Model Kramp GmbH
Otto-Hahn-Straße 41
63456 Hanau
Tel. +49 6181-6750-0

Hepa-Merz 3000 Granulat
Indonesien
GA

Job No.: me4016326				**Created at:** 02.09.2021	**Operator:** ul
Size: 148 x 210 mm (w x h x d)				**1. AC:** 07.09.2021 mf	**5. AC:**
MN XXXXX		**MC** XXXX		**2. AC:**	**6. AC:**
AM 45123		**MZ/AZ** 0000		**3. AC:**	**7. AC:**
Typestyle: Helvetica BQ				**4. AC:**	**8. AC:**
				Type size: 6,8 pt	

Black Stanze

Scale
0 10 20 30 40 50 60 70 80 90 100 110 120 130 measured in mm

reading direction

Hepa-Merz® *GRANULATE*
L-ORNITHINE-L-ASPARTATE

3 g/5 g, Granules for oral solution

COMPOSITION
Each sachet with 5 g contains 3.0 g L-ornithine-L-aspartate.

Excipients: Citric acid, saccharin sodium, sodium cyclamate, povidone 25, fructose, flavourings, orange yellow S (E110).

INDICATIONS
Treatment of concomitant disease and sequelae due to impaired hepatic detoxification activity (e.g.in cirrhosis of the liver) with the symptoms of latent and manifest hepatic encephalopathy.

POSOLOGY AND METHOD OF ADMINISTRATION
Granules for oral solution.

The dissolved contents of 1–2 sachets of Hepa-Merz granules are taken up to 3 times daily.
Hepa-Merz granules are dissolved in plenty of fluid (e.g. a glass of water, tea or juice) and taken with or after meals.

The experiences on the use of the drug in children are limited.

CONTRAINDICATIONS
Severely impaired renal function (renal insufficiency). A serum creatinine value over 3 mg/100 ml can be used as a guideline value.

Hepa-Merz granules must not be taken by patients with known hypersensitivity to L-ornithine-L-aspartate, orange yellow S or any of the excipients.

WARNINGS AND PRECAUTIONS
Hepa-Merz granules contain fructose. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

Hepa-Merz granules contain 1.13 g fructose per sachet (equivalent to 0.11CEU). This should be taken into account in patients with diabetes mellitus.

Any possible fructose intolerabilities should be checked by the attending physician before treatment.

Hepa-Merz granules may be harmful to the teeth (caries) in long-term use.

No data are so far available on the use of the drug in children.

INTERACTION
None known

PREGNANCY AND LACTATION
Pregnancy:
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.

Lactation:
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.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
As a result of the disease, the ability to drive and operate machinery may be impaired during treatment with L-ornithine-L-aspartate.

UNDESIRABLE EFFECTS

Very common:	(≥1/10)
Common:	(≥1/100, <1/10)
Uncommon:	(≥1/1000, <1/100)
Rare:	(≥1/10000, <1/1000)
Very rare:	(<1/10000), not known (cannot be estimated from the available data)

Gastrointestinal disorders
Nausea, vomiting, stomach ache, flatulence and diarrhoea are uncommon occurrences.

Musculoskeletal and connective tissue disorders
In very rare cases, pain in the limbs has been observed.

These undesirable effects are usually transient and do not require withdrawal of the medicine.

Orange yellow S (E110) can trigger allergic reactions.

Overdosage
So far signs of intoxication have not been observed following an overdose of L-ornithine- L-aspartate. Symptomatic treatment is recommended if overdose occurs.

MN XXXXX, XXXXXXXXX, MC XXXX

reading direction

	Approved for printing	(Variation) Procedure No.	Identical to approved texts	Compliant with national requirements	Double checked	Date, Signature
Research and Development	☐					
Regulatory Affairs	☐		Yes ☐	Yes ☐	Yes ☐	
Information Officer	☐					
Legal Department	☐					

DISETUJUI OLEH BPOM : 20/09/2021 EREG100217VR12100095

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PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic group:
Hepatotherapeutics, ATC code: A05BA

In vivo, L-ornithine-L-aspartate exerts its effects through the amino acids, ornithine and aspartate, via two key methods of ammonia detoxification: urea synthesis and glutamine synthesis.

Urea synthesis takes place in the periportal hepatocytes. In these cells, ornithine serves both as an activator of the enzymes ornithinecarbamoyltransferase and carbamoyl phosphate synthetase and also as the substrate of urea synthesis.

Glutamine synthesis is localised in the perivenous hepatocytes. Particularly under pathological conditions, aspartate and other dicarboxylates, including the metabolic products of ornithine, are absorbed into the cells and used there to bind ammonia in the form of glutamine.

Glutamate is an amino acid that binds ammonia under both physiological and patho physio logical conditions. The resulting amino acid glutamine not only represents a form for the excretion of ammonia, but also activates the important urea cycle (intercellular glutamine exchange).

Under physiological conditions, ornithine and aspartate are not limiting for urea synthesis.

Animal studies suggest that the ammoniareducing effect of L-ornithine-L-aspartate is caused by enhanced glutamine synthesis. Individual clinical studies have shown an improved branched-chain amino acid/aromatic amino acid quotient.

Pharmacokinetic properties

L-ornithine-L-aspartate is rapidly absorbed and cleaved to form ornithine and aspartate. Both amino acids have a short elimination half-life of 0.3–0.4 hours. A fraction of the aspartate is recovered in unmetabolised form in the urine.

Preclinical safety data

Preclinical data, based on safety pharmacological studies and chronic toxicity and mutagenicity studies, do not suggest any particular risk to humans following correct administration.

No studies into any carcinogenic potential have been performed.

In a dose-finding study, L-ornithine-L-aspartate was insufficiently investigated in terms of its toxicity in relation to reproduction.

STORAGE

Store below 30°C.

This product should not be used after the expiry date.

PACKAGING

Box,10 sachets containing 5 g granules
Reg. No. DKI0691300222A1

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

ON MEDICAL PRESCRIPTION ONLY
HARUS DENGAN RESEP DOKTER

Manufactured by:

Klocke Pharma-Service GmbH, Appenweier, Germany

Released by:

Merz Pharma GmbH & Co. KGaA, Reinheim, Germany

Imported by:

PT Combiphar, Bandung Barat, Indonesia

MN XXXXX, XXXXXXXXX, MC XXXX

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