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Vsem imetnikom dovoljenj za promet z zdravili, ki vsebujejo ceftriakson

ZAHTEVA ZA PREDLOŽITEV SPREMEMBE TIPA II – dopolnitev povzetka glavnih značilnosti zdravila (SmPC) in navodila za uporabo (PIL) za zdravila, ki vsebujejo ceftriakson zaradi tveganja za nastanek oborine ob sočasni uporabi raztopin, ki vsebujejo kalcij

Spoštovani,

Oktobra 2009 je delovna skupina za farmakovigilanco (PhVWP) ocenila podatke glede tveganja za nastanek oborine, ki nastane pri rekonstituciji ceftriaksona z raztopinami, ki vsebujejo kacij ali pri dajanju ceftriaksona sočasno z infuzijskimi raztopinami, ki vsebujejo kalcij. Na podlagi ocene podatkov je izdala priporočilo za dopolnitev povzetka glavnih značilnosti zdravil in navodil za uporabo zdravil, ki vsebujejo ceftriakson, z novimi informacijami.

Imetnike dovoljenj za promet z zadevnimi zdravili prosimo, da Javni agenciji RS za zdravila in medicinske pripomočke v skladu s Pravilnikom o dovoljenju za promet z zdravilom za uporabo v humani medicini (Uradni list RS, št. 59/2006) predložijo spremembo tipa II najkasneje v 30 dneh po prejemu obvestila. Dodatne informacije in podporna dokumentacija v vlogi niso potrebne. Ta dopis je objavljen tudi na spletni strani JAZMP www.jazmp.si .

Odobreno originalno besedilo spremembe je podano v nadaljevanju.

S spoštovanjem,

dr. Martina Cvelbar, mag.farm., spec.
Direktorica

SPC

Section 4.2 (Posology and method of administration)
Diluents containing calcium, (e.g. Ringer's solution or Hartmann's solution), should not be used to reconstitute ceftriaxone vials or to further dilute a reconstituted vial for IV administration because a precipitate can form. Precipitation of ceftriaxone - calcium can also occur when ceftriaxone is mixed with calcium-containing solutions in the same IV administration line. Therefore, ceftriaxone and calcium-containing

solutions must not be mixed or administered simultaneously (see sections 4.3, 4.4 and 6.2).

Section 4.3 (Contraindications)
Ceftriaxone is contraindicated in:
• premature newborns up to a corrected age of 41 weeks (weeks of gestation + weeks of life),
• full-term newborns (up to 28 days of age) with

- jaundice, or who are hypoalbuminaemic or acidotic because these are conditions in which bilirubin binding is likely to be impaired
- if they require (or are expected to require) IV calcium treatment, or calcium-containing infusions because of the risk of precipitation of ceftriaxone-calcium (see sections 4.4, 4.8 and 6.2).

Section 4.4. (Special warnings and precautions for use)
Interaction with Calcium-Containing Products
Cases of fatal reactions with calcium-ceftriaxone precipitates in lungs and kidneys in premature and full-term newborns aged less than 1 month have been described. At least one of them had received ceftriaxone and calcium at different times and through different intravenous lines. In the available scientific data, there are no reports of confirmed intravascular precipitations in patients, other than newborns, treated with ceftriaxone and calcium-containing solutions or any other calcium-containing products. In vitro studies demonstrated that newborns have an increased risk of precipitation of ceftriaxone-calcium compared to other age groups.
In patients of any age ceftriaxone must not be mixed or administered simultaneously with any calcium-containing IV solutions, even via different infusion lines or at different infusion sites.
However, in patients older than 28 days of age ceftriaxone and calcium-containing solutions may be administered sequentially one after another if infusion lines at different sites are used or if the infusion lines are replaced or thoroughly flushed between infusions with physiological saltsolution to avoid precipitation. In patients requiring continuous infusion with calcium-containing TPN solutions, healthcare professionals may wish to consider the use of alternative antibacterial treatments which do not carry a similar risk of precipitation**.** If use of ceftriaxone is considered necessary in patients requiring continuous nutrition, TPN solutions and ceftriaxone can be administered simultaneously, albeit via different infusion lines at different sites. Alternatively, infusion of TPN solution could be stopped for the period of ceftriaxone infusion, considering the advice to flush infusion lines between solutions. (see sections 4.3, 4.8, 5.2 and 6.2).

Section 4.8 (Undesirable effects)
Rarely, severe, and in some cases fatal, adverse reactions have been reported in preterm and fullterm newborns (aged <28 days) who had been treated with intravenous ceftriaxone and calcium. Precipitations of ceftriaxone-calcium salt have been observed in lung and kidneys post-mortem. The high risk of precipitation in newborns is due to their low blood volume and the longer half life of ceftriaxone compared with adults (see sections 4.3, 4.4 and 5.2).

Section 5.2 (Pharmacokinetic properties)
Pharmacokinetics in special clinical situations

In the first week of life, 80% of the dose is excreted in the urine; over the first month, this falls to levels similar to those in the adults. In infants aged less than 8 days the average elimination halflife is usually two to three times longer than that of young adults.

Section 6.2 (Incompatibilities)
Solutions containing ceftriaxone should not be mixed with or added to other agents. In particular diluents containing calcium, (e.g. Ringer's solution, Hartmann's solution) should not be used to reconstitute ceftriaxone vials or to further dilute a reconstituted vial for IV administration because a precipitate can form. Ceftriaxone must not be mixed or administered simultaneously with calciumcontaining solutions (see section 4.2, 4.3, 4.4 and 4.8).

PIL

No specific wording is proposed for inclusion in the Patient Information Leaflet, as this should be suitably amended to reflect these warnings at a National level. The warning to patients should be updated to reflect that they should inform their healthcare professional if they have recently received or are about to receive calcium (rather than this being a contraindication to treatment).
Where a tearoff sheet for healthcare professionals exists, this should also be amended to strengthen the warnings on incompatibilities, in line with the SmPC.