Thioctic Acid
Thiogamma® Turboset

℞

12 mg/mL (600 mg/50 mL) Solution for Infusion (I.V.)

Alimentary Tract/Metabolism Product

Pharma Code

DESCRIPTION:

The finished product is a yellowish to greenish-yellow solution for infusion.

FORMULATION:

1 injection vial with 50 mL of solution for infusion contains:

Active substance:
Thioctic Acid (as meglumine salt)..... 600 mg
Excipients:
Macrogol 300 ..... 4 g
Meglumine..... 5.00–25.00 mg
Water for
Injection..... approx. 45557.30–45577.30 mg (up to 50 mL)

INDICATION:

Thioctic Acid (Thiogamma® Turboset) is used to treat pain and sensory disturbances (e.g. numbness, burning, tingling, itching, pins and needles like pain) induced by diabetic nerve damage (polyneuropathy), in adults (over 18 years).

DOSAGE, METHOD AND LENGTH OF ADMINISTRATION:

Individual and Daily Doses
In very severe pain and sensory disturbances induced by diabetic nerve damage (polyneuropathy), the recommended dose is 1 vial **Thioctic Acid (Thiogamma® Turboset)** daily (equivalent to 600 mg thioctic acid / 50 mL, solution for infusion) in the initial phase of treatment.

Hepatic impairment:
If you are suffering from any diseases or impairment of the liver, please tell your doctor or pharmacist. Experience is limited in patients with hepatic impairment. Therefore, **Thioctic Acid (Thiogamma® Turboset)** should be used with caution in these situations of diseases or impairment of the liver.

Children and adolescents
Treatment of children and adolescents is not recommended with **Thioctic Acid (Thiogamma® Turboset)**, as there is no clinical experience in this age group

Method of administration
For intravenous use.

Intravenous administration should be done slowly over at least 30 minutes as a short infusion.

The infusion is done directly from the vial using a standard infusion set and the accompanying light-protection bag.

Because of the photosensitivity of the active substance, the injection vial should be removed from the package directly before administration. Ensure that the infusion time does not exceed 30 minutes.

Once vial has been opened, the infusion should be started immediately and the product protected from light using the accompanying light-protection bag.

Duration of administration
Thioctic Acid (Thiogamma® Turboset) is administered over a period of 2–4 weeks in the initial phase of treat-ment.

As nerve damage caused by diabetes (polyneuro-pathy) is a chronic disease you may need a continuation of this treatment. Your doctor or pharmacist will decide what is best for your individual situation. For continuing therapy, it is recommended to use 600 mg thioctic acid as oral administration daily.

If you have forgotten to use **Thioctic Acid (Thiogamma® Turboset)**
Do not take a double dose to make up for a forgotten dose. Your doctor or pharmacist will determine when you receive your next dose of **Thioctic Acid (Thiogamma® Turboset)**. You should discuss this with your doctor or pharmacist.

If you stop using **Thioctic Acid (Thiogamma® Turboset)**
Please do not interrupt or stop taking your treatment with **Thioctic Acid (Thiogamma® Turboset)** without first discussing this with your attendant doctor or pharmacist.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

CONTRAINDICATIONS:

Thioctic Acid (Thiogamma® Turboset) is totally contraindicated in patients with known hypersensitivity to the active substance or to any of the excipients which are contained in the product.

ADVERSE EFFECTS:

In the assessment of side effects the following frequency categories are used:

Very common	(≥1/10)
Common	(≥1/100 to <1/10)
Uncommon	(≥1/1,000 to < 1/100)
Rare	(≥1/10,000 to <1/1,000)
Very rare	(<1/10,000)
Not known	(cannot be estimated from the available data)

Blood and lymphatic system disorders
Very rare: Thrombopathy

Immune system disorders
Frequency unknown:
- Insulin autoimmune syndrome
- Allergic skin reactions (urticaria, itching, eczema, skin rash), systemic allergic reactions (including anaphylactic shock).

Metabolism and nutrition disorders

Frequency unknown: As a result of the improved utilisation of glucose, blood sugar levels may fall. In such cases hypoglycaemia-like symptoms with dizziness, sweating, headaches and impaired vision have been observed.

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Nervous system disorders
Very rare:
- Changes and/or disturbances to the sense of taste
- Convulsion.

Eye disorders
Very rare: Double vision.

Skin and subcutaneous tissue disorders
Very rare: Purpura.

General disorders and administration site conditions
Very rare: Reactions at the point of infusion.

Frequency unknown: After rapid intravenous infusion symptoms such as pressure in the head and respiratory distress may occur, although these abate spontaneously.

OVERDOSE

In case of overdose nausea, vomiting and headache may occur.

In some cases serious, sometimes poisonings with lethal outcome have occurred. Such as
- seizures with loss of consciousness,
- too much acid in the blood (acid-base disturbances with increase of lactic acid in the blood)
- serious disturbances of blood clotting.

This can occur when more than 10 g of thioctic acid is used together with too much alcohol.
In addition, the decrease in blood sugar (hypoglycemia), shock, damage of the muscles (rhabdomyolysis), disintegration of red blood cells (hemolysis), bone marrow damage and multiple organ dysfunction were described after the use of high doses of thioctic acid.

If there is any suspicion of significant overdose with **Thioctic Acid (Thiogamma® Turboset),** You should go prompt and seek transportation to the hospital. You will get treatment according to the general treatment principles for cases of poisoning.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Talk to your doctor or pharmacist before using **Thioctic Acid (Thiogamma® Turboset)**.

Allergic reactions (hypersensitivity reactions) including life-threatening shock (sudden circulatory collapse with hypotension) have been reported in association with the use of **Thioctic Acid (Thiogamma® Turboset)** (see section Possible side effects). Therefore, your treating doctor or pharmacist will monitor you during the administration of **Thioctic Acid (Thiogamma® Turboset)** for the appearance of early symptoms of allergy (e.g. redness, nausea, malaise). If these occur, the treatment must be interrupted immediately; other therapeutic measures may be required.
In some cases severe allergic symptoms may occur in association with **Thioctic Acid (Thiogamma® Turboset)**in diabetic patients not properly set or not properly controlled and with poor general condition.
Patients with a certain human leukocyte antigen genotype (which is more frequent in Japanese and Korean patients, but is also found in Caucasians) are more prone to development of insulin autoimmune syndrome (disorder of the blood glucose regulating hormones with pronounced lowering of blood sugar levels) when treated with thioctic acid. Cases of Insulin Autoimmune Syndrome (IAS) have been reported during

treatment with alpha-lipoic acid. Patients with human leukocyte antigen genotype such as HLA-DRB1*04:06 and HLA-DRB1*04:03 alleles, are more susceptible to develop IAS when treated with alpha-lipoic acid. HLA-DRB1*04:03 allele (susceptibility to IAS odds ratio: 1.6) is especially found in Caucasians, with a higher prevalence in southern than in northern Europe and HLA-DRB1*04:06 allele (susceptibility to IAS odds ratio: 56.6) is especially found in Japanese and Korean patients.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Concomitant administration of cisplatin with **Thioctic Acid (Thiogamma® Turboset)** leads to loss in efficacy of cisplatin.

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The blood-sugar lowering effect of insulin or oral anti-diabetics may be reinforced.
Close monitoring of blood sugar levels is indicated during the thioctic acid therapy, particularly during the initial phase. In individual cases to avoid hypoglycaemia it is necessary to reduce the insulin dose or the dose of the oral anti-diabetics.

Regular intake of alcohol represents a significant risk factor for the development and progression of neuropathic pathologies and thus can impair also the success of treatment with **Thioctic Acid (Thiogamma® Turboset)**. Patients with diabetic polyneuropathy are recommended to avoid the consumption of alcohol. This applies also to therapy-free intervals.

PREGNANCY AND LACTATION

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. In accordance with the general principles of pharmacotherapy, medicinal products should be used during pregnancy and lactation only after careful consideration of the benefit/ risk ratio.

Pregnancy:
Animal studies have not demonstrated teratogenic effects associated with thioctic acid. However, fetal risk in human cannot be ruled out. The available evidence is inconclusive or is inadequate for determining fetal risk when used in pregnant women or women of childbearing potential. There are no adequate studies in humans. It is not known whether thioctic acid crosses the placenta and if it is responsible for any fetal adverse effects.

Breastfeeding:
It is unknown whether thioctic acid is excreted in human breast milk. Breastfeeding women should start treatment with thioctic acid only after stringent determination of indication by a physician, even if the reproductive toxicological studies have not resulted in any evidence relating to an effect on fertility and early embryonal development and it showed no embryotoxic properties.

The effects on the nursing infant from exposure to the drug in milk are unknown. The use of the thioctic acid while breast feeding is not recommended.

PRECLINICAL SAFETY DATA

Acute toxicity
Acute toxicity in test animals has rarely occured. The lethal intravenous dose in rats is about 400 mg/kg body weight, the lethal oral dose in dogs 400–500 mg/kg body weight. In dogs after administration of high doses vomiting, drooling and sedation were observed. In end-stage, tonic-clonic seizures occur.

Chronic toxicity
There are no data for chronic animal toxicity studies.

Mutagenecity and carcinogenecity
Studies of mutagenic potential did not provide evidence of gene or chromosomal mutations. No evidence of a tumorigenic potential of thioctic acid was found in a cancerogenicity study following oral administration in rats. When thioctic acid was co-administratered with cancerogenic N-nitroso-dimethylamine (NDEA), thioctic acid did not have a tumour–promoting effect.

Reproductive toxicity
Thioctic acid has no influence on fertility and early development of the embryo in rats up to a maximum tested oral dose of 68.1 mg/kg body weight. No malformation producing properties were found after intravenous infusion in rabbits at doses up to the maternally toxic range.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties
Pharmacotherapeutic group:
Neuropathy preparation

ATC Code: N07XB01

Thioctic acid (alternativ name = alpha-lipoic acid or short ALA), along with its major metabolite dihydrolipoic acid, is a potent antioxidant via scavenging of oxygen free radicals, redox interaction with other antioxidants, and inhibition of lipid peroxidation. ALA is characterized by high reactivity towards free radicals and is capable of regeneration of vitamins C and E as well as glutathione.

Four main molecular mechanisms have been implicated in glucose-mediated microvascular damage (retinopathy, nephropathy, neuropathy). All seem to reflect a single hyperglycemia-induced initial process of overproduction of superoxide anion by the mitochondrial electron-transport chain. Thus, oxidative stress represents the primary event in the causation of hyperglycemia-induced microvascular complications providing a rationale for the treatment of diabetic neuropathy by antioxidants such as alpha-lipoic acid.

Experimental diabetic neuropathy is characterized by impaired nerve conduction velocity, reduced nerve blood flow, and a variety of metabolic abnormalities in peripheral nerves that have been ascribed to hyperglycemia, abnormal fatty acid metabolism, ischaemic hypoxia, and/or oxidative stress. Alpha-lipoic acid improves nerve blood flow, reduces oxidative stress, and also ameliorates nerve conduction, intraepidermal nerve fiber density, and nocifensive behavior in experimental diabetic neuropathy. Thus, alpha-lipoic acid improves the diagnostic criteria for establishing the presence of somatic diabetic neuropathy in rodent models. These criteria parallel those used in patients to diagnose diabetic neuropathy. Therefore, the experimental evidence supports the concept that the observed favorable effects of Thioctic acid have clinical relevance.

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Pharmacokinetic properties

Biotransformation
Thioctic acid is subject to a first-pass effect in the liver. There is considerable interindividual variation in the systemic availability of thioctic acid. In virtue of oxidation of the side chain and conjugation, alpha-lipoic acid is biotransformed and eliminated predominantly via the kidneys.

Elimination
The plasma half-life of thioctic acid in humans is approximately 25 minutes, while total plasma clearance is 10–15 mL/min/kg. At the end of a 30-minute infusion of 600 mg the plasma levels are approximately 20 µg/mL. Through the use of radioactive marking it has been shown in animal experiments (rats, dogs) that the excretion path is mainly renal at 80–90% in the form of metabolites. Also in humans there are only small quantities of intact substance excreted in the urine. Biotransformation occurs mainly by oxidative side chain shortening (β oxidation) and/ or S-methylation of the corresponding thiols. Thioctic acid reacts in vitro with metal ion complexes (e.g. with cisplatin). Thioctic acid forms difficult-to-dissolve complex compounds with sugar molecules.

CAUTION:
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.
For suspected adverse drug reaction, please report to the FDA: www.fda.gov.ph.

STORAGE:
Store at temperatures not exceeding 30°C.
Protect from light.

AVAILABILITY
50 mL Type II amber glass vial with pink bromobutyl rubber stopper and aluminum seal with white polypropylene flip-off cap (Box of 1's and 10's).

Manufactured by:
Solupharm Pharmazeutische Erzeugnisse GmbH
Industriestraße 3, 34212 Melsungen, Germany

For:
Wörwag Pharma GmbH & Co. KG
Flugfeld-Allee 24, 71034, Böblingen, Germany

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Wörwag Pharma GmbH & Co. KG
Flugfeld-Allee 24, 71034 Böblingen

wörwag PHARMA

VNr. 19-XXXX-00 / xxxxxxx

148 x 420 mm / 8 pt / PC xxxxx

customer:	Wörwag Pharma GmbH & Co. KG			
product:	**Thiogamma Turbo-Set**			
	Beileger / Leaflet			
country:	**Philippinen (PH)**			
dimensions:	148 x 420 mm			
	Solupharm			
font:	DIN Next (size: min. 8 pt / line spacing: min. 3,4 mm)			
colors:	■ black			

date:	21.04.2020	3	19-0420-00	MR
	29.04.2020	9	19-0420-00	JuS
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	29.05.2020	9	19-0520-00	JuS
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	24.01.2023	1	19-0422-00	HB
	31.01.2023	1	19-0422-00	HB (Schreibweise Turboset)
	15.09.2023	1	19-XXXX-00	JuS
	26.09.2023	1	19-XXXX-00	JuS