HIPREX- methenamine hippurate tablet
Validus Pharmaceuticals LLC

Hiprex Tablets

HIPREX®

(methenamine hippurate tablets USP)

To reduce the development of drug-resistant bacteria and maintain the effectiveness of HIPREX (methenamine hippurate tablets USP) and other antibacterial drugs, HIPREX should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

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.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of HIPREX and other antibacterial drugs, HIPREX should be used only to treat or prevent

infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

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

Prescribing HIPREX in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

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**).*

Information for Patients

Patients should be counseled that antibacterial drugs including HIPREX should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When HIPREX is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by HIPREX or other antibacterial drugs in the future.

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.

To report SUSPECTED ADVERSE REACTIONS, contact Validus Pharmaceuticals LLC at

1-866-982-5438 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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 W 1037 in bottles of 100 (NDC 30698-477-01).

Store at 68° to 77°F (20° to 25°C); excursions permitted to 59° to 86°F (15° to 30°C) [See USP Controlled Room Temperature].

Dispense in well-closed, light-resistant container with child-resistant closure.

Manufactured for and Distributed by:
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Product of India

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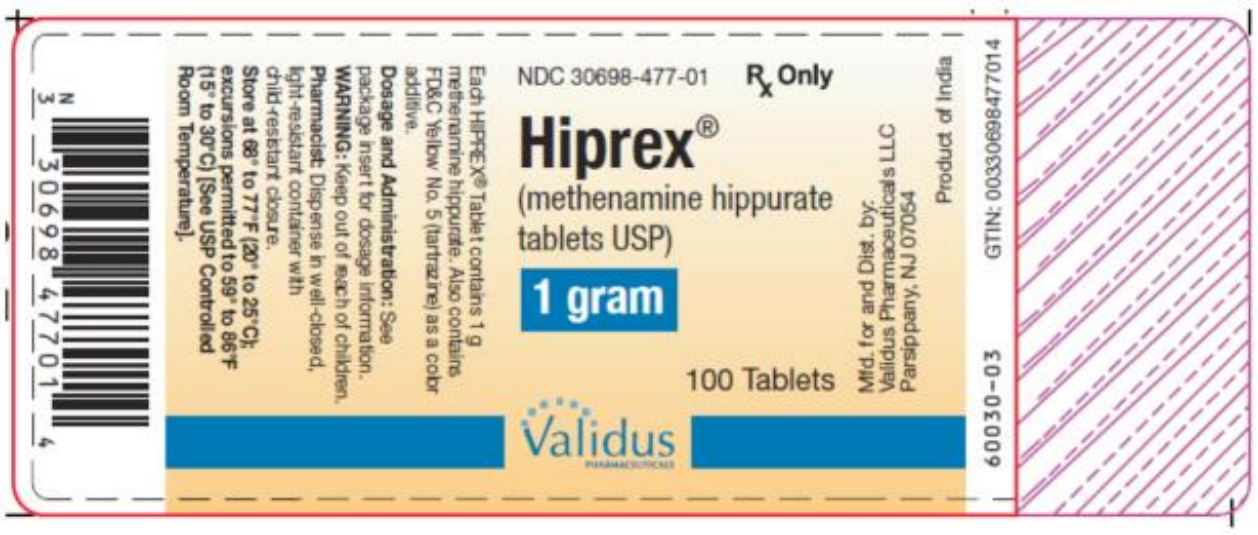
PRINCIPAL DISPLAY PANEL

NDC 30698-477-01
Hiprex®
(methenamine hippurate
Tablets USP)
1 gram
100 Tablets
Rx Only



HIPREX

methenamine hippurate tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:30698-477
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
METHENAMINE HIPPURATE (UNII: M329791L57) (METHENAMINE - UNII:J50OIX95QV)	METHENAMINE HIPPURATE	1 g

Inactive Ingredients

Ingredient Name	Strength
FD&C YELLOW NO. 5 (UNII: I753WB2F1M)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POVIDONE (UNII: FZ989GH94E)	
SACCHARIN SODIUM (UNII: SB8ZUX40TY)	

Product Characteristics

Color	yellow	**Score**	2 pieces
Shape	CAPSULE	**Size**	19mm
Flavor		**Imprint Code**	W;1037
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:30698-477-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	09/09/1976	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA017681	09/09/1976	

Labeler - Validus Pharmaceuticals LLC (801194619)

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