

NOTICE

Our file number: 06-125744-338

The final version of this Health Canada guidance document: **Basic Product Monograph Information for Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)** is now available. Comments and suggestions received from the consultation on the draft version of the guidance were reviewed and considered in the finalization of this document.

This document supercedes the 1997 policy: **Nonsteroidal Anti-inflammatory Group of Drugs (NSAIDs), Revision of the General Basic Guidelines for Product Monographs of and Basic Minimum Information for the Patient Taking** .

Since the posting of the previous guidance document on NSAIDs, several new products belonging to the NSAID sub-group of selective COX-2 inhibitors have been approved in Canada. Continuing post-market experience from this sub-group, and NSAIDs as a whole, have provided new safety information beyond that which was previously described in guidance. In light of this new safety information, that should be conveyed to health practitioners and their patients, Health Canada has developed this updated version of the previous guidance document on the same subject. This guidance is intended to help the pharmaceutical industry revise the content of the Product Monograph and associated labelling materials.

Sponsors will be required to revise their labelling in accordance with the complete guidance through the provision of a supplemental New Drug Submission as follows:

- Sponsors of products belonging to the sub-group of COX-2s, products that exhibit COX-2 properties, and NSAID products of the greatest use in Canada, will be contacted by Health Canada and requested to update to the complete guidance. At the time of this posting these products include, but are not limited to:
 - celecoxib
 - diclofenac
 - ibuprofen
 - indomethacin
 - meloxicam
 - naproxen
- All other sponsors will be required, with any subsequent filing, to revise the labelling of their NSAID products in accordance with the complete guidance.
- All new NSAIDs will be required to be in complete compliance with the guidance.

.../2

Depending on the market status of the Canadian Reference Product (CRP), sponsors of generic products may be permitted to update the labelling of their respective products immediately upon the finalization of the labelling for the CRP.

This and other Guidance documents are available on the website.

Should you have any questions regarding the content of the guidance, please contact

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GUIDANCE DOCUMENT

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

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Également disponible en français sous le titre : 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 governing statutes and regulations. Guidance documents also provide assistance to staff on how Health Canada mandates and objectives should be implemented in a manner that is fair, consistent and effective.

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 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 document, 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 guidance documents.

TABLE OF CONTENTS

| | | |
|----------|---|--------------------|
| 1 | INTRODUCTION | 1 |
| 1.1 | Purpose | 1 |
| 1.2 | Inquiries | 1 |
| 1.3 | Background | 1 |
| 1.4 | Using the Guidance Document | 2 |
| 2 | PRODUCT MONOGRAPH STYLE GUIDE | 2 |
| 3 | PART I: HEALTH PROFESSIONAL INFORMATION | 3 |
| 3.1 | Summary Product Information | 3 |
| 3.2 | Indications and Clinical Use | 3 |
| 3.2.1 | <i>Patient Subsets</i> | 3 |
| 3.2.1.1 | Geriatrics | 3 |
| 3.2.1.2 | Pediatrics | 4 |
| 3.3 | Contraindications | 4 |
| 3.4 | Warnings and Precautions | 6 |
| 3.4.1 | <i>General</i> | 7 |
| 3.4.2 | <i>Carcinogenesis and Mutagenesis</i> | 7 |
| 3.4.3 | <i>Cardiovascular</i> | 7 |
| 3.4.4 | <i>Endocrine and Metabolism</i> | 8 |
| 3.4.4.1 | Corticosteroids | 8 |
| 3.4.5 | <i>Gastrointestinal (GI)</i> | 8 |
| 3.4.6 | <i>Genitourinary</i> | 10 |
| 3.4.7 | <i>Hematologic</i> | 10 |
| 3.4.7.1 | Anti-coagulants | 10 |
| 3.4.7.2 | Anti-platelet Effects | 10 |
| 3.4.7.3 | Blood dyscrasias | 11 |
| 3.4.8 | <i>Hepatic / Biliary / Pancreatic</i> | 11 |
| 3.4.9 | <i>Hypersensitivity Reactions</i> | 12 |
| 3.4.9.1 | Anaphylactoid Reactions | 12 |
| 3.4.9.2 | ASA-Intolerance | 12 |
| 3.4.9.3 | Cross-sensitivity | 12 |
| 3.4.9.4 | Serious skin reactions | 12 |
| 3.4.10 | <i>Immune</i> | 12 |
| 3.4.11 | <i>Infection</i> | 13 |
| 3.4.11.1 | Aseptic Meningitis | 13 |
| 3.4.12 | <i>Neurologic</i> | 13 |
| 3.4.13 | <i>Ophthalmologic</i> | 13 |

| | | |
|----------|---|--------------------|
| 3.4.14 | <i>Peri-Operative Considerations</i> | 13 |
| 3.4.15 | <i>Psychiatric</i> | 13 |
| 3.4.16 | <i>Renal</i> | 14 |
| 3.4.16.1 | Advanced Renal Disease | 14 |
| 3.4.16.2 | Fluid and Electrolyte Balance | 14 |
| 3.4.17 | <i>Respiratory</i> | 15 |
| 3.4.18 | <i>Sexual Function / Reproduction</i> | 15 |
| 3.4.19 | <i>Skin</i> | 15 |
| 3.4.20 | <i>Special Populations</i> | 16 |
| 3.4.20.1 | Pregnant Women | 16 |
| 3.4.20.2 | Nursing Women | 16 |
| 3.4.20.3 | Pediatrics | 16 |
| 3.4.20.4 | Geriatrics | 16 |
| 3.4.21 | <i>Monitoring and Laboratory Tests</i> | 17 |
| 3.5 | <i>Adverse Reactions</i> | 17 |
| 3.5.1 | <i>Adverse Drug Reaction Overview</i> | 17 |
| 3.5.2 | <i>Clinical Trial Adverse Drug Reactions</i> | 17 |
| 3.5.3 | <i>Less Common Clinical Trial Adverse Drug Reactions</i> | 17 |
| 3.5.4 | <i>Abnormal Hematologic and Clinical Chemistry Findings</i> | 17 |
| 3.5.5 | <i>Post-market Adverse Drug Reactions</i> | 17 |
| 3.6 | <i>Drug Interactions</i> | 17 |
| 3.6.1 | <i>Serious Drug Interactions Box</i> | 17 |
| 3.6.2 | <i>Drug-Drug Interactions</i> | 18 |
| 3.6.2.1 | Acetylsalicylic acid (ASA) or other NSAIDs | 18 |
| 3.6.2.2 | Antacids | 18 |
| 3.6.2.3 | Anti-coagulants | 18 |
| 3.6.2.4 | Anti-hypertensives | 18 |
| 3.6.2.5 | Anti-platelet Agents (including ASA) | 19 |
| 3.6.2.6 | Cyclosporin | 19 |
| 3.6.2.7 | Digoxin | 19 |
| 3.6.2.8 | Diuretics | 19 |
| 3.6.2.9 | Glucocorticoids | 19 |
| 3.6.2.10 | Lithium | 19 |
| 3.6.2.11 | Methotrexate | 19 |
| 3.6.2.12 | Oral Contraceptives | 19 |
| 3.6.2.13 | Oral Hypoglycemics | 20 |
| 3.6.2.14 | Selective Serotonin Reuptake Inhibitors (SSRIs) | 20 |
| 3.6.2.15 | Tacrolimus | 20 |
| 3.6.3 | <i>Drug-Food Interactions</i> | 20 |

| | | |
|-------|---|--------------------|
| 3.6.4 | <i>Drug-Herb Interactions</i> | 20 |
| 3.6.5 | <i>Drug-Laboratory Test Interactions</i> | 20 |
| 3.6.6 | <i>Drug-Lifestyle Interactions</i> | 20 |
| 3.7 | Dosage and Administration | 20 |
| 3.7.1 | <i>Dosing Considerations</i> | 20 |
| 3.7.2 | <i>Recommended Dose and Dosage Adjustment</i> | 20 |
| 3.7.3 | <i>Missed Dose</i> | 20 |
| 3.7.4 | <i>Administration</i> | 20 |
| 3.8 | Overdosage | 21 |
| 3.9 | Action and Clinical Pharmacology | 21 |
| 3.9.1 | <i>Mechanism of Action</i> | 21 |
| 3.9.2 | <i>Pharmacokinetics</i> | 21 |
| 3.9.3 | <i>Pharmacodynamics</i> | 21 |
| 3.9.4 | <i>Special Populations and Conditions</i> | 21 |
| 3.10 | Storage and Stability | 21 |
| 3.11 | Special Handling Instructions | 21 |
| 3.12 | Dosage Forms, Composition and Packaging | 21 |
| 4 | PART II: SCIENTIFIC INFORMATION | 22 |
| 4.1 | Pharmaceutical Information | 22 |
| 4.2 | Clinical Trials | 22 |
| 4.3 | Detailed Pharmacology | 22 |
| 4.4 | Microbiology | 22 |
| 4.5 | Toxicology | 22 |
| 4.6 | References | 22 |
| 5 | PART III: CONSUMER INFORMATION | 22 |
| 5.1 | About this Medication | 23 |
| 5.2 | Warnings and Precautions | 24 |
| 5.3 | Interactions with this Medication | 26 |
| 5.4 | Proper Use of this Medication | 27 |
| 5.5 | Side Effects and What to Do about Them | 28 |
| 5.6 | How to Store It: | 30 |
| 5.7 | Reporting Suspected Side Effects | 30 |
| 5.8 | More Information | 30 |

1 INTRODUCTION

1.1 Purpose

This guidance is 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.

1.2 Inquiries

The Director's Office of the Bureau of Metabolism, Oncology and Reproductive Sciences can assist sponsors with questions concerning the preparation and filing of a draft product monograph or if further clarification is required (email: BMORS_enquiries@hc-sc.gc.ca.)

1.3 Background

Nonsteroidal anti-inflammatory drugs (NSAIDs) are used to relieve symptoms, including pain, associated with a variety of musculoskeletal disorders. Selective COX-2 inhibitor NSAIDs are a subclass of the "traditional" NSAIDs. Selective COX-2 inhibitor NSAIDs were first marketed in Canada in 1999 as an alternative to "traditional" NSAIDs, where aggressive marketing cited that fewer gastrointestinal adverse events occurred with their use, when compared to their traditional counterparts. Consequently, selective COX-2 inhibitor NSAIDs have become among the most commonly prescribed drugs in Canada.

In September 2004, Merck voluntarily withdrew Vioxx (rofecoxib) from the market due to concerns that its use resulted in an increased incidence of cardiovascular adverse events, namely myocardial infarction and stroke. In October 2004, scientific, medical and epidemiological experts at Health Canada initiated a comprehensive review of the cardiovascular safety of the COX-2-selective NSAIDs. In April 2005, Pfizer suspended sales of Bextra (valdecoxib), at Health Canada's request, due to concerns of an increased incidence of serious skin reactions, namely erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis. Additional concerns were raised regarding the use of Bextra in the peri-operative setting of coronary artery bypass graft (CABG) surgery as patients who took Bextra after this procedure were more likely to experience cardiovascular / thromboembolic events, deep surgical infections or sternal wound complications when compared with

those who did not take Bextra. External clinicians, epidemiologists, patient representatives and the public were consulted about the safety of selective COX-2 inhibitor NSAIDs at the COX-2 Public Forum and Expert Advisory Panel Meeting held in June 2005.

The NSAID Guidance Document has been updated to reflect the new findings for selective COX-2 inhibitor NSAIDs as well as recommendations from both internal and external experts about the safety of COX-2 selective NSAIDs, in particular, and the entire class of NSAIDs, in general. This guidance document is based on information available as of August 31, 2006. In preparing their Product Monographs, sponsors should also take into consideration any new information that has become available subsequent to this date.

1.4 Using the Guidance Document

The *Guidance for Industry: Basic Product Monograph Information for Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)* is divided into sections that reflect the structure and format of a Product Monograph. This guidance provides specific instructions for each section of the Product Monograph (PM) that needs to be updated in accordance with the NSAID Class Labelling Initiative. Additionally, references are made throughout this guidance to the related *Guidance for Industry: Product Monograph*, which came into effect on October 1, 2004. Instructions to sponsors for completion of the PM are indicated in italicized text and should not be included in the PM.

2 PRODUCT MONOGRAPH STYLE GUIDE

The product monograph consists of three distinct parts:

Part I: Health Professional Information

Contains information required for the safe and appropriate prescribing, dispensing and administering of the medication

Part II: Scientific Information

Contains more in-depth and complete scientific/research information.

Part III: Consumer Information

Contains information derived from Parts I and II written in lay language that helps the consumer understand what the medication is, how to use it, and what the potential side effects are.

For detailed Product Monograph style guidance, please see Section 2 of the *Guidance for Industry: Product Monograph* entitled “Preparing a standard Product Monograph”.

3 PART I: HEALTH PROFESSIONAL INFORMATION

3.1 Summary Product Information

Dosage form, strength, route of administration and a qualitative, alphabetical listing of clinically relevant nonmedicinal ingredients should be presented in a summary table at the beginning of the Product Monograph with a cross-reference to the complete listing in the Dosage Forms, Composition and Packaging section. Clinically relevant nonmedicinal ingredients may include the following (not an exhaustive list): ethanol, gluten, lactose, sulphite and tartrazine.

3.2 Indications and Clinical Use

(Brand Name of Drug) (proper name of drug) is indicated for the following:

Present concise and accurate claims which have met the requirements of the Food and Drug Regulations. This section should contain a point-form listing of the indications, followed by a brief discussion of any relevant clinical information.

Throughout this document, the term NSAIDs refers to both non-selective NSAIDs and selective COX-2 inhibitor NSAIDs, unless otherwise indicated.

For patients with an increased risk of developing CV and/or GI adverse events, other management strategies that do NOT include the use of NSAIDs should be considered first. (See Contraindications and Warnings and Precautions)

Use of (Brand Name of Drug) should be limited to the lowest effective dose for the shortest possible duration of treatment in order to minimize the potential risk for cardiovascular or gastrointestinal adverse events. (See Contraindications and Warnings and Precautions)

(Brand Name of Drug), as a NSAID, does NOT treat clinical disease or prevent its progression.

(Brand Name of Drug), as a NSAID, only relieves symptoms and decreases inflammation for as long as the patient continues to take it.

3.2.1 Patient Subsets

3.2.1.1 Geriatrics:

Evidence from clinical studies and postmarket experience suggests that use in the geriatric population is associated with differences in safety (See **Warnings and Precautions**). *Add a cross-reference to Clinical Trials, if applicable.*

3.2.1.2 Pediatrics:

Safety and efficacy have not been established in the pediatric population (*or provide pertinent information for your drug*).

3.3 Contraindications

(Brand Name of Drug) is contraindicated in:

- the peri-operative setting of coronary artery bypass graft surgery (CABG). Although (Brand Name of Drug) has NOT been studied in this patient population, a selective COX-2 inhibitor NSAID studied in such a setting has led to an increased incidence of cardiovascular/thromboembolic events, deep surgical infections and sternal wound complications.
- the third trimester of pregnancy, because of risk of premature closure of the ductus arteriosus and prolonged parturition
- women who are breastfeeding, because of the potential for serious adverse reactions in nursing infants
- severe uncontrolled heart failure
- known hypersensitivity to (proper name of drug) or to any of the components/excipients
- history of asthma, urticaria, or allergic-type reactions after taking ASA or other NSAIDs (i.e. complete or partial syndrome of ASA-intolerance - rhinosinusitis, urticaria/ angioedema, nasal polyps, asthma). Fatal anaphylactoid reactions have occurred in such individuals. 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 reaction. The potential for cross-reactivity between different NSAIDs must be kept in mind (see **Warnings and Precautions - Hypersensitivity Reactions - Anaphylactoid Reactions**).
- active gastric / duodenal / peptic ulcer, active GI bleeding.
(*This contraindication should remain even for the selective COX-2 inhibitor NSAIDs because serious GI complications are reduced but not eliminated and small bowel adverse events are still a problem.*)
- cerebrovascular bleeding or other bleeding disorders
- inflammatory bowel disease

- severe liver impairment or active liver disease
- severe renal impairment (creatinine clearance <30 mL/min or 0.5 mL/sec) or deteriorating renal disease (individuals with lesser degrees of renal impairment are at risk of deterioration of their renal function when prescribed NSAIDs and must be monitored) (see **Warnings and Precautions - Renal**)
- known hyperkalemia (see **Warnings and Precautions - Renal - Fluid and Electrolyte Balance**)
- children and adolescents less than (*provide age*) years of age

List any other condition(s) 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); e.g. demonstrated allergic-type reactions to sulfonamides, if applicable.

3.4 Warnings and Precautions

Provide the following statements enclosed within a black box as follows:

Risk of Cardiovascular (CV) Adverse Events: Ischemic Heart Disease, Cerebrovascular Disease, Congestive Heart Failure (NYHA II-IV)
(See Warnings and Precautions - Cardiovascular). Add a cross-reference to Clinical Trials, if applicable.

(Brand Name of Drug) is a non-steroidal anti-inflammatory drug (NSAID). Use of some NSAIDs is associated with an increased incidence of cardiovascular adverse events (such as myocardial infarction, stroke or thrombotic events) which can be fatal. The risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.

Caution should be exercised in prescribing (Brand Name of Drug) to any patient with ischemic heart disease (including but NOT limited to acute myocardial infarction, history of myocardial infarction and/or angina), cerebrovascular disease (including but NOT limited to stroke, cerebrovascular accident, transient ischemic attacks and/or amaurosis fugax) and/or congestive heart failure (NYHA II-IV).

Use of NSAIDs, such as (Brand Name of Drug), can promote sodium retention in a dose-dependent manner, through a renal mechanism, which can result in increased blood pressure and/or exacerbation of congestive heart failure. (see also Warnings and Precautions - Renal - Fluid and Electrolyte Balance)

Randomized clinical trials with (Brand Name of Drug) have not been designed to detect differences in cardiovascular events in a chronic setting. Therefore, caution should be exercised when prescribing (Brand Name of Drug).

Risk of Gastrointestinal (GI) Adverse Events (see Warnings and Precautions –Gastrointestinal) Add a cross-reference to Clinical Trials, if applicable.

Use of NSAIDs, such as (Brand Name of Drug), is associated with an increased incidence of gastrointestinal adverse events (such as peptic/duodenal ulceration, perforation, obstruction and gastrointestinal bleeding).

Other clinically significant or life-threatening safety hazards when taking the drug should be highlighted within a black box and immediately follow the above black boxed statements. Information for these serious warnings and precautions may be drawn from any section of the Product Monograph and will be determined in consultation with the sponsor and Health Canada.

3.4.1 *General:*

Frail or debilitated patients may tolerate side effects less well and therefore special care should be taken in treating this population. **To minimize the potential risk for an adverse event, the lowest effective dose should be used for the shortest possible duration.** As with other NSAIDs, caution should be used in the treatment of elderly patients who are more likely to be suffering from impaired renal, hepatic or cardiac function. For high risk patients, alternate therapies that do not involve NSAIDs should be considered.

(Brand Name of Drug) is NOT recommended for use with other NSAIDs, with the exception of low-dose ASA for cardiovascular prophylaxis, because of the absence of any evidence demonstrating synergistic benefits and the potential for additive adverse reactions. (See **Drug Interactions - Drug/Drug Interactions - Acetylsalicylic acid (ASA) or other NSAIDs**)

3.4.2 *Carcinogenesis and Mutagenesis:*

Include any human data if there is evidence that the drug is carcinogenic or mutagenic. Where there is only animal data, a cross reference to the **Toxicology** section should be provided.

3.4.3 *Cardiovascular:*

(Brand Name of Drug) is a non-steroidal anti-inflammatory drug (NSAID). Use of some NSAIDs is associated with an increased incidence of cardiovascular adverse events (such as myocardial infarction, stroke or thrombotic events) which can be fatal. The risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. (Provide a cross-reference to Clinical Trials, if applicable):

Caution should be exercised in prescribing (Brand Name of Drug) to patients with risk factors for cardiovascular disease, cerebrovascular disease or renal disease, such as any of the following (NOT an exhaustive list)

- **Hypertension**
- **Dyslipidemia / Hyperlipidemia**
- **Diabetes Mellitus**
- **Congestive Heart Failure (NYHA I)**
- **Coronary Artery Disease (Atherosclerosis)**
- **Peripheral Arterial Disease**
- **Smoking**
- **Creatinine Clearance < 60 mL/min or 1 mL/sec**

Use of NSAIDs, such as (Brand Name of Drug), can lead to new hypertension or can worsen pre-existing hypertension, either of which may increase the risk of cardiovascular events as described above. Thus blood pressure should be monitored regularly. Consideration should be given to discontinuing (Brand Name of Drug) should hypertension either develop or worsen with its use.

Use of NSAIDs, such as (Brand Name of Drug), can induce fluid retention and edema, and may exacerbate congestive heart failure, through a renally-mediated mechanism. (See **Warnings and Precautions - Renal - Fluid and Electrolyte Balance**).

For patients with a high risk of developing an adverse CV event, other management strategies that do NOT include the use of NSAIDs should be considered first. **To minimize the potential risk for an adverse CV event, the lowest effective dose should be used for the shortest possible duration.**

Provide pertinent product-specific information on cardiovascular thrombotic events including myocardial infarction, sudden death, angina, stroke, transient ischemic attacks and peripheral venous and arterial thromboses. Also provide similar information with respect to hypertension, peripheral edema and congestive heart failure.

3.4.4 Endocrine and Metabolism:

3.4.4.1 Corticosteroids:

(Brand Name of Drug) (proper name of drug) is NOT a substitute for corticosteroids. It does NOT treat corticosteroid insufficiency. Abrupt discontinuation of corticosteroids may lead to exacerbation of corticosteroid-responsive illness. Patients on prolonged corticosteroid therapy should have their therapy tapered slowly if a decision is made to discontinue corticosteroids. (see **Drug Interactions - Drug-Drug Interactions - Glucocorticoids**)

3.4.5 Gastrointestinal (GI):

Serious GI toxicity (sometimes fatal), such as peptic / duodenal ulceration, inflammation, perforation, obstruction and gastrointestinal bleeding, can occur at any time, with or without warning symptoms, in patients treated with NSAIDs, such as (Brand Name of Drug). Minor upper GI problems, such as dyspepsia, commonly occur at any time. Health care providers should remain alert for ulceration and bleeding in patients treated with (Brand Name of Drug), even in the absence of previous GI tract symptoms. Most spontaneous reports of fatal GI

events are in elderly or debilitated patients and therefore special care should be taken in treating this population. **To minimize the potential risk for an adverse GI event, the lowest effective dose should be used for the shortest possible duration.** For high risk patients, alternate therapies that do not involve NSAIDs should be considered. (see **Warnings and Precautions - Special Populations - Geriatrics**)

Patients should be informed about the signs and/or symptoms of serious GI toxicity and instructed to discontinue using (Brand Name of Drug) and seek emergency medical attention if they experience any such symptoms. The utility of periodic laboratory monitoring has NOT been demonstrated, nor has it been adequately assessed. Most patients who develop a serious upper GI adverse event on NSAID therapy have no symptoms. Upper GI ulcers, gross bleeding or perforation, caused by NSAIDs, appear to occur in approximately 1% of patients treated for 3-6 months, and in about 2-4% of patients treated for one year. These trends continue, thus increasing the likelihood of developing a serious GI event at some time during the course of therapy. Even short-term therapy has its risks.

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.

Caution should be taken if prescribing (Brand Name of Drug) to patients with a prior history of peptic / duodenal ulcer disease or gastrointestinal bleeding as these individuals have a greater than 10-fold higher risk for developing a GI bleed when taking a NSAID than patients with neither of these risk factors. Other risk factors for GI ulceration and bleeding include the following: *Helicobacter pylori* infection, increased age, prolonged use of NSAID therapy, excess alcohol intake, smoking, poor general health status or concomitant therapy with any of the following:

- Anti-coagulants (e.g. warfarin)
- Anti-platelet agents (e.g. ASA, clopidogrel)
- Oral corticosteroids (e.g. prednisone)
- Selective Serotonin Reuptake Inhibitors (SSRIs) (e.g. citalopram, fluoxetine, paroxetine, sertraline)

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

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

3.4.6 Genitourinary:

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 a NSAID. Should urinary symptoms occur, in the absence of an alternate explanation, treatment with (Brand Name of Drug) should be stopped to ascertain if symptoms disappear. This should be done before urological investigations or treatments are carried out.

Provide pertinent product-specific information on urinary symptoms.

3.4.7 Hematologic:

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

Provide product-specific data for the effects of your NSAID on platelet function and bleeding time.

3.4.7.1 Anti-coagulants:

Numerous studies have shown that the concomitant use of NSAIDs and anti-coagulants increases the risk of bleeding. Concurrent therapy of (Brand Name of Drug) with warfarin requires close monitoring of the international normalized ratio (INR).

Even with therapeutic INR monitoring, increased bleeding may occur.

3.4.7.2 Anti-platelet Effects:

NSAIDs inhibit platelet aggregation and have been shown to prolong bleeding time in some patients. Unlike acetylsalicylic acid (ASA), their effect on platelet function is quantitatively less, or of shorter duration, and is reversible.

(Brand Name of Drug) and other NSAIDs have no proven efficacy as anti-platelet agents and should NOT be used as a substitute for ASA or other anti-platelet agents for prophylaxis of cardiovascular thromboembolic diseases. Anti-platelet therapies (e.g. ASA) should NOT be discontinued. There is some evidence that use of NSAIDs with ASA can markedly attenuate the cardioprotective effects of ASA. (see **Drug Interactions - Drug-Drug Interactions - Acetylsalicylic Acid (ASA) or other NSAIDs**)

Concomitant administration of (Brand Name of Drug) with low dose ASA increases the risk of GI ulceration and associated complications.

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

3.4.7.3 Blood dyscrasias:

Blood dyscrasias (such as neutropenia, leukopenia, thrombocytopenia, aplastic anemia and agranulocytosis) associated with the use of NSAIDs are rare, but could occur with severe consequences.

Anemia is sometimes seen in patients receiving NSAIDs, including (Brand Name of Drug). This may be due to fluid retention, GI blood loss, or an incompletely described effect upon erythropoiesis. Patients on long-term treatment with NSAIDs, including (Brand Name of Drug), should have their hemoglobin or hematocrit checked if they exhibit any signs or symptoms of anemia or blood loss.

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

3.4.8 Hepatic / Biliary / Pancreatic:

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

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 function 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, liver necrosis and hepatic failure, some of them with fatal outcomes, have been reported with NSAIDs.

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.

3.4.9 Hypersensitivity Reactions:

3.4.9.1 Anaphylactoid Reactions:

As with NSAIDs in general, anaphylactoid reactions have occurred in patients without known prior exposure to (Brand Name of Drug). In post-marketing experience, rare cases of anaphylactic/ anaphylactoid reactions and angioedema have been reported in patients receiving (Brand Name of Drug). (Brand Name of Drug) should NOT be given to patients with the ASA-triad. This symptom complex typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking ASA or other NSAIDs (see **Contraindications**).

3.4.9.2 ASA-Intolerance:

(Brand Name of Drug) should NOT be given to patients with 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 NSAIDs. 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 reaction (see **Contraindications**).

3.4.9.3 Cross-sensitivity:

Patients sensitive to one NSAID may be sensitive to any of the other NSAIDs as well.

3.4.9.4 Serious skin reactions:

(See **Warnings and Precautions - Skin**)

Provide information on demonstrated allergic-type reactions to sulfonamides, if applicable.

3.4.10 Immune:

(See **Warnings and Precautions - Infection- Aseptic Meningitis**)

3.4.11 Infection:

(Brand Name of Drug), in common with other NSAIDs, may mask signs and symptoms of an underlying infectious disease.

3.4.11.1 Aseptic Meningitis:

Rarely, 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 tissue diseases, etc.) seem to be pre-disposed. Therefore, in such patients, the health care provider must be vigilant to the development of this complication.

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

3.4.12 Neurologic:

Some patients may experience drowsiness, dizziness, blurred vision, vertigo, tinnitus, hearing loss, insomnia or depression with the use of NSAIDs, such as (Brand Name of Drug). If patients experience such adverse reaction(s), they should exercise caution in carrying out activities that require alertness.

Provide any specific information related to your product.

3.4.13 Ophthalmologic:

Blurred and/or diminished vision has been reported with the use of NSAIDs. If such symptoms develop (Brand Name of Drug) should be discontinued and an ophthalmologic examination performed. Ophthalmologic examination should be carried out at periodic intervals in any patient receiving (Brand Name of Drug) for an extended period of time.

3.4.14 Peri-Operative Considerations:

(See **Contraindications** - Coronary Artery Bypass Graft Surgery)

3.4.15 Psychiatric:

(See **Warnings and Precautions** – *Neurologic*)

3.4.16 Renal:

Long term administration of NSAIDs to animals has resulted in renal papillary necrosis and other abnormal renal pathology. In humans, there have been reports of acute interstitial nephritis, hematuria, low grade proteinuria and occasionally nephrotic syndrome.

Renal insufficiency due to NSAID use is seen in patients with pre-renal conditions leading to reduction in renal blood flow or blood volume. Under these circumstances, renal prostaglandins help maintain renal perfusion and glomerular filtration rate (GFR). In these patients, administration of a NSAID may cause a reduction in prostaglandin synthesis leading to impaired renal function. Patients at greatest risk of this reaction are those with pre-existing renal insufficiency (GFR < 60 mL/min or 1 mL/s), dehydrated patients, patients on salt restricted diets, those with congestive heart failure, cirrhosis, liver dysfunction, taking angiotensin-converting enzyme inhibitors, angiotensin-II receptor blockers, cyclosporin, diuretics, and those who are 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 a NSAID under stable conditions may decompensate during periods of added stress (e.g. dehydration due to gastroenteritis). Discontinuation of NSAIDs is usually followed by recovery to the pre-treatment state.

Caution should be used when initiating treatment with NSAIDs, such as (Brand Name of Drug), in patients with considerable dehydration. Such patients should be rehydrated prior to initiation of therapy. Caution is also recommended in patients with pre-existing kidney disease.

3.4.16.1 Advanced Renal Disease:

(See **Contraindications**)

3.4.16.2 Fluid and Electrolyte Balance:

Use of NSAIDs, such as (Brand Name of Drug), can promote sodium retention in a dose-dependent manner, which can lead to fluid retention and edema, and consequences of increased blood pressure and exacerbation of congestive heart failure. Thus, caution should be exercised in prescribing (Brand Name of Drug) in patients with a history of congestive heart failure, compromised cardiac function, hypertension, increased age or other conditions predisposing to fluid retention (See **Warnings and Precautions - Cardiovascular**).

Use of NSAIDs, such as (Brand Name of Drug), can increase the risk of hyperkalemia, especially in patients with diabetes mellitus, renal failure, increased age, or those receiving concomitant therapy with adrenergic blockers, angiotensin-converting enzyme inhibitors, angiotensin-II receptor antagonists, cyclosporin, or some diuretics.

Electrolytes should be monitored periodically (see **Contraindications**).

Provide any other pertinent information, including special renal studies performed with your drug.

3.4.17 Respiratory:

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.

3.4.18 Sexual Function / Reproduction:

The use of (Brand Name of Drug), as with any drug known to inhibit cyclooxygenase/prostaglandin synthesis, may impair fertility and is not recommended in women attempting to conceive. Therefore, in women who have difficulties conceiving, or who are undergoing investigation of infertility, withdrawal of (Brand Name of Drug) should be considered.

3.4.19 Skin:

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, photosensitivity reactions, urticaria/angioedema, Stevens-Johnson syndrome, toxic epidermal necrolysis and other serious skin reactions related to your product (if applicable).

Describe any other system warnings or precautions applicable to your drug in a concise manner.

3.4.20 Special Populations:

3.4.20.1 Pregnant Women:

(Brand Name of Drug) is CONTRAINDICATED for use during the third trimester of pregnancy because of risk of premature closure of the ductus arteriosus and the potential to prolong parturition (see Toxicology).

Caution should be exercised in prescribing (Brand Name of Drug) during the first and second trimesters of pregnancy (see Toxicology).

Inhibition of prostaglandin synthesis may adversely affect pregnancy and/or the embryo-foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation after use of a prostaglandin synthesis inhibitor in early pregnancy.

In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

3.4.20.2 Nursing Women:

(See **Contraindications**)

3.4.20.3 Pediatrics:

(See **Contraindications**)

3.4.20.4 Geriatrics:

Patients older than 65 years (referred to in this document as older or elderly) and frail or debilitated patients are more susceptible to a variety of adverse reactions from 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. Older patients are also at risk of lower esophageal injury including 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.

3.4.21 Monitoring and Laboratory Tests:

This section should include important monitoring parameters (e.g., blood pressure), laboratory or other tests (e.g., serum potassium, INR, serum transaminases, serum creatinine, serum urea, blood cell count, etc.) required to monitor response to therapy and possible adverse reactions. The frequency of monitoring before, during and after therapy should be included. Information regarding the range of normal and abnormal values expected in a particular situation should be provided. Appropriate response to particular laboratory values should be included.

3.5 Adverse Reactions

Complete this section using the appropriate subheadings, with reference to the guidance entitled, "Guidance for Industry: Product Monograph".

3.5.1 Adverse Drug Reaction Overview

3.5.2 Clinical Trial Adverse Drug Reactions

3.5.3 Less Common Clinical Trial Adverse Drug Reactions

3.5.4 Abnormal Hematologic and Clinical Chemistry Findings

3.5.5 Post-market Adverse Drug Reactions

Additional reports of serious adverse events temporally associated with (Brand Name of Drug) during worldwide post-marketing experience are included below. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or clearly establish a causal relationship to (Brand Name of Drug) exposure. *(Include this introductory paragraph if you have post-marketing adverse drug reaction data for your drug).*

3.6 Drug Interactions

Complete this section using the appropriate subheadings, with reference to the guidance entitled, "Guidance for Industry: Product Monograph". The pertinent information on the identified drug interactions listed below should be included in a tabular format.

3.6.1 Serious Drug Interactions Box

3.6.2 Drug-Drug Interactions:

3.6.2.1 Acetylsalicylic acid (ASA) or other NSAIDs:

The use of (Brand Name of Drug) in addition to any other NSAID, including over-the-counter ones (such as ASA and ibuprofen) for analgesic and/or anti-inflammatory effects is NOT recommended because of the absence of any evidence demonstrating synergistic benefits and the potential for additive adverse reactions.

The exception is the use of low dose ASA for cardiovascular protection, when another NSAID is being used for its analgesic/anti-inflammatory effect, keeping in mind that combination NSAID therapy is associated with additive adverse reactions.

Some NSAIDs (e.g. ibuprofen) may interfere with the anti-platelet effects of low dose ASA, possibly by competing with ASA for access to the active site of cyclooxygenase-1.

Provide any other pertinent information for your drug.

3.6.2.2 Antacids:

Provide any pertinent information for your drug, including potential pH effects of antacids on dissolution of enteric-coated formulations, if applicable.

3.6.2.3 Anti-coagulants:

(See **Warnings and Precautions – Hematologic - Anti-coagulants**)

3.6.2.4 Anti-hypertensives:

NSAIDs may diminish the anti-hypertensive effect of Angiotensin Converting Enzyme (ACE) inhibitors.

Combinations of ACE inhibitors, angiotensin-II antagonists, or diuretics with NSAIDs might have an increased risk for acute renal failure and hyperkalemia. Blood pressure and renal function (including electrolytes) 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.

3.6.2.5 Anti-platelet Agents (including ASA):

There is an increased risk of bleeding, via inhibition of platelet function, when anti-platelet agents are combined with NSAIDs, such as (Brand Name of Drug) (see **Warnings and Precautions – Hematologic - Anti-platelet Effects**).

3.6.2.6 Cyclosporin:

Provide any pertinent information for your drug (e.g. effects on electrolytes; nephrotoxicity)

3.6.2.7 Digoxin:

Provide any pertinent information for your drug.

3.6.2.8 Diuretics:

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

Provide any other pertinent information for your drug.

3.6.2.9 Glucocorticoids:

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

Provide any other pertinent information for your drug.

3.6.2.10 Lithium:

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

Provide any other pertinent information for your drug.

3.6.2.11 Methotrexate:

Provide any pertinent information for your drug.

3.6.2.12 Oral Contraceptives:

Provide any pertinent information for your drug.

3.6.2.13 Oral Hypoglycemics:

Provide any pertinent information for your drug.

3.6.2.14 Selective Serotonin Reuptake Inhibitors (SSRIs):

Concomitant administration of NSAIDs and SSRIs may increase the risk of gastrointestinal ulceration and bleeding (see **Warnings and Precautions - Gastrointestinal**).

3.6.2.15 Tacrolimus:

Provide any pertinent information for your drug (e.g. nephrotoxicity)

Include any other drug-drug interactions identified for your drug.

3.6.3 Drug-Food Interactions

3.6.4 Drug-Herb Interactions

3.6.5 Drug-Laboratory Test Interactions

3.6.6 Drug-Lifestyle Interactions

This section should include information on interactions with alcohol and smoking, and possible effects on activities requiring alertness (e.g. driving, operating machinery).

3.7 Dosage and Administration

Complete the following table, with reference to the guidance entitled, “Guidance for Industry: Product Monograph”.

3.7.1 Dosing Considerations

3.7.2 Recommended Dose and Dosage Adjustment

3.7.3 Missed Dose

3.7.4 Administration

3.8 Overdosage

This section should include the following:

- *Signs and symptoms of overdosage;*
- *Current recommended management of overdosage;*
- *The human lethal dose, and the maximum dose reported with recovery, with or without residual damage, and*
- *Procedures that, by experience with this or similar type drugs, are known or reasonably expected to be unnecessary or unsuitable.*

Provide any other pertinent information for your drug. Mention if drug is dialyzable.

3.9 Action and Clinical Pharmacology

Complete this section using the appropriate subheadings, with reference to the guidance entitled, “Guidance for Industry: Product Monograph”. Present concise and accurate disclosure of results of pharmacologic, pharmacokinetic, metabolic and bioavailability studies, which could be of help to the prescriber. Data on analgesic/anti-inflammatory equivalence with acetylsalicylic acid (ASA) and other NSAIDs may be presented provided that these are found to be acceptable. 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.

3.9.1 Mechanism of Action

3.9.2 Pharmacokinetics

3.9.3 Pharmacodynamics

3.9.4 Special Populations and Conditions

3.10 Storage and Stability

- Temperature
- Light
- Moisture
- Others

3.11 Special Handling Instructions

3.12 Dosage Forms, Composition and Packaging

4 PART II: SCIENTIFIC INFORMATION

Complete this section using the appropriate subheadings as indicated, with reference to the guidance entitled, “Guidance for Industry: Product Monograph”.

4.1 Pharmaceutical Information

4.2 Clinical Trials

Randomized clinical trials with (Brand Name of Drug) have NOT been designed to detect differences in cardiovascular adverse events in a chronic setting.

Describe special studies or studies in special populations designed to address specific aspects of the drug such as GI or cardiovascular safety.

4.3 Detailed Pharmacology

4.4 Microbiology

4.5 Toxicology

4.6 References

5 PART III: CONSUMER INFORMATION

There should be a header placed at the top of the first page of Part III with the words, “IMPORTANT: PLEASE READ”.

The brand name of the drug in upper case with the proper name of the drug in lower case in brackets below the brand name should be placed at the beginning of the document.

Read this information each time you refill your prescription in case new information has been added.

This leaflet is a summary designed specifically for you to read. It will NOT tell you everything about (Brand Name of Drug). See your health care provider and pharmacist regularly and ask them questions about your health and any medications you take.

5.1 About this Medication

What the medication is used for:

Your health care provider has prescribed (Brand Name of Drug) for you for one or more of the following medical conditions:

Provide a point form listing of all the indications, as outlined in the Indications section of Part I and approved in the Notice of Compliance issued by Health Canada. Any limitations on duration of use also must be stated. No claims can be made that the product is able to treat or modify disease signs or prognosis unless these are supported by evidence-based clinical trials. If the product is intended for use as an adjunct to other measures (e.g. diagnosis, treatment/therapy), this should be included.

What it does:

(Brand Name of Drug) ((proper name of drug)), as a nonsteroidal anti-inflammatory drug (NSAID), can reduce the chemicals produced by your body which cause pain and swelling.

Provide any other mechanisms of action of the drug in brief lay explanation, including how it is expected to work so as to be useful in this instance. If use of co-medication(s) is/are required, this should be noted here.

(Brand Name of Drug), as a nonsteroidal anti-inflammatory drug (NSAID), does NOT cure your illness or prevent it from getting worse. (Brand Name of Drug) can only relieve pain and reduce swelling as long as you continue to take it.

When it should not be used:

DO NOT TAKE (Brand Name of Drug) if you have any of the following medical conditions:

- **Heart bypass surgery (planning to have or recently had)**
- **Severe, uncontrolled heart failure**
- **Bleeding in the brain or other bleeding disorders**
- **Current pregnancy (after 28 weeks of pregnancy)**
- **Currently breastfeeding (or planning to breastfeed)**
- **Allergy to ASA (Acetylsalicylic Acid) or other NSAIDs (Nonsteroidal Anti-Inflammatory Drugs)**
- **Ulcer (active)**
- **Bleeding from the stomach or gut (active)**
- **Inflammatory bowel disease (Crohn's Disease or Ulcerative Colitis)**
- **Liver disease (active or severe)**

- **Kidney disease (severe or worsening)**
- **High potassium in the blood**
- *List, in point form, any other contraindications as outlined in the Contraindications section of Part I which are not listed above.*

Patients who took a drug in the same class as (Brand Name of Drug) after a type of heart surgery (coronary artery bypass grafting (CABG)) were more likely to have heart attacks, strokes, blood clots in the leg(s) or lung(s), and infections or other complications than those who did NOT take that drug.

(Brand Name of Drug) should NOT be used in patients under (*provide age*) years of age since the safety and effectiveness have NOT been established.

What the medicinal ingredient is:

Proper name of drug

What the nonmedicinal ingredients are:

List nonmedicinal ingredients in alphabetical order, as outlined in the Summary Product Information section of Part I.

What dosage forms it comes in:

List available preparations and their respective doses.

5.2 Warnings and Precautions

The following statements should appear in a black box as illustrated below:

If you have, or previously had, any of the following medical conditions, see your health care provider to discuss treatment options other than (Brand Name of Drug):

- **Heart Attack or Angina**
- **Stroke or Mini-stroke**
- **Loss of Vision**
- **Current Pregnancy (less than 28 weeks)**
- **Congestive Heart Failure**

Before taking this medication, tell your health care provider if you have any of the following:

- High blood pressure
- High cholesterol
- Diabetes mellitus or on a low sugar diet
- Atherosclerosis
- Poor circulation to your extremities
- Smoker or ex-smoker
- Kidney disease or urine problems
- Previous ulcer or bleeding from the stomach or gut
- Previous bleeding in the brain
- Bleeding problems
- Family history of allergy to NSAIDs, such as acetylsalicylic acid (ASA), celecoxib, diclofenac, diflunisal, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, mefenamic acid, meloxicam, nabumetone, naproxen, oxaprozin, piroxicam, rofecoxib, sulindac, tenoxicam, tiaprofenic acid, tolmetin, or valdecoxib (NOT a complete list)
- Family history of asthma, nasal polyps, long-term swelling of the sinus (chronic sinusitis) or hives
- Family history of allergy to sulfonamide drugs (*if applicable*)
- Any other medical problem (*List any other diseases of particular importance to this drug product.*)

Also, before taking this medication, tell your health care provider if you are planning to get pregnant.

While taking this medication:

- tell any other doctor, dentist, pharmacist or other health care professional that you see, that you are taking this medication, especially if you are planning to have heart surgery;
- do NOT drink alcoholic beverages while taking this medication because you would be more likely to develop stomach problems;
- fertility may be decreased. The use of (Brand Name of Drug) is not recommended in women trying to get pregnant. In women who have difficulty conceiving, stopping (Brand Name of Drug) should be considered.

5.3 Interactions with this Medication

This section is to ensure consumers are aware of any medications or foods or beverages (e.g. alcohol) known to interact with this medication. Serious or significant interactions should be listed (for example, drug interactions listed in the Serious Drug Interactions box in Part I).

Talk to your health care provider and pharmacist if you are taking any other medication (prescription or non-prescription) such as any of the following (NOT a complete list):

- Acetylsalicylic Acid (ASA) or other NSAIDs
 - e.g. ASA, celecoxib, diclofenac, ibuprofen, indomethacin, ketorolac, meloxicam, naproxen
- Antacids
- Antidepressants
 - Selective Serotonin Reuptake Inhibitors (SSRIs)
 - e.g. citalopram, fluoxetine, paroxetine, sertraline
- Blood pressure medications
 - ACE (angiotensin converting enzyme) inhibitors
 - e.g. enalapril, lisinopril, perindopril, ramipril
 - ARBs (angiotensin II receptor blockers)
 - e.g. candesartan, irbesartan, losartan, valsartan
- Blood thinners
 - e.g. warfarin, ASA, clopidogrel
- Corticosteroids (including glucocorticoids)
 - e.g. prednisone
- Cyclosporin
- Digoxin
- Diuretics
 - e.g. furosemide, hydrochlorothiazide
- Lithium

- Methotrexate
- Oral contraceptives
- Oral hypoglycemics (diabetes medications)
- Tacrolimus
- *List any other medications, vitamins or herbal products of particular importance to this drug product.*

Your health care provider may prescribe low dose ASA (acetylsalicylic acid) as a blood thinner to reduce your risk of having a heart attack or stroke while you are taking (Brand Name of Drug). Take only the amount of ASA prescribed by your health care provider. You are more likely to upset or damage your stomach if you take both (Brand Name of Drug) and ASA than if you took (Brand Name of Drug) alone.

5.4 Proper Use of this Medication

Usual Dose:

Complete the following table for each indication, its corresponding starting dose and maximum daily dose.

| Medical Condition | Age Group | Starting Dose | Maximum Dose (per day) | Maximum Duration of Treatment (days) |
|-------------------|-----------|---------------|------------------------|--------------------------------------|
| | | | | |
| | | | | |

Take (Brand Name of Drug) only as directed by your health care 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 care provider recommended. If possible, you should take the lowest dose of this medication for the shortest time period.** Taking too much (Brand Name of Drug) may increase your chances of unwanted and sometimes dangerous side effects, especially if you are elderly, have other diseases or take other medications.

If you will be using (Brand Name of Drug) for more than 7 days, see your health care provider regularly to discuss whether this medicine is working for you and if it is causing you any unwanted effects.

This medication has been prescribed specifically for you. Do NOT give it to anyone else. It may harm them, even if their symptoms seem to be similar to yours.

(Brand Name of Drug) is NOT recommended for use in patients under (provide age) years of age since safety and effectiveness have NOT been established.

Provide any other specific and essential information for this drug product and its schedule of administration necessary for safe and effective use (e.g. 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).

(Brand Name of Drug) must be taken with food *(or modify as appropriate for your drug)*.

Missed Dose:

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

Overdose:

If you take more than the prescribed dose, contact your health care provider immediately.

5.5 Side Effects and What to Do about Them

(Brand Name of Drug) may cause some side effects, especially when used for a long time or in large doses. When these side effects occur, you may require medical attention. Report all symptoms or side effects to your health care provider.

(Brand Name of Drug) may cause you to become drowsy or tired. Be careful about driving or participating in activities that require you to be alert. If you become drowsy, dizzy or light-headed after taking (Brand Name of Drug), do NOT drive or operate machinery.

(Brand Name of Drug) may cause you to become more sensitive to sunlight. Any exposure to sunlight or sunlamps may cause sunburn, skin blisters, skin rash, redness, itching or discolouration, or vision changes. If you have a reaction from the sun, check with your health care provider. *(Include this paragraph if applicable to your drug.)*

Check with your health care provider IMMEDIATELY if you develop chills, fever, muscle aches or pains, or other flu-like symptoms, especially if they occur before or together with a skin rash. These symptoms may be the first signs of a SERIOUS ALLERGIC REACTION to this medication.

| SERIOUS SIDE EFFECTS AND WHAT TO DO ABOUT THEM | | |
|---|---|--|
| Symptom | STOP taking (Brand Name of Drug) and get emergency medical attention IMMEDIATELY | STOP taking (Brand Name of Drug) and talk to your physician or pharmacist |
| Bloody or black tarry stools | ✓ | |
| Shortness of breath, wheezing, any trouble breathing or chest tightness | ✓ | |
| Skin rash, hives, swelling or itching | ✓ | |
| Blurred vision, or any visual disturbance | ✓ | |
| Any change in the amount or colour of your urine (red or brown) | ✓ | |
| Any pain or difficulty experienced while urinating | | ✓ |
| Swelling of the feet, lower legs; weight gain | | ✓ |
| Vomiting or persistent indigestion, nausea, stomach pain or diarrhea | | ✓ |
| Yellow discolouration of the skin or eyes, with or without itchy skin | | ✓ |
| Malaise, fatigue, loss of appetite | | ✓ |
| Headaches, stiff neck | | ✓ |
| Mental confusion, depression | | ✓ |
| Dizziness, lightheadedness | | ✓ |
| Hearing problems | | ✓ |

Add to the above chart any other common and uncommon but serious side effects specific to your drug product.

This is NOT a complete list of side effects. If you develop any other symptoms while taking (Brand Name of Drug), see your health care provider.

5.6 How to Store It:

Provide storage information (e.g. storage temperature, light exposure, moisture exposure, recommended storage location).

Do NOT keep outdated medicine or medicine no longer needed. Any outdated or unused medicine should be returned to your pharmacist.

Keep out of reach of children.

5.7 Reporting Suspected Side Effects

A box on reporting suspected adverse drug reactions should be included.

5.8 More Information

Date

List the last revised date of Part III of the Product Monograph. It must match the date on the title page of the Product Monograph.