

Rev. November 2003

HIPREX[®]

(methenamine hippurate tablets USP)

DESCRIPTION

Each yellow capsule-shaped tablet contains 1 g Methenamine Hippurate which is the Hippuric Acid Salt of Methenamine (hexamethylene tetramine). The tablet also contains inactive ingredients. FD&C Yellow No. 5 (tartrazine, see PRECAUTIONS), Magnesium Stearate, Povidone, and Saccharin Sodium.

ACTIONS

Microbiology: HIPREX (methenamine hippurate tablets USP) has antibacterial activity because the methenamine component is hydrolyzed to formaldehyde in acid urine. Hippuric acid, the other component, has some antibacterial activity and also acts to keep the urine acid. The drug is generally active against *E. coli*, enterococci and staphylococci. *Enterobacter aerogenes* is generally resistant. The urine must be kept sufficiently acid for urea-splitting organisms such as *Proteus* and *Pseudomonas* to be inhibited.

Human Pharmacology: Within 1/2 hour after ingestion of a single 1-gram dose of HIPREX, antibacterial activity is demonstrable in the urine. Urine has continuous antibacterial activity when HIPREX is administered at the recommended dosage schedule of 1 gram twice daily. Over 90% of methenamine moiety is excreted in the urine within 24 hours after administration of a single 1-gram dose. Similarly, the hippurate moiety is rapidly absorbed and excreted, and it reaches the urine by both tubular secretion and glomerular filtration. This action may be important in older patients or in those with some degree of renal impairment.

INDICATIONS

HIPREX is indicated for prophylactic or suppressive treatment of frequently recurring urinary tract infections when long-term therapy is considered necessary. This drug should only be used after eradication of the infection by other appropriate antimicrobial agents.

CONTRAINDICATIONS

HIPREX (methenamine hippurate tablets USP) is contraindicated in patients with renal insufficiency, severe hepatic insufficiency, or severe dehydration. Methenamine preparations should not be given to patients taking sulfonamides because some sulfonamides may form an insoluble precipitate with formaldehyde in the urine.

WARNING

Large doses of methenamine (8 grams daily for 3 to 4 weeks) have caused bladder irritation, painful and frequent micturition, albuminuria, and gross hematuria.

PRECAUTIONS

1. Care should be taken to maintain an acid pH of the urine, especially when treating infections due to urea-splitting organisms such as *Proteus* and strains of *Pseudomonas*.
2. In a few instances in one study, the serum transaminase levels were slightly elevated

- during treatment but returned to normal while the patients were still taking HIPREX. Because of this report, it is recommended that liver function studies be performed periodically on patients taking the drug, especially those with liver dysfunction.
3. Use in Pregnancy: In early pregnancy the safe use of HIPREX is not established. In the last trimester, safety is suggested, but not definitely proved. No adverse effects on the fetus were seen in studies in pregnant rats and rabbits. HIPREX taken during pregnancy can interfere with laboratory tests of urine estriol (resulting in unmeasurably low values) when acid hydrolysis is used in the laboratory procedure. This interference is due to the presence in the urine of methenamine and/or formaldehyde. Enzymatic hydrolysis, in place of acid hydrolysis, will circumvent this problem.
 4. This product contains FD&C Yellow No. 5 (tartrazine), which may cause allergic-type reactions (including bronchial asthma) in certain susceptible individuals. Although the overall incidence of FD&C Yellow No. 5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity.

Geriatric Use:

Clinical studies of HIPREX did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.

HIPREX is contraindicated in patients with renal insufficiency and severe hepatic insufficiency (see CONTRAINDICATIONS).

ADVERSE REACTIONS

Minor adverse reactions have been reported in less than 3.5% of patients treated. These reactions have included nausea, upset stomach, dysuria, and rash.

DOSAGE AND ADMINISTRATION

1 tablet (1.0 g) twice daily (morning and night) for adults and pediatric patients over 12 years of age. 1/2 to 1 tablet (0.5 to 1.0 g) twice daily (morning and night) for pediatric patients 6 to 12 years of age. Since the antibacterial activity of HIPREX is greater in acid urine, restriction of alkalinizing foods and medications is desirable. If necessary, as indicated by urinary pH and clinical response, supplemental acidification of the urine should be instituted. The efficacy of therapy should be monitored by repeated urine cultures.

HOW SUPPLIED

1-gram scored, capsule-shaped yellow tablets debossed MERRELL 277 in bottles of 100 (NDC 0068-0277-61)

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