All Revised: January 2016 (1st version)

Standard Commodity Classification No. of Japan
873122

Storage : Stored with protection from light at room temperature
Expiration date : Do not use after the expiration date indicated on the outer package.
Caution :See the section "PRECAUTIONS FOR HANDLING"
Prescription drug:
(Caution – Use only pursuant to the prescription issued of physician, etc.)

Sustained-release vitamin B_1 injection

Biogen Injection 50mg

Biogen Injection

<Thiamine disulfide injection solution>

Approval No.	21800AMX10810
Date of listing in the NHI reimbursement price	July 1967
Date of initial marketing in Japan	December 2003
Date of latest reexamination	July 1974

CONTRAINDICATIONS (Biogen Injection is contraindicated in the following patients.)

Patients with a history of hypersensitivity to any ingredient of Biogen Injection.

DESCRIPTION

In a 20 mL ampoule

Brand name	Biogen Injection 50 mg
Ingredient/content	Thiamine disulfide 50 mg
	JP glucose 4 g
Excipient	Glucuronolactone 10 mg, pH adjuster
Description	Colorless to clear pale-yellow aqueous injection
pH	2.5 – 4.0
Osmotic pressure ratio	Ca. 4 (ratio to physiological saline)

INDICATIONS

1. Prevention and treatment of vitamin B_1 deficiency
2. 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.)
3. Wernicke's encephalopathy
4. Shoshin beriberi
5. 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 indication no. 5 when an effect is not achieved.

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.

PRECAUTIONS

1. Adverse Reactions

No such investigations have been performed that can definitely determine the incidence of adverse drug reactions (e.g., Drug Use Results Surveys) in patients treated with this product.

(1) Clinically significant adverse reactions (incidence unknown)

Shock: Since shock may develop, administration should be immediately discontinued and appropriate measures taken when symptoms such as decreased blood pressure, precordial oppression, or dyspnea, etc. develop.

(2) Other adverse reactions

	Incidence unknown
Hypersensitivity Note)	Rash, etc.
Gastrointestinal	Nausea/vomiting, etc.

Note) Administration should be discontinued when hypersensitivity develops.

2. Precautions for Use

(1) **At preparation:** This product should not be mixed with a mixed amino acid injection or an injection showing reducibility.

(2) **Injection rate:** Since angialgia may develop by intravenous administration, this product should be administered as slowly as possible.

PHARMACOLOGY

◇ **Vitamin B_1 effect**

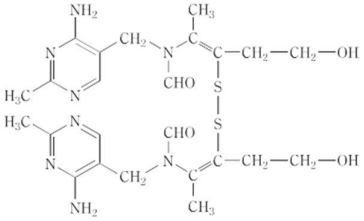
Thiamine disulfide (TDS) does not demonstrate vitamin B_1 activity as it is, but its vitamin B_1 activity is confirmed when reduced by cysteine, etc. *in vitro*.[1] Vitamin B_1 plays an important role in maintaining nerve functions, and its deficiency causes disorders in central nerve and peripheral 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]

◇ **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.

PHYSICOCHEMISTRY

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.

PRECAUTIONS FOR HANDLING

1) Do not use the product if moisture is seen inside the blister package.
2) Do not use the product if the indicator (pink tablet) is blue-violet to blue in color.
3) Store the product in a light-proof container as much as possible.
4) Use the product immediately after opening.

PACKAGING

Biogen Injection 50 mg 20 mL 50ampoules Polyal (snap open polyal)

Polyal (snap open polyal): Polyethylene ampoule

REFERENCES

1) Kawasaki C et al.:Vitamin, **28**, 541（1963）
2) TEXTBOOK OF Medical Physiology 11th EDITION GUYTON & HALL., 926（2010）
3) Present Knowledge in Nutrition, 10th ed., 261（2012）
4) Okuda K et al.:, The Clinical Report, **7**, 1679（1973）

REQUEST FOR LITERATURE SHOULD BE MADE TO:

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Fuso Pharmaceutical Industries, Ltd.
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