Bundesamt für Sicherheit
im Gesundheitswesen

BASG / AGES
Institut LCM
Traisengasse 5, A-1200 Wien

Datum: 23.04.2015
Kontakt: Veronika Iro
Abteilung: REGA
Tel. / Fax: +43 (0) 505 55 – 36247
E-Mail: pv-implemetation@ages.at
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Betreff: Fosfomycin – hältige Arzneispezialitäten – Änderungen der Fach- und Gebrauchsinformationen aufgrund des HBD – PSUR Worksharing Projektes

Sehr geehrte Damen und Herren,

basierend auf der Evaluierung des PSURs im EU-HBD-worksharing Projekt (Verfahrensnummer: FR/H/PSUR/0061/001) kommt es zu der Empfehlung, folgende Ergänzungen in die **Fach- und Gebrauchsinformation** aller Fosfomycin – hältigen Arzneispezialitäten zur intravenösen Verabreichung aufzunehmen.

Sollten diese bereits aufgenommen worden sein, betrachten Sie dieses Schreiben als gegenstandslos.

Core Safety Profile – Fosfomycin IV

4.3 Contraindications

This medicine MUST NO BE USED in the following cases:
- Hypersensitivity to fosfomycin and/or to one of the other ingredients of this medicinal product

4.4 Special warnings and precautions for use

As fosfomycin may rapidly cause the selection of resistant mutants when used alone it must be combined with one or several other antibiotics.

Hypersensitivity reactions, including anaphylaxis and anaphylactic shock, may occur during fosfomycin treatment and may be life-threatening (see section 4.8). If such reaction occurs, fosfomycin should be discontinued and an adequate medical treatment is required.

During prolonged treatment with high doses, blood potassium levels should be monitored in particular in digitalized heart failure patients (possible hypokalaemia, see section 4.8).

In patients with impaired renal function, adjust the dosage according to the renal insufficiency (see section 4.2).

This medicinal product contains 0.33 g sodium per 1 g of product. To be taken into consideration by patients on a controlled sodium diet.

Antibiotic-associated diarrhoea has been reported with the use of nearly all antibacterial agents, including fosfomycin and may range in severity from mild diarrhoea to fatal colitis. Diarrhoea, particularly if severe, persistent and/or bloody, during or after treatment with <Product name> (including several weeks after treatment) may be symptomatic of *Clostridium difficile*-associated disease (CDAD). It is therefore important to consider this diagnosis in patients who develop serious diarrhoea during or after treatment with <Product name>. If CDAD is suspected or confirmed, appropriate treatment should be initiated without delay (see section 4.8). Anti-peristaltic medicinal products are contra-indicated in this clinical situation.

4.5 Interaction with other medicinal products and other forms of interaction

Specific problems concerning the alteration in INR

Numerous cases of increased oral anticoagulant activity have been reported in patients receiving antibiotics. Risk factors include severe infection or inflammation, age and poor general health. Under these circumstances, it is difficult to determinate whether the alteration in INR is due to the infectious disease or its treatment. However, certain classes of antibiotics are more often involved and in particular: fluoroquinolones, macrolides, cyclins, cotrimoxazole and certain cephalosporins.

4.6 Fertility, pregnancy and lactation

Fertility
No effect on fertility has been reported in animal studies. No data are available in human.

Pregnancy
Animal studies do not indicate reproductive toxicity. A large amount of data concerning effectiveness of fosfomycin during pregnancy is available. However, only moderate amount of safety data on pregnant women is available and does not indicate any malformative or feto/neonatal toxicity of fosfomycin.
The use of fosfomycin may be considered during pregnancy, if necessary.

Lactation
Fosfomycin is excreted into human milk at low level after a single injection. The excretion into human milk after repeated doses of fosfomycin is unknown. In case of repeated injections, a decision must be made whether to discontinue breast-feeding or to discontinue/abstain from fosfomycin therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

4.7 Effects on ability to drive and use machines

No specific studies have been performed but patients should be informed that even if no case are been reported with parenteral use of fosfomycin, dizziness have been reported with oral fosfomycin trometamol use. This may influence some patients' ability to drive and use machines.

4.8 Undesirable effects

The frequencies are defined with following conventions: very common (≥1/10); common (≥1/100 and <1/10); uncommon (≥1/1,000 and <1/100); rare (≥1/10,000 and <1/1,000); very rare (<1/10,000), frequency unknown.

Blood and lymphatic system disorders:
Unknown frequency: cases of neutropenia or transient agranulocytosis.

Immune system disorders:
Unknown frequency: anaphylactic reactions including anaphylactic shock hypersensitivity (see section 4.4),.

Gastrointestinal disorders:
Unknown frequency: antibiotic-associated colitis (see section 4.4).

Hepatobiliary disorders:
Unknown frequency: Transaminases increased (ALAT, ASAT), gamma-GT increased.

Skin and subcutaneous tissue disorders:
Common: erythematous eruption
Unknown frequency: skin reactions such as pruritus, urticaria, bullous eruptions, angioedema have been reported.

Metabolism and nutrition disorders:
Common: the high sodium content of fosfomycin may cause fluid and electrolyte disorders leading to edema or disturbances of alertness.

Investigations:
Common: hypernatremia, hypokalemia (see section 4.4).

4.9 Overdose

Experience regarding the overdose of fosfomycin is limited. Cases of hypotonia, somnolence, electrolytes disturbances, thrombocytopenia and hypoprothrombinemia have been reported with parenteral use of fosfomycin. In the event of overdose, treatment should be symptomatic and supportive. Rehydratation is recommended to promote urinary elimination of the drug.

Oben angeführte Textabschnitte stellen eine Mindestanforderung dar, zusätzliche nationale Hinweise in diesen Abschnitten sind zu belassen.