PRESCRIBING INFORMATION

PrPHENAZO®
Phenazopyridine Hydrochloride Tablets
100 mg and 200 mg Tablets

Urinary Analgesic

Bausch Health, Canada Inc.
2150 St-Elzear Blvd. West
Laval, Quebec
H7L 4A8

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PrPHENAZO®
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100 mg and 200 mg Tablets

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Non-medicinal Ingredients
Oral	Tablet 100 mg, 200 mg	FD&C Blue No. 1 Al lake (200mg), FD&C Red No. 40 Al lake (200mg), FD&C Yellow No. 6 Al Lake (200mg), Hydroxypropyl Methyl-Cellulose (200mg), Lactose, Magnesium Stearate, Microcrystalline Cellulose, Mineral Oil (200mg), Polyethylene Glycol (200mg), Povidone (200mg), Shellac Glaze (100mg), Sodium Lauryl Sulphate (200mg), Sodium Starch Glycolate, Stearic Acid (200mg), Talc, Titanium Dioxide (200mg).

INDICATIONS AND CLINICAL USE

PHENAZO (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 antimicrobial therapy controls the infection.
Treatment of a urinary tract infection with phenazopyridine should not exceed 2 days. There is no evidence that the combined administration of phenazopyridine and an antimicrobial provides greater benefit than administration of the antimicrobial alone after 2 days.

Patient subset

Geriatrics (>65 years old)
No data is available

Pediatrics (<16 years old)
No data is available

CONTRAINDICATIONS

PHENAZO is contraindicated in:

- patients who are hypersensitive to the drug or its ingredients.
- patients with renal insufficiency (including glomerulonephritis, uremia, pyelonephritis during pregnancy, or impaired renal function)
- patients with severe liver disease.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Phenazopyridine produces an orange to red colour in the urine and feces and may cause staining. Phenazopyridine may cause discoloration of body fluids and staining of contact lenses has been reported. A yellowish colour of the skin or sclerae may indicate accumulation of phenazopyridine resulting from impaired renal function and necessitates discontinuance of the drug. It should be noted that a decline in renal function is common in elderly patients. 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.

General

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 colour in the urine and feces and may cause staining.

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.

Genitourinary

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

Hepatic/Biliary/Pancreatic
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**).

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 colour of sclerae may indicate accumulation of phenazopyridine (see **Serious Warnings and Precautions**)

Renal
The decline in renal function associated with advanced age should be kept in mind.

Skin
A yellowish colour of the skin may indicate accumulation of phenazopyridine resulting from impaired renal function and necessitates discontinuance of the drug (see **Serious Warnings and Precautions**).

Special Populations

Pregnant Women
Category B:
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 prospective very limited 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 (<16 years old)
Safety and effectiveness in children below the age of 16 have not been established.

Geriatrics (> 65 years old)
Safety and effectiveness in elderly patients above 65 have not been established.

Monitoring and Laboratory Tests

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 (colour interference with Ehrlich's reagent), and urinalysis (spectrophotometric or colour-based tests). Phenazopyridine also imparts an orange-red colour to stools which may interfere with colour tests.

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.

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

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

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

DRUG INTERACTIONS

Drug-Drug Interactions

The medical literature to date suggests that no significant interactions have been reported beside 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 colour reactions (see **Warnings and Precautions**).

Phenazopyridine may interfere with the phenolsulfophthalein (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 colour interference with Ehrlich's reagent. Phenazopyridine may produce falsely elevated readings in the spectrophotofluorimetric screening tests and assays for porphyrins.

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, patient should take it as soon as they 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.

Administration

Administration is by the oral route, preferably after meals.

OVERDOSAGE

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

Methemoglobinemia generally follows a massive, acute overdose. 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. 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.

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

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 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 determined. 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

PHENAZO 100mg and 200mg tablets contain the active ingredient phenazopyridine hydrochloride USP.

Nonmedicinal ingredients: FD&C Blue No. 1 Aluminum Lake (200mg), FD&C Red No. 40 Aluminum Lake (200mg), FD&C Yellow No. 6 Aluminum Lake (200mg), Hydroxypropyl Methylcellulose (200mg), Lactose, Magnesium Stearate, Microcrystalline Cellulose, Mineral Oil (200mg), Polyethylene Glycol (200mg), Povidone (200mg), Shellac Glaze (100mg), Sodium Lauryl Sulphate (200mg), Sodium Starch Glycolate, Stearic Acid (200mg), Talc, Titanium Dioxide (200mg).

Availability

100mg: Each maroon, round film-coated tablet imprinted "25" contains phenazopyridine hydrochloride USP. Bottles of 100 tablets.

200mg: Each maroon, oblong film-coated tablet imprinted "CPC860" contains phenazopyridine hydrochloride USP. Bottles of 100 tablets.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

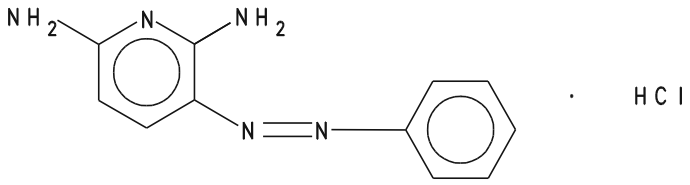
Proper Name: Phenazopyridine hydrochloride

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

Empirical Formula: $C_{11}H_{11}N_5 \cdot HCl$

Molecular Weight: 249.70 g/mol

Structural Formula:



Physicochemical properties

Description: 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 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 exceedingly 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.

REFERENCES

1. Alano FA Jr., Webster GD Jr. Acute renal failure and pigmentation due to phenazopyridine (Pyridium). Ann Intern Med. 1970 Jan;72(1):89-91.

2. Cahan DH. Phenazopyridine overdose and renal failure. JAMA. 1979 Jun 29;241(26):2785.

3. Cohen BL, Bovasso GJ Jr. Acquired methemoglobinemia and hemolytic anemia following excessive pyridium (phenazopyridine hydrochloride) ingestion. Clin Pediatr (Phila). 1971 Sep;10(9):537-40.

4. Eisinger AJ, Jones R. Phenazopyridine-hydrochloride haemolysis. Lancet. 1969 Jan 18;1(7586):151.

5. Goldfinger SE, Marx S. Hypersensitivity hepatitis due to phenazopyridine hydrochloride. N Engl J Med. 1972 May 18;286(20):1090-1.

6. Greenberg MS, Wong H. Methemoglobinemia and Heinz body hemolytic anemia due to phenazopyridine hydrochloride. N Engl J Med. 1964 Aug 27;271:431-5.

7. Herlihy TE. Phenazopyridine and aseptic meningitis. Ann Intern Med. 1987 Jan;106(1):172-3.

8. Hollifield RD, Conklin JD. A method for determining nitrofurantoin in urine in the presence of phenazopyridine hydrochloride and its metabolites. Clin Chem. 1970 Apr;16(4):335-8.

9. Hood JW, Toth WN. Jaundice caused by phenazopyridine hydrochloride. JAMA. 1966 Dec 26;198(13):1366-7.

10. Johnson WJ, Chartrand A. The metabolism and excretion of phenazopyridine hydrochloride in animals and man. Toxicol Appl Pharmacol. 1976 Aug;37(2):371-6.

11. Marcelín-Jiménez G, Angeles AP, Martínez-Rossier L, Fernández S A. Ciprofloxacin bioavailability is enhanced by oral co-administration with phenazopyridine: a pharmacokinetic study in a Mexican population. Clin Drug Investig. 2006;26(6):323-8.

12. McEwen J, Paterson C. Drugs and false-positive screening tests for porphyria. Br Med J. 1972 Feb 12;1(5797):421.

13. Meshali MM, El-Sabbagh H. Effect of adsorption of phenazopyridine hydrochloride on its bioavailability in human. Pharmazie. 1981 Dec;36(12):867-8.

14. Randazzo GP, Ford EA, Glauser FL. Methemoglobinemia caused by acute overdosage of phenazopyridine. West J Med. 1975 May;122(5):427-9.

15. Tishler M, Abramov A. Phenazopyridine-induced hemolytic anemia in a patientwith G6PD deficiency. Acta Haematol. 1983;70(3):208-9.

16. Wander HJ, Pascoe DJ. Phenylazopyridine hydrochloride poisoning. report of case and review of literature. Am J Dis Child. 1965 Jul;110:105-7.

17. Zelenitsky SA, Zhanel GG. Phenazopyridine in urinary tract infections. Ann Pharmacother. 1996 Jul-Aug;30(7-8):866-8.

PART III: CONSUMER INFORMATION

PrPHENAZO®
Phenazopyridine Hydrochloride Tablets
100 mg and 200 mg Tablets

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 PHENAZO™ was approved for sale in Canada and is designed specifically for consumers. This leaflet is a summary and will not tell you everything about PHENAZO™. 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 PHENAZO 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.

PHENAZO 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:
PHENAZO is excreted in the urine where it exerts a topical analgesic effect on the mucosa of the 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 PHENAZO if you have any of the following medical conditions:

- **hypersensitive to the drug or its ingredients**
- **kidney disorders**
- **severe liver disease**

PHENAZO should NOT be used in patients under 16 years of age since the safety and effectiveness have NOT been established.

What the medicinal ingredient is:
Phenazopyridine Hydrochloride 100mg and 200 mg

What the important nonmedicinal ingredient are:
FD&C Blue No. 1 Aluminum Lake (200mg), FD&C Red No. 40 Aluminum Lake (200mg), FD&C Yellow No. 6 Aluminum Lake (200mg), Hydroxypropyl Methylcellulose (200mg), Lactose, Magnesium Stearate, Microcrystalline Cellulose, Mineral Oil (200mg), Polyethylene Glycol (200mg), Povidone (200mg), Shellac Glaze (100mg), Sodium Lauryl Sulphate (200mg), Sodium Starch Glycolate, Stearic Acid (200mg), Talc, Titanium Dioxide (200mg).

What dosage forms it comes in:
Each Tablet contains 100 mg or 200mg of Phenazopyridine Hydrochloride

WARNING AND PRECAUTIONS

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

- **hypersensitive to the drug or its ingredients**
- **kidney problems**
- **severe liver disease**

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

Usual Dose

Medical Condition	Age Group	Starting Dose	Maxi-mum Dose (per day)	Maximum Duration of Treatment (days)
Symptomat	>16	200 mg	1200mg	2

ic relief of pain, burning, urgency, frequency, and other discomforts caused by infection, trauma, surgery, endoscopic procedures, or the passage of sounds or catheters.	years	3 times daily after meals		

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

If you will be using PHENAZO 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. PHENAZO is NOT recommended for use in patients under 16 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 PHENAZO exactly as your doctor has prescribed.
PHENAZO 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.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

PHENAZO 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.

PHENAZO may turn your skin or the whites of your eyes to a yellowish tone. If you have such symptoms check with your health care provider.

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

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

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom	**STOP taking PHENAZO and talk to your physician or pharmacist**	**STOP taking PHENAZO and get emergency medical attention IMMEDIATELY**
Headaches, stiff neck	✔	
Shortness of breath, wheezing, any trouble breathing or chest tightness		✔
Skin rash, hives, swelling 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	✔	

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 (15-

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 (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) 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.

Keep out of reach of children.

MORE INFORMATION

This document plus the full product monograph prepared for health professionals can be obtained by contacting the sponsor, Bausch Health, Canada Inc. at 1-800-361-4261.

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