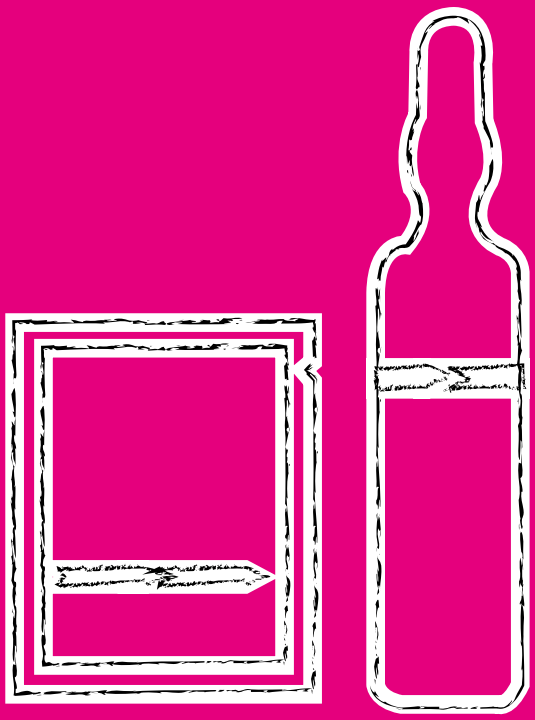
OPTIMAL USE
OF HEPA-MERZ® IN
HEPATIC ENCEPHALOPATHY (HE)
PRESCRIBING CONSIDERATIONS



Hepa-Merz®
L-ornithine-L-aspartate

40 years of effective and safe HE management

Hepa-Merz® – convenient and easy to use in HE

Hepa-Merz® (L-ornithine-L-aspartate; LOLA) is available in the following pharmaceutical forms:[1]

- Granules: Hepa-Merz®
  1 sachet contains 3 g of LOLA
- Infusion concentrate: 10 ml
  concentrate contains 5 g of LOLA in water for injection

Using Hepa-Merz® for the management of all stages of HE

Hepa-Merz® indications:

- Treatment of concomitant disease and sequelae due to impaired detoxification activity (e.g. liver cirrhosis) with symptoms of latent and manifest HE[1]
- Hepa-Merz® Infusion is indicated especially for the treatment of pre-coma and coma[1]

Hepa-Merz® contraindications:

- Patients with kidney failure (serum creatinine level of over 3 mg/100 ml can be taken as a guide)[1]
- Hepa-Merz® should be avoided in pregnancy and whilst breast feeding[1]

Hepa-Merz® – formulation and dosing:[1]

	Hepa-Merz® Granules	**Hepa-Merz® Infusion Concentrate**
Active ingredient	3 g L-ornithine-L-aspartate per sachet.[1]	5 g L-ornithine-L-aspartate 10 ml ampoule (with water for injection).[1]
Administration	Dissolved in plenty of liquid (a glass of water, tea or juice).[1]	Hepa-Merz® Infusion Concentrate can be mixed with the usual infusion solutions. For reasons of venous tolerability, one should not dissolve more than 6 ampoules per 500 ml infusion solution. The maximum infusion rate is 5 g LOLA (corresponding to the content of 1 ampoule) per hour. If the liver function is substantially impaired, the flow rate must be adjusted to the patient's individual condition in order to prevent nausea and vomiting.[1]
Dosage	The dissolved contents of 1–2 sachets up to 3 times a day.[1]	Unless otherwise prescribed up to 4 amps/day pre-coma or coma: up to 8 amp/24 h, depending on severity of condition.[1]
Indication	Treatment of disorders that accompany, or are secondary to, hepatic detoxification impairment (e.g. liver cirrhosis) with symptoms of latent and manifest HE.[1]	Treatment of disorders that accompany, or are secondary to, hepatic detoxification impairment (e.g. liver cirrhosis) with symptoms of latent and manifest HE, especially the treatment of incipient clouding of consciousness (pre-coma) and clouding of consciousness (coma).[1]
Contraindiction	Severe impaired renal function (kidney failure) (guide value: serum creatinine >3 mg/100ml).[1]	Severe renal dysfunction (serum creatinine >3 mg/100ml).[1]
Adverse effects	Not known	Nausea (occasionally); vomiting (rare)*
Drug-drug Interactions	Not known	Not known
Other ingredients	Citric acid (anhydrous); saccharin sodium; sodium cyclamate; fructose; Povidone K 25; flavours; colouring agent E110.[1]	Water for injections.
Advice for people with diabetes	1 sachet of granules contains 1.13 g fructose.[1]	None
Usage during pregnancy and location periowd	No harmful effects of LOLA during pregnancy or lactation period have so far been reported. Administration of during pregnancy should therefore be avoided. If treatment with Hepa-Merz® Granules is considered necessary, careful consideration should be given to the benefit versus risk ratio.[1]	No clinical data are available on the use of Hepa-Merz® Infusion concentrate in pregnancy. The administration of Hepa-Merz® Infusion concentrate in pregnancy should be avoided. It is not known if LOLA passes into breast milk. Administration of Hepa-Merz® should therefore be avoided during lactation. If treatment with Hepa-Merz® is thought necessary, the benefits and risks should be assessed.[1]

* LOLA- therapy is generally very well tolerated and adverse reactions may occur rarely, in the form of mild gastrointestinal disturbances. To prevent such reactions, a maximum infusion rate of 5 g LOLA infusion concentrate per hour is recommended.[1]

Optimal use of Hepa-Merz® in HE

Hepa-Merz® Prescribing Information

Hepa-Merz® Granules. Active substance: L-ornithine-L-aspartate. **Composition:** One sachet with 5 g of Granules contains: **Active substance:** 3 g L-ornithine-L-aspartate. **Excipients:** citric acid, saccharin sodium, sodium cyclamate, povidone 25, fructose, flavorings, orange yellow S (E110). Note for diabetics: One sachet of Hepa-Merz® Granules contains 1.13 g of fructose (corresponds to approx. 0.11 BU). **Therapeutic indications:** Treatment of concomitant disease and sequelae due to impaired detoxification activity (e.g. in cirrhosis of the liver) with the symptoms of latent and manifest hepatic encephalopathy. **Contraindications:** Absolute: Hypersensitivity to L-ornithine-L-aspartate, orange yellow S or any of the other excipients. Severely impaired renal function (renal insufficiency). A serum creatinine value over 3 mg/100 ml can be used as a guideline value. Relative: Pregnancy and lactation: No clinical data are available relating to intake of Hepa-Merz® Granules during pregnancy. No exhaustive animal studies have been performed for L-ornithine-L-aspartate, to investigate its toxicity in relation to reproduction. Administration of Hepa-Merz® Granules during pregnancy should therefore be avoided. If, however, treatment with Hepa-Merz® Granules is considered necessary, careful consideration should be given to the benefit versus risk ratio. It is not known whether L-ornithine-L-aspartate is excreted into the breast milk. Administration of Hepa-Merz® Granules should therefore be avoided during lactation. If, however, treatment with Hepa-Merz® Granules is considered necessary, careful consideration should be given to the benefit versus risk ratio. **Undesirable effects:** Uncommon (≥ 1/1000 to < 1/100): Nausea, vomiting, stomach ache, flatulence, diarrhea. Very rare (< 1/10000): Pain in the limbs. These undesirable effects are usually transient and do not require withdrawal of the medicine. Orange yellow S (E110) can trigger allergic reactions. **Warnings:** Hepa-Merz® Granules contain fructose. Patients with rare hereditary problems of fructose intolerance should not take this medicine. **Further precautions:** As a result of the disease, the ability to drive and operate machinery may be impaired during treatment with L-ornithine-L-aspartate.

Hepa-Merz® Infusion concentrate. Active substance: L-ornithine-L-aspartate. **Composition:** One ampoule of 10 ml contains: **Active substance:** 5 g L-ornithine-L-aspartate. **Excipients:** Water for injections. **Therapeutic indications:** Latent and manifest hepatic encephalopathy. **Contraindications:** Absolute: Hypersensitivity to L-ornithine-L-aspartate. Severe renal impairment (renal failure). A serum creatinine level in excess of 3 mg/100 ml can be taken as a guide. Relative: Pregnancy and lactation: There are no clinical data available on the use of Hepa-Merz® Infusion concentrate in pregnancy. L-ornithine-L-aspartate has been investigated for reproduction toxicity only to a limited extent in experimental animal studies. The administration of Hepa-Merz® Infusion concentrate in pregnancy should therefore be avoided. If treatment with Hepa-Merz® is nevertheless thought to be necessary, the benefits and risks should be carefully assessed. It is not known whether L-ornithine-L-aspartate passes into breast milk. Administration of Hepa-Merz® should therefore be avoided during lactation. If treatment with Hepa-Merz® is nevertheless thought to be necessary, the benefits and risks should be carefully assessed. **Undesirable effects:** Uncommon (≥ 1/1000 to < 1/100): Nausea. Rare (≥ 1/10000 to < 1/1000): vomiting. Frequency not known (frequency cannot be estimated from the available data): hypersensitivity, anaphylactic reaction. Generally however, the gastrointestinal symptoms are transient, and do not necessitate discontinuation of treatment. They disappear on reduction of the dose or the infusion rate. **Further precautions:** Hepa-Merz® concentrate for solution for infusion can be mixed with the usual infusion solutions. So far no peculiarities have been observed with regard to miscibility. However, the ampoules should be admixed to the infusion solution only immediately before application. At high doses of Hepa-Merz® Infusion concentrate, serum and urine urea levels should be monitored. If liver function is substantially impaired, the infusion rate must be adjusted to the individual patient in order to prevent nausea and vomiting. Depending on the underlying disease, the ability to drive and operate machines may also be impaired on treatment with L-ornithine-L-aspartate. Hepa-Merz® Infusion concentrate must not be injected into an artery. Status: January 2013. Merz Pharmaceuticals GmbH, 60048 Frankfurt.

Reference: 1. Specialist information Hepa-Merz® Infusion Concentrate. Specialist information Hepa-Merz® Granules. Hepa-Merz® Summary of Product Characteristics.

For more information, visit **www.merz.com**