



HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use mesalamine delayed-release tablets safely and effectively. See full prescribing information for mesalamine delayed-release tablets.

MESALAMINE Delayed-release Tablets, for oral use

Initial U.S. Approval: 1987

RECENT MAJOR CHANGES

Warnings and Precautions, Interference with Laboratory Tests (5.6), 08/2013

INDICATIONS AND USAGE

Mesalamine delayed-release tablets are locally acting 5-aminosalicylic acid (5-ASA) indicated for the induction of remission in adults with active, mild to moderate ulcerative colitis and for the maintenance of remission of ulcerative colitis. (1)

DOSAGE AND ADMINISTRATION

For induction of remission of active, mild to moderate ulcerative colitis, two to four 1.2 g tablets taken once daily with food. (1, 2) For maintenance of remission of ulcerative colitis, two 1.2 g tablets taken once daily with food. (1, 2)

DOSAGE FORMS AND STRENGTHS

Delayed-Release Tablets: 1.2 g (3)

CONTRAINDICATIONS

Patients with known hypersensitivity to salicylates or aminosaliclates or to any of the ingredients of mesalamine delayed-release tablets. (4)

WARNINGS AND PRECAUTIONS

- Renal impairment may occur. Assess renal function at the beginning of treatment and periodically during treatment. (5.1)
- Mesalamine-induced acute intolerance syndrome has been reported. Observe patients closely for worsening of these symptoms while on treatment. (5.2)
- Use caution when treating patients who are hypersensitive to sulfasalazine. (5.3)
- Mesalamine-induced cardiac hypersensitivity reactions (myocarditis and pericarditis) have been reported. (5.3)

- Hepatic failure has been reported in patients with preexisting liver disease. Use caution when treating patients with liver disease. (5.4)
- Upper GI tract obstruction may delay onset of action. (5.5)
- Use of mesalamine may lead to spuriously elevated test results when measuring urinary normetanephrine by liquid chromatography with electrochemical detection. (5.6)

ADVERSE REACTIONS

- The most common adverse reactions (incidence $\geq 2\%$) are ulcerative colitis, headache, flatulence, liver function test abnormality, and abdominal pain. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Zydus Pharmaceuticals USA Inc. at 1-877-993-8779 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Nephrotoxic agents including NSAIDs: renal reactions have been reported. (7.1)
- Azathioprine or 6-mercaptopurine: blood disorders have been reported. (7.2)

USE IN SPECIFIC POPULATIONS

- Renal impairment: Use mesalamine delayed-release tablets with caution in patients with a history of renal disease. (5.1, 7.1, 8.5, 13.2)
- Nursing Women: Caution should be exercised when administered to a nursing woman. (8.3)
- Geriatric Patients: Monitor blood cell counts in geriatric patients. (8.5)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 10/2014

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE
Mesalamine delayed-release tablets are indicated for the induction of remission in patients with active, mild to moderate ulcerative colitis and for the maintenance of remission of ulcerative colitis.

2 DOSAGE AND ADMINISTRATION
The recommended dosage for the induction of remission in adult patients with active, mild to moderate ulcerative colitis is two to four 1.2 g tablets taken once daily with a meal for a total daily dose of 2.4 g or 4.8 g. The recommended dosage for the maintenance of remission is two 1.2 g tablets taken once daily with a meal for a total daily dose of 2.4 g.

3 DOSAGE FORMS AND STRENGTHS
Mesalamine Delayed-release Tablets, 1.2 g are pale red-brown, oval-shaped, biconvex, bevel film-coated tablets debossed with the "711" on one side and plain on other side.

4 CONTRAINDICATIONS
Mesalamine delayed-release tablets are contraindicated in patients with known hypersensitivity to salicylates or aminosaliclates or to any of the ingredients of mesalamine delayed-release tablets [see Warnings and Precautions (5.3), Description (11), Adverse Reactions (6.2)].

5 WARNINGS AND PRECAUTIONS

5.1 Renal Impairment
Renal impairment, including minimal change nephropathy, acute and chronic interstitial nephritis, and, rarely, renal failure, has been reported in patients given products such as mesalamine delayed-release tablets that contain mesalamine or are converted to mesalamine. It is recommended that patients have an evaluation of renal function prior to initiation of mesalamine delayed-release tablets therapy and periodically while on therapy. Exercise caution when using mesalamine delayed-release tablets in patients with known renal dysfunction or a history of renal disease. In animal studies, the kidney was the principal organ for toxicity [see Drug Interactions (7.1) and Nonclinical Toxicology (13.2)].

5.2 Mesalamine-Induced Acute Intolerance Syndrome
Mesalamine has been associated with an acute intolerance syndrome that may be difficult to distinguish from an exacerbation of ulcerative colitis. Although the exact frequency of occurrence has not been determined, it has occurred in 3% of patients in controlled clinical trials of mesalamine or sulfasalazine. Symptoms include cramping, acute abdominal pain and bloody diarrhea, and sometimes fever, headache, and rash. Observe patients closely for worsening of these symptoms while on treatment. If acute intolerance syndrome is suspected, promptly discontinue treatment with mesalamine delayed-release tablets.

5.3 Hypersensitivity Reactions
Some patients who have experienced a hypersensitivity reaction to sulfasalazine may have a similar reaction to mesalamine delayed-release tablets or to other compounds that contain or are converted to mesalamine. Mesalamine-induced cardiac hypersensitivity reactions (myocarditis and pericarditis) have been reported with mesalamine delayed-release tablets and other mesalamine medications. Caution should be taken in prescribing this medicine to patients with conditions predisposing them to the development of myocarditis or pericarditis.

5.4 Hepatic Impairment
There have been reports of hepatic failure in patients with preexisting liver disease who have been administered mesalamine. Caution should be exercised when administering mesalamine delayed-release tablets to patients with liver disease.

5.5 Upper GI Tract Obstruction
Pyloric stenosis or other organic or functional obstruction in the upper gastrointestinal tract may cause prolonged gastric retention of mesalamine delayed-release tablets which would delay mesalamine release in the colon.

5.6 Interference with Laboratory Tests
Use of mesalamine may lead to spuriously elevated test results when measuring urinary normetanephrine by liquid chromatography with electrochemical detection because of the similarity in the chromatograms of normetanephrine and mesalamine's main metabolite, N-acetylamino salicylic acid (N-Ac-5-ASA). An alternative, selective assay for normetanephrine should be considered.

6 ADVERSE REACTIONS
The most serious adverse reactions seen in mesalamine delayed-release tablets clinical trials or with other products that contain or are metabolized to mesalamine are:

- Renal impairment, including renal failure [See Warnings and Precautions (5.1)]
- Mesalamine-induced acute intolerance syndrome [See Warnings and Precautions (5.2)]
- Hypersensitivity reactions [See Warnings and Precautions (5.3)]
- Hepatic impairment, including hepatic failure [See Warnings and Precautions (5.4)]

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. Mesalamine delayed-release tablets have been evaluated in 1368 ulcerative colitis patients in controlled and open-label trials.

Induction of Remission
In two 8 week placebo-controlled clinical trials involving 535 ulcerative colitis patients, 356 received 2.4 g/day or 4.8 g/day mesalamine delayed-release tablets and 179 received placebo. The most frequent adverse reaction leading to discontinuation from mesalamine delayed-release tablets therapy was exacerbation of ulcerative colitis (0.8%). Pancreatitis occurred in less than 1% of patients during clinical trials and resulted in discontinuation of therapy with mesalamine delayed-release tablets in patients experiencing this event. Adverse reactions occurring in mesalamine delayed-release tablets or placebo groups at a frequency of at least 1% in two 8 week, double-blind, placebo-controlled trials are listed in Table 1. The most common adverse reactions with mesalamine delayed-release tablets 2.4 g/day and 4.8 g/day were headache (5.6% and 3.4%, respectively) and flatulence (4% and 2.8%, respectively).

Table 1
Adverse Reactions in Two Eight-Week Placebo-Controlled Trials Experienced by at Least 1% of the Mesalamine Delayed-release Tablets Group and at a Rate Greater than Placebo*

Adverse Reaction	Mesalamine Delayed-release Tablets 2.4 g/day (n = 177)	Mesalamine Delayed-release Tablets 4.8 g/day (n = 179)	Placebo (n = 179)
Headache	10 (5.6%)	6 (3.4%)	1 (0.6%)
Flatulence	7 (4%)	5 (2.8%)	5 (2.8%)
Liver Function Test Abnormal	1 (0.6%)	4 (2.2%)	2 (1.1%)
Alopecia	0	2 (1.1%)	0
Pruritus	1 (0.6%)	2 (1.1%)	2 (1.1%)

* Adverse reactions for which the placebo rate equalled or exceeded the rate for at least one of the mesalamine delayed-release tablets treatment groups were abdominal pain, dizziness, dyspepsia, and nausea. The following adverse reactions, presented by body system, were reported infrequently (less than 1%) by mesalamine delayed-release tablets-treated ulcerative colitis patients in the two controlled trials.

Cardiac Disorder
Tachycardia

Vascular Disorders
Hypertension, hypotension

Skin and Subcutaneous Tissue Disorders
Acne, prurigo, rash, urticaria

Gastrointestinal Disorders
Abdominal distention, colitis, diarrhea, pancreatitis, rectal polyp, vomiting

Investigations
Decreased platelet count

Musculoskeletal and Connective Tissue Disorders
Arthralgia, back pain

Nervous System Disorders
Somnolence, tremor

Respiratory, Thoracic and Mediastinal Disorders
Pharyngolaryngeal pain

General Disorders and Administrative Site Disorders
Asthenia, face edema, fatigue, pyrexia

Ear and Labyrinth Disorders
Ear pain

Maintenance of Remission of Ulcerative Colitis
The dose evaluated in three studies of mesalamine delayed-release tablets given for the maintenance of remission in patients with ulcerative colitis was 1.2 g twice daily or 2.4 g/once daily. One of these studies was a 6-month double-blind comparator study while two were 12-to 14-month open-label studies. The most common adverse reactions with mesalamine delayed-release tablets in the maintenance arms of long-term trials were colitis ulcerative (5.8%), headache (2.9%), liver function test abnormal (2.3%), and abdominal pain (2.2%). Of the 1082 subjects in the all maintenance studies pooled, 1.9% had severe adverse reactions. The most common severe adverse reactions were gastrointestinal disorders; these were mainly symptoms associated with ulcerative colitis.

Table 2
Adverse Reactions in Three Maintenance Trials Experienced by at Least 1% of the Mesalamine Delayed-release Tablets Group (maintenance phases of trials)

Adverse Reaction	n	%
Colitis ulcerative	63	(5.8%)
Headache	31	(2.9%)
Liver function test abnormal	25	(2.3%)
Abdominal pain	24	(2.2%)
Diarrhea	18	(1.7%)
Abdominal distention	14	(1.3%)
Abdominal pain upper	13	(1.2%)
Dyspepsia	13	(1.2%)
Back pain	13	(1.2%)
Rash	13	(1.2%)
Arthralgia	12	(1.1%)
Fatigue	11	(1.0%)
Hypertension	10	(1.0%)

The following adverse reactions, presented by body system, were reported infrequently (less than 1%) by mesalamine delayed-release tablets-treated ulcerative colitis patients in the three long-term maintenance trials (maintenance phases of these trials):

Cardiac Disorder
tachycardia

Skin and Subcutaneous Tissue Disorders
acne, alopecia, pruritis, urticaria

Gastrointestinal Disorders
colitis, flatulence, nausea, pancreatitis, rectal polyp, vomiting

Nervous System Disorders
dizziness

Respiratory, Thoracic and Mediastinal Disorder
pharyngolaryngeal pain

General Disorders and Administrative Site Disorders
asthenia, pyrexia

Ear and Labyrinth Disorders
ear pain

