DESCRIPTION

MOTRIN Tablets contain the active ingredient ibuprofen, which is 2-(2-carboxyethoxy)phenylpropionic acid. Ibuprofen is a white powder with a melting point of 74-77°C and is very slightly soluble in water (< 1 mg/mL) and readily soluble in organic solvents such as ethanol and aceton.

The structural formula is represented below:

\[
\begin{align*}
\text{CH}_3 & \quad \text{CH}_2 \quad \text{OH} \\
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{C} \quad \text{OH} \\
\text{CH}_3 & \quad \text{CH}_2 \quad \text{OH} \\
\text{CH}_3 & \quad \text{CH}_2 \quad \text{OH} \\
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{C} \quad \text{OH}
\end{align*}
\]

MOTRIN, a nonsteroidal anti-inflammatory agent, is available in 400 mg, 600 mg, and 800 mg tablets for oral administration. Inactive ingredients: carnauba wax, colloidal silicon dioxide, croscarmellose sodium, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, propylene glycol, titanium dioxide.

CLINICAL PHARMACOLOGY

MOTRIN Tablets contain ibuprofen which possesses analgesic and antipyretic activities. In mode of action, like that of other nonsteroidal anti-inflammatory agents, is not completely understood, but may be related to prostaglandin synthetase inhibition.

In clinical studies in patients with rheumatoid arthritis and osteoarthritis, MOTRIN has been shown to be comparable to aspirin in controlling pain and inflammation and to be associated with a statistically significant reduction in the milder gastrointestinal side effects (see ADVERSE REACTIONS). MOTRIN may be well tolerated in some patients who have had gastrointestinal side effects with aspirin, but these patients when treated with MOTRIN should be carefully followed for signs and symptoms of gastrointestinal ulceration and bleeding. Although it is not definitely known whether MOTRIN causes less gastric ulceration than aspirin, in one study involving 885 patients with rheumatoid arthritis treated for up to one year, there were no reports of gastric ulceration with MOTRIN whereas frank ulceration was reported in 13 patients in the aspirin group (statistically significant p<.001).

Gastroscopic studies at varying doses show an increased tendency toward gastric irritation at higher doses. However, at comparable doses, gastric irritation is approximately half that seen with aspirin. Studies using 14C-labeled red cells indicate that fecal blood loss associated with MOTRIN Tablets in doses up to 2400 mg daily did not exceed the normal range, and was significantly less than that seen in aspirin-treated patients.

In clinical studies in patients with rheumatoid arthritis, MOTRIN has been shown to be comparable to indomethacin in controlling the signs and symptoms of disease activity and to be associated with a statistically significant reduction of the milder gastrointestinal (see ADVERSE REACTIONS) and CNS side-effects.

MOTRIN may be used in combination with gold salts or other corticosteroids.

Controlled studies have demonstrated that MOTRIN is a more effective analgesic than propoxyphene for the relief of epistaxis pain, pain following dental extraction procedures, and for the relief of the symptoms of primary dysmenorrhea.

In patients with primary dysmenorrhea, MOTRIN has been shown to reduce elevated levels of prostaglandin activity in the menstrual fluid and to reduce existing and active inflammation with pressure, as well as the frequency of uterine contractions. The probable mechanism of action is to inhibit prostaglandin synthesis rather than simply to provide analgesia.

The ibuprofen in MOTRIN is rapidly absorbed. Peak serum ibuprofen levels are generally attained one to two hours after administration. With single doses up to 800 mg, a linear relationship exists between amount of drug administered and the area under the serum drug concentration vs time curve. Above 800 mg, however, the area under the curve increases less than proportionally to increases in dose. There is no evidence of drug accumulation or enzyme induction.

The administration of MOTRIN Tablets either under fasting conditions or immediately before meals yields quite similar serum ibuprofen concentration-time profiles. When MOTRIN Tablets are administered immediately after a meal, there is a reduction in the rate of absorption but no appreciable decrease in the extent of absorption. The bioavailability of the drug is minimally altered by the presence of food.

CNS effects, such as dizziness, drowsiness, headache or blurring of vision have been reported. If a patient develops such symptoms while receiving MOTRIN Tablets, the drug should be discontinued.

MOTRIN is also indicated for the treatment of primary dysmenorrhea.

Since there have been no controlled clinical trials to demonstrate whether or not there is any beneficial effect or harmful interaction with the use of MOTRIN in conjunction with aspirin, the combination cannot be recommended (see Drug Interactions).

Controlled clinical trials to establish the safety and effectiveness of MOTRIN in children have not been conducted.

CONTRAINDICATIONS

MOTRIN Tablets should not be used in patients who have previously exhibited hypersensitivity to the drug, or in individuals with the syndrome of nasal polyps, angioedema and bronchospastic reactivity to aspirin or other nonsteroidal anti-inflammatory agents. Anaphylactoid reactions have occurred in such patients.

WARNINGS

Risk of GI Ulceration, Bleeding and Perforation with Nonsteroidal Anti-Inflammatory Therapy:

Serious gastrointestinal toxicity such as bleeding, ulceration, and perforation, can occur at any time, with or without warning symptoms, in patients treated chronically with nonsteroidal anti-inflammatory drugs. Although minor upper gastrointestinal problems, such as dyspepsia, are common, usually developing early in therapy, physicians should remain alert for ulceration and bleeding in patients treated chronically with nonsteroidal anti-inflammatory drugs even in the absence of previous GI tract symptoms. In patients observed in clinical trials of several months to two years duration, symptomatic upper GI ulcers, gross bleeding or perforation appear to occur in approximately 1% of patients treated for three to six months, and in about 2-4% of patients treated for one year. Physicians should inform patients about the signs and/or symptoms of serious GI toxicity and what steps to take if they occur.

Studies to date have not identified any subset of patients not at risk of developing peptic ulceration and bleeding. Except for the history of serious GI events and other risk factors known to be associated with peptic ulcer disease, such as alcoholism, smoking, etc., no risk factors (eg, age, sex) have been associated with increased risk. Elderly or debilitated patients seem to tolerate ulceration or bleeding less well than other individuals and most spontaneous reports of fatal GI events are in this population. Studies to date are inadequate concerning the relative risk of various nonsteroidal anti-inflammatory agents in causing such reactions. High doses of any such agents probably carry a greater risk of these reactions, although controlled clinical trials showing this do not exist in most cases. In considering the use of relatively large doses (within the recommended dosage range), sufficient benefit should be anticipated to offset the potential increased risk of GI toxicity.

PRECAUTIONS

General Precautions

Blurred and/or diminished vision, scotomata, and/or changes in color vision have been reported. If a patient develops such complaints while receiving MOTRIN Tablets, the drug should be discontinued, and the patient should have an ophthalmologic examination which includes central visual fields and color vision testing.

Fluid retention and edema have been reported in association with MOTRIN; therefore, the drug should be used with caution in patients with a history of cardiac decompensation or hypertension.
Motrin
brand of ibuprofen tablets

MOTRIN like other nonsteroidal anti-inflammatory agents, can in rare instances cause an exaggerated in patients with underlying hemostatic defects, mortality associated with ibuprofen. Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported with ibuprofen as with other non-steroidal anti-inflammatory drugs. Such reactions are rare, but in the absence of liver tests have occurred, should be evaluated for evidence of the development of more serious hepatic reaction while on therapy with MOTRIN. Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported with ibuprofen as with other non-steroidal anti-inflammatory drugs. Such reactions are rare, but in the absence of liver tests has been observed with other non-steroidal anti-inflammatory drugs. The mechanism is unknown. With daily doses of 3200 mg, the total decrease in hemoglobin of less than 1 gram if there are no signs of bleeding, is probably not clinically important.

In two postmarketing clinical studies the incidence of a decreased hemoglobin level was greater than previously reported. Decrease in hemoglobin of 1 gram or more was observed in 17.1% of 193 patients on 1600 mg ibuprofen system daily (estrogen-free), and in 23.8% of 189 patients taking 2400 mg of ibuprofen daily (rheumatoid arthritis). Positive studies in blood tests and elevated serum creatinine levels were also observed in these studies. Aseptic Meningitis: Aseptic meningitis with fever and coma has been observed on rare occasions in patients on ibuprofen therapy. Although it is probably more likely to occur in patients with systemic lupus erythematosus and related connective tissue diseases, it has been reported in patients who do not have an underlying chronic disease. If signs of meningitis develop in a patient on MOTRIN, the possibility of its being related to MOTRIN should be considered.

Renal Effects: As with other nonsteroidal anti-inflammatory drugs, long-term administration of ibuprofen to animals has resulted in renal necrosis and other abnormal renal pathology. In humans, there have been reports of acute interstitial nephritis with blood dyscrasias, purpura, and occasionally nephrotic syndrome.

A second form of renal toxicity has been seen in patients with preterminal conditions leading to a reduction in renal blood flow or blood volume, where the renal prostaglandins have a supportive 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 may precipitate overt renal insufficiency. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and elderly. Discontinuation of non-steroidal anti-inflammatory drug therapy is typically followed by recovery to the pretreatment state. Those patients at high risk who chronically take MOTRIN should have renal function monitored if they have signs of renal lesions which may be consistent with mild azotemia, such as malaise, fatigue, loss of appetite, etc. Occasional patients may develop some elevation of serum creatinine and BUN levels without signs of symptoms.

Motrin
brand of ibuprofen tablets

Since ibuprofen is eliminated primarily by the kidneys, patients with significantly impaired renal function should be closely monitored; and a reduction in dosage should be anticipated to avoid drug accumulation. Prospective studies on the safety of ibuprofen in neonates, MOTRIN is not recommended for use in nursing mothers. However, because of the limited nature of the studies, and the possible adverse effects of prostaglandin-inhibiting drugs on neonates, MOTRIN is not recommended for use in nursing mothers.

ADVERSE REACTIONS

The most frequent type of adverse reaction occurring with Motrin Tablets is gastrointestinal. In controlled clinical trials the percentage of patients reporting one or more gastrointestinal complaints ranged from 9% to 16%.

In controlled studies when MOTRIN was compared to aspirin and indomethacin in equally effective doses, the overall incidence of gastrointestinal complaints was about half that seen in either the aspirin- or indomethacin-treated patients. Adverse reactions observed during controlled clinical trials at an incidence greater than 1% are listed in the table. Those reactions listed in Column one encompass over 3,000 patients. More than 500 of these patients were treated for periods of at least 54 weeks.

Still other reactions occurring less frequently than 1 in 100 were reported in controlled clinical trials and in postmarketing experience.

These reactions have been divided into two categories: Column two of the table lists reactions with therapy with MOTRIN where the probability of a causal relationship exists: for the reactions in Column three, a causal relationship with MOTRIN has not been established.

Reported side effects were higher at doses of 3200 mg/day than at doses of 2400 mg or less per day in clinical trials of patients with rheumatoid arthritis. The increases in incidence were slight and still within the range observed in the table.

OVERDOSAGE

Approximately 1/2 hour after the reported ingestion of from 7 to 10 MOTRIN Tablets (400 mg), a 10-month old child weighing 12 kg was seen in the hospital emergency room, apneic and cyanotic, responding only to painful stimuli. This type of stimulus, however, was sufficient to induce respiration. A gastric lavage and parental fluids with added cimetidine were given; a greenish-yellow fluid was aspirated from the stomach with no evidence to indicate the presence of ibuprofen. Two hours after ingestion the child’s condition seemed stable; she still responded only to painful stimuli and was observed to have periods of apnea lasting from 5 to 10 seconds. She was admitted to intensive care and sodium bicarbonate was administered as well as infusions of dextrose and normal saline. By four hours post-ingestion the child’s condition appeared to be a reasonably stable, she was taken by her mother to respond to spoken commands. Blood level of ibuprofen was 102.9 µg/mL, approximately 8/5 hours after accidental ingestion. At 12 hours she appeared to be completely recovered.

In two other reported cases where children (each weighing approximately 10 kg) accidentally, acutely ingested approximately 120 mg/kg, there were no signs of acute intoxication or late sequelae. Blood level in one child 90 minutes after ingestion was 700 µg/mL. — about 16 times the peak levels seen in absorption-excretion studies.

A 19-year old male who had taken 8,000 mg of ibuprofen over a period of a few hours complained of diziness and syncope was noted. After administration, parotidial hyperemia and three days bed...
Motrin Tablets are available in the following strengths, colors and sizes:

- 400 mg (white, round, imprinted with MOTRIN 400)
  - Bottles of 100 NDC 0009-7385-01
  - Bottles of 500 NDC 0009-7385-02
  - Unit dose blister of 100 NDC 0009-7385-04
- 600 mg (white, elliptical, imprinted with MOTRIN 600)
  - Bottles of 90 NDC 0009-7386-05
  - Bottles of 100 NDC 0009-7386-01
  - Bottles of 270 NDC 0009-7386-09
  - Bottles of 500 NDC 0009-7386-82
  - Unit dose blister of 100 NDC 0009-7386-04

DOSAGE AND ADMINISTRATION

- Do not exceed 3200 mg total daily dose. If gastrointestinal complaints occur, administer MOTRIN Tablets with meals or milk.

Rheumatoid arthritis and osteoarthritis, including flare-ups of chronic disease:

- Suggested Dosage: 1200 mg-3200 mg daily (300 mg qid; 400 mg, 600 mg or 800 mg tid or qid) Individual patients may show a better response to 3200 mg daily, as compared with 2400 mg, although in well-controlled clinical trials patients on 3200 mg did not show a better mean response in terms of efficacy. Therefore, when treating patients with 3200 mg/day, the physician should observe sufficient increased clinical benefits to offset potential increased risk.

- The dose should be tailored to each patient, and may be lowered or raised depending on the severity of symptoms either at time of initiating drug therapy or as the patient responds or fails to respond.

- In general, patients with rheumatoid arthritis seem to require higher doses of MOTRIN than do patients with osteoarthritis.

- The smallest dose of MOTRIN that yields acceptable control should be employed. A linear blood level dose-response relationship exists with single doses up to 800 mg (See CLINICAL PHARMACOLOGY for effects of food on rate of absorption).

- The availability of four tablet strengths facilitates dosage adjustment.

- In chronic conditions, a therapeutic response to therapy with MOTRIN is sometimes seen in a few days to a week but most often is not achieved for at least 3 to 4 weeks. After a satisfactory response has been achieved, the patient’s dose should be reviewed and adjusted as required.

- Mild to moderate pain: 400 mg every 4 to 6 hours as necessary for relief of pain.

- In controlled analgesic clinical trials, doses of MOTRIN greater than 400 mg were no more effective than the 400 mg dose.

  **Dysmenorrhea**: For the treatment of dysmenorrhea, beginning with the earliest onset of such pain, MOTRIN should be given in a dose of 400 mg every 4 hours as necessary for the relief of pain.

**GASTROINTESTINAL**

- Nausea*, epigastric pain*, diarrhea, abdominal distress, nausea and vomiting, indigestion, constipation, abdominal cramps or pain, fullness of GI tract (blunting and flattening)

**CENTRAL NERVOUS SYSTEM**

- Dizziness*, headache, nervousness

**DERMATOLOGIC**

- Rash* (including maculopapular type), pruritus

**SPECIAL SENSES**

- Tinnitus

**HEMATOLOGIC**

- Neutropenia, agranulocytosis, aplastic anemia, hemolytic anemia (sometimes Coombs positive), thrombocytopenia with or without purpura, eosinophilia, decreases in hemoglobin and hematocrit (see PRECAUTIONS)

**METABOLIC/ENDOCRINE**

- Decreased appetite

**CARdioVASCULAR**

- Edema, fluid retention (generally responds promptly to drug discontinuation) (see PRECAUTIONS)

**ALLERGIC**

- Syndrome of abdominal pain, fever, chills, nausea and vomiting, anaphylaxis, bronchospasm (see CONTRAINDICATIONS)

**REnal**

- Acute renal failure (see PRECAUTIONS), decreased creatinine clearance, polyuria, azotemia, cystitis, hematuria

**MISCELLANEOUS**

- Dry eyes and mouth, gingival ulcer, rhinitis

* Reactions occurring in 3% to 9% of patients treated with MOTRIN. (Those reactions occurring in less than 3% of the patients are unmarked.)

** Reactions are classified under "Probable Causal Relationship" (PCR) if there has been one positive rechallenge or if three or more cases occur which might be causally related. Reactions are classified under "Causal Relationship Unknown" if seven or more events have been reported but the criteria for PCR have not been met.