

PRODUCT MONOGRAPH

Pr PYRIDIUM®

Phenazopyridine Hydrochloride Tablets USP

100 and 200 mg

Urinary Tract Analgesic



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PYRIDIUM®
Phenazopyridine Hydrochloride Tablets USP

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Nonmedicinal Ingredients
oral	Tablet 100 mg, 200 mg	Carnauba wax, cornstarch, D&C red No. 7, FD&C blue No. 2, FD&C yellow No. 6, gelatin, lactose, magnesium stearate, methylcellulose, sodium starch glycolate, sucrose, titanium dioxide and white wax.

INDICATIONS AND CLINICAL USE

Adults (≥18 years old):

PYRIDIUM® (Phenazopyridine Hydrochloride) is indicated for the symptomatic relief of pain, burning, urgency, frequency, and other discomforts resulting from irritation of the mucosa of the lower urinary tract caused by infection, trauma, surgery, endoscopic procedures, or the passage of sounds or catheters.

Phenazopyridine is compatible with antimicrobial therapy and can help relieve pain and discomfort during the interval before an antimicrobial therapy controls the infection.

Treatment with phenazopyridine should not exceed 2 days because of potential organ damage. (See **Warnings and Precautions**)

Geriatrics (>65 years old): No data are available

Pediatrics (< 18 years old): No data are available

CONTRAINDICATIONS

PYRIDIUM® is contraindicated in:

- patients who are hypersensitive to the drug or its ingredients.
- patients with renal insufficiency or any liver disease.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

A yellowish color of the skin or sclerae may indicate accumulation of phenazopyridine resulting from impaired renal function or overdose or taking the drug for more than two days, and necessitates discontinuance of the drug. It should be noted that a decline in renal function is common in elderly patients. Phenazopyridine produces an orange to red color in the urine and feces, and may cause staining. Phenazopyridine may cause discoloration of body fluids and staining of contact lenses. Phenazopyridine may mask pathological conditions and interfere with laboratory test values using colorimetric, spectrophotometric or fluorometric analysis methods.

Cautious use in patients with G-6-PD deficiency is advised since these patients are susceptible to oxidative hemolysis and may have greater potential to develop hemolytic anemia.

Patient Counselling by the physician:

- The patient should be advised to take phenazopyridine with or following food or after eating a snack to reduce stomach upset.
- The patient should be advised that phenazopyridine produces an orange to red color in the urine and feces, and may cause staining.
- The patient should be advised that treatment with Pyridium should not exceed 2 days.
- The patient should be advised to discontinue Pyridium and contact their doctor immediately if they notice a yellowish color of the skin or sclerae (white of the eye).

Carcinogenesis and Mutagenesis

Long-term administration of phenazopyridine has been associated with tumors of the large intestine in rats and of the liver in mice. Available epidemiological data are insufficient to evaluate the carcinogenicity of phenazopyridine in humans. In vitro studies indicate that phenazopyridine in the presence of metabolic activation is mutagenic in bacteria and mutagenic and clastogenic in mammalian cells.

Striated muscles

Treatment with phenazopyridine should not exceed 2 days. 2,3,6-triaminopyridine, a metabolite of phenazopyridine, caused extensive injury to the skeletal muscle and, to a lesser extent, the heart muscle in rats in a toxicology study. Caution is advised when giving phenazopyridine to patients with a heart condition or to patients with any neuromuscular condition.

Hepatic/Biliary/Pancreatic

Phenazopyridine is contraindicated in patients with any liver disease. (See **Contraindications**)

Renal

Phenazopyridine is contraindicated in patients with renal insufficiency. The decline in renal function associated with advanced age should be kept in mind. There are no data available in elderly patients.

Phenazopyridine produces an orange to red color in the urine (See **Serious Warnings and Precautions**).

Hematologic

Patients with G-6-PD deficiency are susceptible to oxidative hemolysis and may have greater potential to develop hemolytic anemia (See **Serious Warnings and Precautions**). Phenazopyridine should not be used in patients with G-6-PD Mediterranean as hemolysis may occur at normal doses in these patients.

Infection

The use of phenazopyridine for relief of symptoms should not delay definitive diagnosis and treatment of causative conditions. The drug should be used for symptomatic relief of pain and not as a substitute for specific surgery or antimicrobial therapy.

Ophthalmologic

A yellowish color of sclerae (white of the eye) may indicate accumulation of phenazopyridine resulting from impaired renal function or overdose or taking for more than two days, and necessitates discontinuance of the drug. (See **Serious Warnings and Precautions**).

Skin

A yellowish color of the skin may indicate accumulation of phenazopyridine resulting from impaired renal function or overdose or taking for more than two days, and necessitates discontinuance of the drug. (See **Serious Warnings and Precautions**).

Special Populations

Pregnant Women

Reproductive studies with phenazopyridine (in combination with sulfacytine) in rats given up to 110 mg/kg/day and in rabbits given up to 39 mg/kg/day during organogenesis revealed no evidence of harm to offspring.

One very limited prospective study in humans demonstrated that phenazopyridine traverses the placenta into the fetal compartment. There are no adequate and well-controlled studies in pregnant women. Therefore, phenazopyridine should be used in pregnant women only if the benefit clearly outweighs the risk.

Nursing Women

It is unknown if the drug is excreted in human milk. Because many drugs are excreted in human milk precaution should be exercised.

Pediatrics (<18 years old)

Safety and effectiveness in children below the age of 18 have not been established.

Geriatrics (> 65 years old)

Safety and effectiveness in elderly patients above 65 have not been established.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

Gastrointestinal: nausea, vomiting and diarrhea.

Nervous System: headache, aseptic meningitis.

Integumentary: rash, pruritus, discoloration, jaundice,.

Renal: renal toxicity usually associated with overdose, renal calculi.

Hematologic: methemoglobinemia, hemolytic anemia, potential hemolytic agent in G-6-PD deficiency, sulfhemoglobinemia, neutropenia, leukopenia, pancytopenia.

Body as a Whole: anaphylactoid-like reaction and hypersensitivity hepatitis.

Special Senses: visual disturbances, eye irritation, ear pain, reversible loss of color vision.

Other: hepatic toxicity usually associated with overdose, discoloration of body fluids.

DRUG INTERACTIONS

Drug-Drug Interactions

The medical literature suggests that no significant interactions have been reported besides the one mentioned below.

Table 1 Established or Potential Drug-Drug Interactions

<Proper name>	Ref	Effect	Clinical comment
Ciprofloxacin	Theoretical	↑ Ciprofloxacin bioavailability	Caution is warranted

Drug-Laboratory Test Interactions

Due to its properties as an azo dye, Phenazopyridine HCl may interfere with urinalysis based on spectrometry or color reactions (See Warnings and Precautions).

Phenazopyridine may interfere with the phenolsulfonphthalein (PSP) excretion test of kidney function; butanol may be used to extract phenazopyridine from the final alkaline urine dilution to give accurate results.

Phenazopyridine may interfere with urinary glucose tests. Phenazopyridine may interfere with urinary ketone tests using sodium nitroprusside or Gerhardt ferric chloride by producing interfering colors. Phenazopyridine may interfere with urinary urobilinogen determinations because of color interference with Ehrlich's reagent. Phenazopyridine may produce falsely elevated readings in the spectrophotofluorimetric screening tests and assays for porphyrins.

Phenazopyridine may interfere with laboratory test values using colorimetric, photometric or fluorometric analysis methods. Altered urine laboratory test values may include ketone (sodium nitroprusside), bilirubin (foam test, talc-disk-Fouchet-spot test, Franklin's tablet-Fouchet test, p-nitrobenzene diazonium p-toluene sulfonate reagent), diacetic acid (Gerhardt ferric chloride test), free hydrochloric acid, glucose (glucose oxidase tests), 17-hydroxycorticosteroids (modified Glenn-Nelson), 17-ketosteroids (Holtorff Koch modification of Zimmerman), porphyrins, albumin (discolors bromophenol blue test areas of commercial reagent strips, nitric acid ring test), phenolsulfophthalein, urobilinogen (color interference with Ehrlich's reagent), and urinalysis (spectrophotometric or color-based tests). Phenazopyridine also imparts an orange-red color to stools which may interfere with color tests.

DOSAGE AND ADMINISTRATION

Recommended Dose and Dosage Adjustment

Adults: 200 mg 3 times daily after meals.

When used concomitantly with an antibacterial agent for the treatment of a urinary tract infection, the administration of phenazopyridine should **not** exceed 2 days. If symptoms persist, the patient should be re-evaluated.

Missed Dose

If a dose is missed, patients should take it as soon as they remember. If it is near the time of the next dose, patients should skip the missed dose and resume their usual dosing schedule. Patients should not double the dose to catch up.

Administration

Administration is by the oral route, preferably after meals.

OVERDOSAGE

For management of a suspected drug overdose contact your regional Poison Control Centre.

Exceeding the recommended dose in patients with normal renal function or administering the recommended dose to patients with reduced renal function (common in elderly patients) may lead to increased serum levels and toxic reactions.

Methemoglobinemia generally follows a massive, acute overdose. Oxidative Heinz body hemolytic anemia also may occur, and “bite cells” (degmacytes) may be present in a chronic overdosage situation. Red blood cell G-6-PD deficiency may predispose to hemolysis; however, hemolysis may occur at normal doses in patients with G-6-PD Mediterranean. Renal toxicity and occasional failure and hepatic impairment may also occur.

Treatment: Treatment is symptomatic and supportive. Methylene blue, 1 to 2 mg/kg/dose given i.v. as a 1% solution as needed, should cause prompt reduction of the methemoglobinemia and disappearance of the cyanosis which is an aid in diagnosis.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Phenazopyridine is excreted in the urine where it exerts a topical analgesic effect on the mucosa of the lower urinary tract. This action helps to relieve pain, burning, urgency and frequency. The precise mechanism of action is unknown.

Pharmacokinetics

The pharmacokinetic properties of phenazopyridine have not been fully elucidated. Phenazopyridine and its metabolites are rapidly excreted by the kidneys. In a small number of healthy subjects, 90% of a 600 mg/day oral dose of phenazopyridine was eliminated in the urine in 24 hours, 41% as unchanged drug and 49% as metabolites.

STORAGE AND STABILITY

Store at controlled room temperature, 15-30°C.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Composition

PYRIDIUM[®] 100 mg: Each reddish brown, coated tablet, imprinted with a white PD 180 monogram on one side, contains: phenazopyridine HCl 100 mg. Nonmedicinal ingredients: carnauba wax, cornstarch, D&C red No. 7, FD&C blue No. 2, FD&C yellow No. 6, gelatin, lactose, magnesium stearate, methylcellulose, sodium starch glycolate, sucrose, titanium dioxide and white wax. Energy: 1.76 kJ (0.42 kcal)/100 mg. Sodium: 0.32 mg. gluten-, paraben-, sulfite- and tartrazine-free. Bottles of 100.

PYRIDIUM[®] 200 mg: Each reddish brown, coated tablet, imprinted with a white PD 181 monogram on one side, contains: phenazopyridine HCl 200 mg. Nonmedicinal ingredients: carnauba wax, cornstarch, D&C red No. 7, FD&C blue No. 2, FD&C yellow No. 6, gelatin, lactose, magnesium stearate, methylcellulose, sodium starch glycolate, sucrose, titanium dioxide and white wax. Energy: 3.52 kJ (0.84 kcal)/200 mg. Sodium: 0.32 mg. gluten-, paraben-, sulfite- and tartrazine-free. Bottles of 100.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

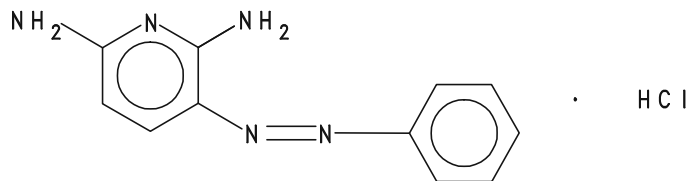
Proper Name: Phenazopyridine hydrochloride

Chemical Name: 2, 6-pyridinediamine, 3-(phenylazo)-, monohydrochloride.

Empirical Formula: C₁₁H₁₁N₅ •HCl

Molecular Weight: 249.70

Structural Formula:



Physicochemical properties: Brick-red microcrystals with a slight violet luster or a purple powder.
Slightly bitter taste.

DETAILED PHARMACOLOGY

Phenazopyridine Hydrochloride exerts a topical analgesic effect on the mucosa of the lower urinary tract. This action helps to relieve pain, burning, urgency and frequency. The precise mechanism of action is not known.

Phenazopyridine HCl is rapidly excreted by the kidneys, with as much as 65% of an oral dose being excreted unchanged in the urine.

TOXICOLOGY

Toxic reactions to phenazopyridine, an azo dye, appear to be rare. Metabolism of phenazopyridine results in the formation of large quantities of aniline, and the production of methemoglobinemia by phenazopyridine is probably due to the aniline metabolites. Because the azo dye is deposited in the skin, yellow skin pigmentation has been noted in cases of azo dye intoxication.

The oral administration of phenazopyridine hydrochloride to dogs showed that the drug accumulated selectively in lacrimal and nictitans glands and the glands of Moll, and caused a reduction of tear flow. The drug or its metabolic derivative was detectable by light microscopy as an accumulation in the cytoplasm within 48 hours after drug administration. Electron microscopy showed that the product detected was localized in secretory granules. The results suggest that phenazopyridine hydrochloride affects the synthesis of secretory granules and causes progressive destruction of affected cells.

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PART III: CONSUMER INFORMATION

PYRIDIUM[®]

(Phenazopyridine Hydrochloride)

Tablets USP

Read this information each time you refill your prescription in case new information has been added. This leaflet is part III of three-part ``Product Monograph`` published when PYRIDIUM[®] was approved for sale in Canada and is designed specifically for consumers. This leaflet is a summary and will not tell you everything about PYRIDIUM[®]. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

Your health care provider has prescribed PYRIDIUM[®] for you for one or more of the following medical conditions:

- Pain, burning, urgency, frequency, and other discomforts resulting from lower urinary tract caused by infection, trauma, surgery, endoscopic procedures, or the passage of sounds or catheters.

PYRIDIUM[®] is indicated for short-term use and can only relieve symptoms; it is not a treatment for the underlying cause of the symptoms.

What it does:

PYRIDIUM[®] is excreted in the urine where it exerts a topical analgesic effect on the mucosa of the lower urinary tract. This action helps to relieve pain, burning, urgency and frequency. The precise mechanism of action is unknown.

When it should not be used:

DO NOT TAKE PYRIDIUM[®] if you have any of the following medical conditions:

- hypersensitive to the drug or its ingredients
- renal insufficiency
- severe liver disease

PYRIDIUM[®] should NOT be used in patients under 18 -years of age since the safety and effectiveness have NOT been established.

What the medicinal ingredient is:

Phenazopyridine Hydrochloride

What the non medicinal ingredient are:

Carnauba wax, cornstarch, D&C red No. 7, FD&C blue No. 2, FD&C yellow No. 6, gelatin, lactose, magnesium stearate, methylcellulose, sodium starch glycolate, sucrose, titanium dioxide and white wax.

What dosage forms it comes in:

Each Tablet USP contains 100 mg or 200mg of Phenazopyridine Hydrochloride

WARNING AND PRECAUTIONS

If your skin or the whites of your eyes develop a yellowish tone, it may indicate that your kidneys are not eliminating the medication as they should. STOP TAKING THE DRUG AND NOTIFY YOUR DOCTOR IMMEDIATELY.

If you have, or previously had, any of the following medical conditions, see your health care provider to discuss treatment options other than PYRIDIUM[®]:

- hypersensitive to the drug or its ingredients
- renal insufficiency
- severe liver disease

Phenazopyridine produces an orange to red color in the urine and feces, and may cause staining. Staining of contact lenses has also been reported. If you are older, your doctor will watch you more closely, since the kidneys work less effectively with age.

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

- G-6-PD deficiency
- renal insufficiency
- severe liver disease
- Any other medical problem

INTERACTIONS WITH THIS MEDICATION

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):

- Ciprofloxacin

No other interactions have been reported

PROPER USE OF THIS MEDICATION

Adults

Usual Dose: 200 mg 3 times daily after meals.

Take PYRIDUM[®] 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 PYRIDUM[®] may increase your chances of unwanted and sometimes dangerous side effects, especially if you are elderly, have other diseases.

If you will be using PYRIDUM[®] for more than 2 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. PYRIDUM[®] is **NOT** recommended for use in patients under 18 years of age since safety and effectiveness have **NOT** been established.

Follow all directions given to you by your doctor or pharmacist carefully. They may differ from the information contained in this leaflet. **If you do not understand the instructions on the pack or bottle, ask your doctor or pharmacist for help.**

Take PYRIDUM[®] exactly as your doctor has prescribed.

PYRIDUM[®] must be taken after meals.

Missed Dose

If a dose is missed, you should take it as soon as you remember. If it is near the time of the next dose, skip the missed dose and resume your usual dosing schedule. Do not double the dose to catch up.

Overdose

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

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM		
Symptom	STOP taking (Brand Name of Drug) and talk to your physician or pharmacist	STOP taking (Brand Name of Drug) and get emergency medical attention IMMEDIATELY
Headaches, stiff neck		✓
Shortness of breath, wheezing, any trouble breathing or chest tightness		✓
Skin rash, hives, swelling of the neck, throat or tongue or itching		✓
Blurred vision, or any visual disturbance	✓	
nausea, vomiting and diarrhea.	✓	
Yellow discoloration of the skin or whites of the eyes with or without itchy skin	✓	

Check with your health care provider IMMEDIATELY if you develop chills, fever, muscle aches or pains, or other flu like symptoms, swelling of the neck and throat and tongue, 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.**

This is NOT a complete list of side effects. If you develop any other symptoms while taking PYRIDIUM[®], see your health care provider. These side effects are rare.

HOW TO STORE IT

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

Keep the tablets in a dry place at normal room temperature (below 30°C) in the packaging that they come in.

Keep out of sight and reach of children.

PYRIDIUM[®] 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.

PYRIDIUM[®] may turn your skin or the whites of your eyes to a yellowish tone. If you have such symptoms contact health care provider immediately.

MORE INFORMATION

This document plus the full product monograph prepared for health professionals can be found at <http://www.erfa.net> or by contacting the sponsor, ERFA Canada Inc. at 1-888-922-3133.

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REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

1. Report online at
www.healthcanada.gc.ca/medeffect
2. Call toll-free at 1-866-234-2345
3. Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701D
Ottawa, Ontario
K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.