
PONSETIL

(Mefenamic Acid Capsules, USP)

Rx Only

PON-PI-1

DESCRIPTION

Ponsetil (mefenamic acid) is a member of the fenamate group of nonsteroidal anti-inflammatory drugs (NSAIDs). It is a white, odorless, crystalline powder with a melting point of 203–207°C and water solubility of 0.55mg/mL, at pH 7.4. It is a 2-methyl-2H-1,4-benzoxazin-3(4H)-one. The molecular weight is 241.3. Its molecular formula is C_{16}H_{14}NO_3.

The structural formulas of mefenamic acid are as follows:

![Structural formulas of mefenamic acid]

CLINICAL PHARMACOLOGY

Pharmacodynamics

Ponsetil is a nonsteroidal anti-inflammatory drug (NSAID) that exhibits anti-inflammatory, analgesic, and antipyretic activities. It is related to aspirin-like agents, like that of other NSAIDs, is not completely understood but may be related to prostaglandin synthetase inhibition.

Pharmacokinetics

Absorption

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Distribution

Mefenamic acid has been reported as being greater than 95% bound to plasma proteins. Ponsetil is up to 98% bound to plasma proteins. The apparent volume of distribution (Vd) estimated following a 150-mg dose of mefenamic acid was 108 L/kg.

Metabolism

Mefenamic acid is metabolized by cytochromes P450 enzymes (CYP3A3/4) and CYP2C19. Further metabolism is through glucuronidation and sulfation. The metabolites of mefenamic acid are excreted in the urine.

Excretion

Approximately 30% of a mefenamic acid dose is excreted into the urine, primarily as glucuronides of mefenamic acid (6%), 3-hydroxymefenamic acid (25%) and mefenamic acid (25%) and their metabolites. The metabolic fate of the drug accounts for up to 25% of the dose, mostly in the form of unconjugated 3-carboxylic acid.

OVERDOSAGE

Skin and appendages - angioedema, toxic epidermal necrosis, erythema multiforme, purpura, erythematous rash, urticaria, angioneurotic edema, jaundice, photosensitivity, pruritus, rashes

Respiratory - respiratory depression, pneumonia

Cardiovascular system - tachycardia, hypotension, myocardial infarction, palpitations, arrhythmia, chest pain

Gastrointestinal system - gastrointestinal bleeding, gastric perforation, hematemesis, melena, hematochezia, nausea, vomiting, epigastric pain

泌尿系统 - renal failure, interstitial nephritis

Neurological system - convulsions, coma, hallucinations, depression

Other adverse reactions, which occur rarely are:

Skin and appendages - alopecia, photosensitivity, pruritus, sweat

Sensory system - visual impairment

Respiratory system - asphyxia

Hemic and lymphatic system - agranulocytosis, hemolytic anemia, aplastic anemia, PONSETIL

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Patients with asthma may have aspirin-sensitive asthma. The use of aspirin in patients with asthma is contraindicated.

Fluid Retention and Edema

Ponstel who may be adversely affected by alterations in platelet function, such as those seen in patients with a history of thrombosis or stroke. Unlike aspirin, their effect on platelet function is quantitatively less, or qualitatively different.

NSAIDs inhibit platelet aggregation and have been shown to prolong bleeding time in patients with a history of thrombosis or stroke. This may reduce the likelihood of the occurrence of thrombotic or thromboembolic events in patients with a prior history of thrombosis or stroke.

Anemia is sometimes seen in patients receiving NSAIDs, including Ponstel. This may be related to decreases in hematocrit or hemoglobin levels, or to diarrhea, which can lead to a decrease in iron stores.

Advanced Renal Disease

In cases with pre-existing advanced kidney disease, treatment with Ponstel is not recommended (see CONTRAINDICATIONS).

Pregnancy

In pregnancy, as with other NSAIDs, Ponstel should be avoided because it may cause premature closure of the ductus arteriosus.

PRECAUTIONS

General

Ponstel cannot be expected to substitute for corticosteroids or to treat corticosteroid withdrawal syndrome. It is not known whether patients with corticosteroid withdrawal syndrome will be able to taper off corticosteroids without developing symptoms of withdrawal.

Patients on prolonged corticosteroid therapy should have therapy tapered slowly if a decision is made to discontinue corticosteroids.

Because Ponstel reduces inflammation, it may disguise the diagnostic signs for detecting complications of porcine pseudococcal endocarditis.

Hepatic Effects

Borderline elevations of one or more liver function tests may occur in up to 15% of patients taking Ponstel, including Ponstel. These laboratory abnormalities may persist or resolve without any apparent consequence. There have been rare reports of severe hepatic reactions, including fulminant and fatal hepatic failure, over the course of treatment with NSAIDs. Withdrawal of the drug has been associated with recovery. A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver function test is noted, should be evaluated for hepatic impairment. Even in the absence of symptoms and/or signs of hepatic impairment, patients should be advised not to take additional medications that could increase liver toxicity. Conditions that increase the risk for hepatic complications include alcoholism and other liver disorders, severe dehydration, or concomitant use of drugs that are potentially hepatotoxic.

In patients with impaired renal function, liver function tests may be increased.

NSAIDs should be prescribed with extreme caution in patients with a history of liver disease because of the risk of serious hepatic reactions including fulminant hepatic necrosis and fatal hepatic failure.

Gastrointestinal (GI) Effects - Risk of GI Ulceration, Bleeding, and Perforation

Serious gastrointestinal toxicity, such as inflammation, bleeding, ulcers, and perforation of the stomach, small intestine, or large intestine, can occur at any time, with or without warning symptoms, in patients treated with non-steroidal anti-inflammatory drugs (NSAIDs). Minor gastrointestinal problems, such as dyspepsia, are common and may also occur at any time during NSAID therapy. Therefore, physicians and patients should remain alert for and be especially watchful in the presence of previous GI tract symptoms. Patients should be informed about the signs and symptoms of serious GI toxicity and the steps to take if they occur. For patients with a history of peptic ulcer disease, therapy with NSAIDs should be initiated only after careful consideration has been given to the advisability of continuing treatment. Only one or two patients in 1,000 treated with agents which inhibit prostaglandin synthesis (e.g., aspirin, indomethacin, flurbiprofen) may develop gastric erosions or ulcers which appear to occur in approximately 1% of patients treated for 3 months, and in about 2-5% 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; however, even short-term therapy is not without risk.

NSAIDs should be prescribed with extreme caution in those with a prior history of ulcer disease or in those who have had peptic ulcer disease in the past. NSAIDs, like aspirin, have a greater than 10-fold higher risk of developing a GI tract lesion than those with neither of these risk factors. In addition to a past history of peptic ulcer disease, pharmacoeconomic studies have identified other cardiovascular or cerebrovascular conditions or conditions that may increase the risk for GI bleeding such as: treatment with other non-steroidal anti-inflammatory drugs, treatment with corticosteroids, treatment with acetylsalicylic acid (ASA) therapy, alcoholism, smoking, use of corticosteroids, ulcer, and poor general health status.

Anaphylactoid Reactions

As with other NSAIDs, anaphylactoid reactions may occur in patients without known prior exposure to NSAIDs. For this reason, Ponstel should be given cautiously to patients with a history of drug allergy. In such patients, an antihistaminic agent should be administered concurrently with NSAID therapy. Treatment of anaphylactoid reactions therefore should include, at a minimum, discontinuation of the drug, the use of adrenalin and other standard symptomatic measures.

Adverse Reactions

In a single dose study (n=6), ingestion of an antacid containing 1.7-gram of magnesium hydroxide and 2.7-gram of calcium carbonate decreased plasma levels of mefenamic acid by 125% and 36%, respectively.1

Nonsteroidal anti-inflammatory drugs (NSAIDs) are classified as pregnancy category C. Ponstel should not be used in patients with pre-existing renal disease. In preclinical studies, NSAIDs have a tendency to increase renal papillary necrosis and other renal, hepatic and bone marrow toxicity. In patients with renal disease, decreased urine output and/or elevation of serum creatinine may occur.

Pregnancy

Any woman who is pregnant should be apprised of the potential hazard to the fetus of exposure to NSAIDs. Only when the benefits are thought to outweigh the risks should Ponstel be used in the second and third trimesters.

Antacids:

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Warfarin:

The anticoagulant effect of warfarin is not altered by coadministration of Ponstel. However, a small but statistically significant decrease in anticoagulant effect was observed in subjects coadministering warfarin and ketoprofen (see CLINICAL PHARMACOLOGY, INTERACTIONS).

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