1 NAME OF THE MEDICINAL PRODUCT

Methenamine hippurate 1 g tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 1 g methenamine hippurate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

White to off- white colored, capsule shaped, biconvex tablets, debossed with "H" and "1" on either side of breakline on one side and plain on other side with approximate length 20.00 mm & width 8.00 mm.

The tablet can be divided into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Methenamine hippurate is indicated in the prophylaxis and treatment of urinary tract infections:

1. As maintenance therapy after successful initial treatment of acute infections with antibiotics.
2. As long-term therapy in the prevention of recurrent cystitis.
3. To suppress urinary infection in patients with indwelling catheters and to reduce the incidence of catheter blockage.
4. To provide prophylaxis against the introduction of infection into the urinary tract during instrumental procedures.

5. Asymptomatic bacteriuria.

4.2 Posology and method of administration

Posology
Adults: 1 g twice daily.

In patients with catheters the dosage may be increased to 1 g three times daily.

Paediatric population:

Children under 6 years: Not recommended.

Children: *6-12 years:* 500 mg twice daily.

Older people:
No special dosage recommendations.

Method of administration

The tablets may be halved, or they can be crushed and taken with a drink of milk or fruit juice if the patient prefers.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Hepatic dysfunction, renal parenchymal infection, severe dehydration, metabolic acidosis, severe renal failure (creatinine clearance or GFR<10ml/min.) or gout. Methenamine hippurate may be used where mild (20-50 ml/min.) to moderate (10-20ml/min.) renal insufficiency is present. (If the GFR is not available the serum creatinine concentration can be used as a guide.). Methenamine hippurate should not be administered concurrently with sulphonamides because of the possibility of crystalluria, or with alkalising agents, such as a mixture of potassium citrate.

4.4 Special warnings and precautions for use

None.

4.5 Interaction with other medicinal products and other forms of interaction

Methenamine hippurate should not be given/administered concurrently with sulphonamides because of the possibility of crystalluria, or with alkalising agents such as potassium citrate. Concurrent use with acetazolamide should be avoided as the desired effect of hexamine will be lost.

Depending on the type of analysing method used, methenamine can affect the determination of steroids, catecholamines and 5 hydroxyindole acetic acid from urine and give false results.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is inadequate evidence of safety of methenamine hippurate in human pregnancy, but it has been in wide use for many years without apparent ill consequence. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of methenamine hippurate during pregnancy.

Breast-feeding
Methenamine is excreted in breast milk but the quantities will be insignificant to the infant. Mothers can therefore breast feed their infants.

Fertility
There are no human data available on fertility. Data from studies in rats do not indicate any effects on female fertility, effects on male fertility have not been adequately tested (see section 5.3).

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

Adverse events are listed below by system organ class and frequency. Frequencies are defined as:

Very common (≥1/10)
Common (≥1/100 and <1/10)
Uncommon (≥1/1000 and <1/100)
Rare (≥1/10,000 and <1/1000)
Very rare (<1/10,000)
Not known (cannot be estimated from the available data).

Gastrointestinal disorders
Uncommon: gastric irritation, irritation of the bladder, nausea, vomiting
Not known: Diarrhoea, abdominal pain

Skin and subcutaneous disorders
Uncommon: Rash, pruritus

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Vomiting and haematuria may occur. These can be treated by the use of an anti-emetic and drinking copious quantities of water respectively. Bladder symptoms can be treated by the consumption of copious quantities of water and 2-3 teaspoonfuls of bicarbonate of soda.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: urinary antibacterial agent, ATC code: J01XX05
Methenamine hippurate is a urinary antibacterial agent with a wide antibacterial spectrum covering both gram-positive and gram-negative organisms. Urinary antibacterial activity can be shown within 30 minutes of administration.

The chemical structure of methenamine hippurate is such that a two-fold antibacterial action is obtained:

1. The slow release of the bactericidal formaldehyde, from the methenamine part, in the urine; acid pH is necessary for this reaction to occur. It is obtained and maintained there by the presence of hippuric acid.
2. The bacteriostatic effect of hippuric acid itself on urinary tract pathogens.

5.2 Pharmacokinetic properties

Methenamine hippurate is readily absorbed from the gastro-intestinal tract and excreted via the kidney.
Plasma concentrations of methenamine hippurate reach maximum 1-2 hours after a single dose and then decline with a half-life of about 4 hours.
Methenamine recovered in the urine corresponds to about 80% of the dose given per 12 hours.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on repeated dose toxicity studies. No carcinogenicity or genotoxicity data are available for methenamine hippurate. Methenamine did not demonstrate any carcinogenic potential in long term studies in rodents.

In limited studies in pregnant rabbits with methenamine hippurate at approximately 3 times the clinical dose based on body surface area, there was increased post-implantation loss resulting in lower litter sizes and a limited occurrence of fetal deformities including shortness of tail and malrotation of limbs. No effects on development were noted at doses equivalent to the clinical dose. Methenamine hippurate, administered at approximately 3 times the clinical dose, based on body surface area, did not adversely affect the fertility of female rats. Effects on male fertility have not been adequately studied.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal silicon dioxide
Povidone
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicine does not require any special storage conditions.

6.5 Nature and contents of container

Methenamine hippurate tablets are available in Alu-Alu blister pack and HDPE bottle pack with a polypropylene screw cap.

Pack sizes:

Blister packs: 7, 8, 10, 20, 21, 60, 100 and 105 tablets.

HDPE packs: 60 and 100 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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PL 25298/0236

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