

## PRODUCT MONOGRAPH

### **Children's MOTRIN\* Suspension**

(Ibuprofen Oral Suspension McNEIL Std., 100 mg/5 mL)

### **Infant's MOTRIN\* Suspension Drops**

(Ibuprofen Oral Suspension McNEIL Std., 40 mg/mL)

### **Children's/Junior Strength MOTRIN\* Chewable Tablets**

(Ibuprofen Tablets McNEIL Std., 50 mg and 100 mg)

### **Junior Strength MOTRIN\* Caplets**

(Ibuprofen Tablets USP, 100 mg)

Analgesic/Antipyretic

McNeil Consumer Healthcare  
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N1K 1A5

Date of Preparation: December 12, 1996  
Date of Revision: August 28, 1998  
July 8, 1999  
June 7, 2000  
August 4, 2000  
October 12, 2000  
December 5, 2000  
January 26, 2001  
April 5, 2001  
June 7, 2001  
January 23, 2002  
April 24, 2003  
February 25, 2005  
June 29, 2005  
October 17, 2005  
March 22, 2006  
June 29, 2006

Control # 104799

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## Children's MOTRIN\*

### PART I: HEALTH PROFESSIONAL INFORMATION

#### SUMMARY PRODUCT INFORMATION

<b>Route of Administration</b>	<b>Dosage Form / Strength</b>	<b>Clinically Relevant Nonmedicinal Ingredients</b>
Oral	100 mg/5 mL ibuprofen oral suspension	None <i>For a complete listing see Dosage Forms, Composition and Packaging section.</i>
Oral	40 mg/mL ibuprofen oral suspension	None <i>For a complete listing see Dosage Forms, Composition and Packaging section.</i>
Oral	50 mg and 100 mg ibuprofen tablets	None <i>For a complete listing see Dosage Forms, Composition and Packaging section.</i>
Oral	100 mg ibuprofen caplets	None <i>For a complete listing see Dosage Forms, Composition and Packaging section.</i>

#### INDICATIONS AND CLINICAL USE

Children's MOTRIN\* (ibuprofen) is indicated for:

- Temporary relief of minor aches and pains in muscles, bones and joints, headache, fever, the aches and fever due to the common cold or flu, immunizations, toothache (dental pain), sore throat, earache. (Arthritis Advisory Committee; 1983, Proceeding of Joint Meeting of Arthritis Drug Advisory Committee & Nonprescription Drug Advisory Committee; 1995)

#### CONTRAINDICATIONS

Children's MOTRIN\* (ibuprofen) should not be used in patients:

- who have previously exhibited hypersensitivity to it or in individuals who are known to have a sensitivity (manifested as asthma, bronchospasm, hypotension, angioedema, laryngeal edema, swelling, shock or urticaria) to acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (Arthritis Advisory Committee; 1983).

- with acute peptic ulcer or gastrointestinal bleeding.
- during pregnancy or in nursing mothers because its safety under these conditions has not been established.
- with Systemic Lupus Erythematosus as an anaphylaxis like reaction with fever may occur, particularly when ibuprofen has been administered previously. Aseptic meningitis has also been reported.
- who are children and are suffering from dehydration as a result of acute diarrhea, vomiting or lack of fluid intake

## **WARNINGS AND PRECAUTIONS**

### **General**

Several medical conditions which can predispose patients to the adverse effects of non-steroidal anti-inflammatory drugs in general may be applicable to ibuprofen.

Patients taking Children's MOTRIN\* should be cautioned to report to their physician unusual signs or symptoms which might be a manifestation of GI ulceration or bleeding, blurred vision or other ocular symptoms, skin rash, tinnitus, dizziness, weight gain, edema or respiratory difficulties.

Children's MOTRIN\* should be used with caution in patients with a history of cardiac failure or kidney disease because of the possibility of aggravating pre-existing states of fluid-retention or edema (Arthritis Advisory Committee; 1983). Mild impairment of renal function (decreased renal blood flow and glomerular filtration rate) can occur at maximal doses of ibuprofen. Renal papillary necrosis has been reported.

Also, patients with underlying medical or pharmacologically-induced hemostatic defects could also experience further prolongation of bleeding time through the inhibition of platelet aggregation induced to varying degrees by this class of drugs (Arthritis Advisory Committee; 1983).

Long-term ingestion of combinations of analgesics has been associated with the condition analgesic nephropathy. It is therefore appropriate that patients be discouraged from long-term unsupervised consumption of analgesics, particularly in combination. Patients should be directed to consult a physician if their underlying condition requires administration of Children's MOTRIN\* for more than 3 days for fever or 5 days for pain, nor should Children's MOTRIN\* usually be administered with acetaminophen or acetylsalicylic acid (Arthritis Advisory Committee; 1983).

A general precaution seems appropriate for patients with any serious medical condition to consult a physician before using Children's MOTRIN\* as an analgesic or antipyretic (Arthritis

Advisory Committee; 1983).

### **Carcinogenesis and Mutagenesis**

See Toxicology Section.

### **Cardiovascular**

Conditions such as congestive heart failure and hypertension may be aggravated by sodium retention and edema caused by ibuprofen in such patients.

### **Endocrine and Metabolism**

If Children's MOTRIN\* is taken in conjunction with prolonged corticosteroid therapy and it is decided to discontinue this therapy, the corticosteroid should be tapered slowly to avoid exacerbation of disease or adrenal insufficiency.

### **Gastrointestinal**

Gastrointestinal side effects to ibuprofen have been reported including dyspepsia, heartburn, nausea, vomiting, anorexia, diarrhea, constipation, stomatitis, flatulence, bloating, epigastric pain, abdominal pain, and peptic ulcer with GI bleeding or perforation which could have a fatal outcome (Arthritis Advisory Committee; 1983). Children's MOTRIN\* ibuprofen should therefore be given only under close supervision to patients with a history of upper gastrointestinal tract disease.

Occasionally serious gastrointestinal side effects have been associated with the anti-inflammatory uses of ibuprofen. Minor gastrointestinal complaints have also been reported during the clinical use of ibuprofen at analgesic doses. Therefore, if occasional and mild heartburn, upset stomach or stomach pain were to occur with its use, the administration of Children's MOTRIN\* with food or milk is recommended. Patients should be advised to seek the consultation of a physician if gastrointestinal side effects occur, persist or appear to worsen (Arthritis Advisory Committee; 1983).

### **Hematologic**

Children's MOTRIN\* ibuprofen, like other nonsteroidal anti-inflammatory agents, can inhibit platelet aggregation but the effect is quantitatively less than that seen with acetylsalicylic acid. Ibuprofen has been shown to prolong bleeding time (but within the normal range) in normal subjects. Because this prolonged bleeding effect may be exaggerated in patients with underlying haemostatis defects, Children's MOTRIN\* ibuprofen should be avoided by persons with intrinsic coagulation defects and by those on anticoagulant therapy.

### **Immune**

Anaphylactoid reactions have occurred after administration of ibuprofen to patients with known acetylsalicylic acid or other NSAID sensitivity manifested as asthma, swelling, shock or hives (Arthritis Advisory Committee; 1983).

### **Ophthalmologic**

Tinnitus, blurred and/or diminished vision, scotoma, and/or changes in colour vision have been reported. If a patient develops such complaints while taking Children's MOTRIN, the drug should be discontinued. Patients with any visual disturbances or eye complaints during therapy should have an ophthalmologic examination.

### **Renal**

Like other non-steroidal anti-inflammatory agents, ibuprofen inhibits renal prostaglandin synthesis which may decrease renal function and cause sodium retention.

Advanced age, hypertension, use of diuretics, diabetes, atherosclerotic cardiovascular disease, chronic renal failure, cirrhosis and conditions which may be associated with dehydration appear to increase the risk of renal toxicity. Children's MOTRIN\* should therefore be used with caution when these risk factors are present.

### **Respiratory**

Ibuprofen may elicit an asthma attack in individuals with a history of asthma, but who have no history of allergy or asthma induced by aspirin and other NSAIDs (Antonicelli & Tagliabracci; 1995, Ayres *et al.*; 1987, Friedlander *et al.*; 1994)

### **Special Populations**

#### **Pregnant Women:**

No evidence specifically identifies exposure to analgesic doses of ibuprofen as a cause of harm to either mother or fetus during pregnancy (Arthritis Advisory Committee, 1983; Barry *et al.*, 1984). Non-steroidal anti-inflammatory drugs in general, however, are known to affect the action of prostaglandin synthetase which could alter a variety of the physiological functions of prostaglandins or platelets during delivery such as facilitating uterine contraction in the mother, closure of the ductus arteriosus in the fetus, and platelet-related haemostasis. Patients should therefore be advised not to use Children's MOTRIN\* during pregnancy without the advice of a physician, particularly during the last trimester (Arthritis Advisory Committee; 1983). Clinical information is limited on the effects of ibuprofen in pregnancy.

**Nursing Women:** Pharmacokinetic studies indicated that following oral administration of ibuprofen 400 mg the level of drug which appeared in breast milk was below detection levels of 1 µg/mL. The amount of ibuprofen to which an infant would be exposed through this source was considered negligible (Albert & Gernaat; 1984). However, since the absolute safety of ibuprofen ingested under these circumstances has not been determined, nursing mothers should be advised to consult a physician before using Children's MOTRIN\* (Arthritis Advisory Committee; 1983).

**Geriatrics:** Although Children's MOTRIN\* is labelled specifically for children, particular caution should be observed should it be administered to elderly patients, as they are more likely to be taking other medications or have pre-existing disease states which can increase the likelihood of the complications that have been associated with ibuprofen. Elderly patients appear

to be more susceptible to the central nervous system disease reactions; cognitive dysfunction (forgetfulness, inability to concentrate, a feeling of separation from the surroundings) in such patients has been reported.

## **ADVERSE REACTIONS**

### **Adverse Drug Reaction Overview**

Experience reported with prescription use of ibuprofen has included the following adverse reactions. Note: Reactions listed below under Causal Relationship Unknown are those where a causal relationship could not be established; however, in these rarely reported events, the possibility of a relationship to ibuprofen also cannot be excluded. The adverse reactions most frequently seen with ibuprofen therapy involve the gastrointestinal system.

## Clinical Trial Adverse Drug Reactions

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

**Table 1 - Incidence of Adverse Events Attributed to Ibuprofen .**

Adverse Effect	Incidence 3-9%	Incidence 1-3%
Gastrointestinal	<ul style="list-style-type: none"> <li>▪ nausea</li> <li>▪ epigastric pain</li> <li>▪ heartburn</li> </ul>	<ul style="list-style-type: none"> <li>▪ diarrhea</li> <li>▪ abdominal distress</li> <li>▪ nausea and vomiting</li> <li>▪ indigestion</li> <li>▪ constipation</li> <li>▪ abdominal cramps and pain</li> <li>▪ gastrointestinal tract fullness (bloating or flatulence)</li> </ul>
Central Nervous System	<ul style="list-style-type: none"> <li>▪ dizziness</li> </ul>	<ul style="list-style-type: none"> <li>▪ headache</li> <li>▪ nervousness</li> </ul>
Dermatologic	<ul style="list-style-type: none"> <li>▪ rash (including maculopapular type)</li> </ul>	<ul style="list-style-type: none"> <li>▪ pruritis</li> </ul>
Special Senses		<ul style="list-style-type: none"> <li>▪ tinnitus</li> </ul>
Metabolic		<ul style="list-style-type: none"> <li>▪ decreased appetite</li> <li>▪ edema</li> <li>▪ fluid retention (generally responds promptly to drug discontinuation)</li> </ul>

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

Gastrointestinal: gastric or duodenal ulcer with bleeding and/or perforation, gastrointestinal hemorrhage, melena, hepatitis, jaundice, abnormal liver function (SGOT, serum bilirubin and alkaline phosphatase).

Central Nervous System: Depression, insomnia.

Dermatologic: vesiculobullous eruptions, urticaria, erythema multiforme.



Special Senses: amblyopia (blurred and/or diminished vision, scotomata and/or changes in colour vision).

Cardiovascular: congestive heart failure in patients with marginal cardiac function, elevated blood pressure.

Allergic: Anaphylaxis.

Hematologic: leukopenia and decreases in haemoglobin and hematocrit.

#### Reports with an Unknown Causal Relationship

Central Nervous System: paresthesias; hallucinations; dream abnormalities; aseptic meningitis has been reported in patients with systemic lupus erythematosus or other connective tissue disease; aseptic meningitis and meningioencephalitis, in one case accompanied by eosinophilia in the cerebrospinal fluids, has been reported in patients who took ibuprofen intermittently and did not have any connective tissue disease; cognitive dysfunction has been observed in elderly patients who took ibuprofen.

Dermatologic: alopecia, Stevens-Johnson Syndrome have been reported.

Special Senses: conjunctivitis, diplopia; optic neuritis.

Hematologic: hemolytic anemia; thrombocytopenia; granulocytopenia; bleeding episodes (e.g. purpura, epistaxis, hematuria, menorrhagia); auto-immune hematological anemia occurred in one patient taking 400 mg of ibuprofen three times a day for ten days; fatal aplastic anemia was reported in one patient who took 600 mg per day for 8 months.

Cardiovascular: arrhythmias (sinus tachycardia, sinus bradycardia, palpitations).

Allergic: fever, serum sickness, lupus erythematosus syndrome.

Endocrine: gynecomastia; hypoglycemic reaction; menstrual delays of up to two weeks and dysfunctional uterine bleeding; occurred in nine patients taking ibuprofen 400 mg three times a day for three days before menses.

Renal: decreased creatinine clearance, polyuria, azotemia.

#### Abnormal Hematologic and Clinical Chemistry Findings

Gastrointestinal: The generally modest elevations of serum transaminase activity that has been observed are usually without clinical sequelae but severe, potentially fatal toxic hepatitis can occur.

Renal: Renal blood flow glomerular filtration rate decreased in patients with mild impairment of

renal functions who took 1200 mg/day of ibuprofen for one week. Renal papillary necrosis has been reported. A number of factors appear to increase the risk of renal toxicity.

## **DRUG INTERACTIONS**

### **Overview**

Although ibuprofen binds to a significant extent to plasma proteins, interactions with other protein-bound drugs occur uncommonly. Nevertheless, caution should be observed when other drugs also having a high affinity for protein binding sites are used concurrently. Some observations have suggested a potential for ibuprofen to interact with digoxin, methotrexate, phenytoin and lithium salts. However, the mechanisms and clinical significance of these observations are presently not known

A general precaution is appropriate for patients to assure the compatibility of Children's MOTRIN\* with their other prescribed medications through consultation with a physician (Arthritis Advisory Committee; 1983).

### **Drug-Drug Interactions**

#### **Coumarin Type Anticoagulants**

Several short-term controlled studies failed to show that ibuprofen significantly affected prothrombin time or a variety of other clotting factors when administered to individuals on Coumarin-type anticoagulants. However, bleeding has been reported when ibuprofen and other NSAID agents have been administered to patients on Coumarin-type anticoagulants. The use of Children's MOTRIN\* in patients who are taking anticoagulants should therefore be avoided because of the possibility of enhanced GI bleeding or an additive effect due to ibuprofen's reversible anti-platelet action.

#### **Acetylsalicylic Acid**

Animal studies show that ASA given with NSAIDs, including ibuprofen, yields a net decrease in anti-inflammatory activity with lowered blood levels of the non-ASA drug. Single dose bioavailability studies in normal volunteers have failed to show an effect of ASA on ibuprofen blood levels. Correlative clinical studies have not been done.

Since there have been no controlled trials to demonstrate whether there is any beneficial or harmful interaction with use of ibuprofen in conjunction with ASA, the combination can not be recommended.

The platelet inhibiting effects of ibuprofen, although less potent and of shorter duration than those induced by acetylsalicylic acid, warrant cautionary supervision by a physician before co-administration of Children's MOTRIN\* and anti-coagulants.

#### **Other Anti-Inflammatory Agents (NSAIDs)**

The addition of Children's MOTRIN\* to a pre-existent prescribed NSAID regimen in patients with a condition such as rheumatoid arthritis may result in increased risk of adverse effects.

### Diuretics

Ibuprofen, because of its fluid retention properties, can decrease the diuretic and anti-hypertensive effects of diuretics, and increased diuretic dosage may be needed. Patients with impaired renal function taking potassium-sparing diuretics who develop ibuprofen-induced renal insufficiency might be in serious danger of fatal hyperkalemia.

### Acetaminophen

Although interactions have not been reported, concurrent use with Children's MOTRIN\* is not advisable.

## **DOSAGE AND ADMINISTRATION**

### **Recommended Dose and Dosage Adjustment**

#### Prescribed Dosage and Administration:

**Fever Reduction:** For reduction of fever in children up to 12 years of age, the dosage should be adjusted on the basis of the initial temperature level. The recommended dose is 5 mg/kg if the baseline temperature is less than 102.5°F (39.1°C) or 10 mg/kg if the baseline temperature is 102.5°F (39.1°F) or greater. The duration of fever reduction is generally 6 to 8 hours. The recommended maximum daily dose is 40 mg/kg.

**Analgesia:** For relief of mild to moderate pain in children up to 12 years of age, the recommended dosage is 10 mg/kg, every 6 to 8 hours. The recommended maximum daily dose is 40 mg/kg. Doses should be given so as not to disturb the child's sleep pattern.

**Individualization of Dosage:** The dose of Children's MOTRIN\* should be tailored to each patient, and may be lowered or raised from the suggested doses depending on the severity of symptoms either at the time of initiating drug therapy or as the patient responds or fails to respond.

Limited data suggests that, after the initial dose of Children's MOTRIN\*, subsequent doses may be lowered and still provide adequate fever control (McEnvoy; 1997). In a situation when lower fever would require the Children's MOTRIN\* 5 mg/kg dose in a child with pain, the dose that will effectively treat the predominant symptom should be chosen.

#### OTC Dosage and Administration

**Mild to Moderate pain or fever:** The OTC Dosing recommendation is based on a single dose of ibuprofen of approximately 7.5 mg/kg for either pain or fever.

**Adults:** MOTRIN\* brand of ibuprofen is available for adults in table/caplet/gelcap form. The equivalent adult dosage of Children's MOTRIN\* Suspension (100 mg/5 mL) is 200 – 400 mg (2 to 4 teaspoons or 10 – 20 mL) as required every 4 to 6 hours, not to exceed 1200 mg (12

teaspoons or 60 mL) in 24 hours unless directed by a physician.

Children: Children’s MOTRIN\* Ibuprofen

Age	Weight		Single Dose <sup>1</sup>			
	lbs.	kg	Suspension: 100 mg/5 mL	Infant’s Suspension Drops: 40 mg/mL	Tablets: 50 mg	Tablets/Caplets: 100 mg
0 to 3 mos**	6 to 11	2.5 to 5.4		Calculate based on weight and target dose 7.5 mg/kg 0.625 mL = 25 mg 1.25 mL = 50 mg		
4 to 11 mos*	12 to 17	5.5 to 7.9	½ tsp = 2.5 mL = 50 mg	1.25 ml = 50 mg		
12 to 23 mos*	18 to 23	8 to 10.9	¾ tsp = 3.75 mL = 75 mg	1.875 mL = 75 mg		
2 to 3 yrs	24 to 35	11 to 15.9	1 tsp = 5 mL = 100 mg		2 tablets = 100 mg	
4 to 5 yrs	36 to 47	16 to 21.9	1 ½ tsp = 7.5 mL = 150 mg		3 tablets = 150 mg	
6 to 8 yrs	48 to 59	22 to 26.9	2 tsp = 10 mL = 200 mg		4 tablets = 200 mg	2 tablets/caplets = 200 mg
9 to 10 yrs	60 to 71	27 to 31.9	2 ½ tsp = 12.5 mL = 250 mg		5 tablets = 250 mg	2 ½ tablets/caplets = 250 mg
11 yrs	72 to 95	32 to 43.9	3 tsp = 15 mL = 300 mg		6 tablets = 300 mg	3 tablets/caplets = 300 mg

<sup>1</sup> Single dose may be given every 6 to 8 hours as needed but do not exceed 4 doses per day unless advised by your doctor.

\* Only Infant’s MOTRIN\* Suspension Drops are labelled for children under 2 years of age. Consumer labelling for Children’s MOTRIN\* Suspension 100 mg/5 mL does not offer dosing for children under 2 years of age; therefore these doses are provided as a guide for professional recommendations to consumers.

\*\* Infant’s MOTRIN\* Suspension Drops 40 mg/mL are labelled “as directed by a doctor” for children under 4 months of age.

Do not take for fever for more than 3 days or pain for more than 5 days unless directed by a physician. If the painful area is red or swollen, if condition deteriorates or new symptoms occur, consult a physician.

**Administration**

Take with food or milk if mild upset stomach occurs with use.

**OVERDOSAGE**

Clinical Features

A clear pattern of clinical features associated with accidental or intentional overdose of ibuprofen has not been established. Reported cases of overdose have often been complicated by co-ingestions or additional suicidal gestures. The range of symptoms observed has included nausea, vomiting, abdominal pain, drowsiness, nystagmus, diplopia, headache, tinnitus, impaired renal function, coma and hypotension. A review of 4 fatalities associated with ibuprofen

overdose indicates other contributing factors co-existed so it would be difficult to identify the toxicity of ibuprofen as a specific cause of death. (Barry *et al.*; 1984, Court *et al.*; 1984).

Post-ingestion blood levels may be useful to confirm a diagnosis and to quantify the degree of exposure but otherwise have not been helpful in predicting clinical outcome. Generally, full recovery can be expected with appropriate symptomatic management.

The following cases of overdose have been reported: A 19 month old child, 1-1/2 hours after the ingestion of 7 to 10 X 400 mg tablets of ibuprofen presented apnea, cyanosis and responded only to painful stimuli. After treatment with O<sub>2</sub>, NaHCO<sub>3</sub>, infusion of dextrose and normal saline, the child was responsive and 12 hours after ingestion appeared completely recovered. Blood levels of ibuprofen reached 102.9 µg/mL, 8-1/2 hours after the accident. Two other children weighing approximately 10 kg, had taken an estimated 120 mg/kg. There were no signs of acute intoxication or late sequelae. In 1 child the ibuprofen blood level at 90 minutes after ingestion was approximately 700 µg/mL. A 19 year old male who ingested 8000 mg of ibuprofen reported dizziness and nystagmus was noted. He recovered with no reported sequelae after parenteral hydration and 3 days of bed rest.

#### Management of Overdose

General measures to reduce absorption such as gastric lavage, administration of activated charcoal or ipecac-induced emesis are appropriate particularly within 1 to 4 hours of ingestion. Routine symptomatic and supportive treatment is then recommended as follow-up (Court *et al.*; 1984).

## **ACTION AND CLINICAL PHARMACOLOGY**

### Mechanism of Action

The basic mechanism of the pharmacological actions of ibuprofen, like other NSAID's, has not been precisely determined. It is generally thought to be related to the inhibition of prostaglandin synthesis (Flower *et al.*; 1985).

### Pharmacodynamics

**Ibuprofen:** Ibuprofen is a member of the class of agents commonly known as non-steroidal anti-inflammatory drugs (NSAID). Consistent with this classification, ibuprofen exhibits anti-inflammatory activity at higher dosage ranges (Brooks *et al.*; 1973). At lower adult single doses (200 – 400 mg) relevant to the non-prescription analgesic/antipyretic indications and dosage strength, ibuprofen relieves pain of mild to moderate intensity (Cooper *et al.*; 1977, Gollardo & Rossi; 1980, Jain *et al.*; 1984, Vecchio *et al.*; 1983, Ihles; 1980) and reduces fever (Gaitonde *et al.*; 1973, Sheth *et al.*; 1973, Sheth *et al.*; 1980, Simila *et al.*; 1976). Clinical studies have also confirmed the analgesic (Bertin *et al.*; 1991, Schachtel & Thoden; 1993) and antipyretic (Walson *et al.*; 1989, Wilson *et al.*; 1991) effects of ibuprofen in children. Analogous to acetylsalicylic acid, the prototype of this class, this analgesic/antipyretic activity of ibuprofen occurs at lower doses than necessary for anti-inflammatory effects which are thought to require sustained

administration of higher individual doses (Flower *et al.*; 1985).

### **Pharmacokinetics**

**Absorption:** Ibuprofen is rapidly absorbed after oral administration with peak plasma levels usually occurring within 1 to 2 hours. Oral absorption is estimated to be 80% of the dose. Both the rate of ibuprofen absorption and peak plasma concentrations are reduced when the drug is taken with food, but, bioavailability as measured by total area under the concentration-time curve is minimally altered.

A single 200 mg oral dose study in 6 fasting healthy men produced a peak plasma concentration of 15.0 µg/mL at 0.75 hr (Adams *et al.*; 1967). Another study using a single oral 400 mg dose in humans produced a peak serum level of  $31.9 \pm 8.8$  µg/mL 0.5 hours after ingestion, and at 16 hours serum concentrations had dropped to 1 µg/mL (Kaiser & Martin; 1978). Comparable serum levels and time to peak within 1-2 hours were confirmed by other investigations with 200 mg and 400 mg solid doses (Kaiser & Vangiessen; 1974, Glass & Swannell; 1978). A multiple dose study of administration of a 200 mg ibuprofen tablet three times a day for 2 weeks showed no evidence of accumulation of ibuprofen (Mills *et al.*; 1973). As is true with most tablet and suspension formulations, Children's MOTRIN\* Suspension is absorbed somewhat faster than a tablet with a time to peak generally within one hour.

**Distribution:** Clinical studies indicate a duration of clinical effect for up to 8 hours. Ibuprofen like most drugs of its class, is highly protein bound (>99% bound at 20 µg/mL) (Mills *et al.*; 1973, Kober & Sjöholm; 1980). Based on oral dosing data there is an age- or fever-related change in volume of distribution for ibuprofen. Febrile children <11 years old have a volume of approximately 0.2 L/kg while adults have a volume of approximately 0.12 L/kg. The clinical significance of these findings is unknown (McEnvoy; 1997). Tissue distribution of ibuprofen is also extensive in humans. Studies comparing synovial fluid levels with serum concentrations indicated that equilibration time post-ingestion occurred within approximately 3 to 5 hours (Glass & Swannell; 1978).

**Metabolism:** Ibuprofen is rapidly metabolized through oxidation and glucuronic acid conjugation with urinary excretion of the inactive metabolites usually complete with 24 hours. In humans, ibuprofen is extensively metabolized with approximately 84% recoverable in the urine, primarily as conjugated hydroxyl- and carboxy- metabolites, with only approximately 1% excreted unchanged (Albert & Gernaat; 1984). Less than 10% is excreted unchanged in the urine (Albert & Gernaat; 1984). The 2 major metabolites of ibuprofen in humans have been found to have no activity in the ultraviolet erythema test in guinea pigs and in the acetylcholine-induced mouse writhing test at doses of 10 mg/kg and 15 mg/kg respectively (Adams, Cliffe *et al.*; 1969).

**Excretion:** Ibuprofen is rapidly metabolized and eliminated in the urine. The excretion of ibuprofen is virtually complete 24 hours after the last dose. It has a biphasic plasma elimination time curve with a half-life of approximately 2.0 hours. There is no difference in the observed terminal elimination rate or half-life between children and adults, however, there is an age- or fever-related change in total clearance (McEnvoy; 1997). This suggests that the observed

difference in clearance is due to differences in the volume of distribution of ibuprofen, as described above. The clinical relevance of these differences in clearance is unknown, although extensive clinical experience with ibuprofen in children at the pertinent dosage range (5 - 10 mg/kg) indicates a wide margin of safety.

### **Special Populations and Conditions**

**Pediatrics:** The pharmacokinetics of ibuprofen has also been studied in humans. Although there is little evidence of clinically significant age dependent kinetics in febrile children ages 3 months to 12 years (Kauffman *et al.*; 1989), some differences in the pharmacokinetic parameters of volume of distribution and clearance have been observed between adults and children (McEnvoy; 1997). Controlled clinical trials comparing doses between 5 and 10mg/kg of ibuprofen and 10-15 mg/kg of acetaminophen have been conducted in children 6 months to 12 years of age with fever primarily due to viral illnesses. In these studies, there were few differences between treatments in fever reduction in the first hour and maximum fever reduction occurred between 2 and 4 hours. There was some evidence that the higher dosage range of ibuprofen (10 mg/kg) resulted in a prolonged duration of effect (from 6 to 8 hours) and that it was more effective for children with higher baseline temperatures (above 102.5°F/39.1°C) but the numbers of patients were not adequate to draw definitive conclusions. In children with baseline temperatures at or below 102.5°F (39.1°C) both ibuprofen doses and acetaminophen were equally effective in their maximum effect.

**Geriatrics:** Studies demonstrate no significant alterations in ibuprofen pharmacokinetics in the elderly or in children (Albert *et al.*; 1984, Kauffman *et al.*; 1989).

**Hepatic Insufficiency:** Ibuprofen pharmacokinetics has also been studied in patients with alcoholic liver disease who have been assessed to have fair to poor hepatic function. Results suggest despite the liver being the primary organ of metabolism of ibuprofen, its kinetic parameters are not substantially altered by this condition (Juhl *et al.*; 1983).

### **STORAGE AND STABILITY**

Suspension/Suspension Drops: Store in tightly closed container at room temperature; 15°C to 30°C (59°F to 86°F). Avoid high humidity and excessive heat (40°C, 104°F).

Tablets/Caplets: Store at room temperature; 15°C to 30°C (59°F to 86°F).

### **SPECIAL HANDLING INSTRUCTIONS**

None.

## DOSAGE FORMS, COMPOSITION AND PACKAGING

Children's MOTRIN\* Suspension is available in Berry, Dye-Free Berry, Grape, Bubblegum and Tropical Punch flavours in bottles of 30 mL and 120 mL:

Medicinal Ingredient: 100 mg/5 mL ibuprofen

Non-Medicinal Ingredients:

### Berry Flavour

Acesulfame Potassium  
Citric Acid  
D&C Yellow no. 10  
FD&C Red No. 40  
Flavour  
Glycerin  
Hydroxy propyl distarch phosphate  
Polysorbate 80  
Purified Water  
Sodium Benzoate  
Sucrose  
Xanthan Gum

### Dye-Free Berry

Acesulfame Potassium  
Citric Acid  
Flavour  
Glycerin  
Hydroxy propyl distarch phosphate  
Polysorbate 80  
Purified Water  
Sodium Benzoate  
Sucrose  
Xanthan Gum

### Grape Flavour

Acesulfame Potassium  
Citric Acid  
D&C Red No. 33  
FD&C Blue No. 1  
FD&C Red No. 40  
Flavour  
Glycerin  
Hydroxy propyl distarch phosphate  
Polysorbate 80  
Purified Water  
Sodium Benzoate  
Sucrose  
Xanthan Gum

### Bubblegum Flavour

Acesulfame Potassium  
Citric Acid  
FD&C Red No. 40  
Flavour  
Glycerin  
Hydroxy propyl distarch phosphate  
Polysorbate 80  
Purified Water  
Sodium Benzoate  
Sucrose  
Xanthan Gum

### Tropical Punch Flavour

Acesulfame Potassium  
Citric Acid  
FD&C Red No. 40  
Flavour  
Glycerin  
Hydroxy propyl distarch phosphate  
Polysorbate 80  
Potassium Sorbate  
Purified Water  
Sodium Benzoate  
Sucralose  
Sucrose  
Xanthan Gum



Infant's MOTRIN\* Suspension Drops is available in Berry and Dye-free Berry flavours, in bottles of 7.5 mL, 15 mL and 30 mL:

Medicinal Ingredient: 40 mg/mL ibuprofen

Non-Medicinal Ingredients:

Berry Flavour

Citric Acid  
Corn Starch  
FD&C Red No. 40  
Flavour  
Glycerin  
Polysorbate 80  
Purified Water  
Sodium Benzoate  
Sorbitol  
Sucrose  
Xanthan Gum

Dye-free Berry Flavour

Citric Acid  
Corn Starch  
Flavour  
Glycerin  
Polysorbate 80  
Purified Water  
Sodium Benzoate  
Sorbitol  
Sucrose  
Xanthan Gum

Children's MOTRIN\* Chewable Tablets are available in Grape and Orange flavours, in bottles of 24. The orange flavour tablet is round, light orange in colour, having an orange odour. The grape flavour tablet is round, purple in colour, having a grape odour. The tablets are debossed with "MO" and "50" on one side and scored on the other side.

Junior Strength MOTRIN\* Chewable Tablets are available in Grape and Orange flavours, in bottles of 24. Junior Strength MOTRIN\* Chewable Tablets, Grape Flavour is also available in pouches of 2. The orange flavour tablet is round, light orange in colour, having an orange odour. The grape flavour tablet is round, purple in colour, having a grape odour. The tablets are debossed with "MO" and "100" on one side and scored on the other side.

Medicinal Ingredient:            50 mg ibuprofen/tablet (Children's MOTRIN\*)  
   100 mg ibuprofen/tablet (Junior Strength MOTRIN\*)

Non-Medicinal Ingredients (Children's MOTRIN\* Tablets and Junior Strength MOTRIN\* Tablets):

Grape Flavour

Acesulfame Potassium  
Aspartame  
Citric Acid  
D&C Red No. 7 calcium lake  
D&C Red No. 30 aluminum lake  
FD&C Blue No. 1 aluminum lake  
Flavour  
Fumaric acid  
Hydroxyethyl cellulose  
Hypromellose  
Magnesium Stearate  
Mannitol  
Microcrystalline cellulose  
Povidone  
Sodium lauryl sulphate  
Sodium starch glycolate

Orange Flavour

Acesulfame Potassium  
Aspartame  
Citric acid  
FD&C Yellow No. 6 aluminum lake  
Flavour  
Fumaric Acid  
Hydroxyethyl cellulose  
Hypromellose  
Magnesium stearate  
Mannitol  
Microcrystalline cellulose  
Povidone  
Sodium lauryl sulfate  
Sodium starch glycolate

Junior Strength MOTRIN\* Caplets are available in pouches of 2 and blisters of 8 or 16:

Medicinal Ingredient: 100 mg ibuprofen/tablet

Non-medicinal Ingredients: Carnauba wax  
Colloidal silicon dioxide  
Corn starch  
D&C Yellow No. 10  
FD&C Yellow No. 6  
Hypromellose  
Microcrystalline cellulose  
Pharmaceutical glaze  
Polydextrose  
Polyethylene glycol  
Pregelatinized starch  
Propylene glycol  
Sodium starch glycolate  
Titanium dioxide  
Triacetin

## PART II: SCIENTIFIC INFORMATION

### PHARMACEUTICAL INFORMATION

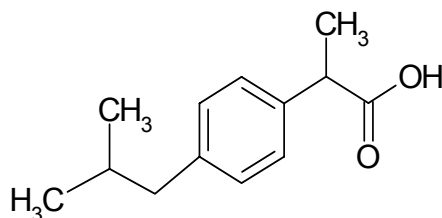
#### Drug Substance

Proper name: Ibuprofen

Chemical name: (±)-2-(p-isobutylphenyl) propionic acid

Molecular mass: 206.28

Structural formula:



Physicochemical properties:

- White crystalline powder with a characteristic odour and slight taste
- Very slightly soluble in water and very soluble in alcohol and other common organic solvents
- Apparent pKa 5.2.
- Melting point is 75°C to 75.5°C

## CLINICAL TRIALS

### Comparative Bioavailability Studies

#### Summary Table of the Comparative Bioavailability Data: Infant's MOTRIN\* Suspension Drops (40 mg/mL) – From Measured Data

Geometric Mean				
Arithmetic Mean (CV%)				
Parameter		Test 5 mL, 40 mg/mL (Fasted)	Reference <sup>†</sup> 10 mL, 20 mg/mL (fasted)	% Ratio of Geometric Means
AUC <sub>T</sub>	GM	71.4	68.9	104
(µg.h/mL)	AM	72.7 (19%)	70.0 (19%)	
AUC <sub>I</sub>	GM	72.9	70.2	104
(µg.h/mL)	AM	74.3 (19%)	71.3 (19%)	
AUC <sub>RefTmax</sub>	GM	9.8	10.1	97
(µg.h/mL)	AM	11.7 (63%)	11.5 (58%)	
C <sub>max</sub>	GM	23.6	21.4	110
(µg/mL)	AM	24.1 (21%)	21.9 (22%)	
T <sub>max</sub> (h)		1.0 (59%)	0.8 (46%)	
T <sub>½</sub> (h)		2.2 (46%)	2.2 (47%)	

The T<sub>max</sub> and T<sub>½</sub> parameters are expressed as the arithmetic means (SD) only.

<sup>†</sup> Original Childrens MOTRIN\* Ibuprofen Suspension marketed in Canada by McNeil Consumer Healthcare (1997)

**Summary Table of the Comparative Bioavailability Data: Children's MOTRIN\*  
Suspension (100 mg/5 mL) – From Measured Data**

Geometric Mean				
Arithmetic Mean (CV%)				
Parameter		Test <sup>‡</sup> 10 mL, 20 mg/mL (Fasted)	Reference <sup>†</sup> 10 mL, 20 mg/mL (fasted)	% Ratio of Geometric Means
AUC <sub>T</sub>	GM	68	64.9	105
(µg.h/mL)	AM	69.4 (22%)	66.4 (22%)	
AUC <sub>I</sub>	GM	68.9	65.8	105
(µg.h/mL)	AM	70.4 (22%)	67.3 (22%)	
AUC <sub>RefTmax</sub>	GM	8.34	7.71	108
(µg.h/mL)	AM	10.97 (78.9%)	9.52 (68.6%)	
C <sub>max</sub>	GM	22.3	20.4	109
(µg/mL)	AM	22.8 (21%)	21.0 (25%)	
T <sub>max</sub> (h)		0.53 (45%)	0.76 (60%)	
T <sub>½</sub> (h)		2.06 (17%)	2.08 (14%)	

The T<sub>max</sub> and T<sub>½</sub> parameters are expressed as the arithmetic means (SD) only.

<sup>†</sup> Original Childrens MOTRIN\* Ibuprofen Suspension marketed in Canada by McNeil Consumer Healthcare (1997)

<sup>‡</sup> Reformulated Children's MOTRIN\* Ibuprofen Suspension marketed in Canada by McNeil Consumer Healthcare (2000)

The results of a study to compare the bioavailability of Children's MOTRIN\* Chewable Tablets, 50 mg and Junior Strength MOTRIN\* Chewable Tablets, 100 mg to the original formulation of Children's MOTRIN\* Suspension are summarized in the following table.

**Summary Table of the Comparative Bioavailability Data: Children's/Junior Strength MOTRIN\* Ibuprofen Chewable Tablets (Total dose 200 mg) – From measured data**

Geometric Mean						
Arithmetic Mean (CV%)						
Parameter		Test A 2 x 100 mg (fasted)	Test B 4 x 50 mg (fasted)	Reference <sup>†</sup> 10 mL, 20 mg/mL (fasted)	% Ratio of Geometric Means	
					A:R	B:R
AUC <sub>T</sub>	GM	66.1	64.5	62.9	105	103
(µg.h/mL)	AM	67.3 (21%)	65.5 (20%)	64.1 (21%)		
AUC <sub>I</sub>	GM	67.2	66.7	63.8	105	105
(µg.h/mL)	AM	68.4 (21)	67.7 (19%)	65.1 (21%)		
C <sub>max</sub>	GM	17.6	16.4	21.2	83	77
(µg/mL)	AM	18.1 (24%)	16.7 (19%)	22 (29%)		
T <sub>max</sub> (h)		1.93 (32%)	1.95 (36%)	0.69 (63%)		
T <sub>½</sub> (h)		2.3 (36%)	2.5 (63%)	2.1 (15%)		

The T<sub>max</sub> and T<sub>½</sub> parameters are expressed as the arithmetic means (SD) only.

<sup>†</sup> Original Childrens MOTRIN\* Ibuprofen Suspension marketed in Canada by McNeil Consumer Healthcare (1997)

The results of a study to compare the bioavailability of reformulated Junior Strength MOTRIN\* Chewable Tablets, 100 mg and the original formulation of Junior Strength MOTRIN\* Chewable Tablets, 100 mg are summarized in the following table.

**Summary Table of the Comparative Bioavailability Data: Children's/Junior Strength MOTRIN\* Ibuprofen Chewable Tablets (Total dose 200 mg) – From Measured Data**

Geometric Mean			
Arithmetic Mean (CV%)			
Parameter	Test 5 mL, 40 mg/mL (Fasted)	Reference <sup>†</sup> 10 mL, 20 mg/mL (fasted)	% Ratio of Geometric Means
AUC <sub>T</sub> GM	67.1	68.5	97.96
(µg.h/mL) AM	68.7 (23)	70.0 (22)	
AUC <sub>I</sub> GM	70.4	71.6	98.32
(µg.h/mL) AM	72.4 (24)	73.5 (24)	
C <sub>max</sub> GM	15.5	16.8	92.26
(µg/mL) AM	15.9 (23)	17.1 (20)	
T <sub>max</sub> <sup>†</sup> (h)	2.8 (40)	2.2 (45)	
T <sub>½</sub> <sup>†</sup> (h)	1.9 (17)	1.9 (14)	

There were no adjustments made in pharmacokinetic parameters for drug content

The T<sub>max</sub> and T<sub>½</sub> parameters are expressed as the arithmetic means (CV%) only.

<sup>†</sup> Original Junior Strength MOTRIN\* Chewable Tablets marketed in Canada by McNeil Consumer Healthcare (2001)

**Clinical Trials:**

The efficacy of ibuprofen as an analgesic and antipyretic has been demonstrated by a variety of clinical studies and pain models.

**Dental Pain**

In adults, the effects of a drug on post-surgical dental extraction pain serves as a standard model for relief of pain of mild to moderate intensity. Ibuprofen 200 mg and 400 mg has been clearly demonstrated to provide pain relief significantly superior to placebo. When compared to the "standard" non-prescription analgesics, ibuprofen 200 mg is found to be comparable to ASA 650 mg (Cooper *et al.*; 1977, Cooper; 1984).

**Sore Throat or Ear Pain (Pediatric Models)**

In children 6-12 years, ibuprofen 10 mg/kg was found to be effective for the relief of pain using a sore throat model, both post-op sore throat (tonsillectomy) (Bertin *et al.*; 1991) and pharyngitis due to upper respiratory infection (Schachtel & Thoden; 1993).

Controlled clinical trials comparing doses of 5 and 10 mg/kg ibuprofen and 12.5 mg/kg acetaminophen have been conducted in children 5-12 years of age with sore throat pain believed due to an infectious agent or ear pain believed due to acute otitis media. All 3 active treatments provided significant pain relief versus placebo within 1 to 2 hours of administration and had a duration of action of up to 6 hours. There were no statistically significant differences among the



3 active treatments in the degree of maximum pain relief, although the trends favoured ibuprofen 10 mg/kg. Ibuprofen 5 mg/kg demonstrated pain relief comparable to acetaminophen 12.5 mg/kg. Ibuprofen 10 mg/kg demonstrated greater pain relief than acetaminophen 12.5 mg/kg from 3 to 6 hours after administration. A pediatric dosage schedule has been developed for Children's MOTRIN\* based on an ibuprofen dose of approximately 7.5 mg/kg body weight.

### Dysmenorrhea

Nonsteroidal anti-inflammatory drugs which inhibit prostaglandin synthesis such as ibuprofen, are particularly suitable for management of primary dysmenorrhea. Menstrual pain is now thought to result from abnormal uterine activity, which is secondary to increased production and release of endometrial prostaglandins at the time of menstruation.

Several adequate and well-controlled clinical trials provide substantial evidence of the safety and efficacy of ibuprofen at doses of 200 to 400 mg in relieving the pain of menstrual cramps (Molla & Donald; 1974, Shapiro & Diem; 1981, Gookin *et al.*; 1983).

A summary of trials of ibuprofen in the treatment of dysmenorrhea indicates the usual dose administered to be 400 mg. The few studies which are available at a 200 mg dosage indicate superiority of both ibuprofen 200 mg and 400 mg compared with ASA 650 mg (Dawood; 1984).

### Pain of Osteoarthritis

Several controlled clinical studies in adults provide substantial evidence of the safety and efficacy of ibuprofen at doses of 1200 mg or less per day in relieving the pain of osteoarthritis (Miller *et al.*; 1975, deBlecourt; 1975, Chahade *et al.*; 1976, Tylson & Glynne; 1980, Ruoff *et al.*; 1982). Collectively these studies support an indication for the temporary relief of minor pains of arthritis and, in conjunction with single dose analgesia studies, support the broader indication for the temporary relief of minor aches and pains.

### Headache

Ibuprofen has also been used satisfactorily in the management of headache. The efficacy of 200 mg of ibuprofen has been reported to be significantly superior to placebo and ASA 650 mg in the treatment of muscle contraction headaches (Vecchio *et al.*; 1983). No differences in the frequency of side effects were found in the treatment groups. Similar results were reported in a study with patients referred to a Headache Clinic with frequent muscle contraction headaches (Diamond; 1983).

### Soft Tissue Injury

Several studies also document the efficacy of analgesic doses of ibuprofen in the treatment of soft tissue injuries such as muscular aches or athletic injuries (Muckle; 1974, Naustion; 1973).

### Fever

Studies of its efficacy in the management of fever in adults and children demonstrate ibuprofen to be an effective antipyretic (Gaitonde *et al.*; 1973, Sheth *et al.*; 1980, Sinila *et al.*; 1976, Walson *et al.*; 1989, Wilson *et al.*; 1991), with a duration of action of up to 8 hours when administered at a dose of 7.5 mg/kg.

One controlled clinical trial comparing a single dose of ibuprofen 7.5 mg/kg with acetaminophen 12.5 mg/kg demonstrated the superiority of ibuprofen over an 8-hour period.

## DETAILED PHARMACOLOGY

### Ibuprofen

Several aspects of the pharmacokinetics of ibuprofen have been studied *in vivo* in rats, rabbits, dogs and baboons.

Studies in rats indicate that while limited absorption of ibuprofen occurs in the stomach, the principal site of absorption is the intestine. Single dose studies using C<sub>14</sub> labelled ibuprofen in rats, rabbits and dogs show rapid absorption rates (Adams, Bough *et al.*; 1969).

Tissue distribution studies performed in rats after both single and repeated doses of 20 mg/kg of C<sub>14</sub> labelled ibuprofen demonstrate broad distribution with accumulation of radioactivity in the thyroid, adrenals, ovaries, fat and skin. Transplacental passage of ibuprofen was also noted with similar plasma levels measured in both the pregnant rats and fetuses (Adams, Bough *et al.*; 1969).

Protein binding studies with plasma levels of 20 µg/mL indicate the percent bound in rats 96%, dogs 99%, baboons 95% and humans 99 (Mills *et al.*; 1973).

Four metabolites of ibuprofen have been found in the plasma of rabbits, 3 in rats, none in dogs, 2 in baboons and 2 in humans, with the liver suggested as the principal organ of metabolism (Adams, Bough *et al.*; 1969, Mills *et al.*; 1973). Excretion of metabolites was noted to varying degrees through both urine and feces indicating species variability in the bile and kidney excretion ratios.

While the mechanism of action of ibuprofen is not definitely known, it is generally believed to involve the inhibition of prostaglandin synthesis. Inhibition of prostaglandin biosynthesis prevents sensitization of tissues by prostaglandins to other inflammatory, pain and thermoregulatory mediators, hence accounting for the activity of ibuprofen and other nonsteroidal anti-inflammatory drugs against pain, inflammation and fever (Flower *et al.*; 1985).

Inhibition of prostaglandin synthesis by ibuprofen has been demonstrated in several different experimental models: bull seminal vesicle microsomes (Cushman & Cheung; 1976), stomach, duodenum, kidney and brain of the rat, (Fitzpatrick & Wynaida; 1976) microsomal preparations from rabbit brain and kidney medulla (Szczeklik *et al.*; 1976)

The analgesic efficacy of ibuprofen has been demonstrated in several animal models: phenylbenzoquinone-induced writhing in the mouse, acetylcholine-induced writhing in the mouse, the Randall-Selitto inflamed paw model in the rat, the mouse hot plate and adjuvant-induced arthritis model in the rat (Arparicio; 1977, Adams, Cliffe *et al.*; 1969, Romer; 1980).

The antipyretic activity of ibuprofen has been demonstrated in yeast-induced fever in rats (Arparicio; 1977, Adams, Cliffe *et al.*; 1969, Romer; 1980).

## MICROBIOLOGY

Not applicable.

## TOXICOLOGY

### Ibuprofen

Toxicity studies have been conducted using a variety of species, including: mice, rats, rabbits, guinea pigs and beagle dogs.

### Acute Toxicity Studies

Single-dose acute toxicity studies indicate that ibuprofen in lethal doses depresses the central nervous system of rodents and that large doses are ulcerogenic in both rodents and nonrodents. Ulcerogenesis may occur with both parenteral and oral administration indicating that the mechanism may have both a systemic as well as topical component.

Acute toxicity of ibuprofen in the rodent was studied in a number of models.

Single graded doses of ibuprofen were administered by oral intubation or by intraperitoneal or subcutaneous injection to groups of 10 male albino mice and male albino rats. Gross reactions were observed and mortalities recorded over a period of 14 days. The LD<sub>50</sub> values determined by this method were 800 mg/kg orally and 320 mg/kg intraperitoneally in the mouse and 1600 mg/kg orally and 1300 mg/kg subcutaneously in the rat. Acute signs of poisoning were prostration in mice, and sedation, prostration, loss of righting reflex and laboured respiration in rats. Death occurred within 3 days from perforated gastric ulcers in mice and intestinal ulceration in rats, irrespective of the route of administration (Adams & Bough *et al.*; 1969).

Similar LD<sub>50</sub> determinations in other strains of rats and mice are summarized in the table below.

### **Acute Toxicity in Rodents (LD<sub>50</sub>)**

Species	Route	LD <sub>50</sub> Range (mg/kg)
Albino Mice <sup>ab</sup>	Oral	800-1000
	Intraperitoneal	320
Albino Rats <sup>a</sup>	Oral	1600
	Subcutaneous	1300
Sprague Dawley Rat <sup>c</sup>		1050
Long Evans Rat <sup>d</sup>		1000

<sup>a</sup> Adams, Bough *et al.*, 1969

<sup>b</sup> Aparicio, 1977

<sup>c</sup> Fukawa *et al.*, 1982

<sup>d</sup> Cioli *et al.*, 1980

In a comparison of several non-steroidal anti-inflammatory drugs (NSAID) including ibuprofen,

male rats were sacrificed and the stomachs removed and examined for ulceration either 3 or 24 hours after oral administration of various single doses of ibuprofen (Atkinson & Leach; 1976). Using a standard scoring technique a mean score for each dosage group was calculated and the ulcerogenic potential was expressed as a minimum ulcerogenic dose. The minimum oral ulcerogenic dose for ibuprofen in rats was calculated to be 6-13 mg/kg.

Another group studied the production of gastrointestinal lesions in the rat comparing ulcerogenic doses of ibuprofen and other NSAIDs after oral or intravenous administration (Cioli *et al.*; 1980). Both male and female Long Evans rats were used in all experiments. Prior to drug administration the animals were fasted for 8 hours. After treatment they were fed a normal diet and sacrificed after 17 hours. Gastric and intestinal mucosa was examined for presence of ulcers. The ulcerogenic dose in 50% of treated animals (UD<sub>50</sub>) was calculated. The UD<sub>50</sub> following oral administration of ibuprofen was determined to be 70 mg/kg while for intravenous ibuprofen it was 210 mg/kg. The intestinal UD<sub>50</sub> was 88 mg/kg following oral and 172 mg/kg with intravenous administrations. A calculated "severity index" of gastric lesions was higher by the oral than the IV route at all doses tested.

Studies of the ulcerogenic potential of ibuprofen are summarized in the table below.

#### Single Dose Ulcerogenicity Studies in Rodents

Species	Route	UD <sub>50</sub> * (mg/kg)	MUD** (mg/kg)
Long Evans Rat <sup>a</sup>	Oral	70	50
	IV	210	-
Sprague Dawley Rat <sup>b</sup>	Oral	-	6-13

\*ulcerogenic dose in 50% treated animals

\*\*minimum ulcerogenic dose

<sup>a</sup>Cioli *et al.*, 1980

<sup>b</sup>Atkinson and Leach, 1976

Acute toxicity has also been studied in dogs.

Various single oral doses of ibuprofen were administered to dogs with subsequent hematologic examination and biochemical analyses of blood and urine, and examination of feces for occult blood (Adams, Bough *et al.*; 1969). Gross examination of the major organs occurred after the animals were sacrificed. No ill effects were seen following doses of 20 or 50 mg/kg. Oral doses of 125 mg/kg or greater produced emesis, scouring, albuminuria, fecal blood loss and erosions in the gastric antrum and pylorus.

Multiple dose ulcerogenicity studies of ibuprofen have also been conducted.

Rats were dosed by the oral route for a specific number of consecutive days, then sacrificed for examination. The ulcerogenic effect of oral ibuprofen was graded and reported by various scoring systems such as percent of animals in whom ulcers were produced by a specific dose, or the UD<sub>50</sub>.

In one typical such study, Long Evans rats were administered comparative NSAIDs orally once a

day for 5 days (Cioli *et al.*; 1980). The gastric and small intestinal mucosa were then examined for ulceration. The UD<sub>50</sub>, MUD and potency ratio of the drugs tested were calculated. The minimal ulcerogenic doses of ibuprofen were 25 mg/kg for the stomach and 50 mg/kg for the intestine.

Similar studies of multiple dose ulcerogenic potential of ibuprofen are summarized in the table below.

#### Multiple Oral Dose Toxicity Studies

Species	Daily Dose	Duration	Ulcerogenic Factor
Albino Rat <sup>a</sup>	400 mg/kg	30 hours	Ulcers in 100%
Albino Rat <sup>b</sup>		4 days	UD <sub>50</sub> = 455 mg/kg/day UD <sub>28</sub> = 240 mg/kg/day
Long Evans Rat <sup>c</sup>		5 days	MUD = 25 - 50 mg/kg/day
Sprague Dawley Rat <sup>d</sup>	5.8 - 225 mg/kg	10 days	None
Albino Rat <sup>e</sup>	7.5 mg/kg 180 mg/kg	26 weeks 26 weeks	None Ulcers in 20%
Dog <sup>e</sup>	4 mg/kg 8 mg/kg 16 mg/kg	30 days 30 days 30 days	None 100% 100%

<sup>a</sup>Parmer and Ghosh, 1981

<sup>b</sup>Aparicio, 1977

<sup>c</sup>Cioli *et al.*, 1980

<sup>d</sup>Paroli *et al.*, 1978

<sup>e</sup>Adams, Bough *et al.*, 1969

No other organ systems were generally noted to be significantly affected by these chronic administration studies. In one 30 day study (Dudkeiwicz; 1970), Wistar rats receiving 157 mg/kg/day ibuprofen had serum transaminase levels approximately double of those of a control, untreated group. Lower doses of ibuprofen in the same study had no significant effect on the activity of these enzymes.

Chronic toxicity studies in dogs demonstrated no gross or clinical signs of toxicity at 4, 8 or 16 mg/kg/day for 30 days (Adams, Bough *et al.*; 1969). However, in all dogs given 8 or 16 mg/kg/day, postmortem examination revealed gastric ulcers or erosions. No lesions were observed in dogs given 4 mg/kg/day.

A more complete assessment of chronic toxicity of ibuprofen in dogs studied the effects of administration of oral doses of 0, 2, 4 or 26 mg/kg/day over 26 weeks (Adams & Bough *et al.*; 1969). Periodic blood, urine and fecal sample analyses were performed. Histologic examination of selected organs and tissues was performed at the completion of the study. During the 26 week period, some reversible signs of gastrointestinal disturbance characterized by frequent vomiting, diarrhea, occasional passage of fresh blood and weight loss occurred in the 2 female dogs but not the males receiving 16 mg/kg ibuprofen. Occult blood was irregularly detected in fecal samples but urinalysis, liver function tests and other hematologic and blood biochemical values were not altered significantly. Gross examination of organs was normal except for ulcerative lesions in

the gastrointestinal tract of organs of all dogs receiving 16 mg/kg/day. Dogs given 2 and 4 mg/kg/day suffered no adverse reactions or gastrointestinal damage.

A study to evaluate the potential carcinogenic activity of ibuprofen involved administration of a minimum of 100 mg/kg/day to mice for 80 weeks and 60 mg/kg/day to rats for 2 years (Adams, Bough et al.; 1970). The proportion of animals with tumours of all types examined did not differ from those in the control group. The studies confirm that in the rat and mouse, ibuprofen does not induce tumours of the liver or other organs. Further, despite prolonged treatment, no other drug-induced hepatic lesions were seen in either species.

Teratogenicity studies of ibuprofen have been conducted in rabbits and rats (Adams, Bough *et al.*, 1969). Results of the experiments indicate that ibuprofen is not teratogenic when given in toxic doses to rabbits nor is there embryotoxic or teratogenic activity in pregnant rats even when administered in ulcerogenic doses.

Effects of ibuprofen on circular strips of fetal lamb ductus arteriosus indicate that exposure may produce contraction of the ductus (Coceani; 1979). Such an effect might be anticipated because of the known prostaglandin inhibiting properties of ibuprofen.

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**PART III: CONSUMER INFORMATION**  
**Children's MOTRIN\* Suspension**  
**(Ibuprofen Oral Suspension McNEIL Std., 100 mg/5 mL)**  
**Pain Reliever / Fever Reducer**  
**Up to 8 hour relief of fever.**

Only selected information is contained on the package label. This information is a summary and will not tell you everything about Children's MOTRIN\* Suspension. Contact your doctor or pharmacist if you have any questions about the drug.

**ABOUT THIS MEDICATION**

**What the medication is used for:**

The effective, temporary relief of:

- Fever
- and temporary relief of the minor aches and pains due to:
- Sore throat
  - Earache
  - Colds
  - Flu
  - Headache
  - Toothache
  - Immunization
  - Body aches, sprains and strains

**What it does:**

Ibuprofen is a member of a class of drugs called non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs work within the body by blocking the production of substances called prostaglandins, which are involved in the development of pain and inflammation.

**When it should not be used:**

You should not use Children's MOTRIN\* Suspension if:

- your child is taking ibuprofen, acetylsalicylic acid (ASA) or other pain or fever medication
- your child is oversensitive to one of the ingredients (symptoms include

facial or throat swelling, shortness of breath, low blood pressure)

- your child has peptic ulcers or gastrointestinal bleeding (bleeding in the urine or stool)
- your child has Systemic lupus Erythmatosus
- your child is suffering from dehydration caused by diarrhea, vomiting or lack of fluid
- you are pregnant or nursing

**WARNINGS AND PRECAUTIONS**

**BEFORE giving Children's MOTRIN\* Suspension to your child, talk to your doctor or pharmacist if:**

- your child is dehydrated (significant fluid loss) due to continued vomiting, diarrhea or lack of fluid intake
- your child is suffering from stomach pain
- your child has peptic ulcers, high blood pressure, heart failure, serious kidney or liver disease, asthma, or is under a doctor's care for any other serious condition or are taking any other drug.
- your child has a history of gastrointestinal disease, blood clotting problems or taking an anticoagulant

Also, see to your doctor if:

- your child does not get any relief within 24 hours.
- redness or swelling is present in the painful area
- a sore throat is severe, lasts for more than 2 days or occurs with fever, headache, rash, nausea or vomiting.
- your child develops any vision problems (blurred or reduced vision, colour changes)
- any new symptoms appear

**INTERACTIONS WITH THIS MEDICATION**

Talk to your doctor if your child is taking coumarin-type anticoagulants, diuretics (water tablets), digoxin, methotrexate,

phenytoin, lithium salt, as some drug interaction could occur.

**SIDE EFFECTS AND WHAT TO DO ABOUT THEM**

If unusual symptoms or any of the following reactions develop during treatment stop use and see a doctor immediately:

- skin rash or itching, dizziness, any change in vision, ringing or buzzing in the ears, nausea or vomiting, abdominal pain or cramps, diarrhea or constipation, heartburn, bloating, fluid retention, indigestion, headache, decreased appetite

**SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM**

Symptom / effect		Talk with your doctor or pharmacist	
		Only if severe	In all cases
Common	Dizziness		✓
Uncommon	Blurred/reduced vision		✓
	Vision colour changes		✓
	Ringing in ears		✓
	Blood in urine or stool		✓
	Swelling of mouth, throat and extremities		✓
	Difficulty breathing		✓
	Abdominal pain	✓	
	Severe skin rash		✓
	Weight gain/fluid retention	✓	
	Bruising	✓	

This is not a complete list of side effects. For any unexpected side effects while taking Children’s MOTRIN\* Suspension, talk to your doctor or pharmacist.

**HOW TO STORE IT**

Store at room temperature, 15°C - 30°C (59°F to 86°F).

Keep this and all medication out of the reach of children.

Child resistant package.

**PROPER USE OF THIS MEDICATION**

Usual dose:

Shake suspension well before use. Use only the enclosed measuring cup or a measured teaspoon to dose this product. Do not use any other dosing device. Measure dose with the dosage cup provided and ensure the complete dose is taken.

For accurate dosing, follow the instructions carefully. Find the right dose on the chart. If possible, use weight to dose, otherwise use age.

Weight		Age Years	Single Oral Dose	
lbs.	kg		mL	tsp
Under 24	Under 11	Under 2	Use Infant’s MOTRIN* Suspension Drops	
24-35	11-15.9	2-3	5	1
36-47	16-21.9	4-5	7.5	1 ½
48-59	22-26.9	6-8	10	2
60-71	27-31.9	9-10	12.5	2 ½
72-95	32-43.9	11	15	3

Single dose may be repeated every 6 to 8 hours as needed. Do not exceed 4 doses of ibuprofen per day unless advised by a doctor.

Do not use for more than 3 days for fever or 5 days for pain unless directed by a doctor. While uncommon, if stomach upset occurs, Children’s MOTRIN\* Suspension can be given with food or milk. If stomach upset persists, talk to your doctor.

Pregnant and nursing women should talk to a doctor before taking any MOTRIN\* product.

Adults & children 12 years of age and older: MOTRIN\* IB brand is available in tablets, caplets or gelscaps. The equivalent adult dosage of Children’s MOTRIN\* Suspension is 200-400 mg (2-4 teaspoons or 10-20 mL) every 4 to 6 hours as needed, not to exceed 1200 mg (12 teaspoons or 60 mL) per day.

Overdose:

In case of accidental overdose, even if there are no symptoms, call a doctor or Poison Control centre at once.

**REPORTING SUSPECTED SIDE EFFECTS**

To monitor drug safety, Health Canada collects information on serious and unexpected effects of drugs . If you suspect you have had a serious or unexpected reaction to this drug you may notify Health Canada by:

toll-free telephone: 866-234-2345

toll-free fax 866-678-6789

By email: [cadrmp@hc-sc.gc.ca](mailto:cadrmp@hc-sc.gc.ca)

By regular mail:

National AR Centre

Marketed Health Products Safety and Effectiveness

Information Division

Marketed Health Products Directorate

Tunney's Pasture, AL 0701C

Ottawa ON K1A 0K9

*NOTE: Before contacting Health Canada, you should contact your physician or pharmacist.*

**MORE INFORMATION**

Product Monograph available to doctors, dentists and pharmacists.

? Contact McNeil Customer Healthcare at: 1-888-6MOTRIN (1-888-666-8746)

Last revised: October 4, 2005

### PART III: CONSUMER INFORMATION

**Infants' MOTRIN\* Suspension Drops**  
**(Ibuprofen Oral Suspension**  
**McNEIL Std., 40 mg/mL)**  
**Pain Reliever / Fever Reducer**  
**Up to 8 hour relief of fever.**

Only selected information is contained on the bottle label. This information is a summary and will not tell you everything about Infants' MOTRIN\* Suspension Drops. Contact your doctor or pharmacist if you have any questions about the drug.

#### ABOUT THIS MEDICATION

##### What the medication is used for:

The effective, temporary relief of:

- Fever
- and temporary relief of the minor aches and pains due to:
- Sore throat
  - Earache
  - Colds
  - Flu
  - Headache
  - Toothache
  - Immunization
  - Body aches, sprains and strains

##### What it does:

Ibuprofen is a member of a class of drugs called non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs work within the body by blocking the production of substances called prostaglandins, which are involved in the development of pain and inflammation.

##### When it should not be used:

You should not use Infants' MOTRIN\* Suspension Drops if:

- your child is taking ibuprofen, acetylsalicylic acid (ASA) or other pain or fever medication
- your child is oversensitive to one of the ingredients (symptoms include

facial or throat swelling, shortness of breath, low blood pressure)

- your child has peptic ulcers or gastrointestinal bleeding (bleeding in the urine or stool)
- your child has Systemic lupus Erythmatosus
- your child is suffering from dehydration caused by diarrhea, vomiting or lack of fluid
- you are pregnant or nursing

#### WARNINGS AND PRECAUTIONS

**BEFORE** giving Infant's MOTRIN\* Suspension Drops to your child, talk to your doctor or pharmacist if:

- your child is dehydrated (significant fluid loss) due to continued vomiting, diarrhea or lack of fluid intake
- your child is suffering from stomach pain
- your child has asthma, or is under a doctor's care for any other serious condition or is taking any other drug
- your child has a history of gastrointestinal disease, blood clotting problems, or taking an anticoagulant.

Also, see to your doctor if:

- your child does not get any relief within 24 hours.
- redness or swelling is present in the painful area
- a sore throat is severe, lasts for more than 2 days or occurs with fever, headache, rash, nausea or vomiting.
- your child develops any vision problems (blurred or reduced vision, colour changes)
- any new symptoms appear

#### INTERACTIONS WITH THIS MEDICATION

Talk to your doctor if your child is taking coumarin-type anticoagulants, diuretics (water tablets), digoxin, methotrexate, phenytoin, lithium salt, as some drug interaction could occur.

**SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM**

**PROPER USE OF THIS MEDICATION**

Usual dose:

Shake suspension well before use.

Infant's MOTRIN\* concentrated drops are not the same concentration as Children's MOTRIN\* Suspension. Measure dose with oral syringe provided and ensure the complete dose is taken. Oral syringe should be rinsed and dried between uses. Replace child-resistant cap after each use. For accurate dosing, only use the enclosed oral syringe and follow the instructions carefully. If possible, dose according to body weight.

Weight		Age	Single Oral Dose
lbs.	kg	Months	mL
Under 12	Under 5.5	Under 4	As directed by a doctor
12-17	5.5-7.9	4-11	1.25
18-23	8-10.9	12-23	1.875

Single dose may be repeated every 6 to 8 hours as needed. Do not exceed 4 doses of ibuprofen per day unless advised by a doctor.

Do not use for more than 3 days for fever or 5 days for pain unless directed by a doctor. While uncommon, if stomach upset occurs, Infant's MOTRIN\* Suspension Drops can be given with food or milk. If stomach upset persists, talk to your doctor.

Overdose:

In case of accidental overdose, even if there are no symptoms, call a doctor or Poison Control centre at once.

**SIDE EFFECTS AND WHAT TO DO ABOUT THEM**

If unusual symptoms or any of the following reactions develop during treatment stop use and see a doctor immediately:

- skin rash or itching, dizziness, any change in vision, ringing or buzzing in the ears, nausea or vomiting, abdominal pain or cramps, diarrhea or constipation, heartburn, bloating, fluid retention, indigestion, headache, decreased appetite.

Symptom / effect		Talk with your doctor or pharmacist	
		Only if severe	In all cases
Common	Dizziness		✓
Uncommon	Blurred/reduced vision		✓
	Vision colour changes		✓
	Ringing in ears		✓
	Blood in urine or stool		✓
	Swelling of mouth, throat and extremities		✓
	Difficulty breathing		✓
	Abdominal pain	✓	
	Severe skin rash		✓
	Weight gain/fluid retention	✓	
	Bruising	✓	

This is not a complete list of side effects. For any unexpected side effects while taking Infants' MOTRIN\* Suspension Drops, talk to your doctor or pharmacist.

**HOW TO STORE IT**

Store at room temperature, 15°C - 30°C (59°F to 86°F).

Keep this and all medication out of the reach of children.

Child resistant package.



**REPORTING SUSPECTED SIDE EFFECTS**

To monitor drug safety, Health Canada collects information on serious and unexpected effects of drugs . If you suspect you have had a serious or unexpected reaction to this drug you may notify Health Canada by:

toll-free telephone: 866-234-2345

toll-free fax 866-678-6789

By email: [cadrmp@hc-sc.gc.ca](mailto:cadrmp@hc-sc.gc.ca)

By regular mail:

National AR Centre

Marketed Health Products Safety and Effectiveness

Information Division

Marketed Health Products Directorate

Tunney's Pasture, AL 0701C

Ottawa ON K1A 0K9

*NOTE: Before contacting Health Canada, you should contact your physician or pharmacist.*

**MORE INFORMATION**

Product Monograph available to doctors, dentists and pharmacists.

? Contact McNeil Customer Healthcare at: 1-888-6MOTRIN (1-888-666-8746)

Last revised: October 4, 2005

### PART III: CONSUMER INFORMATION

Children's MOTRIN\* Chewable Tablets  
(Ibuprofen Tablets McNEIL Std., 50 mg)  
Pain Reliever / Fever Reducer  
Up to 8 hour relief of fever.

Only selected information is contained on the package label. This information is a summary and will not tell you everything about Children's MOTRIN\* Chewable Tablets. Contact your doctor or pharmacist if you have any questions about the drug.

#### ABOUT THIS MEDICATION

**What the medication is used for:**  
The effective, temporary relief of:

- Fever
- and temporary relief of the minor aches and pains due to:
- Sore throat
  - Earache
  - Colds
  - Flu
  - Headache
  - Toothache
  - Immunization
  - Body aches, sprains and strains

**What it does:**

Ibuprofen is a member of a class of drugs called non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs work within the body by blocking the production of substances called prostaglandins, which are involved in the development of pain and inflammation.

**When it should not be used:**

You should not use Children's MOTRIN\* Chewable Tablets if:

- your child is taking ibuprofen, acetylsalicylic acid (ASA) or other pain or fever medication

- your child is oversensitive to one of the ingredients (symptoms include facial or throat swelling, shortness of breath, low blood pressure)
- your child has peptic ulcers or gastrointestinal bleeding (bleeding in the urine or stool)
- your child has Systemic lupus Erythmatosus
- your child is suffering from dehydration caused by diarrhea, vomiting or lack of fluid
- you are pregnant or nursing

#### WARNINGS AND PRECAUTIONS

**BEFORE** giving Children's MOTRIN\* Chewable Tablets to your child, talk to your doctor or pharmacist if:

- your child is dehydrated (significant fluid loss) due to continued vomiting, diarrhea or lack of fluid intake
- your child is suffering from stomach pain
- your child has peptic ulcers, high blood pressure, heart failure, serious kidney or liver disease, asthma, is under a doctor's care for any serious condition or is taking any other drug
- your child has a history of gastrointestinal disease, blood clotting problems or taking an anticoagulant

Also, see to your doctor if:

- your child does not get any relief within 24 hours.
- redness or swelling is present in the painful area
- a sore throat is severe, lasts for more than 2 days or occurs with fever, headache, rash, nausea or vomiting
- your child develops any vision problems (blurred or reduced vision, colour changes)
- any new symptoms appear

**Caution Phenylketonurics:** contains phenylalanine (aspartame)

**INTERACTIONS WITH THIS MEDICATION**

Talk to your doctor if your child is taking coumarin-type anticoagulants, diuretics (water tablets), digoxin, methotrexate, phenytoin, lithium salt, as some drug interaction could occur.

**PROPER USE OF THIS MEDICATION**

Usual dose:

For accurate dosing, follow the instructions carefully. Find the right dose on the chart. If possible, use weight to dose, otherwise use age.

Weight		Age	Single Oral Dose
lbs.	kg	Years	Tablets
Under 24	Under 11	Under 2	As directed by a doctor
24-35	11-15.9	2-3	2
36-47	16-21.9	4-5	3
48-59	22-26.9	6-8	4

Single dose may be repeated every 6 to 8 hours as needed. Do not exceed 4 doses of ibuprofen per day unless advised by a doctor.

Do not use for more than 3 days for fever or 5 days for pain unless directed by a doctor. While uncommon, if stomach upset occurs, Children’s MOTRIN\* Chewable Tablets can be given with food or milk. If stomach upset persists, talk to your doctor.

Overdose:

In case of accidental overdose, even if there are no symptoms, call a doctor or Poison Control centre at once.

**SIDE EFFECTS AND WHAT TO DO ABOUT THEM**

If unusual symptoms or any of the following reactions develop during treatment stop use and see a doctor immediately:

- skin rash or itching, dizziness, any change in vision, ringing or buzzing in the ears, nausea or vomiting, abdominal pain or cramps, diarrhea or constipation, heartburn, bloating, fluid retention, indigestion, headache, decreased appetite

**SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM**

Symptom / effect		Talk with your doctor or pharmacist	
		Only if severe	In all cases
Common	Dizziness		✓
Uncommon	Blurred/reduced vision		✓
	Vision colour changes		✓
	Ringing in ears		✓
	Blood in urine or stool		✓
	Swelling of mouth, throat and extremities		✓
	Difficulty breathing		✓
	Abdominal pain	✓	
	Severe skin rash		✓
Weight gain/fluid retention	✓		
	Bruising	✓	

This is not a complete list of side effects. For any unexpected side effects while taking Children’s MOTRIN\* Chewable Tablets, talk to your doctor or pharmacist.

**HOW TO STORE IT**

Store at room temperature, 15°C - 30°C (59°F to 86°F).

Keep this and all medication out of the reach of children.

Child resistant package.

**REPORTING SUSPECTED SIDE EFFECTS**

To monitor drug safety, Health Canada collects information on serious and unexpected effects of drugs . If you suspect you have had a serious or unexpected reaction to this drug you may notify Health Canada by:

toll-free telephone: 866-234-2345

toll-free fax 866-678-6789

By email: [cadrmpp@hc-sc.gc.ca](mailto:cadrmpp@hc-sc.gc.ca)

By regular mail:

National AR Centre

Marketed Health Products Safety and Effectiveness

Information Division

Marketed Health Products Directorate

Tunney's Pasture, AL 0701C

Ottawa ON K1A 0K9

*NOTE: Before contacting Health Canada, you should contact your physician or pharmacist.*

**MORE INFORMATION**

Product Monograph available to doctors, dentists and pharmacists.

? Contact McNeil Customer Healthcare at: 1-888-6MOTRIN (1-888-666-8746)

Last revised: October 4, 2005

**PART III: CONSUMER  
INFORMATION**

**Junior Strength MOTRIN\* Caplets  
(Ibuprofen Tablets USP, 100 mg)**

or

**Junior Strength MOTRIN\* Chewable  
Tablets**

**(Ibuprofen Tablets McNEIL Std., 100  
mg)**

**Pain Reliever / Fever Reducer  
Up to 8 hour relief of pain.**

Only selected information is contained on the package label. This information is a summary and will not tell you everything about Junior Strength MOTRIN\*. Contact your doctor or pharmacist if you have any questions about the drug.

**ABOUT THIS MEDICATION**

**What the medication is used for:**

The effective, temporary relief of:

- Fever
- and temporary relief of the minor aches and pains due to:
- Sore throat
  - Earache
  - Colds
  - Flu
  - Headache
  - Toothache
  - Immunization
  - Body aches, sprains and strains

**What is does:**

Ibuprofen is a member of a class of drugs called non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs work within the body by blocking the production of substances called prostaglandins, which are involved in the development of pain and inflammation.

**When it should not be used:**

You should not use Junior Strength MOTRIN\* if:

- your child is taking ibuprofen, acetylsalicylic acid (ASA) or other pain or fever medication
- your child is oversensitive to one of the ingredients (symptoms include facial or throat swelling, shortness of breath, low blood pressure)
- your child has peptic ulcers or gastrointestinal bleeding (bleeding in the urine or stool)
- your child has Systemic lupus Erythmatosus
- your child is suffering from dehydration caused by diarrhea, vomiting or lack of fluid
- you are pregnant or nursing

**WARNINGS AND PRECAUTIONS**

**BEFORE giving Junior Strength MOTRIN\* to your child, talk to your doctor or pharmacist if:**

- your child is dehydrated (significant fluid loss) due to continued vomiting, diarrhea or lack of fluid intake
- your child is suffering from stomach pain
- your child has peptic ulcers, high blood pressure, heart failure, serious kidney or liver disease, asthma, is under a doctor's care for any serious condition or is taking any other drug
- your child has a history of gastrointestinal disease, blood clotting problems or taking anticoagulants

Also, see to your doctor if:

- your child does not get any relief within 24 hours.
- redness or swelling is present in the painful area
- a sore throat is severe, lasts for more than 2 days or occurs with fever, headache, rash, nausea or vomiting.
- your child develops any vision problems (blurred or reduced vision, colour changes)
- any new symptoms appear

**Caution Phenylketonurics (*Chewable Tablets Only*): contains phenylalanine (aspartame).**

**INTERACTIONS WITH THIS MEDICATION**

Talk to your doctor if your child is taking coumarin-type anticoagulants, diuretics (water tablets), digoxin, methotrexate, phenytoin, lithium salt, as some drug interaction could occur.

**PROPER USE OF THIS MEDICATION**

Usual dose:

For accurate dosing, follow the instructions carefully. Find the right dose on the chart. If possible, use weight to dose, otherwise use age.

Weight		Age	Single Oral Dose
lbs.	kg	Years	Tablets/Caplets
48-59	22-26.9	6-8	2
60-71	27-31.9	9-10	2 ½
72-95	32-43.9	11	3

Single dose may be repeated every 6 to 8 hours as needed. Do not exceed 4 doses of ibuprofen per day unless advised by a doctor.

Do not use for more than 3 days for fever or 5 days for pain unless directed by a doctor. While uncommon, if stomach upset occurs, Junior Strength MOTRIN\* Tablets/Caplets can be given with food or milk. If stomach upset persists, talk to your doctor.

Overdose:

In case of accidental overdose, even if there are no symptoms, call a doctor or Poison Control centre at once.

**SIDE EFFECTS AND WHAT TO DO ABOUT THEM**

If unusual symptoms or any of the following reactions develop during treatment stop use and see a doctor immediately:

- skin rash or itching, dizziness, any change in vision, ringing or buzzing in the ears, nausea or vomiting, abdominal pain or cramps, diarrhea or constipation, heartburn, bloating, fluid retention, indigestion, headache, decreased appetite

**SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM**

Symptom / effect		Talk with your doctor or pharmacist	
		Only if severe	In all cases
Common	Dizziness		✓
Uncommon	Blurred/reduced vision		✓
	Vision colour changes		✓
	Ringing in ears		✓
	Blood in urine or stool		✓
	Swelling of mouth, throat and extremities		✓
	Difficulty breathing		✓
	Abdominal pain	✓	
	Severe skin rash		✓
	Weight gain/fluid retention	✓	
	Bruising	✓	

This is not a complete list of side effects. For any unexpected side effects while taking Junior Strength MOTRIN\*, talk to your doctor or pharmacist.

**HOW TO STORE IT**

Store at room temperature, 15°C - 30°C (59°F to 86°F).

Keep this and all medication out of the reach of children.

Child resistant package.

**REPORTING SUSPECTED SIDE EFFECTS**

To monitor drug safety, Health Canada collects information on serious and unexpected effects of drugs . If you suspect you have had a serious or unexpected reaction to this drug you may notify Health Canada by:

toll-free telephone: 866-234-2345

toll-free fax 866-678-6789

By email: [cadrmp@hc-sc.gc.ca](mailto:cadrmp@hc-sc.gc.ca)

By regular mail:

National AR Centre

Marketed Health Products Safety and Effectiveness

Information Division

Marketed Health Products Directorate

Tunney's Pasture, AL 0701C

Ottawa ON K1A 0K9

*NOTE: Before contacting Health Canada, you should contact your physician or pharmacist.*

**MORE INFORMATION**

Product Monograph available to doctors, dentists and pharmacists.

? Contact McNeil Customer Healthcare at: 1-888-6MOTRIN (1-888-666-8746)

Last revised: June 29, 2006