Bundesamt für Sicherheit
im Gesundheitswesen

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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/0064/001) kommt es zu der Empfehlung, folgende Ergänzungen in die **Fach- und Gebrauchsinformation** aller Fosfomycin – hältigen Arzneispezialitäten zur oralen Verabreichung aufzunehmen.

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

Core Safety Profile – Fosfomycin oral

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and precautions for use

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 never be re-administrated and an adequate medical treatment is required.

Antibiotic-associated diarrhoea has been reported with 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.

Renal insufficiency: urinary concentrations of fosfomycin remain effective for 48 hours after an usual dose if creatinine clairance is above 10 ml/min.

<Product name> contains sucrose. Its use is not recommended in patients with hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency.

4.5 Interaction with other medicinal products and other forms of interaction

Food may delay the absorption of the active ingredient of <Product name>, with consequent slight decrease in peak plasma levels and urinary concentrations. It is therefore preferable to take the medicine on an empty stomach or about 2 – 3 hours after meals.

Specific problems concerning the alteration in INR
Numerous cases of increased antivitamin K antagonists 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
At the present time, single-dose treatments are not suitable to treat urinary tract infections in pregnant women.
Animal studies do not indicate reproductive toxicity. A large amount of safety data concerning effectiveness of fosfomycin during pregnancy is available. However, only moderate amount of data on pregnant women is available and does not indicate any malformative or feto/neonatal toxicity of fosfomycin.

Lactation
Fosfomycin is excreted into human milk at low level after a single injection. Therefore fosfomycin can be used during breastfeeding, after a single oral dose.

4.7 Effects on ability to drive and use machines

No specific studies have been performed but patients should be informed that dizziness have been reported. This may influence some patients' ability to drive and use machines.

4.8 Undesirable effects

The most common adverse reactions following the single-dose administration of fosfomycin trometamol involve the gastrointestinal tract, mainly diarrhoea. These events are usually self-limited in duration and resolve spontaneously.
The following table displays ADRs that have been reported with the use of <Product name> from either clinical-trial or post-marketing experiences.
The displayed frequency categories use the following convention:
Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to <1/1 000); very rare (<1/10 000), not known (cannot be estimated form the available data)
Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System organ class	**Adverse drug reactions**			
	Common	**Uncommon**	**Rare**	**Not known**
Infections and infestations	vulvovaginitis			
Immune system disorders				anaphylactic reactions including anaphylactic shock, hypersensitivity
Nervous system disorders	Headache, dizziness			
Gastro-intestinal disorders	Diarrhoea, nausea	Vomiting, abdominal pain		Antibiotic-associated colitis (see section 4.4)
Skin and subcutaneous tissue disorders		Rash, urticaria, pruritus		Angioedema

4.9 Overdose

Experience regarding the overdose of oral fosfomycin is limited. However 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.