PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

PrASACOL™ 800

Mesalamine Tablets (Delayed-Release) *
Tablets, 800 mg, Oral

Mfr. Std.

Lower Gastrointestinal Anti-inflammatory

Allergan Inc.
85 Enterprise Blvd., Suite 500
Markham, Ontario
L6G 0B5
www.allergan.ca

Date of Initial Approval:
April 26, 2005

Date of Revision:
March 18, 2021

Submission Control No: 245722

* also referred to as 5-aminosalicylic acid (5-ASA)

RECENT MAJOR LABEL CHANGES

WARNINGS AND PRECAUTIONS, Renal	04/2020
WARNINGS AND PRECAUTIONS, Acute Intolerance Syndrome	03/2021
WARNINGS AND PRECAUTIONS, 7.1.2 Breast-feeding	03/2021

TABLE OF CONTENTS

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

ASACOL 800 (800 mg mesalamine delayed-release tablets) is indicated for:

- treatment of moderately active ulcerative colitis.

1.1 Pediatrics

Pediatrics: No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2 Geriatrics

Geriatrics: No data are available to Health Canada; therefore, Health Canada has not authorized an indication for geriatric use.

2 CONTRAINDICATIONS

ASACOL 800 (800 mg tablet) is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

ASACOL 800 (800 mg tablet) is contraindicated in:

- patients with a history of sensitivity to salicylates
- patients with severe renal impairment (GFR<30 mL/min/1.73 m^2) and/or severe hepatic impairment (see WARNINGS & PRECAUTIONS – Renal and Hepatic/Biliary/Pancreatic)
- patients with existing gastric or duodenal ulcer
- patients with urinary tract obstruction
- patients unable to swallow the intact tablets

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions

- **Hypersensitivity:** If toxic or hypersensitivity reactions occur, the drug should be discontinued. In assessing liver and joint complications, it should be kept in mind that these are frequently associated with ulcerative colitis.

- **Renal:** Renal impairment, including minimal change nephropathy, acute and chronic interstitial nephritis, and renal failure has been reported in patients taking mesalamine products**.** Asacol 800 (800 mg tablet) is contraindicated in patients with severe renal impairment (see CONTRAINDICATIONS). It is recommended that all patients have an evaluation of renal function prior to initiation of Asacol 800 (800 mg tablet) tablets and periodically while on Asacol 800 (800 mg tablet) therapy. For patients with moderate or mild renal impairment, see WARNINGS AND PRECAUTIONS.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

Abrupt discontinuation of Asacol 800 (800 mg tablet) is not recommended, and may result in relapse.

Interchangeability between Asacol (400 mg tablet) and Asacol 800 (800 mg tablet) has not been established. For information on the Asacol (400 mg tablet), please refer to the current Product Monograph for the Asacol (400 mg tablet) tablet.

4.2 Recommended Dose and Dosage Adjustment

For the treatment of moderately active ulcerative colitis: Usual daily adult dose is 6 Asacol 800 (800 mg tablet) tablets, taken orally in divided doses. Asacol 800 (800 mg tablet) may be given without regards to meals.

For alternate dosing for moderately active ulcerative colitis, see the Asacol (400 mg tablet) Product Monograph.

Patients with ulcerative colitis should be made aware that ulcerative colitis rarely remits completely. It is important for patients to comply with the dosage prescribed by their doctors; by doing so, the risk of relapse can be substantially reduced.

Health Canada has not authorized an indication for pediatric use.

4.3 Administration

Swallow tablets whole, taking care not to break the outer coating. The outer coating is designed to remain intact, to protect the active ingredient until it reaches the terminal ileum, where the tablet coating dissolves and the contents of the tablet are released into the terminal ileum and colon.

Take Asacol 800 (800 mg tablet) tablets only as prescribed. Do not change the number or frequency of tablets ingested without first consulting your physician.

What appears to be intact or partially intact tablets may infrequently appear in the stool. If this occurs repeatedly, consult your physician.

4.4 Missed Dose

If a dose of this medication has been missed, it should be taken as soon as possible. However, if it is almost time for the next dose, skip the missed dose and go back to the regular dosing schedule. Do not take double the dose.

5 OVERDOSAGE

There is no clinical experience with overdose of Asacol 800 (800 mg tablet). Mesalamine is not metabolized to salicylate. There is no specific antidote for mesalamine overdose, and treatment is symptomatic and supportive.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table – Dosage Forms, Strengths, Composition and Packaging.

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
oral	Mesalamine Delayed Release Tablets, 800 mg	colloidal silicon dioxide, dibutyl phthalate, edible black ink (ammonium hydroxide, n-butyl alcohol, shellac glaze [modified] in SD-45, propylene glycol, synthetic black iron oxide), Eudragit®-L {methacrylic acid copolymer Type A (USP)}, Eudragit®-S {methacrylic acid copolymer Type B (USP)}, iron oxide red, iron oxide yellow, lactose, magnesium stearate, polyethylene glycol, polyvinylpyrrolidone, sodium starch glycolate, and talc

Asacol 800 (800 mg tablet) tablets are available for oral administration as red-brown, capsule-shaped, enteric coated tablets, printed in black ink with “WC 800”.

Each red-brown capsule-shaped enteric coated tablet of Asacol 800 (800 mg tablet) contains 800 mg mesalamine. Asacol 800 (800 mg tablet) colon-targeted tablets are coated with a special acrylic-based resin, Eudragit®-S {methacrylic acid copolymer Type B (USP)}, which dissolves at pH 7 or greater, that delays release of the mesalamine until the tablets reach the terminal ileum. A second enteric coating which begins to dissolve earlier in the gastrointestinal tract is added after the Eudragit®-S. The outer coating consists of a combination of Eudragit®-S and another acrylic-based resin, Eudragit®-L {methacrylic acid copolymer Type A (USP)}.

Asacol 800 (800 mg tablet) colon-targeted tablets are supplied in bottles of 180 tablets each.

7 WARNINGS AND PRECAUTIONS

Please see the Serious Warnings and Precautions Box at the beginning of Part I: Health Professional Information.

General
Asacol 800 (800 mg tablet) and other mesalamine-containing products have differences in formulation and release characteristics that may lead to differences in concentrations of mesalamine delivered to the colon. If it is deemed necessary to switch from one mesalamine-containing product to another mesalamine-containing product, the prescriber should carefully assess the overall benefit-risk analysis based on the patient's clinical conditions and on all available information for the various mesalamine-containing products.

Acute Intolerance Syndrome
Mesalamine has been implicated in the production of an acute intolerance syndrome characterized by cramping, acute abdominal pain and bloody diarrhea, sometimes fever, headache and a rash; in such cases prompt withdrawal is required. The patient's history of sulfasalazine intolerance, if any, should be re-evaluated. If a rechallenge is performed later in order to validate the hypersensitivity, it should be carried out under close supervision and only if clearly needed, giving consideration to reduced dosage. The possibility of increased absorption of mesalamine and concomitant renal tubular damage as noted in the preclinical studies must be kept in mind. Patients on mesalamine 1000 mg, especially those on concurrent oral products which contain or release mesalamine and those with pre-existing renal disease, should be carefully monitored with urinalysis, BUN and creatinine testing.

Carcinogenesis and Mutagenesis
Preclinical animal data are provided in the Toxicology section.

Driving and Operating Machinery
There are no data available on the effects of mesalamine on ability to drive and use machines.

Gastrointestinal
Acute exacerbation of the symptoms of colitis, characterized by cramping, abdominal pain, bloody diarrhea, and occasionally by fever, headache, malaise, pruritus, rash, and conjunctivitis, has been reported in 3% of patients in controlled clinical trials of Asacol (400 mg tablet) versus sulfasalazine. This reaction has been reported after initiation of other mesalamine-containing products, and was reported by 2% of patients receiving Asacol 800 (800 mg tablet) in two controlled clinical trials. Symptoms usually abate when mesalamine therapy is discontinued.

Patients with pyloric stenosis may have prolonged gastric retention of Asacol 800 (800 mg tablet) tablets that could delay release of mesalamine in the colon.

What appears to be intact or partially intact tablets may be observed in the stool.

Hepatic/Biliary/Pancreatic
Caution should be exercised when using Asacol 800 (800 mg tablet) (or other compounds that contain or are converted to mesalamine or its metabolites) in patients with hepatic dysfunction.

In assessing liver complications, it should be kept in mind that these are frequently associated with ulcerative colitis.

There have been reports of hepatic failure and increased liver enzymes in patients with pre-existing liver disease when treated with mesalamine products. Therefore, Asacol 800 (800 mg tablet) is contraindicated in patients with severe hepatic impairment (see CONTRAINDICATIONS). In patients with mild to moderate liver function impairment, caution should be exercised and Asacol 800 (800 mg tablet) should only be used if the expected benefit clearly outweighs the risks to the patients. Appropriate assessment and monitoring of liver function should be performed.

Immune

Hypersensitivity

Some patients who have experienced a hypersensitivity reaction to sulfasalazine may have a similar reaction to Asacol 800 (800 mg tablet) tablets or to other compounds that contain, or are converted to, mesalamine. Asacol 800 (800 mg tablet) does not contain a sulfa moiety, thus sulfa-related side effects are avoided. These patients should be instructed to discontinue therapy if signs of rash or fever become apparent. In case of an allergic reaction, appropriate measures (standard of care) should be taken.

Monitoring and Laboratory Tests

It is recommended that all patients have an evaluation of renal function prior to initiation of Asacol 800 (800 mg tablet) tablets and periodically while on Asacol 800 (800 mg tablet) therapy.

It is recommended that appropriate assessment and monitoring of liver function should be performed.

Renal

Reports of renal impairment, including minimal change nephropathy, and acute or chronic interstitial nephritis have been associated with mesalamine products and pro-drugs of mesalamine. Cases of nephrolithiasis have been reported with the use of mesalamine, including stones with a 100% mesalamine content. It is recommended to ensure adequate fluid intake during treatment. Asacol 800 (800 mg tablet) is contraindicated in patients with severe renal impairment (see CONTRAINDICATIONS). In patients with mild to moderate renal dysfunction, history of renal disease or taking concomitant nephrotoxic drugs, caution should be exercised and Asacol 800 (800 mg tablet) should be used only if the benefits outweigh the risks. It is recommended that all patients have an evaluation of renal function prior to initiation of therapy and periodically while on treatment.

7.1 Special Populations

7.1.1 Pregnant Women

There are no adequate and well controlled studies of Asacol 800 (800 mg tablet) use in pregnant women. Limited published data on the class of mesalamine products show an increased rate of preterm birth, stillbirth and low birth weight. These adverse pregnancy outcomes are also associated with active inflammatory bowel disease. Mesalamine crosses the placenta. Animal reproduction studies of mesalamine found no evidence of fetal harm.

Mesalamine should be used during pregnancy only if the benefits clearly outweigh the risks to the fetus.

Dibutyl phthalate (DBP) is an inactive ingredient in Asacol 800 (800 mg tablet)'s enteric coating, and in animal studies at doses >80 times the human dose based on body surface area, maternal DBP was associated with external and skeletal malformations and adverse effects on the male reproductive system. Asacol 800 (800 mg tablet) should be used during pregnancy only if the potential benefit justifies the potential risk.

7.1.2 Breast-feeding

Literature reports indicate that, following oral or rectal administration of mesalamine-containing products to lactating women, small amounts of 5-ASA and higher concentrations of the metabolite N-acetyl-5-ASA are found in breast milk. While the clinical significance of this has not been determined, caution should be exercised when Asacol 800 (800 mg tablet) tablets are administered to a nursing woman.

When mesalamine is used in nursing women, infants should be monitored for changes in stool consistency. If the infant develops diarrhea, breast-feeding should be discontinued. Cases of diarrhea in breastfed infants exposed to mesalamine have been reported.

Isolated weight decrease in nursing infant has been reported during post-marketing experience with mesalamine.

Dibutyl phthalate (DBP), an inactive ingredient in the enteric coating of Asacol 800 (800 mg tablet), and its primary metabolite mono-butyl phthalate (MBP) are excreted into human milk. The clinical significance of this has not been determined.

7.1.3 Pediatrics

Pediatrics: Safety and effectiveness of Asacol 800 (800 mg tablet) therapy in patients younger than 18 years of age has not been established. Therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4 Geriatrics

Geriatrics: Less than 10% of patients in the Asacol 800 (800 mg tablet) clinical trial were > 65 years of age. Patients in this age range were not significantly different from the overall patient population with respect to safety and efficacy responses.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Asacol is generally well tolerated. The most commonly reported adverse reactions were nausea, diarrhea, abdominal pain and headache. Other common adverse reactions seen in clinical trials with Asacol were acute exacerbation of ulcerative colitis symptoms, abnormal hepatic functions tests and rash. Adverse events seen in clinical trials with Asacol tablets have generally been mild and reversible, and have seldom resulted in discontinuation of treatment.

8.2 Clinical Trial Adverse Reaction

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

In two double-blind, randomized 6 week, parallel-group design clinical trials in patients with mildly to moderately active ulcerative colitis, the safety and efficacy of Asacol 800 (800 mg tablet), dosed at 4.8 g/day, was compared to the safety and efficacy of Asacol (400 mg tablet), dosed at 2.4 g/day. In these trials, the overall incidence of adverse events was comparable between the two treatment groups, and similar to that observed previously with Asacol (400 mg tablet) therapy. Table 1 presents adverse events assessed as possibly or probably related to the study drug in 1% or more of patients in either treatment group.

Table 1
Adverse Events Assessed as Possibly or Probably Related to Study Drug Occurring in >=1% in Either Treatment Group by MedDRA PT

Event	2.4g/day Asacol (400 mg Tablet) (N=349) n (%)	4.8g/day Asacol (800 mg Tablet) (N=338) n (%)
Gastrointestinal disorders		
Abdominal Distention	5 (1.4%)	1 (0.3%)
Abdominal Pain	7 (2.0%)	3 (0.9%)
Nausea	6 (1.7%)	8 (2.4%)
Ulcerative Colitis	4 (1.1%)	3 (0.9%)
Vomiting	3 (0.9%)	4 (1.2%)
Nervous system disorders		
Headache	13 (3.7%)	12 (3.6%)

8.3 Abnormalities Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Elevated AST or ALT, elevated alkaline phosphatase, elevated serum creatinine and BUN.

8.4 Post-Market Adverse Reactions

In addition to the adverse events listed above, the following adverse events have also been reported in controlled clinical trials, open-label studies, literature reports, or foreign and domestic marketing experience. Because many of these events were reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The relationship of the reported events to Asacol is unclear in many cases, some, including anorexia, joint pain, pyoderma gangrenosum, oral ulcers, and anemia, are sometimes part of the clinical presentation of ulcerative colitis.

Blood and lymphatic system disorders: agranulocytosis (rare), aplastic anemia (rare), leukopenia, anemia, thrombocytopenia, eosinophilia, lymphadenopathy.
Cardiac disorders: pericarditis (rare), myocarditis (rare), palpitations.

Ear and labyrinth disorders: ear pain, tinnitus, deafness, ear congestion, ear disorder, vertigo.
Eye disorders: amblyopia, blurred vision, conjunctivitis, eye pain, lacrimation disorder, vision abnormality.
Gastrointestinal disorders: dry mouth, stomatitis, oral ulcers, dyspepsia, eructation, flatulence, pancreatitis, gastritis, gastroenteritis, gastrointestinal bleeding, abdominal enlargement, perforated peptic ulcer (rare), constipation, rectal hemorrhage, bloody diarrhea, tenesmus, rectal disorder, stool abnormality.
General disorders and administration site conditions: facial edema, edema, peripheral edema, asthenia, drug fever (rare), chills, malaise, pain, chest pain, flu syndrome, infection, mesalamine-induced acute intolerance syndrome.
Hepatobiliary disorders: hepatic impairment, including hepatic failure or hepatitis (rare), cholecystitis. Asymptomatic elevations of liver function tests have occurred in patients taking Asacol tablets. These elevations usually resolve during continued therapy or with discontinuation of Asacol. When any elevations in liver enzymes are assessed, it should be kept in mind that hepatic complications are frequently associated with inflammatory bowel disease.
Immune system disorders: anaphylactic reaction, allergic reaction, lupus-like syndrome, Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).
Infections and infestations: pharyngitis,sinusitis, vaginal moniliasis.
Metabolism and nutrition disorders: anorexia, increased appetite.
Musculoskeletal and connective tissue disorders: back pain, gout, rheumatoid arthritis, arthritis, arthralgia, joint disorder, myalgia, hypertonia, leg cramps, neck pain.
Nervous system disorders: somnolence, dizziness, tremor, paresthesia, migraine, taste perversion, peripheral neuropathy (rare), Guillain-Barré syndrome (rare), transverse myelitis (rare).
Psychiatric disorders: anxiety, confusion, depression, decreased libido, emotional lability, hyperesthesia, insomnia, nervousness.
Respiratory, thoracic and mediastinal disorders: epistaxis, rhinitis, dyspnea, increased cough, asthma exacerbation, pleuritis, bronchitis, pneumonia, allergic and interstitial lung disease, eosinophilic pneumonia, interstitial pneumonitis, lung disorder.
Skin and subcutaneous tissue disorders: alopecia, psoriasis (rare), pyoderma gangrenosum (rare), erythema nodosum, acne, dry skin, sweating, pruritus, Stevens-Johnson Syndrome (SJS), urticaria.
Renal and urinary disorders: interstitial nephritis (rare), minimal change nephropathy (rare), nephrolithiasis, renal failure (rare) (see also WARNINGS AND PRECAUTIONS), cystitis, urinary tract infection, dysuria, urinary urgency, increased urination, hematuria, urine abnormality.
Reproductive system and breast disorders: dysmenorrhea, epididymitis, menorrhagia, prostate disorder, vaginitis.
Vascular disorders: vasodilation.

9 DRUG INTERACTIONS

9.1 Overview

There are no known drug interactions with Asacol (400 mg tablet). No drug interaction studies were performed with Asacol 800 (800 mg tablet). In clinical trials of Asacol 800 (800 mg tablet), there were no restrictions on the concomitant use of antacids, H2-receptor antagonists, proton-pump inhibitors, or other preparations affecting gastrointestinal pH. In subgroup analyses, patients receiving H2-receptor antagonists or proton-pump inhibitors were not

significantly different from the overall patient population with respect to safety and efficacy response.

9.2 Drug-Drug Interactions

The hypoglycaemic effect of sulfonylureas may be enhanced when administered with aminosalicylates (oral antidiabetics may be displaced from the binding sites of plasma proteins). 5- ASA was reported to inhibit coumarin anticoagulants, resulting in thrombosis.

Concomitant treatment with mesalamine may increase the risk of myelosuppression in patients receiving azathioprine or 6-mercaptopurine. The concurrent use of mesalamine with azathioprine or 6-mercaptopurine may increase the risk for blood dyscrasia. If concomitant use of mesalamine and azathioprine or 6-mercaptopurine cannot be avoided, monitor blood tests, including complete blood cell counts and platelet counts.

The concurrent use of mesalamine with known nephrotoxic agents, including nonsteroidal anti-inflammatory drugs (NSAIDs) may increase the risk of nephrotoxicity. Monitor patients taking nephrotoxic drugs for changes in renal function and mesalamine-related adverse reactions.

9.3 Drug-Food Interactions

Administration of the Asacol 800 (800 mg tablet) tablet immediately following a high fat meal had no significant effect on the extent of exposure to 5-ASA and N-acetyl-5-ASA based on AUC and percent of dose excreted in urine (Ae%). A reduction of approximately 50% was observed in Cmax, due to significantly delayed tmax when dosed following a high fat meal compared to dosing under fasting condition. However, no impact was observed on the safety profile or systemic exposure to 5-ASA and N-acetyl-5ASA in the clinical trials where doses were given without regards to meals. Therefore, Asacol 800 (800 mg tablet) can be taken in a fasted or fed state.

9.4 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.5 Drug-Laboratory Test Interactions

Several reports of possible interference with measurements, by liquid chromatography, of urinary normetanephrine causing a false-positive test result have been observed in patients exposed to sulfasalazine or its metabolite, mesalamine/mesalazine.

10 ACTION AND CLINICAL PHARMACOLOGY

10.1 Mechanism of Actions

The active ingredient in Asacol 800 (800 mg tablet) is mesalamine (5-aminosalicylic acid, also referred to as 5-ASA). The available evidence suggests that mesalamine has a topical anti-inflammatory effect on the colon, where it inhibits prostaglandin and leukotriene synthesis.

10.2 Pharmacokinetics

Tables 2 and 3 presents the mean pharmacokinetic parameters of 5-ASA and N-acetyl-5-ASA (N-Ac-5-ASA) following single and multiple dosing of Asacol 800 (800 mg tablet) in healthy subjects.

Table 2 Summary of mean pharmacokinetic parameters of 5-ASA following single and multiple dosing in healthy subjects

	AUC_{tlast} (ng●h/mL)	AUC (ng●h/mL)	C_{max} (ng/mL)	T_{max} (h)	t_{lag} (h)	$t_{1/2,z}$ (h)	$\%A_e$ (%)
Single dose mean (1 x 800 mg)	3449.2	3548.2	354.03	9.61	6.20	13.41	0.21
Multiple dose (4.8 g/day x 6 Days)	-	20282.0[a]	4972.1	2.63	-	11.89	9.28

AUC_{tlast} is the area under the plasma concentration-time curve from time zero to the last quantifiable concentration
AUC is the area under the plasma concentration-time curve from time zero to infinity
Cmax is the maximum plasma concentration
T_{max} is the time at which C_{max} is observed
t_{lag} is the lag time before the onset of drug absorption
$t_{1/2,Z}$ is the terminal exponential half-life
$\%A_e$ is the percentage of dose excreted in urine
[a] AUC_T is the area under the plasma concentration-time curve over a dosing interval.

Table 3 Summary of mean pharmacokinetic parameters of N-Ac-5-ASA following single and multiple dosing in healthy subjects

	AUC_{tlast} (ng●h/mL)	AUC (ng●h/mL)	C_{max} (ng/mL)	T_{max} (h)	t_{lag} (h)	$t_{1/2,z}$ (h)	$\%A_e$ (%)
Single dose mean (1 x 800 mg)	19900.8	22034.2	1028.68	11.13	5.39	13.62	12.04
Multiple dose (4.8 g/day x 6 Days)	-	24864.0[a]	4614.78	3.13	-	19.56	19.01

AUC_{tlast} is the area under the plasma concentration-time curve from time zero to the last quantifiable concentration
AUC is the area under the plasma concentration-time curve from time zero to infinity
Cmax is the maximum plasma concentration
T_{max} is the time at which C_{max} is observed
t_{lag} is the lag time before the onset of drug absorption
$t_{1/2,Z}$ is the terminal exponential half-life
$\%A_e$ is the percentage of dose excreted in urine
[a] AUC_T is the area under the plasma concentration-time curve over a dosing interval.

Asacol 800 (800 mg tablet) tablets have a special acrylic-based resin coating, which does not allow the drug to be released below pH 7. The coating delays release of mesalamine until the tablets reach the terminal ileum and colon. Asacol 800 (800 mg tablet) demonstrated expected enteric coating properties that were comparable to those of the Asacol (400 mg tablet) tablet, as indicated by *in-vitro* dissolution data as well as prolonged t_{max} and t_{lag} following oral administration.

Absorption
Once released in the colon, mesalamine is minimally absorbed and plasma levels are similar to those found in previous studies following oral administration of doses given as 400 mg tablets. The bioequivalence between Asacol 800 (800 mg tablet) and Asacol (400 mg tablet) tablets has not been established. Following oral administration of a single, 800 mg tablet under fasting conditions, the time to peak plasma concentration (t_{max}) is approximately 10 hours while the terminal elimination half-life ($t1/2_{elm}$) is 12 to 19 hours for both mesalamine and its metabolite, N-acetyl-5-ASA.

Human studies conducted using radiological and serum markers, with the 400 mg tablets, showed that the Asacol (400 mg tablet) coating delayed release of mesalamine until the terminal ileum was reached. Other studies with mesalamine compared its absorption when administered as an enema (a readily available dosage form) and when released for absorption in the stomach, small intestine, and colon relative to an intravenous dose. Results indicated that once released in the colon, mesalamine was minimally absorbed and plasma levels were similar to those found following rectal administration. Approximately 20% of the administered dose released was absorbed, with about 80% available for topical activity in the colon. The extent of systemic exposure to mesalamine is similar in fasted and fed subjects.

Metabolism
Mesalamine, on absorbed, is rapidly acetylated through the gut mucosal wall and by the liver.

Elimination
Absorbed mesalamine is mainly excreted by the kidney, as N-acetyl-5-ASA.

11 STORAGE, STABILITY AND DISPOSAL

Store at controlled room temperature (15°C – 30°C).

PART II: SCIENTIFIC INFORMATION

12 PHARMACEUTICAL INFORMATION

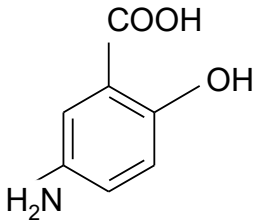
Drug Substance

Proper name: mesalamine or 5- aminosalicylic acid

Chemical name: 5-amino-2-hydroxybenzoic acid, also referred to as 5-aminosalicylic acid or 5-ASA.

Molecular formula and molecular mass: $C_7H_7NO_3$ Molecular Weight 153.1

Structural formula:



Physicochemical properties: Mesalamine is an off-white to light-brown powder that decomposes at 280°C and is slightly soluble in water. It darkens upon exposure to air, high humidity or light over a period of several months.
pK_a Values: pK_1 = 2.74, pK_2 = 5.80.

13 CLINICAL TRIALS

13.1 Trial Design and Study Demographics

In the pivotal double-blind, randomized, multiple-site, controlled study in newly and previously diagnosed patients who were experiencing a flare-up of mildly to moderately active ulcerative colitis, patients were randomly assigned to receive either 2.4 g/day (Asacol 400 mg tablet) or 4.8 g/day (Asacol 800 (800 mg tablet)) for 6 weeks. A total of 301 patients were randomized to the treatment groups. In this study, a large subgroup (n = 180) of patients with moderately active ulcerative colitis was identified using the predefined stratum of baseline disease severity. Additional analyses looking at the primary, secondary and tertiary efficacy endpoints were performed in this subgroup of patients. The data from these analyses supports the efficacy of Asacol 800 (800 mg tablet) at 4.8 g/day in moderately active ulcerative colitis patients.

In the pivotal clinical trial with Asacol 800 (800 mg tablet), moderately active ulcerative colitis was determined by a Physician Global Assessment (PGA) which included clinical and endoscopic evaluations scored as a 2 on a 0 (normal) to 3 (severe) scale.

The baseline demographic characteristics for the moderately active ulcerative colitis patients are presented in Table 4.

Table 4 Summary of baseline demographic characteristics for clinical trials in patients with moderately active ulcerative colitis

Study #	Trial design	**Dosage, route of administration and duration**	**Study subjects (n=number)**	**Mean age (Range)**	**Gender**
Study 1	double-blind, randomized, multiple-site, controlled study	2.4 g/day (400 mg tablets orally for 6 weeks)	n=96	43.0 (18-74)	45.8% M 54.2% F
		4.8 g/day (800 mg tablets orally for 6 weeks)	n=84	45.4 (20-76)	47.6% M 52.4% F

There were no statistically significant differences for any baseline demographic or anthropometric characteristic, or history of ulcerative colitis between patients with moderately active ulcerative colitis enrolled into the two treatment groups. With respect to baseline disease state characteristics, patients in the two treatment groups were not statistically different except for stool frequency scores in which more patients in the 4.8 g/day group had slightly higher stool frequency scores.

Patients enrolled into the study presented with either proctitis, proctosigmoiditis, left-sided colitis, or pancolitis and the length of disease ranged from less than one year to greater than 10 years.

In another double-blind, randomized, multiple-site, controlled study (Study 2) in newly and previously diagnosed patients who were experiencing a flare up of moderately active ulcerative colitis, patients were randomly assigned to receive either 2.4 g/day (Asacol 400 mg tablet) or 4.8 g/day (Asacol 800 (800 mg tablet)) for 6 weeks. A total of 386 patients were randomly assigned to treatment groups; 268 with moderate disease. The two moderately active ulcerative colitis treatment groups were comparable with respect to baseline demographic, disease history, and disease severity characteristics. Results from this study support the efficacy of Asacol 800 (800 mg tablet) at 4.8 g/day in moderately active ulcerative colitis patients.

13.2 Study Results

In both studies, the percentage of patients with moderately active ulcerative colitis who were classified as a treatment success after 6 weeks of therapy based on the intent-to-treat study population are presented in Table 5.

Table 5 Summary of Treatment Outcomes at Week 6 (Intent-to-treat Population With Moderate Disease [PGA = 2] at Baseline)

	Pivotal Study		Study 2		Pooled	
	2.4 g/day Asacol (400 mg Tablet) N = 223 n (%)	**4.8 g/day Asacol (800 mg Tablet)** N = 200 n (%)	**2.4 g/day Asacol (400 mg Tablet)** N = 223 n (%)	**4.8 g/day Asacol (800 mg Tablet)** N = 200 n (%)	**2.4 g/day Asacol (400 mg Tablet)** N = 223 n (%)	**4.8 g/day Asacol (800 mg Tablet)** N = 200 n (%)
Treatment Success [(a)]	53 (57.0%)	55 (72.4%)	77 (59.2%)	89 (71.8%)	130 (58.3%)	144 (72.0%)
Treatment Failure	40 (43.0%)	21 (27.6%)	53 (40.8%)	35 (28.2%)	93 (41.7%)	56 (28.0%)
p-value [(b)]	0.0384		0.0357		0.0034	

(a) Treatment success was defined as improvement from baseline at Week 6. Improvement from baseline was defined as either a complete response (remission) or partial response (improvement) to treatment. A complete response was defined as a PGA score of 0 and complete resolution of the following clinical assessments: stool frequency, rectal bleeding, PFA, and sigmoidoscopy findings. A partial response was defined as improvement from baseline in the PGA score, accompanied by improvement from baseline in at least 1 of the clinical assessments listed above, and no worsening in any of the remaining clinical assessments. Treatment failure was defined as: 1) PGA score that stayed the same or worsened from baseline (regardless of whether the other clinical assessments resolved), 2) worsening of any clinical assessments at Week 6, or 3) withdrawal from the study due to an AE or lack of treatment effect.

(b) 4.8 g/day compared to 2.4 g/day, from Chi-square test for 2000082 and 2000083, and stratified by protocol using the Cochran-Mantel-Haenszel test for pooled analysis.

The results of these studies for moderately active disease patients are consistent with those of a previous trial, in which the majority of patients were moderate disease patients (77%), where 4.8 g/day was administered using Asacol 400 mg tablets and 74% of patients were classified as treatment success. The findings in the Asacol 800 (800 mg tablet) studies are consistent with the fact that a higher dose of mesalamine shows greater efficacy in patients with more severe disease. Demonstrated efficacy of the Asacol 800 (800 mg tablet) tablet, administered at 4.8 g/day in the population of patients with moderately active disease, provides this population with an alternate formulation allowing daily ingestion of fewer tablets. Interchangeability between Asacol (400 mg tablet) and Asacol 800 (800 mg tablet) has not been established. For information on the Asacol (400 mg tablet), please refer to the current Product Monograph for the Asacol (400 mg tablet) tablet.

Physician's Global Assessment and Individual Symptom and Sigmoidoscopy Scores at Weeks 3 and 6

The percentage of patients whose individual clinical assessments (stool frequency score, rectal bleeding score, and PFA score), sigmoidoscopy score, and PGA score improved from baseline at Weeks 3 and 6 from both studies (pooled data) are presented in Table 6.

Table 6 Distribution of Treatment Improvement for Physician's Global Assessment and Individual Symptoms at Weeks 3 and 6
Excluding Patients With Both Baseline and Visit Scores of Zero (Patients with Moderate Disease [PGA = 2] at Baseline)

	Visit Week 3		Visit Week 6	
	2.4 g/day Asacol (400 mg Tablet) N = 223 n (%)	**4.8 g/day Asacol (800 mg Tablet)** N = 200 n (%)	**2.4 g/day Asacol (400 mg Tablet)** N = 223 n (%)	**4.8 g/day Asacol (800 mg Tablet)** N = 200 n (%)
PGA	122 (63.5%)	130 (71.8%)	139 (73.2%)	152 (84.9%)*
Stool Frequency	107 (59.4%)	112 (64.7%)	126 (70.8%)	126 (75.4%)
Rectal Bleeding	110 (65.5%)	128 (74.4%)	130 (76.5%)	137 (81.5%)
PFA	100 (62.5%)	90 (58.8%)	130 (76.5%)	108 (72.0%)
Sigmoidoscopy	100 (62.5%)	111 (61.3%)	129 (67.9%)	140 (78.2%)*

Patients with no treatment outcome at Week 6 were excluded from this analysis. For patients who have a baseline score but have no score at visit, the improvement status cannot be determined. These patients were also excluded from this analysis.
* = Between-treatment difference is statistically significant ($p<0.05$) using the Cochran-Mantel-Haenszel test stratified by protocol.
N = number of patients in treatment group with treatment outcome at Week 6
n(%) = number and percentage (n/Total x 100) of patients in treatment with specified outcome in specified parameter

In both studies, more patients showed improvement on 4.8 g/day compared to 2.4 g/day across the clinical assessments (stool frequency, rectal bleeding, sigmoidoscopy and PGA). From pooled results, 4.8 g/day showed statistically significant superiority in the sigmoidoscopy and PGA scores at 6 weeks.

Results from both studies (pooled data) demonstrate that the median time to resolution of increased stool frequency, rectal bleeding, and the composite of both symptoms were shorter for the 4.8 g/day group than for the 2.4 g/day group. In addition, the difference between groups was statistically significant for the median time to resolution of rectal bleeding (9 days for 4.8 g/day group vs 16 days for 2.4 g/day group) and the composite of both symptoms (19 days for 4.8 g/day group vs 29 days for 2.4 g/day group), favouring the 4.8 g/day group.

Quality-of-life Scores
The quality-of-life scores derived from the Inflammatory Bowel Disease Questionnaire (IBDQ) at Weeks 3 and 6 from both studies (pooled data) are presented in Table 7.

Table 7 Mean Change from baseline in Inflammatory Bowel Disease Questionnaire Scores at Weeks 3 and 6 (Patients with Moderate Disease [PGA = 2] at Baseline)

	Visit Week 3		Visit Week 6		Exit	
	2.4 g/day Asacol (400 mg Tablet) N = 235 n Mean	**4.8 g/day Asacol (800 mg Tablet)** N = 213 n Mean	**2.4 g/day Asacol (400 mg Tablet)** N = 235 n Mean	**4.8 g/day Asacol (800 mg Tablet)** N = 213 n Mean	**2.4 g/day Asacol (400 mg Tablet)** N = 235 n Mean	**4.8 g/day Asacol (800 mg Tablet)** N = 213 n Mean
Total	189 30.1*	183 33.7*	183 42.6*	176 45.0*	212 36.4*	193 40.2*
Bowel	190 11.4*	182 13.1*	183 16.4*	176 17.4*	212 14.4*	193 15.6*
Systemic	191 4.3*	184 5.1*	185 6.1*	177 6.8*	214 5.2*	194 5.9*
Emotional	187 9.9*	181 11.1*	182 13.9/	175 14.8*	211 11.8*	192 13.2*
Social	191 4.2*	182 4.6*	186 5.9*	176 5.9*	215 4.7*	193 5.3*

Exit is the Week 6 visit for those who completed the study and the withdrawal visit for those who dropped out.
N = number of patients in treatment group with treatment outcome at Week 6
n = number of patients from which statistics were calculated.
* = Change from baseline using t-test is statistically significant ($p<0.0001$).

Quality of life pooled data from both studies using the IBDQ showed statistically significant improvement from baseline in both treatment groups at both week 3 and week 6. No statistically significant differences were seen between treatment groups; however, there was a trend for scores to favour 4.8 g/day dosing over 2.4 g/day dosing.

14 NON-CLINICAL TOXICOLOGY

Acute Toxicity Studies: The acute peroral LD_{50} value for mesalamine is reported to be 5000 mg/kg in mice and 4594 mg/kg in rats.

Subacute Toxicity Studies: Rats (2/sex/group) were administered mesalamine orally at dosages of 0, 40, 120, 360, and 1080 mg/kg/day for 14 days. One female rat (1080 mg/kg/day) died, most probably of renal failure complicated by gastric mucosal injury. Drug-related changes in the clinical chemistry assays (increased serum urea nitrogen, serum creatinine and serum total proteins, and decreased albumin/globulin ratios) occurred only at the 1080 mg/kg/day level. Drug-related histomorphologic effects were present in the kidneys (1080 mg/kg/day) and gastrointestinal tracts (360 and 1080 mg/kg/day) of treated rats.

A similar study in rabbits resulted in diarrhea during the first week (males, 1080 mg/kg/day). Urinalysis revealed slight increases in proteinuria, bilirubinuria, and urinary acetone in the high dose group.

No drug-related effects were observed when rabbits were given 227.3 mg/kg/day rectally (suppository) for 12 days.

Chronic Toxicity Study: Dogs (2/sex/group) were administered Asacol tablets at oral dosages of 40, 120, and 200 mg/kg/day for one year. Control dogs received placebo tablets. Histopathology and clinical chemistry assessment showed no evidence of drug-related effects.

Carcinogenicity: Dietary mesalamine was determined not to be carcinogenic in rats at doses as high as 480 mg/kg/day in one two year study, and 840 mg/kg/day in a second two year study. Similarly, dietary mesalamine was not carcinogenic in mice at 2000 mg/kg/day. These doses are 15, 26 and 62.5 times the maximum recommended human maintenance dose of Asacol (400 mg tablet) of 1.6 g/day (32 mg/kg/day if 50 kg body weight assumed.)

Genotoxicity: Mesalamine was not mutagenic in two bacterial test systems (Ames assay and K. pneumoniae test) with and without metabolic activation. No evidence of teratogenicity was observed when mesalamine was administered orally at a dosage of 480 mg/kg/day to pregnant rats and rabbits.

Reproductive and Developmental Toxicology: The effects of oral mesalamine on fertility and gestation indices were investigated in rats at doses up to 480 mg/kg/day. No effects on fertility or gestation parameters were noted in these studies.

Special Studies: Two studies to assess the potential renal toxicity of mesalamine in a rat model have been reported in the literature. In an acute study, rats were given a single massive intravenous injection, at dose levels between 214 and 872 mg/kg. The animals killed 24-96 hours after the injection presented lesions in the proximal cortical tubules as well as renal papillary necrosis. The former lesion was reversible by one week post-administration. In a second study, using a more clinically relevant dosing regimen, rats were dosed up to 200 mg/kg p.o. for 4 weeks. No drug-related effects were observed.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

PrAsacol™ 800
Mesalamine Delayed-Release Tablets

Read this carefully before you start taking **Asacol 800** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Asacol 800**.

Serious Warnings and Precautions

- **Stop taking Asacol 800 if you have an allergic reaction to this drug. Speak to your doctor immediately or go to the nearest emergency department. Symptoms of allergic reaction may include itching, hives, swelling in face or hands, tightness in chest, trouble breathing.**
- **Asacol 800 contains the medicinal ingredient mesalamine. Kidney failure has been reported in patients taking Asacol 800 as well with drugs that contain mesalamine.**
- **Speak to your doctor if you have a history of kidney problems before using Asacol 800. Taking Asacol 800 may worsen your kidney condition. Your doctor may check your kidney function before you begin Asacol 800 and during your treatment.**

What is Asacol 800 used for?
To treat symptoms related to ulcerative colitis when the condition of the disease is moderate. Ulcerative colitis is where the large bowel (colon) and back passage (rectum) becomes red and swollen (inflamed).

How does Asacol 800 work?
Asacol 800 is an anti-inflammatory drug for the bowel. Asacol 800 is believed to stop the production of certain substances in your body that cause swelling (inflammation). Asacol 800 tablets are designed to prevent the medicine from being released early.

What are the ingredients in Asacol 800?
Medicinal ingredients: mesalamine, otherwise known as 5-aminosalicylic acid or 5-ASA
Non-medicinal ingredients: colloidal silicon dioxide, dibutyl phthalate, edible black ink (ammonium hydroxide, n-butyl alcohol, shellac glaze [modified] in SD-45, propylene glycol, synthetic black iron oxide), Eudragit®-L {methacrylic acid copolymer Type A (USP)}, Eudragit®-S {methacrylic acid copolymer Type B (USP)}, iron oxide red, iron oxide yellow, lactose, magnesium stearate, polyethylene glycol, polyvinylpyrrolidone, sodium starch glycolate and talc.

Asacol 800 comes in the following dosage form:
800 mg tablet

Do not use Asacol 800 if:

- You are allergic to mesalamine (5-ASA) or any of the ingredients in Asacol 800.
- You have a history of sensitivity to salicylates, for example acetylsalicylic acid (i.e. Aspirin®).
- You have severe liver problems.
- You have severe kidney problems.
- You have an ulcer in the stomach or intestines.
- You have a blocked urinary tract.
- You are unable to swallow the whole tablet.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Asacol 800. Talk about any health conditions or problems you may have, including if you:

- have higher than normal blood urea nitrogen (BUN) levels (renal function test)
- have a history of kidney problems
- have pyloric stenosis. Pyloric Stenosis is a condition in where the passage from the stomach to the small intestine is narrow or blocked. Pyloric stenosis may keep the Asacol 800 tablet from reaching the colon as quickly as it normally would.
- are taking other ulcerative colitis drugs that contain Mesalamine. Speak to your doctor before switching your treatment to Asacol 800
- had an allergic reaction to sulfasalazine. Stop taking Asacol 800 and speak to your doctor if you experience a rash or a fever.

Other warnings you should know about:

Treatment with Asacol 800 can increase your risk of certain side effects, including:

- **Liver problems**: You may develop liver function problems, including liver failure.
- **Kidney Stones**: You may develop kidney stones when using Asacol 800. Be sure to drink enough liquids while you are taking Asacol 800. Speak to your doctor about how much water or other liquids you should be drinking. Symptoms of kidney stones may include:
    - blood in urine
    - urinating more often
    - pain in back, side, stomach and groin
- **Acute Intolerance Syndrome:** Mesalamine, the medicinal ingredient in Asacol 800, can cause Acute Intolerance Syndrome. Your doctor may monitor your kidney function if you have kidney disease while on treatment. Speak to your doctor immediately if you experience any of the following symptoms:
    - cramping
    - sudden abdominal pain
    - bloody diarrhea
    - fever
    - headache
    - rash
- **Colitis (inflamed colon):** Asacol 800 can cause the symptoms of colitis to worsen. Speak to your doctor immediately if you suddenly experience any of the following symptoms:
    - cramping
    - abdominal pain
    - bloody diarrhea

- fever
- headache
- rash or itchy skin
- eye infection

Pregnancy and breastfeeding:
If you are pregnant, able to get pregnant or think you are pregnant, there are specific risks you should discuss with your doctor.

- Tell your doctor right away if you become pregnant or think you are pregnant during treatment with Asacol 800.
- Taking Mesalamine during pregnancy have been reported to cause:
  - early Labor
  - stillbirth (death of baby)
  - low birth weight of baby
- If you breastfeed your baby while taking Asacol 800, your baby could develop / start to have diarrhea. It is important to monitor your baby's stool and contact your doctor right away if they have diarrhea. Your doctor may advise you to stop breastfeeding your baby.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Asacol 800:

- Aminosalicylates. Taking Asacol 800 with aminosalicylates may increase your risk of developing a blood clot.
- Azathioprine, 6-mercaptopurine. Taking Asacol 800 with these drugs may increase your risk of developing a blood disorder.
- Nonsteroidal anti-inflammatory drugs (NSAID). Taking Asacol 800 with these drugs may increase your risk of side effects to your kidneys.

How to take Asacol 800:

- Take Asacol 800 exactly as your doctor tells you to take it. Do NOT take more of it than prescribed. Speak to your doctor or pharmacist if you are not sure.
- Take the exact dose your doctor tells you to take during remission. Following your doctor's instructions can reduce the risk of your symptoms returning.
- Do NOT stop using Asacol 800 abruptly.
- Swallow tablets whole. Do NOT crush or chew the tablet.
- The whole tablet or a part of it may occasionally appear in your stool. Speak to your doctor if this occurs frequently.

Usual Adult Dose:
Treatment of moderate ulcerative colitis:
Take six 800 mg tablets daily in divided doses.

Overdose:

If you think you have taken too much Asacol 800, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:
If a dose of this medication has been missed, it should be taken as soon as possible. However, if it is almost time for the next dose, skip the missed dose and go back to the regular dosing schedule. Do not take double the dose.

What are possible side effects from using Asacol 800?

These are not all the possible side effects you may feel when taking Asacol 800. If you experience any side effects not listed here, contact your healthcare professional.

Side effects may include:

- anxiety, confusion or nervousness
- bloated stomach
- diarrhea
- difficulty sleeping
- headache or migraine
- increased appetite
- menstrual (period) pain
- nausea
- rash
- pain in groin, joints, neck or back
- sore throat
- vomiting

Your doctor may run tests, including a blood test, to check your liver function and blood cell counts.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
COMMON			
Worsening of your ulcerative colitis symptoms		✓	
UNCOMMON			
Kidney stones (hard little pebbles that form in your kidneys) blood in urine, urinating more often, pain in your back, side, belly or groin		✓	
Chest pain		✓	
Stomach pain		✓	
RARE			
Ear Problems: pain, contestation, noise, ringing in ear or vertigo (a sense of spinning dizziness)	✓		
Eye problems: blurred vision, eye pain, or pink eye (infection)		✓	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Fever (higher than normal body temperature)		✓	
Fast heartbeat: pounding, fluttering, racing, skipping beats, chest discomfort or shortness of breath			✓
Allergic (hypersensitivity) reactions itching, rash, swelling of face or hands, tightness in chest, trouble breathing			✓
Lung Problems (thickening and scaring of lung tissues): Shortness of breath, fast, shallow breathing, dry cough	✓		
Kidney problems changes in urine output, cloudy or tea-coloured urine, blood in the urine, weight gain (from retaining fluid), confusion, swelling of the eyes, hands, legs, and feet Additional less specific symptoms may include: drowsiness, fatigue, nausea, vomiting, rash, persistent itching, and back pain		✓	
Liver problems severe abdominal pain or distension, nausea, vomiting, drop in appetite, bloating, together with yellowing of the skin and eyes, and abnormal liver function tests		✓	
Acute intolerance syndrome cramping, stomach pain, bloody and excessive stools, fever, headache and rash			✓
Stevens-Johnson syndrome (SJS) (severe skin rash): redness, blistering and/or peeling of the skin and/or inside of the lips, eyes, mouth, nasal passages or genitals, accompanied by fever, chills, headache, cough, body aches or swollen glands			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:
Asacol 800 should be stored at controlled room temperature (15℃ – 30℃).

Keep out of reach and sight of children.

If you want more information about Asacol 800:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (http://hc-sc.gc.ca/index-eng.php); the manufacturer's website www.allergan.ca, or by calling 1-800-668-6424.

ASACOL™ is a trademark of Medeva Pharma Suisse SA, used under license by Allergan Inc.

This leaflet was prepared by Allergan Inc.

Last Revised March 18, 2021