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im Gesundheitswesen

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Ihr Zeichen:

PHV issue Ranitidin

Sehr geehrte Damen und Herren,

basierend auf der Evaluierung des PSURs im EU-HBD-worksharing Projekt (Verfahrensnummer: (IT/H/PSUR/0016/002 und (IT/H/PSUR/0016/003) kommt es zu der Empfehlung, folgende Ergänzungen in die **Fach- und Gebrauchsinformation** aller Ranitidin– hältigen Arzneispezialitäten aufzunehmen.

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

Fachinformation:

4.3 Contraindications

Ranitidine products are contraindicated in patients known to have hypersensitivity to any component of the preparation.

4.4 Warnings and Precautions

The possibility of malignancy should be excluded before commencement of therapy in patients with gastric ulcer [and if indications include dyspepsia; patients of middle age and over with new or recently changed dyspeptic symptoms must be included] as treatment with ranitidine may mask symptoms of gastric carcinoma.

Ranitidine is excreted via the kidney and so plasma levels of the drug are increased in patients with renal impairment.

The dosage should be adjusted as detailed above in section 4.2 in Renal impairment.

Rare clinical reports suggest that ranitidine may precipitate acute porphyric attacks. Ranitidine should therefore be avoided in patients with a history of acute porphyria.

In patients such as the elderly, persons with chronic lung disease, diabetes or the immunocompromised, there may be an increased risk of developing community acquired pneumonia.

A large epidemiological study showed an increased risk of developing community acquired pneumonia in current users of ranitidine alone versus those who had stopped treatment, with an observed adjusted relative risk increase of 1,82 (95% CI 1,26-2,64).

Oral formulations only:

Regular supervision of patients who are taking non-steroidal anti-inflammatory drugs concomitantly with ranitidine is recommended, especially in the elderly and in those with a history of peptic ulcer. [Mandatory statement if indications include NSAID associated peptic ulcer].

Chewable Tablets, Effervescent Tablets:

As ranitidine chewable and effervescent tablets contain aspartame they should be used with caution in patients with phenylketonuria.

Chewable Tablets:

Ranitidine chewable tablets contain 2.6 g of sucrose per tablet. This should be considered when prescribing ranitidine chewable tablets to patients who must restrict their sugar intake.

Long-term treatment with ranitidine chewable tablets increases the risk of dental caries. It is important that adequate dental hygiene is maintained.

Effervescent Tablets:

Ranitidine effervescent tablets contain sodium *(see section 6.1 for sodium content).*

Care should therefore be taken in treating patients in whom sodium restriction is indicated.

Injection:

The use of higher than recommended doses of i.v. H2- antagonists has been associated with rises in liver enzymes when treatment has been extended beyond five days.

Bradycardia in association with rapid administration of ranitidine injection has been reported rarely, usually in patients with factors predisposing to cardiac rhythm disturbances. Recommended rates of administration should not be exceeded.

(NB aspartame warning for aspartame-containing formulation of effervescent tablets only).

Syrup:

Zantac syrup contains approximately 7.5%w/v ethanol (alcohol), i.e. up to 405 mg per 5ml spoonful which is equivalent to about 11ml of beer or 5ml of wine. It is harmful for those suffering from alcoholism. It should be taken into account in pregnant or lactating women, high risk groups (those suffering from alcoholism, liver disease, epilepsy, brain injury or disease) and children (see section 4.2). It may modify or increase the effect of other medicines.

4.5 Interactions

Ranitidine has the potential to affect the absorption, metabolism or renal excretion of other drugs. The altered pharmacokinetics may necessitate dosage adjustment of the affected drug or discontinuation of treatment.

Interactions occur by several mechanisms including:

1) Inhibition of cytochrome P450-linked mixed function oxygenase system:

Ranitidine at usual therapeutic doses does not potentiate the actions of drugs which are inactivated by this enzyme system such as diazepam, lidocaine, phenytoin, propranolol and theophylline.

There have been reports of altered prothrombin time with coumarin anticoagulants (e.g. warfarin). Due to the narrow therapeutic index, close monitoring of increased or decreased prothrombin time is recommended during concurrent treatment with ranitidine.

2) Competition for renal tubular secretion:

Since ranitidine is partially eliminated by the cationic system, it may affect the clearance of other drugs eliminated by this route. High doses of ranitidine (e.g. such as those used in the treatment of Zollinger-Ellison syndrome) may reduce the excretion of procainamide and N-acetylprocainamide resulting in increased plasma levels of these drugs.

3) Alteration of gastric pH:

The bioavailability of certain drugs may be affected. This can result in either an increase in absorption (e.g. triazolam, midazolam, glipizide) or a decrease in absorption (e.g. ketoconazole, atazanavir, delaviridine, gefitnib).

Oral Formulations:

There is no evidence of an interaction between ranitidine and amoxicillin and metronidazole.

If high doses (2 g) of sucralfate are co-administered with ranitidine the absorption of the latter may be reduced. This effect is not seen if sucralfate is taken after an interval of 2 hours.

4.6 Pregnancy and Lactation

Fertility

There are no data on the effects of ranitidine on human fertility. There were no effects on male and female fertility in animal studies (see section 5.3).

Pregnancy

Ranitidine crosses the placenta. Like other drugs ranitidine should only be used during pregnancy if considered essential.

Lactation

Ranitidine is excreted in human breast milk. Like other drugs ranitidine should only be used during breast-feeding if considered essential.

4.7 Ability to perform tasks that require judgement, motor or cognitive skills

None reported.

4.8 Adverse Reactions

The following convention has been utilised for the classification of undesirable effects: very common (>1/10), common (>1/100, <1/10), uncommon (>1/1000, <1/100), rare (>1/10,000, <1/1000), very rare (<1/10,000).

Adverse event frequencies have been estimated from spontaneous reports from post-marketing data.

Blood & Lymphatic System Disorders

Very Rare: Blood count changes (leucopenia, thrombocytopenia). These are usually reversible. Agranulocytosis or pancytopenia, sometimes with marrow hypoplasia or marrow aplasia.

Immune System Disorders

Rare: Hypersensitivity reactions (urticaria, angioneurotic oedema, fever, bronchospasm, hypotension and chest pain).

Very Rare: Anaphylactic shock

Unknown: dyspnoea

These events have been reported after a single dose.

Psychiatric Disorders

Very Rare: Reversible mental confusion, depression and hallucinations.

These have been reported predominantly in severely ill patients, in elderly and in nephropatic patients.

Nervous System Disorders

Very Rare: Headache (sometimes severe), dizziness and reversible involuntary movement disorders.

Eye Disorders

Very Rare: Reversible blurred vision.

There have been reports of blurred vision, which is suggestive of a change in accommodation.

Cardiac Disorders

Very Rare: As with other H2 receptor antagonists bradycardia, A-V block and tachycardia *(for all formulations).*

Asystole *(for injection only).*

Vascular Disorders

Very Rare: Vasculitis.

Gastrointestinal Disorders

Very Rare: Acute pancreatitis, diarrhoea

Uncommon: abdominal pain, , constipation, nausea (these symptoms mostly improved during continued treatment).

Hepatobiliary Disorders

Rare: Transient and reversible changes in liver function tests.

Very Rare: Hepatitis (hepatocellular, hepatocanalicular or mixed) with or without jaundice, these were usually reversible.

Skin and Subcutaneous Tissue Disorders

Rare: Skin rash.

Very Rare: Erythema multiforme, alopecia.

Musculoskeletal and Connective Tissue Disorders

Very Rare: Musculoskeletal symptoms such as arthralgia and myalgia.

Renal and Urinary Disorders

Very rare: Acute interstitial nephritis .

Rare: elevation of plasma creatinine (usually slight; normalised during continued treatment)

Reproductive System and Breast Disorders

Very Rare: Reversible impotence, breast symptoms and breast conditions (such as gynaecomastia and galactorrhoea)

Paediatric population

The safety of ranitidine has been assessed in children aged 0 to 16 years with acid-related disease and was generally well tolerated with an adverse event profile resembling that in adults. There are limited long term safety data available, in particular regarding growth and development.

4.9 Overdosage

Symptoms and Signs

Ranitidine is very specific in action and no particular problems are expected following overdosage with ranitidine formulations.

Treatment

Symptomatic and supportive therapy should be given as appropriate.

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