Revised: August 2022 (1st version)

Standard Commodity Classification No. of Japan
873122

Storage: Stored at room temperature
Shelf life: 2 years

Approval No.	21800AMX10810
Date of Initial Marketing in Japan	December 2003

Sustained-release Vitamin B_1 Injection
Thiamine Disulfide Injection

Prescription drug:
(Caution – Use only pursuant to the prescription issued of physician, etc.)

Biogen Injection 50mg "FUSO"

2. CONTRAINDICATIONS

(This drug is contraindicated to the following patients.)
Patients with a history of hypersensitivity to any ingredient of this product.

3. COMPOSITION AND PRODUCT DESPRICTION

3.1 Composition

Product name	Biogen Injection 50 mg "FUSO"	
Volume	20 mL	
Active Ingredients	In one ampoule, Thiamine disulfide Japanese Pharmacopoeia glucose	 20 mg 4 g
Inactive Ingredients	In one ampoule, Glucuronolactone pH adjuster	 10 mg
Description	Colorless to clear pale-yellow aqueous injection	
pH	2.5 – 4.0	
Osmotic pressure ratio	Ca. 4 (ratio to physiological saline)	

3.2 Product Description

Product name	Biogen Injection 50 mg "FUSO"
Dosage form	Aqueous injection
Appearance	Clear and colorless to pale yellow liquid
pH	2.5 – 4.0
Osmotic pressure ratio (ration to saline)	3.9 – 4.3

4. INDICATIONS

- Prevention and treatment of vitamin B_1 deficiency
- Supplementation of vitamin B_1 when its demand increases and intake from meals is insufficient (wasting disease, hyperthyroidism, during pregnancy and delivery, nursing women, vigorous physical work, etc.)
- Wernicke's encephalopathy
- Beriberi-caused heart failure
- Vitamin B_1 deficiency or metabolic disorder presumed to be involved in the following diseases: neuralgia, myalgia/arthralgia, peripheral neuritis/peripheral nerve palsy, gastrointestinal hypomotility such as constipation, post-operative paresis of intestine.

Biogen Injection should not be aimlessly administered for the above indications when an effect is not achieved.

6. DOSAGE AND ADMINISTRATION

Usually, for adults, gradually administer 5 - 100 mg of Biogen Injection per day as thiamine disulfide by intravenous injection.
The dose may be increased or decreased according to age and symptom.

9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS

9.7 Pediatric Use

Clinical trials have not been conducted to evaluate the efficacy and safety of this drug in children.

11. ADVERSE REACTIONS

The following adverse reactions may occur, so please monitor the patient closely and take appropriate measures such as discontinuing the drug if any adverse reactions are observed.

11.1 Clinically Significant Adverse Reaction

11.1.1 Shock (Incidence unknown)

Administration should be immediately discontinued and appropriate measures taken when symptoms such as decreased blood pressure, precordial oppression, or dyspnea, etc. develop.

11.2 Other Adverse Reactions

	Incidence Unknown
Hypersensitivity	Rash
Gastrointestinal	Nausea/vomiting

14. PRECOUTIONS CONCERNING USE

14.1 Precautions Concerning Administration of the Drug

Since Angialgia may develop by intravenous administration, this product should be administered as slowly as possible.

18. PHARMACOLOGY

18.1 Mechanism of Action

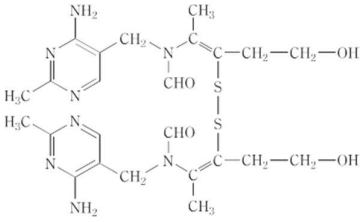
Thiamine disulfide (TDS) does not demonstrate vitamin B_1 activity as it is, but its vitamin B_1 activity is confirmed when reduced by cysteine, etc. *in vitro*.[1] Vitamin B_1 plays an important role in maintaining nerve functions, and its deficiency causes disorders in central nerve and peripheral nerve systems.[2] Beriberi is a disease caused by vitamin B_1 deficiency accompanied by paresthesia and pain of the leg, and these symptoms are improved by administration of vitamin B_1.[3]

18.2 Sustained Effect[4]

After a single intravenous administration of TDS 100 mg and vitamin B_1 hydrochloride 120 mg (equivalent to TDS 100 mg) in healthy adult men, the total vitamin B_1 concentration in whole blood after 8 hours was lowered to baseline in the vitamin B_1 group. However, a concentration equivalent to 1 to 2 hours after dosing in the vitamin B_1 group was maintained in the TDS group, and the effect of TDS for sustaining blood concentration of vitamin B_1 was demonstrated. The difference in changes of vitamin B_1 blood concentration after intravenous administration may be explained by the considerable amount of TDS remaining in the blood and transferred to blood cells after administration without being reduced to vitamin B_1, as well as the high rate of transfer to blood cells for TDS compared with vitamin B_1.

19. PHYSICOCHEMICAL PROPERTIES

Nonproprietary name: Thiamine disulfide
Structural formula:



Molecular formula : $C_{24}H_{34}N_8O_4S_2$
Molecular weight : 562.71
Chemical name : *N,N'*-{Dithiobis[2-(2-hydroxyethyl)-1-methyl-2,1-ethenediyl]}bis{*N*-[(4-amino-2-methyl-5-pyrimidinyl)methyl]formamide}

Description: Thiamine disulfide occurs as white to light yellowish white powder. It is odorless or has a slight characteristic odor and a slightly bitter taste. It is slightly soluble in ethanol (95), and practically insoluble or insoluble in water or diethyl ether. It is soluble in dilute hydrochloric acid or dilute nitric acid. Saturated aqueous solution is nearly neutral.

20. PRECAUTIONS FOR HANDLING

20.1 The blister package should not be opened until the product is used, as it is packaged in a light-shielding and gas-barrier packaging material and contains an oxygen absorber to maintain quality.
20.2 Check the color of the indicator (oxygen detector) before opening the blister package. If it is blue to purple, do not use.
20.3 Do not expose the indicator to direct sunlight in order for it to work properly.
20.4 Do not use the product in the following cases

- When the blister package is damaged
- When water droplets or crystals are observed inside the blister package or on the surface of the container.
- When the solution is leaking from the container.
- When there is any abnormality in the properties or other characteristics of the solution.

22. PACKAGING

20mL, 50 Plastic ampoules (with oxygen absorber)

23. REFERENCES

1) Kawasaki, et al: Vitamin, 1963, 28, 541-545
2) Arthur C. Guyton and others: Guyton's Physiology, original 11th edition Elsevier Japan Ltd., 2010, 926
3) Lucien Bettendorff: Present Knowledge in Nutrition, 10th edition, 2012, 261-279
4) Okuda K et al: The Clinical Report, 1973, 7, 1679-1690

26. MARKETING AUTHORIZATION HOLDER, ETC

26.1 Marketing Authorization Holder,

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