: 68071-4006-2

**Naproxen 500mg**

**#20 Tablets**

Each tablet contains:  
Naproxen, USP 500mg

Capsule-Shaped White/Off-White Scored  
Tablet Debossed: "140" on the un-scored  
side

Product #: P0153020

**Rx Only**

Naproxen 500mg

Lot: 000000 NDC: 68071-4006-02  
MFR NDC: 49483-618-50 Exp.: 00-00

Naproxen 500mg

Lot: 000000 NDC: 68071-4006-02  
MFR NDC: 49483-618-50 Exp.: 00-00



GTIN 00368071400625  
Serial# 00000000002  
Exp. Date 00-00  
LOT#: 000000

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

Manufactured by: 3  
Marksans Pharma Ltd. Verna,  
Goa-403 722 India  
Packaged By:  
NuCare Pharmaceuticals, Inc.  
Orange, CA 92867

Patent Instructions

Take \_\_\_\_\_ every \_\_\_\_\_  
hours \_\_\_\_\_ times a day.

68071400602\*#20\*000000\*000000

Rev 01/01/19

WARNING: KEEP OUT OF REACH OF CHILDREN

STORE AT CONTROLLED TEMPERATURE 59-86°F.

**NAPROXEN**

naproxen tablet

**Product Information**

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:68071-4006(NDC:49483-618)
Route of Administration	ORAL		

**Active Ingredient/Active Moiety**

Ingredient Name	Basis of Strength	Strength
NAPROXEN (UNII: 57Y76R9ATQ) (NAPROXEN - UNII:57Y76R9ATQ)	NAPROXEN	500 mg

**Inactive Ingredients**

Ingredient Name	Strength
CROSCARMELOSE SODIUM (UNII: M28OL1HH48)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POVIDONE (UNII: FZ989GH94E)	

**Product Characteristics**

Color	white	Score	2 pieces
Shape	CAPSULE	Size	16mm
Flavor		Imprint Code	140
Contains			

**Packaging**

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:68071-4006-1	10 in 1 BOTTLE; Type 0: Not a Combination Product	07/17/2017	
2	NDC:68071-4006-7	14 in 1 BOTTLE; Type 0: Not a Combination Product	07/17/2017	



3	NDC:68071-4006-5	15 in 1 BOTTLE; Type 0: Not a Combination Product	07/17/2017	
4	NDC:68071-4006-2	20 in 1 BOTTLE; Type 0: Not a Combination Product	07/17/2017	
5	NDC:68071-4006-3	30 in 1 BOTTLE; Type 0: Not a Combination Product	07/17/2017	
6	NDC:68071-4006-4	40 in 1 BOTTLE; Type 0: Not a Combination Product	07/17/2017	
7	NDC:68071-4006-6	60 in 1 BOTTLE; Type 0: Not a Combination Product	07/17/2017	
8	NDC:68071-4006-9	90 in 1 BOTTLE; Type 0: Not a Combination Product	07/17/2017	

## Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA091416	07/06/2016	

**Labeler** - NuCare Pharmaceuticals, Inc. (010632300)

## Establishment

Name	Address	ID/FEI	Business Operations
NuCare Pharmaceuticals, Inc.		010632300	repack(68071-4006)

Revised: 2/2021

NuCare Pharmaceuticals, Inc.