Bundesamt für Sicherheit
im Gesundheitswesen

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PHV issue: Folinsäure

Sehr geehrte Damen und Herren,

basierend auf der Evaluierung des PSURs im EU-HBD-worksharing Projekt (Verfahrensnummern: IT/H/PSUR/0024/001-002) kommt es zu der Empfehlung, folgende Ergänzungen in die **Fach- und Gebrauchsinformation** aller Folinsäure – hältigen Arzneispezialitäten aufzunehmen.

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

SmPC wording
4.8 Undesirable effects

[All therapeutic indications:]
Immune system disorders
Very rare (<0.01%): allergic reactions, including anaphylactoid / anaphylactic reactions, and urticaria.
Psychiatric disorders
Rare (0.01-0.1%): insomnia, agitation and depression after high doses.
Gastrointestinal disorders
Rare (0.01-0.1%): gastrointestinal disorders after high doses.
Neurological disorders
Rare (0.01-0.1%): increase in the frequency of attacks in epileptics (see also section 4.5 Interactions).
General disorders and administration site conditions
Uncommon (0.1-1%): fever has been observed after administration of <active substance> as solution for injection.

[Combination therapy with 5-fluorouracil only:]
Generally, the safety profile depends on the applied regimen of 5-fluorouracil due to enhancement of the 5-fluorouracil induced toxicities.
Metabolism and Nutritional Disorder:
Not known: Hyperammonaemia
Blood and lymphatic system disorders:
Very common: bone marrow failure, including fatal cases
General disorders and administration site conditions
Very common: (severe) mucosal toxicity, mucositis, including stomatitis and chelitis. Fatalities have occurred as a result of mucositis
Skin and subcutaneous tissue disorders:

Common: Palmar-Plantar Erythrodysaesthesia
Monthly regimen:
Gastrointestinal disorders
Very common (>10%): vomiting and nausea
No enhancement of other 5-fluorouracil induced toxicities (e.g. neurotoxicity).
Weekly regimen:
Gastrointestinal disorders
Very common (>10%): diarrhoea with higher grades of toxicity, and dehydration, resulting in hospital admission for treatment and even death.]

Leaflet wording

4. POSSIBLE SIDE EFFECTS

[All therapeutic indications:]
Very rare: may affect up to 1 in 10,000 people
• severe allergic reaction - you may experience a sudden itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing), and you may feel you are going to faint. This is a serious side effect. You may need urgent medical attention.

Uncommon: may affect up to 1 in 100 people
• fever

Rare: may affect up to 1 in 1,000 people:
• an increase in convulsions (fits) in patients with epilepsy
• depression
• agitation
• problems with the digestive system
• difficulty sleeping (insomnia)

[Combination therapy with 5-fluorouracil only:]
If you receive <active substance> in combination with an anticancer medicine containing fluoropyrimidines, it is more likely that you experience the following side effects of this other medicine:
Very common: may affect more than 1 in 10 people
• nausea
• vomiting
• severe diarrhoea
• drying out which may be due to diarrhea
• inflammation of the lining of the intestine and mouth (life-threatening conditions have occurred)
• reduction in the number of blood cells (including life-threatening conditions)

Common
• redness and swelling of the palms of the hands or the soles of the feet which may cause the skin to peel (hand-foot syndrome)

Not known: frequency cannot be estimated from the available data
• elevated ammonia level in the blood

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