

ATTACHMENT 1

NOTICE

Our file number: 03-110926-952

Release of Draft Guidance Document: Guidance for Industry - Basic Product Monograph Information for Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

The above referenced draft guidance was released by Health Canada for consultation and is being posted on the Therapeutic Products Directorate Website¹ for information and comment.

This draft guidance document is an update of a previous guidance on the same subject that has been posted on the TPD Website since March 17, 1997. Since that time, several new NSAIDs belonging to the group of selective COX-II inhibitors have been approved in Canada and continuing postmarket experience has provided new information about NSAIDs, in general. Recognizing that the guidance document needed to be updated, TPD commissioned an external expert rheumatologist to prepare a revised draft guidance, which was then reviewed by an Expert Panel at a workshop on NSAIDs held on August 22-23, 2002. The Expert Panel's recommendations for revision were considered by a Working Group on NSAIDs with representation from TPD and the Marketed Health Products Directorate (MHPD) and a revised draft document was circulated within TPD for comment. The result of these deliberations is the above-referenced draft guidance that is being posted for comment.

It is also important to note that amendments to draft documents may occur as a result of regulatory consultations and subsequent deliberations within Health Canada.

Comments provided to Health Canada should be submitted no later than September 9, 2003 in order to allow sufficient time for their assessment.

Comments should be directed to

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¹ *As a PDF file format under Activites/Consultation*



DRAFT GUIDANCE FOR INDUSTRY
Basic Product Monograph Information for Nonsteroidal
Anti-Inflammatory Drugs (NSAIDs)

Published by authority of the
Minister of Health

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Health Products and Food Branch
Guidance Document

Our mission is to help the people of Canada maintain and improve their health.

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Également disponible en français sous le titre: Ébauche ligne directrice à l'intention de l'industrie: Information de base sur la monographie des anti-inflammatoires non stéroïdiens (AINS)

FOREWORD

Guidance documents are meant to provide assistance to industry and health care professionals on **how** to comply with the policies and governing statutes and regulations. They also serve to provide review and compliance guidance to staff, thereby ensuring that mandates are implemented in a fair, consistent and effective manner.

Guidance documents are administrative instruments not having force of law and, as such, allow for flexibility in approach. Alternate approaches to the principles and practices described in this document *may be* acceptable provided they are supported by adequate scientific justification. Alternate approaches should be discussed in advance with the relevant program area to avoid the possible finding that applicable statutory or regulatory requirements have not been met.

As a corollary to the above, it is equally important to note that Health Canada reserves the right to request information or material, or define conditions not specifically described in this guidance, in order to allow the Department to adequately assess the safety, efficacy or quality of a therapeutic product. Health Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

This document should be read in conjunction with the accompanying notice and the relevant sections of other applicable guidances.

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1. GENERAL BASIC GUIDANCES: PRODUCT MONOGRAPHS FOR NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs)

INTRODUCTION

These guidances are intended to harmonize and to update the prescribing information for nonsteroidal anti-inflammatory drugs (NSAIDs) indicated for controlling pain and inflammation associated with rheumatic diseases and other less severe conditions. Each product monograph is expected to contain objective, adequate and concise information on properties common to the active component and specific to the drug product. It should provide guidance on the safe and effective use of the drug, not only to the practitioner but also to the patient.

Appropriate information is required on chronic and short term use and on the effects of the drug in patient populations for which it is indicated.

Structure and organization of Product Monographs for nonsteroidal anti-inflammatory drugs (NSAIDs):

The title page should present:

- Description of the document i.e. Product Monograph or Prescribing Information.
- Name of the drug product.
- Generic name of the active ingredient.
- Pharmaceutical dosage form and dosage strength.
- Pharmacologic /Therapeutic classification.
- Name and address of the drug manufacturer.
- Submission number.
- Date of preparation and revision.

NAME OF THE DRUG

Give trade name, generic name, pharmaceutical dosage form and dosage strength.

PHARMACOLOGICAL/ THERAPEUTIC CLASSIFICATION

"Non-Steroidal Anti-inflammatory Drug".

Note: Description of additional properties may be added if authorized under the conditions of the NOC.

ACTIONS AND CLINICAL PHARMACOLOGY

Present concise and accurate disclosure of results of pharmacologic, pharmacokinetic, metabolic and bioavailability studies which could be of help to the prescriber. Data on therapeutic equivalence with acetylsalicylic acid (ASA) and other NSAIDs may be presented provided that these are found to be acceptable. Available data on pharmacokinetics in elderly and other special populations or diseases should be included as applicable.

Note: In Canada the name ASPIRIN is a registered trade name; its use should be restricted to data generated with that specific brand of drug product.

Clinical Studies:

Provide a description of the pivotal clinical studies that have been submitted for Regulatory approval and constitute the data that are the bases for the Indications for the drug. Special studies or studies in special populations designed to address specific aspects of the drug such as GI or cardiovascular safety would go in this location.

INDICATIONS AND CLINICAL USE

Indications:

Present concise and accurate claims which have met the requirements of the *Food and Drug Regulations*.

CONTRAINDICATIONS

The following are contraindications to the use of (Name of Drug):

Active gastric or duodenal ulcer, a history of recurrent ulceration, or active inflammatory disease of the gastrointestinal system.

This contraindication should remain even for the selective COX-II inhibitors because serious GI complications are reduced but not eliminated and small bowel adverse events are still a problem.

Known or suspected hypersensitivity to the drug or other non-steroidal anti-inflammatory drugs. The potential for cross-reactivity between different NSAIDs must be kept in mind.

(Name of the drug) should not be used in patients with the complete or partial syndrome of ASA-intolerance (rhinosinusitis, urticaria/angioedema, nasal polyps, asthma) in whom asthma, anaphylaxis, urticaria/angioedema, rhinitis or other allergic manifestations are precipitated by ASA or other nonsteroidal anti-inflammatory agents. Fatal anaphylactoid reactions have occurred in such individuals. As well, individuals with the above medical problems are at risk of a severe reaction even if they have taken NSAIDs in the past without any adverse effects.

Accumulating data on challenge studies with selective COX-II inhibitors in ASA-intolerant patients may result in modifications of this Contraindication

Significant hepatic impairment or active liver disease.

Severely impaired or deteriorating renal function (creatinine clearance <30 ml/min).

(Name of Drug) should not be used in the presence of known hyperkalemia (also see "Precautions" section under "Fluid and Electrolyte Balance").

Describe any other condition where the specified drug product or its active ingredient should not be used or where the use presents hazard(s) which outweigh anticipated benefit(s).

WARNINGS AND PRECAUTIONS

Gastrointestinal System (GI)

Serious GI toxicity, such as ulceration, perforation, obstruction and gastrointestinal bleeding, sometimes severe and occasionally fatal, can occur at any time, with or without symptoms in patients treated with nonsteroidal anti-inflammatory drugs (NSAIDs) including (Name of this drug).

GI symptoms, such as dyspepsia, are common, usually developing early in therapy. Health providers should remain alert for ulceration and bleeding in patients treated with non-steroidal anti-inflammatory drugs, even in the absence of previous GI tract symptoms.

In patients observed in clinical trials of such agents, symptomatic upper GI ulcers, gross bleeding, or perforation occur in approximately 1% of patients treated for 3-6 months and in about 2-4% of patients treated for one year. The risk continues beyond one year. The incidence of these complications is related to dose, past history of known ulcer disease, and advanced age (see Special Populations).

Add specific data for your NSAID on the risk of these GI adverse events. Include prevalence at 1 and 2 years and beyond if available and also prevalence according to the age of patients.

(Name of this drug) should be given under close medical supervision to patients with a history of ulcer of the upper gastrointestinal tract or inflammatory disease of the gastrointestinal tract such as ulcerative colitis and Crohn's disease. In these cases the health provider must weigh the benefits of treatment against the possible hazards.

Health providers should inform patients about the signs and symptoms of serious GI toxicity and instruct them to contact a health provider immediately if they experience persistent dyspepsia or other symptoms or signs suggestive of gastrointestinal ulceration or bleeding.

Because serious GI tract ulceration and bleeding can occur without warning symptoms, health providers should follow chronically treated patients and watch for the signs and symptoms of ulceration and bleeding and should inform the patients of the importance of this follow-up.

If ulceration is suspected or confirmed, or if GI bleeding occurs, (Name of Drug) should be discontinued immediately, appropriate treatment instituted and the patient monitored closely.

No studies, to date, have identified any group of patients *not* at risk of developing ulceration and bleeding. The major risk factors are a prior history of serious GI events and increasing age. Possible risk factors include *Helicobacter pylori* infection, excess alcohol intake, smoking, and concomitant oral steroids, anti-coagulants, anti-platelet agents (including ASA), or selective serotonin reuptake inhibitors (SSRIs).

Statement regarding experience with drug under consideration in above types of patients may be added if data addressing the issue are available from studies.

Please provide any other pertinent information including special GI studies performed with your drug.

Special Populations

- Use in the Elderly

Patients older than 65 years (hereafter referred to as older or elderly) and frail or debilitated patients are most susceptible to a variety of adverse reactions from nonsteroidal anti-inflammatory drugs (NSAIDs); the incidence of these adverse reactions increases with dose and duration of treatment. In addition, these patients are less tolerant

to ulceration and bleeding. Most reports of fatal GI events are in this population, especially those with cardiovascular disease. Older patients are also at risk of lower esophageal ulceration and bleeding.

For such patients, consideration should be given to a starting dose lower than the one usually recommended, with individual adjustment when necessary and under close supervision.

Additional statements outlining studies and experiences in the elderly SPECIFYING the exact numbers, ages, sex distribution and concurrent illnesses and drugs should be added. Specify if no experience with this drug exists in the elderly.

- Use in pregnancy, labour and lactation

NSAIDs have no consistent adverse effect in the first trimester of pregnancy. Until more is known about the safety of (Name of Drug), it should not be used during pregnancy. In the latter half of pregnancy, due to the diverse recorded and potential effects of NSAIDs such as premature closure of the ductus arteriosus and pulmonary hypertension or oligohydramnios, it is recommended that the use of these agents be avoided. If therapeutic use in pregnancy is required, the pregnancy should be managed by obstetricians or other health providers with particular expertise in high risk pregnancies.

Present additional information on safety and risks.

- Use in children (age 12 and under)

Present information on safety and risks.

Provide any additional warning statements which would be required for each specific drug product or its dosage form.

Renal Function

Long term administration of nonsteroidal anti-inflammatory drugs to animals has resulted in renal papillary necrosis and other abnormal renal pathology. In humans, there have been reports of acute interstitial nephritis with hematuria, proteinuria, and occasionally nephrotic syndrome.

A second form of renal toxicity has been seen in patients with pre-renal conditions leading to 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 non-steroidal anti-inflammatory drug may cause a dose dependent reduction in prostaglandin formation and may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function (Glomerular Filtration Rate (GFR) < 60 ml/min or 1 ml/sec), patients on salt restricted diets, those with congestive heart failure, cirrhosis, liver dysfunction, those taking diuretics, angiotensin-converting enzyme inhibitors, angiotensin-II receptor blockers, cyclosporin, ASA and the elderly. Serious or life-threatening renal failure has been reported in patients with normal or impaired renal function after short-term therapy with NSAIDs. Even patients at risk who demonstrate the ability to tolerate an NSAID under stable conditions may decompensate during periods of added stress, for example during states of fluid restriction as can occur during gastroenteritis. Discontinuation of nonsteroidal anti-inflammatory therapy is usually followed by recovery to the pretreatment state.

NSAIDs can increase the risk of hyperkalemia (see "Fluid and Electrolyte Balance"). In patients on dialysis, NSAIDs should be used with caution.

Please provide any other information including special renal studies performed with your drug.

Fluid and Electrolyte Balance

Fluid retention and edema have been observed in patients treated with (Name of Drug). Therefore, as with many other NSAIDs, the possibility of precipitating congestive heart failure in elderly patients or those with compromised cardiac function should be borne in mind. (Name of Drug) should be used with caution in patients with heart failure, hypertension or other conditions predisposing to fluid retention. Ask patients who are at risk for fluid retention to weigh themselves at regular intervals to assist in monitoring for fluid accumulation. With nonsteroidal anti-inflammatory treatment there is a potential risk of hyperkalemia, particularly in patients with conditions such as diabetes mellitus or renal failure; elderly patients; or in patients receiving concomitant therapy with angiotensin-II receptor antagonists, adrenergic blockers, angiotensin-converting enzyme inhibitors or some diuretics. Patients at risk should be monitored periodically during long-term therapy.

Please provide any other pertinent information.

Genitourinary Tract

Some NSAIDs are associated with persistent urinary symptoms (bladder pain, dysuria, urinary frequency), hematuria or cystitis. The onset of these symptoms may occur at any time after the initiation of therapy with an NSAID. Should urinary symptoms occur, in the absence of an alternate explanation, treatment with (Name of Drug) should be stopped to ascertain if symptoms disappear. This should be done before urological investigations or treatments are considered.

Hepatic Function

As with other nonsteroidal anti-inflammatory drugs, borderline elevations of one or more liver enzyme tests (AST, ALT, ALP) may occur in up to 15% of patients. These abnormalities may progress, may remain essentially unchanged, or may be transient with continued therapy.

If available, provide any specific data for your NSAID on the incidence of hepatic function abnormalities.

A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of a more severe hepatic reaction while on therapy with this drug. Severe hepatic reactions including jaundice and cases of fatal hepatitis have been reported with nonsteroidal anti-inflammatory drugs.

Although such reactions are rare, if abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop (e.g. jaundice), or if systemic manifestations occur (e.g. eosinophilia, associated with rash, etc.), this drug should be discontinued.

If there is a need to prescribe this drug in the presence of impaired liver function, it must be done under strict observation.

Hematology

Drugs inhibiting prostaglandin biosynthesis interfere with platelet function to varying degrees; therefore, patients who may be adversely affected by such an action, such as those on anticoagulants or suffering from hemophilia or platelet disorders should be carefully observed when (Name of Drug) is administered.

- Antiplatelet effects

Anti-platelet agents are used for the prevention of thrombosis or to reduce the risk of non-fatal myocardial infarction (MI), non-fatal cerebral thrombosis or embolism, and death in the following clinical situations: acute MI, secondary prevention following MI, patients with a history of transient ischemic attack(s), ischemic stroke, chronic stable angina, unstable angina or coronary artery disease. Whether anti-platelet agents confer significant benefit as primary prevention in low-risk patient populations remains unclear.

Anti-platelet agents are used to prevent thrombotic complications in patients undergoing procedures such as coronary angioplasty, coronary artery bypass or carotid endarterectomy. They are used to prevent thrombosis in patients with atrial fibrillation who cannot take warfarin.

(Name of Drug) and other NSAIDs have no proven efficacy as anti-platelet agents and cannot be used as a substitute for Acetylsalicylic Acid (ASA) or other antiplatelet agents under these conditions.

Concomitant administration of (Name of Drug) with low dose ASA increases the risk of GI ulceration and associated complications. If the two drugs must be used together, extra caution is warranted.

Provide any other pertinent information including ASA prophylaxis, interaction between low dose ASA and (Name of Drug) and any other interaction.

- Anticoagulants

Numerous studies have shown that the concomitant use of NSAIDs and anticoagulants increases the risk of GI adverse events, such as ulceration and bleeding. Concurrent therapy of (Name of Drug) with warfarin requires close monitoring of INR.

Even with therapeutic INR monitoring, increased bleeding may occur.

- Blood dyscrasias

Blood dyscrasias (such as neutropenia, leukopenia, thrombocytopenia, aplastic anemia and agranulocytosis) associated with the use of non-steroidal anti-inflammatory drugs are rare, but could occur with severe consequences.

Present any data available for your NSAID regarding the incidence of treatment-related thrombocytopenia, leukopenia, anemia, etc.

Cardiovascular Function

Some patients with pre-existing hypertension may develop worsening of blood pressure control when placed on an NSAID and regular monitoring of blood pressure should be performed under such circumstances. NSAIDs may exacerbate congestive heart failure.

Provide pertinent information on the issue of cardiovascular thrombotic events (myocardial infarction, sudden death, angina, stroke, transient ischemic attacks and peripheral venous and arterial thromboses).

Respiratory Disorders

ASA-induced asthma is an uncommon but very important indication of ASA and NSAID sensitivity. It occurs more frequently in patients with asthma who have nasal polyps.

Hypersensitivity Reactions

- **Cross-sensitivity:** Patients sensitive to any one of the nonsteroidal anti-inflammatory drugs may be sensitive to any of the other NSAIDs also.

- **ASA-Intolerance:** As with NSAIDs in general, some patients may experience urticaria and angioedema upon exposure to (Name of Drug). (Name of Drug) should not be given to patients with the complete or partial syndrome of ASA-intolerance (See Contraindications).

- **Serious Skin Reactions:** In rare cases, serious skin reactions such as Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis and erythema multiforme have been associated with the use of some NSAIDs. Because the rate of these reactions is low, they have usually been noted during post-marketing surveillance in patients taking other medications also associated with the potential development of these serious skin reactions. Thus, causality is not clear. These reactions are potentially life threatening but may be reversible if the causative agent is discontinued and appropriate treatment instituted. Patients should be advised that if they experience a skin rash they should discontinue their NSAID and contact their physician for assessment and advice, including which additional therapies to discontinue.

Provide pertinent information on the development of sulfonamide allergy, urticaria/angio-oedema, Steven's Johnson syndrome, toxic epidermal necrolysis and other serious skin reactions related to your product.

Central Nervous System

Some patients may experience drowsiness, dizziness, blurred vision, vertigo, tinnitus or hearing loss with the use of (Name of Drug). If patients experience these side effects, they should exercise caution in carrying out activities that require alertness.

Provide any specific information related to your product

- Aseptic Meningitis

In occasional rare cases, with some NSAIDs, the symptoms of aseptic meningitis (stiff neck, severe headaches, nausea and vomiting, fever or clouding of consciousness) have been observed. Patients with autoimmune disorders (systemic lupus erythematosus, mixed connective tissues diseases, etc.) seem to be pre-disposed. Therefore, in such patients, the health provider must be vigilant to the development of this complication.

Add any data from studies or other sources, including post-marketing surveillance, that exist.

Infection

In common with other anti-inflammatory drugs, (Name of Drug) may suppress fever.

Other Organ Systems

Provide pertinent information.

Information Health Providers should provide to Patients

Provide pertinent information.

Drug Interactions

List known interaction(s): _____ . Preface the specific comments below with a statement such as: "Caution is suggested when: (NAME OF DRUG) is used with (list of drugs of theoretical concern), because there is a potential for interaction.

- Acetylsalicylic acid (ASA) or other NSAIDs

The use of (Name of Drug) in addition to any other NSAID, including over the counter ones (such as ASA and ibuprofen) is not recommended because of the absence of any evidence demonstrating synergistic benefits and the potential for additive side effects.

Also, some NSAIDs may interfere with the anti-platelet effects of low dose ASA, possibly by competing with ASA for access to the active site of cyclooxygenase-I.

Provide any specific information for your product, including whether this potential interaction has been studied.

Provide any other pertinent information.

- Anti-Platelet Agents (including ASA): See WARNINGS AND PRECAUTIONS section on Hematology - Anti-platelet Effects.

- Anticoagulants: See WARNINGS AND PRECAUTIONS section on Hematology - Anticoagulants.

- Digoxin

Provide pertinent information.

- Oral hypoglycemics

Provide pertinent information.

- Anti-hypertensives

NSAIDs may diminish the antihypertensive effect of Angiotensin Converting Enzyme (ACE) inhibitors.

Combinations of ACE inhibitors, diuretics and NSAIDs might have an increased risk for acute renal failure and hyperkalemia. Blood pressure and kidney function should be monitored more closely in this situation, as occasionally there can be a substantial increase in blood pressure.

Provide any other pertinent information for your drug.

- Diuretics

Clinical studies as well as post-marketing observations have shown that NSAIDs can reduce the effect of diuretics.

Provide pertinent information for your drug.

- Glucocorticoids

Some studies have shown that the concomitant use of NSAIDs and oral glucocorticoids increases the risk of GI side effects such as ulceration and bleeding. This is especially the case in older (>65 years of age) individuals.

Provide any other pertinent information.

- Antacids

Provide pertinent information.

- Methotrexate

Provide pertinent information.

- Lithium

Monitoring of plasma lithium concentrations is advised when stopping or starting an NSAID, as increased lithium concentrations can occur.

Provide any other pertinent information.

- Oral Contraceptives

Provide pertinent information.

- Other Drug interactions

Provide pertinent information.

- Clinical Laboratory Tests

Provide pertinent information on effect of (NAME OF DRUG) on International Normalized Ratio (Prothrombin) (INR) and any other relevant information.

ADVERSE REACTIONS

Please organize presentation by disclosing the frequency of adverse events reported for this drug, drug product and dosage form. In an introductory statement give the extent of safety experience with your product.

Provide a general statement:

"The most common adverse reactions encountered with nonsteroidal anti-inflammatory drugs are gastrointestinal, of which gastric or duodenal ulcer, with or without bleeding, is the most severe. Fatalities have occurred, particularly in the elderly."

Provide the discontinuation rates due to the most common adverse reactions seen with your product.

List adverse events, their frequency and severity under the following headings. In addition, summarize the information in tabular format.

- **Gastrointestinal**
- **Allergic**
- **Central Nervous System**
- **Dermatologic**
- **Cardiovascular**
- **Special senses**
- **Hematologic**
- **Renal**
- **Hepatic**
- **Respiratory**
- **Other**

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Provide information. Mention if drug is dialysable.

DOSAGE AND ADMINISTRATION

Provide detailed and specific information. Mention when to give in relation to food.

Adults

Elderly and debilitated

Other age groups

Other special populations

Patient Monitoring Guidelines

Indications for Discontinuing Treatment

PHARMACEUTICAL INFORMATION

**Provide a detailed description as per current Therapeutic Products Directorate
Guidances for Product Monographs.**

AVAILABILITY and STORAGE

**Provide a detailed description as per current Therapeutic Products Directorate
Guidances for Product Monographs.**

INFORMATION TO THE PATIENT

Provide an appropriate text as per attached guidances.

PHARMACOLOGY

Describe.

CLINICAL PHARMACOLOGY

Describe. Include also bioavailability data.

TOXICOLOGY

Describe.

REPRODUCTION STUDIES

Describe effects of (NAME OF DRUG) and NSAIDs in general on conception and early pregnancy including statement to discuss these issues with your health provider when contemplating starting a family.

CARCINOGENICITY AND MUTAGENICITY

Describe.

OTHER SAFETY DATA

Identify and describe.

BIBLIOGRAPHY

- **Include: "Information Letter, Health Canada. Nonsteroidal Anti-inflammatory Drugs. DD-33; August 21, 1985."**
- **Please provide other relevant updated references.**
- **For quotations and listing use a system and abbreviations recommended by Index Medicus.**
- **Complete texts of references quoted should be available in the submission.**

2. BASIC MINIMUM INFORMATION FOR THE PATIENT TAKING NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs)

INTRODUCTION

These guidances are intended to serve as an update to the section on Information for the Patient in Product Monographs (PMs) for nonsteroidal anti-inflammatory drugs (NSAIDs) in order to provide guidance to patients on the safe and effective use of these drugs.

This product is approved for the control of pain and inflammation associated with arthritis. It may also be approved for other non-arthritic health problems such as fever and headache. In addition to the general information in this leaflet, it is expected manufacturers will add information specific to each drug product.

INFORMATION FOR THE PATIENT

Before you begin taking (Name of Drug), you should read this information carefully and keep it to read again as you need to. Your Pharmacist may also be able to give you more information about (Name of Drug). This leaflet does not take the place of careful discussions with your health providers (e.g. doctors, nurses, pharmacists, etc.) about the benefits and risks of (Name of Drug).

WHAT IS (Name of Drug)

(Name of Drug), which has been prescribed to you by your health provider, is one of a large group of non-steroidal anti-inflammatory drugs (also called NSAIDs) and is used to treat the symptoms of certain types of arthritis (**define other cleared indications**) and for certain short term conditions associated with inflammation and pain. NSAIDs help to relieve joint swelling and pain. If your health provider tells you to stop taking them temporarily for good reasons, you may feel more uncomfortable but it will not lead to an irreversible damaging effect.

Take (Name of Drug) only as prescribed by your health provider. Do not take more of it, do not take it more often and do not take it for a longer period of time than your health provider ordered. Taking too much of any medicine may increase the chance of unwanted side effects, especially if you are an elderly patient, you have other diseases and need to take other medications.

Be sure to take (Name of Drug) regularly as prescribed by your health provider. In some types of arthritis, up to two weeks may pass before you feel the benefits of this medicine. Your health provider may decide to change the amount you should take based on how you respond to the medication and according to side effects that you and your health provider are monitoring.

STOMACH UPSET IS ONE OF THE COMMON SIDE EFFECTS WITH NSAIDs.

If you get an upset stomach when taking (Name of Drug), try taking it with food or milk. To prevent irritation of the esophagus, do not take the medication immediately before lying down or going to bed. If such circumstances become necessary, take (Name of Drug) with a glass of water or milk, swallow several times, and remain upright for 20 to 30 minutes before lying down.

Provide any other specific and essential information for this drug product and its schedule of administration necessary for safe and effective use (eg. if it is an extended-release or delayed-release product, and whether or not the drug product can be crushed, chewed, or broken and if capsules can or cannot be emptied out).

Do not take ASA (acetylsalicylic acid), ASA-containing compounds, ibuprofen or other NSAIDs, or other drugs used to treat the symptoms of arthritis while taking (Name of Drug) unless told to do so by your health provider. Taking more than one NSAID will not work better to control your arthritis symptoms, except in a very few specific cases. However, you may take low dose ASA prescribed by your health provider to help reduce the chance of having heart attacks and strokes.

If your health provider prescribes this medication for you to use over a long period of time, your health provider should check your health during regular visits to ensure that this medicine is working and not causing you unwanted harm.

**BEFORE TAKING THIS MEDICATION TELL YOUR HEALTH PROVIDERS
(INCLUDING PHARMACISTS) IF YOU**

- are allergic to or have had a reaction to (Name of Drug) or other NSAIDs (such as ASA or ibuprofen). Any reaction, such as hives (urticaria, swelling of the throat or face (angioedema), the beginning or worsening of asthma, or sudden collapse (anaphylaxis) suggests severe allergy to this type of medication. You must not take (Name of Drug) if any of these things apply to you.
- have had asthma, nasal polyps, long-standing swelling of the sinus (chronic sinusitis) or long-standing hives (chronic urticaria). This increases your chance of having one of the above reactions. If any of these things apply to you, carefully talk about it with your health provider before taking (Name of Drug).
- have a history of stomach upset, stomach ulcers, bleeding from the stomach, stomach perforation, bowel problems, liver or kidney diseases;
- have blood or urine abnormalities;

- have high blood pressure, a history of stroke or mini-strokes, heart pain (angina), heart attack, heart failure or blocked artery in your heart;
- are pregnant or plan to get pregnant while taking this medication. (Name of Drug) should not be used in late pregnancy because it may harm the unborn baby.
- are breast feeding or plan to breast feed while taking this medication;
- are taking any other medication (either prescription or over-the-counter products) such as other NSAIDs, high blood pressure medications, blood thinners, prednisone, vitamins or herbal products;

list any other medications of particular importance to this drug product

- have any other medical problem(s) such as bleeding problems, liver problems, kidney problems, etc.

list any other diseases of particular importance to this drug product

- have trouble controlling your use of alcohol
- **List any other diseases of particular importance to this drug product.**

Provide any other warnings specific to your drug product.

A section on drug interactions should be provided.

WHILE TAKING THIS MEDICATION

- check with your health provider **immediately** if you experience unexpected weakness or if you vomit any blood or have black (looking like tar) or bloody stools; (*Position this information prominently.*)
- tell any other health provider, dentist or pharmacist that you talk to or see, that you are taking this medication;
- Be cautious when doing activities which require alertness.
- check with your health provider if you are not getting any relief from your arthritis or if any other problems with your health come up;

- report any unusual reactions to (Name of Drug) to your health provider. This is very important to do because it will help your health provider to catch and prevent future problems or side effects.
- check with your health provider **immediately** if you develop a skin rash, especially in combination with chills, fever, muscle aches or pains, or other flu-like symptoms. This is especially important if they happen shortly before, or together with, a skin rash. Very rarely, these side effects may be the first signs of a serious reaction to this medication;
- With mild decreases in kidney function the addition of (Name of Drug) can lead to more serious kidney failure. Loss of moisture in the body (dehydration), which may happen when the body is overheated due to too much physical activity or being out in the sun for a long period of time or when you have diarrhea, may cause a person's kidney to stop working fully. Consideration should be given to temporarily stopping the NSAID and consulting your health provider if you are suffering such added physical stress.

Provide any other comments specific to your drug product.

YOUR REGULAR MEDICAL CHECKUPS ARE ESSENTIAL.

SIDE EFFECTS OF THIS MEDICATION

Along with its beneficial effects, (Name of Drug) like other NSAIDs, may cause some undesirable reactions, especially when used for a long time or in large doses.

Elderly, frail or debilitated patients often seem to experience more frequent or more severe side effects.

Although not all of these side effects are common, when they do occur they may require medical attention.

CHECK WITH YOUR HEALTH PROVIDER IMMEDIATELY IF ANY OF THE FOLLOWING ARE NOTED

- bloody or black tarry stools (SUGGEST that you may be bleeding internally);
- shortness of breath, wheezing, any trouble in breathing, or tightness in the chest (SUGGEST that you may be having an attack of asthma, heart failure or a heart attack);
- skin rash, hives, swelling of the face or throat, or itching (SUGGEST an allergic-like reaction);
- vomiting or long-standing indigestion, nausea, stomach pain or diarrhea (SUGGEST stomach or intestinal problems);

- yellow discolouration of the skin or eyes (SUGGESTS possible liver problems);
- any major change in the amount of or colour of your urine (dark red or brown) (SUGGESTS possible kidney problems);
- swelling of the feet or lower legs, (SUGGESTS fluid retention and possible kidney or heart failure);
- unusual tiredness;

Provide any other side effects specific to your drug product.

Other side effects not listed above may also happen in some patients. If you notice any other side effects, check with your health provider.

DOSING

Provide dosing information for each approved indication and age group.

WHAT TO DO IF YOU MISS A DOSE

Provide information on what to do if a patient misses one or more doses.

STORAGE

Provide storage information (eg. where to store, such as cupboard or fridge).

(NAME OF DRUG) IS NOT RECOMMENDED FOR USE IN PATIENTS UNDER (provide age) YEARS OF AGE SINCE SAFETY AND EFFECTIVENESS HAVE NOT BEEN ESTABLISHED.

DO NOT KEEP OUTDATED MEDICINE OR MEDICINE NO LONGER NEEDED.

Return any unneeded medicine to a pharmacist.

KEEP OUT OF THE REACH OF CHILDREN.

THIS MEDICATION HAS BEEN PRESCRIBED FOR YOUR MEDICAL PROBLEM. DO NOT GIVE IT TO ANYONE ELSE.

ALWAYS REMEMBER, IF YOU REQUIRE MORE INFORMATION ON THIS DRUG, IF YOU THINK YOU ARE HAVING A SIDE EFFECT, OR IF YOU ARE UNCLEAR HOW TO TAKE THE DRUG, TALK TO YOUR HEALTH PROVIDER.