Bundesamt für Sicherheit
im Gesundheitswesen

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PHV issue: Mepivacain

Sehr geehrte Damen und Herren,

basierend auf der Evaluierung des PSURs im EU-HBD-worksharing Projekt (Verfahrensnummer: DK/H/PSUR/0057/001) kommt es zu der Empfehlung, folgende Ergänzungen in die **Fach- und Gebrauchsinformation** aller Mepivacain – hältigen Arzneispezialitäten aufzunehmen.

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

Amendments to the Product Information

Proposed addition to SmPC Section 4.2 (new/modified text in bold):

Special populations

Hepatic impairment
A dose reduction for surgical anaesthesia is not necessary in patients with impaired hepatic function. When prolonged blocks are used e.g., by repeated administration the repeated doses of mepivacaine should be reduced by 50% in patients with Child's grade C liver disease and a total 24 hour dose of 750 mg mepivacaine should not be exceeded (see section 4.4).

Renal impairment
A dose reduction for surgical anaesthesia up to 24 h is not necessary in patients with renal dysfunction (see sections 4.4 and 5.2).

Proposed addition to SmPC Section 4.4 (new/ modified text in bold):

- Patients with advanced liver disease or severe renal dysfunction.
In patients with advanced liver disease (Child's grade C), data from lidocaine suggest that clearance may be reduced by approximately 50% (see 4.2).

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A clinically relevant decrease in mepivacaine clearance is expected only in patients with severe renal insufficiency (CL(cr) <30 mL/min) who are not receiving haemodialysis.
The decreased clearance is not expected to impact the occurrence of toxicity caused by high plasma concentrations after single doses for surgical anaesthesia. In chronic renal failure, however, clearance of the renally excreted metabolite PPX is impaired and accumulation may occur after repeated administration (see section 4.2)

Proposed addition to SmPC Section 5.2

Impaired renal function has little or no influence on the tolerability of mepivacaine when used short-term for surgical anaesthesia. Mepivacaine plasma concentrations were evaluated after axillary block with mepivacaine without adrenaline (600 mg for axillary block and 50 mg for supplementation) in 8 patients with end-stage chronic renal failure.
Total plasma concentrations expressed in ug/mL as medians and their ranges were: 1.69 (1.23--7.78) at 5 min, 5.61 (4.36--8.19) at 30 min, 8.28 (3.83--11.21) at 60 min, 7.93 (5.63--11.1) at 90 min and 6.49 (5.56--8.35) at 150 min. No symptoms of toxicity were observed (Rodríguez et al 2001). In comparison, patients without renal insufficiency receiving 600 mg of mepivacaine for axillary plexus block had mean total plasma concentrations of 3.33 ug/mL with a highest single value of 5.21 ug/mL (Cockings 1987). Patients with chronic renal failure have increased concentrations of AAG and therefore increased plasma protein binding and increased total concentrations, whereas the pharmacologically active unbound concentration of mepivacaine may not be increasing into the range where toxicity occurs.
The renal clearance of the metabolite PPX is significantly correlated with creatinine clearance. A lack of correlation between total exposure, expressed as AUC, with creatinine clearance indicates that the total clearance of PPX includes a non-renal elimination in addition to renal excretion. Some patients with impaired renal function may show an increased exposure to PPX resulting from a low non renal clearance. Due to the reduced CNS toxicity of PPX as compared to mepivacaine the clinical consequences are considered negligible in short-term treatment.

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