OMETON
(Omeprazole)
Powder and solvent for solution for injection IV

COMPOSITION:
Each vial contains omeprazole sodium, equivalent to omeprazole 40 mg.
Each ampoule contains 10 ml of solvent for injection.

PHARMACEUTICAL FORM AND PRESENTATION:
Powder and solvent for solution for injection.
Package containing one vial and one solvent ampoule (10 ml)

PHARMACO-TERAPEUTIC GROUP:
VII-3-b.3-Gastric antisecretory agents.

THE MARKETING AUTHORIZATION HOLDER:
LABESFAL - Laboratórios Almiro, S.A.
Campo de Besteiros, Portugal

THERAPEUTIC-INDICATIONS:
Duodenal ulcer
Benign gastric ulcer
Esophageal reflux
Maintenance treatment of esophageal reflux in order to prevent relapses
Prevention and treatment of gastric and duodenal ulcers produced by long-term treatments with NSAIDs.
Symptomatic treatment of gastro esophageal reflux
In association with appropriate therapeutic antibacterial regimens used in the eradication of H. pylori in patients with H. pylori associated with peptic ulcers.
Zollinger-Ellison syndrome.
Acidic dyspepsia treatment

CONTRA-INDICATIONS:
Known hypersensitivity to any of the constituents of the formulation.
Association with clarithromycin is contra-indicated in patients with hepatic insufficiency.

SIDE-EFFECTS:
Gastrointestinal effects:
Frequently (10%-1%): Diarrhea, constipation, flatulence (possibly with abdominal pain), nausea and vomiting. In most cases, these symptoms become milder with continuation of the therapy.
Rarely (0,1%-0,01%): a brown coloration of the tongue and benign glandular cists were observed during joint administration with clarithromycin; both are reversible with the interruption of therapy.
Very rarely (<0,01%): Dry mouth, stomatitis, candidiasis or pancreatitis

Hepatic effects:
Less frequently (1%-0,1%): Increase in liver enzymes
Very rarely (<0,01%): Hepatitis with or without jaundice, hepatic failure and encefalophaty in patients with a pre-existent severe liver disease.

Blood and lymphatic system effects:
Very rarely (<0,01%): Variations in blood counts, reversible thrombocytopenia, leucopenia or pancytopenia and agranulocytosis.
Rarely (0,1%-0,01%): Hipochromy, mycrocitic anemia in children.

Skin and subcutaneous effects:
Less frequently (1%-0,1%): Pruritus, cutaneous eruption, alopecia, erythema multiforme or photosensitivity and increased sweating
Very rarely: Stevens-Johonson syndrome or toxic epidermal necrolysis.

Skeletic Muscle effects
Rarely (0,1%-0,01%): Muscular weakness, myalgic and arthritic symptoms.

Renal effects:
Very rarely (< 0,01%): interstitial nephritis.

Nervous system effects:
Frequently (10%-1%): Somnolence, insomnia, vertigo and headaches.
Rarely (0,1%-0,01%): Paresthesia, slight headaches, lightheadness, reversible mental confusion and hallucinations.
Very rarely (<0,01%): Agitation and depressive reactions, specially in patients severely ill and in geriatric patients.

Sensorial organs effects:
Less frequently (1%-0,1%): blurred vision, hearing dysfunction or taste disturbance. These symptoms disappear with therapy interruption.

Hypersensitivity effects
Very rarely (<0,01%): urticaria, high body temperature, angioedema or anaphylactic shock, allergic vasculitis and fever.

Other side effects
Less frequently (1%-0,1%): peripheral oedema (resolved with therapy interruption)
Very rarely (<0,01%): hyponatremia, gynaecomastia

INTERACTIONS:
Omeprazole undergoes oxidative metabolism, which involves the cytochrome P450 enzyme system and can therefore delay the elimination of certain drugs.

Monitorisation is recommended in patients receiving:
Diazepam, phenytoin, warfarin (Drugs metabolized by hepatic oxidation): Omeprazole may delay their elimination. A dose reduction may be necessary (specially in the case of the phenytoin). Other drugs that may be affected are haxabarbital, citalopram, imipramine, clomipramine, etc.
Disulfiram: Omeprazole may inhibit the hepatic metabolism of disulfiram. Isolated cases of muscular stiffness possibly related have been reported.
Plasma concentration of Omeprazole and clarithromycin are increased during concomitant oral administration.
There is no evidence of an interaction with phenacetin, theophyline, caffeine, propenolol, metoprolol, cyclosporin, lidocaine, quinidine, oestradiol, amoxycillin or antiacids when Omeprazole is given orally.
Due to the low intragastric acidity, the absorption of ketoconazole or itraconazole may be reduced during the treatment with omeprazole, as with other acid secretion inhibitors.
The absorption of Omeprazole given orally is not affected by alcohol or food.
Simultaneous treatment with Omeprazole and digoxin in healthy subjects led to a 10% increase in the bioavailability of digoxin as a consequence of the increased intragastric pH.
Omeprazole may reduce the oral absorption of Vitamin B12. Such fact should be taken into account in patients with low levels, and who are under a long-term therapy.

PRECAUTIONS:
In case of gastric ulcer, it is recommended to verify the benign nature of the ulcer before starting the treatment.
In patients with a positive *Helicobacter pylori* test, the microorganism should be eradicated threw the eradication therapy.
Decreased gastric acidity due to any means including proton-pump inhibitors, increases gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with acid-reducing drugs may lead to a slightly increased risk of gastrointestinal infections, such as Salmonella and Campylobacter.
In patients taking Diazepam or Phenytoin, it may be necessary to reduce the amount.
Theophylline and antivitamines K: special physician checking is recommended.
Omeprazole should be used with caution in geriatric patients and in patients with renal and hepatic impairment. For patients with severe hepatic impairment, a dosage of 20 mg per day is advised.
Before treating ulcers related with NSAIDs, the discontinuation of this cause should be considered.
Maintenance treatment of ulcers associated with the ingestion of NSAIDs should be restricted to risk patients.
In long-term treatments, especially over one year, the physician should revise the therapy and evaluate the benefit-risk relationship.
Care should be taken in patients with renal or hepatic impairment taking combined therapy.
Omeprazole should not be used in infants or children younger then 2

Table containing Important Omeprazole Interactions

Other medicinal products	Cause	Effect
Diazepam (and probably other benzodiazepines), S-Warfarin, Phenytoin	Interaction with the enzyme CYP 2C of the cytochrome 450.	Prolonged elimination time, increase of plasmatic levels.
Ketoconazole, Itraconazole (and other drugs with absorption dependent on pH)	Elevation of gastric pH	Reduced absorption
Digoxin	Elevation of gastric pH	Increase of 10% in bioavailability
Clarithromycin, Roxithromycin, Erythromycin (and probably other macrolides)	Variation of gastric pH and hepatic metabolism.	High plasmatic concentrations, increase of bioavailability and of omeprazoles half-life.
Alcohol, Amoxycillin, Budesonide, Quinidine, Caffeine, Diclofenac, Estradiol, Lidocaine, Metropolol, Metronidazole, Naproxen, Fenacetina, Piroxicam, Propanolol, S-Warfarin, Theophylline.		No pharmacokinetic variation.

years.
In patients severely ill, sight and hearing should be monitorized, since isolated cases of blindness and deafness have occurred with the injectable form of omeprazole.

EFFECTS ON PREGNANT WOMEN AND NEONATES:
There is no evidence on the safety of Omeprazole in human pregnancy. Animal studies have revealed no teratogénico effect.
As precaution, it is recommended:
to not administer Omeprazole during the first three months of pregnancy;
avoid in the following months unless there is no safer alternative.
Omeprazole should not be given to breast feeding woman.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
Due to the pharmacological properties of Omeprazole, no effects are foreseen.
Besides very rare cases of side effects to the Central nervous system or to sight, no effects on driving capacity are to be expected.

EXCIPIENTS:
The powder of Omeprazole contains sodium hydroxide.
The solvent contains: polyethylene glycol 400, citric acid monohydrated and water for injection.

DOSAGE AND ADMINISTRATION:
When oral administration is not suitable, for example in severe cases, a dosage of 40 mg per day is recommended. With this dosage there is an immediate decrease of intragastric acidity, with an average decrease of 90% in 24 hours.
In the Zollinger-Ellison Syndrome, the dosage should be individually adjusted. Higher dosages or more frequent dosages may also be indicated.
The IV solution for injection of Omeprazole is prepared by mixing the solvent with the lyophilizate. The content of the vial should be completely dissolved in the 10 ml of solvent. No other solvent should be used. The following technique should be used:
1.With a syringe collect 10 ml of solvent from the ampoule;
2.Slowly join 5 ml of the solvent to the lyophilizate;
3.Remove as much air as possible from the vial in order to reduce the positive pressure. This will facilitate the addition of the remaining solvent.
4.Add the remaining solvent and certify that the ampoule is empty;
5.Shake the vial in order to guarantee a proper mixture of the lyophilizate with solvent.
6.The reconstituted solution should be kept under 25ºC and for a period of 4 hours.

The solution for injection should only be administered intravenously and should not be mixed with other intravenous solutions.
The injection solution should be given slowly over a period of at least two and a half minutes, with a maximum rate of 4 ml per minute.

Use one only treatment on one only patient.
Do not use the solution if it contains any particle.
Any portion not used should be rejected.

Use in children over 2 years of age with severe esophageal reflux:
There is limited experience of use in children.
Omeprazole should only be used in children with severe esophageal reflux resistant to other therapies. Treatment should be initiated in a pediatric hospital.
Continuous control of pH and genotypic determination (in regard to CYP 2C19 situation) may be done and are appropriate for a good therapeutic response.

The following dosage should be considered:
Weight 10 kg to 20 kg: 10 mg/day
Weight over 20 kg: 20 mg/day
(Approximately 1 mg/kg/day)
Duration of the treatment is normally 4 to 8 weeks and should not exceed 12 weeks due to the lack of experience with long-term treatments in children.

Maintenance treatment of esophageal reflux in order to prevent relapses:
The usual dose is of 10 to 20 mg per day, depending on the clinical response.

Zollinger-Ellison Syndrome:
Dosage should be individually adjusted and supervised by the physician.
The initial recommended dosage is of 60 mg once a day. Above 80 mg per day, the dosage should be divided in two administrations. In patients with Zollinger-Ellison Syndrome the treatment has no duration limit.

Prevention and treatment of gastric and duodenal ulcers produced by long-term treatments with NSAIAs:
The usual dose is of 20 mg per day. The duration of the treatment is of 4 to 8 weeks.

Symptomatic treatment of gastro esophageal reflux:
The usual dose is of 10 to 20 mg per day, depending on the clinical response. The duration of the treatment is of 2 to 4 weeks.
If the symptoms do not decrease in 2 week of treatment, further inves

should be conducted.

Eradication treatment:
Patients with gastric and duodenal ulcers due to H. pylori infection should be treated with an appropriate combination of antibiotics, appropriate regime and appropriate dosage.
The selection of the adequate regime should be based on the patients' tolerability and on the therapeutic guidelines. The following combinations were tested:
Omeprazole 20 mg, Amoxycillin 1000 mg, Clarithromycin 500 mg, all 2 times a day
Omeprazole 20 mg, Clarithromycin 250 mg, Metronidazol 400-500mg, all 2 times a day

The eradication treatment has the duration of 1 week. In order to avoid the development of resistance, duration of treatment should not be reduced.
In patients with active ulcers, the treatment may be prolonged by raw mono-therapy with Omeprazole.

The combined therapy with metronidazol should not be the first choice, since animal studies have induced suspicion that metronidazol is mutagenic.

Acidic dyspepsia treatment:
The usual dose is of 20 mg per day. Patients may answer to a 10 mg dose, so this could be considered to be the initial dose. In case the symptoms are not controlled in a 4 week period, with 20 mg omeprazole per day, additional investigation is recommended.

Use in elderly:
Dosage adjustment is not necessary.

Impaired renal function:
Dosage adjustment is not necessary in patients with impaired renal function.

Impaired hepatic function:
As half-life is increased in patients with impaired hepatic function, the dose requires adjustment and a daily dose of 10 mg to 20 mg may be sufficient.

OVERDOSE:
A single oral dose up to 160 mg has been well tolerated.
Besides symptomatic treatments there is no specific recommendation for the overdose situation.

Any detected undesirable symptom, which is not mentioned in this text, should be reported to your physician or your pharmacist.

EXPIRY DATE:
Do not use after expiry date printed in the package.
Reconstituted solutions remain stable for 4 hours.

STORAGE INSTRUCTIONS:
Store under 25°C, protected from light and humidity.

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