SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Bevione 50 mg/ml solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

[Invented name] contains thiamine (vitamin B1).

Each ml solution contains 50 mg thiamine hydrochloride.
Each 2 ml ampoule contains 100 mg thiamine hydrochloride.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Aqueous, clear, colourless or almost colourless solution, free of visible particles.

The osmolality is approximately 350 mOsmol/kg.
The pH of the drug product is approximately 3.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

[Invented name] is indicated for prevention and treatment of symptomatic thiamine deficiency (e.g. beriberi and Wernicke-Korsakoff syndrome) due to malabsorption/malnutrition.

4.2 Posology and method of administration

Posology

Exact dose, duration of therapy and method of administration will depend on the patient´s clinical status and response to treatment. [Invented name] is administered via intramuscular or slow intravenous injection, preferably in divided doses, until the symptoms resolve or plateau.

The following posology is recommended for Beriberi and Wernicke-Korsakoff syndrome:
Adults
Beriberi:
- Treatment: 10 mg – 20 mg by intramuscular injection or slow intravenous infusion (over 30 minutes) 3 times/day for up to 2 weeks. If severe life threatening form of beriberi (e.g. shoshin beriberi): 100 mg to 300 mg/day by slow intravenous infusion.
- Maintenance treatment: the treatment should be continued with an adapted oral form of vitamin B1.

Wernicke-Korsakoff syndrome associated with alcohol use disorder:
- Prophylaxis in patients with high risk (e.g. hospitalized patients managed for alcohol withdrawal in presence of malnutrition): 250 mg by intramuscular or intravenous route 1 time/day for 3 to 5 days.

- Treatment: 500 mg by intravenous route 3 times/day for at least 2 days. In case of favorable response the treatment can be continued with 250 mg by intramuscular or intravenous route 1 time/day for 5 days or until there is no further improvement.
- Maintenance treatment: the treatment should be continued with an adapted oral form of vitamin B1.

Patients suffering from an underlying thiamine deficiency to whom glucose is being administered should receive 100 mg thiamine hydrochloride in each of the first few liters of IV fluid to avoid precipitating heart failure. Intake of glucose quickly provokes a depletion of the reserves, and precipitates or aggravates a Wernicke encephalopathy(see section 4.4).

Paediatric population
There is only limited experience with therapy in children and adolescents.

Beriberi:
- Treatment: 10 mg to 25 mg/day by intramuscular injection or slow intravenous infusion for 2 weeks. IV doses of 100 mg/day or even higher may be needed in severe cases, for example 500 mg three times a day could be used (see section 5.1).
- Maintenance treatment: the treatment should be continued with an adapted oral form of vitamin B1.

Elderly
There are no data available in the elderly. No dose adjustment is recommended for this population. Interactions with other medicines should be considered (see sections 4.5 and 5.2).

Renal impairment
The influence of renal impairment on the pharmacokinetics of thiamine has not been evaluated. No dose adjustment is recommended, but caution is advised when treating patients with renal impairment (see sections 4.4 and 5.2).

Hepatic impairment
The influence of hepatic impairment on the pharmacokinetics of thiamine has not been evaluated. No dose adjustment is recommended, but caution is advised when treating patients with hepatic impairment (see section 5.2).

Method of administration
[Invented name] should be administrated by slow intravenous or intramuscular route.

The intravenous injection is administrated slowly over 30 minutes.

For intramuscular administration, use the undiluted drug solution.

For instructions on dilution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Warnings
- Parenteral route must be used only when rapid restauration of thiamine is necessary (e.g. Wernicke-Korsakoff syndrome) or when oral route is ineffective (e.g. in case of vomiting, malabsorption).
- The 50 mg/ml solution will be less painful when administered by IM route.
- Anaphylactic reactions leading to shock have been reported after thiamine hydrochloride parenteral administration (see section 4.8).This risk increases in case of repeated doses. An intradermal test

dose is recommended prior parenteral administration in patients suspected to be drug sensitive. **Emergency medical equipment for treating anaphylactic shocks must be easily available.**
- **To reduce the risk of anaphylactic shock and reactions at the injection site, the intravenous injection must be administered slowly (over 30 minutes).** Fast IV administration of 100 mg thiamine hydrochloride is associated with an immediate burning sensation in the arm after injection in the IV line, lasting seconds to minutes. This reaction can be avoided by slow administration into larger veins with higher IV fluid flow rates (see section 4.8).
- As thiamine plays the role of enzymatic cofactor in the normal metabolism of glucides, an important intake of glucose quickly provokes a depletion of the reserves, and precipitates or aggravates a Wernicke encephalopathy in patients suffering from an underlying thiamine deficiency. It is consequently recommended to administer thiamine intravenously before or simultaneously with administration of glucose by bolus or by infusion (see sections 4.2 and 4.8).
- Patients with renal impairment may need an extra careful monitoring (see sections 4.2 and 5.2).
- This medicine contains less than 1 mmol sodium (23 mg) per 2 ml ampoule, that is to say essentially “sodium-free”.

Interference with laboratory tests
Thiamine can give false positive results for urobilinogen determination by the Ehrlich's reaction (urine test) and for uric acid determination by the phosphotungstene method. High doses of thiamine may interfere with Schack and Waxler spectrophotometric assays of theophylline plasma concentration.

4.5 Interaction with other medicinal products and other forms of interaction

Medicines that may decrease the effect of thiamine
- The thiamine antagonists: 5-fluorouracil, other fluoropyrimidines (e.g. capecitabine) and ifosfamide.
- Diuretics, e.g. furosemide that may increase urinary thiamine excretion.

Thiamine deficiency can occur with the chronic use of these medicines. Consider high-dose thiamine supplementation during the treatment with these medicines.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or limited amount of data from the use of thiamine in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3). The use of the product is individualized based on condition and requirements in pregnant women and can be used in pregnant women if use is necessary to correct deficiencies and if benefits overweight risks.
Caution should be exercised when prescribing to pregnant women. The risk of anaphylactic reactions present during parenteral administration must be taken into account.

Breastfeeding
Thiamine is excreted in human milk. At recommended daily intake levels no effects on the breastfed newborns/infants are anticipated. However, there is insufficient information on the levels and possible effects of excretion of thiamine in human milk after administration of high levels of thiamine (> 50 mg/day). A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from thiamine therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.

Fertility
No relevant data is available.

4.7 Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed. However, patients should be cautioned to see how they react before driving or operating machinery.

4.8 Undesirable effects

Adverse effects with thiamine are rare, but hypersensitivity reactions have occurred, mainly after parenteral administration. These reactions have ranged in severity from very mild to very rarely, fatal anaphylactic shock. Pain and an immediate burning sensation in the arm have been reported after a fast intravenous administration.

The possible side effects are listed below. The frequency of the possible side effects is defined as: Very common (>1/10). Common (>1/100, <1/10). Uncommon (>1/1,000, <1/100). Rare (>1/10,000, <1/1,000). Very rare (<1/10,000). Unknown (cannot be estimated from the available data).

The side effects are presented by System Organ Class and in order of decreasing seriousness within each frequency category.

Organ system	**Undesirable effects**	**Frequency**
Immune system disorders	Allergic or anaphylactic reactions (with respiratory depression, pruritus, shock and abdominal pain) [1]	Unknown
Skin and subcutaneous tissue disorders	Contact dermatitis (which can appear after administration to sensitized individuals)	Unknown
General disorders and administration site conditions	Injection site reactions (pain, burning in the arm) [2]	Unknown

[1] Reaction observed after repeated injections of high doses from 25 mg to 100 mg thiamine hydrochloride, at intervals of more than 7 days. These reactions are frequently preceded by sneeze or transient pruritus. The risk of anaphylactic shock can be reduced by a slow administration over 30 minutes.
[2] Fast intravenous administration of 100 mg thiamine hydrochloride is associated with an immediate burning sensation in the arm after injection in the IV line, lasting seconds to minutes. This reaction can be avoided by a slow administration into larger veins with higher IV fluid flow rates (see section 4.4).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Symptoms and signs
Thiamine is widely used, serious toxicity is not expected.
Single parenteral doses of 100 mg to 500 mg have been given with no toxic effects reported. Toxicity is uncommon following oral ingestion, excessive doses are usually excreted rapidly in the urine.

Treatment
In the unlikely event of overdosage, treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: vitamin B1 plain. ATC code: A11D-A01

Mechanism of action
The principal physiological role of thiamine is as a coenzyme in carbohydrate metabolism, where thiamine pyrophosphate (TPP) is required for several stages in the breakdown of glucose to provide energy.
The organ systems principally affected by thiamine deficiency are the nervous, cardiovascular, muscular and gastrointestinal systems.

Clinical efficacy and safety
In early stages of severe deficiencies like Wernicke-Korsakoff syndrome or Shoshin beriberi, parenteral administration of thiamine rapidly reverses the clinical symptoms. The improvement of symptoms is sufficient to make the diagnosis, even if serum thiamine measurement is not available.

In Wernicke-Korsakoff syndrome, early recognition and treatment is important, both because of the risk of collapse and sudden death, and to prevent irreversible damage to the CNS. Korsakoff symptoms respond less well to treatment than those associated with Wernicke's encephalopathy, and may indeed only become evident on treatment. This justifies the recommended high doses for the treatment (see section 4.2).

Paediatric population

In one case report, a 13 years old male was treated with high doses of thiamine: 100 mg/day then 500 mg three times a day. The patient completely recovered after 20 days of replacement therapy (see section 4.2).

5.2 Pharmacokinetic properties

Absorption
Thiamine is rapidly and completely absorbed after intramuscular administration.

Distribution
In blood, 90% of thiamine is incorporated in blood cells. The remaining part in the plasma is non-specifically bound to several proteins, especially albumin. Thiamine is widely distributed to most body tissues. It is not known if thiamine crosses placenta. Thiamine is excreted in human breast milk.
Within the cell, thiamine is mostly present as diphosphate.
Thiamine is a water-soluble vitamin and only little thiamine is stored in the body.

Biotransformation and elimination
Thiamine is metabolised in the liver. Several urinary metabolites of thiamine have been identified in humans. Little or no unchanged thiamine is excreted in urine following administration of physiologic doses; however, following administration of large doses, both unchanged thiamine and metabolites are excreted after tissue stores become saturated.

Specific groups of patients

Renal impairment
The influence of renal impairment on the pharmacokinetics of thiamine has not been evaluated. No dose adjustment is required in patients with renal impairment. However, as elimination through the urine is the main excretion pathway, extra careful monitoring in these patients is advisable (see sections 4.2 and 4.4).

Dialysed patients are at high risk of being deficient in vitamin B1.

Hepatic impairment

The influence of hepatic impairment on the PK of thiamine has not been evaluated. No dose adjustment is required in patients with hepatic impairment but caution is advised in these patients (see section 4.2).

Effect of gender, race and weight
The influence of gender, race and weight has not been established, and there are no data concerning the effect of these factors on the PK of thiamine.

Paediatric population
There is only limited experience with therapy in paediatric population (see section 4.2).

Elderly
There are no pharmacokinetic data in the elderly. No dose adjustment is recommended for this population (see section 4.2).

5.3 Preclinical safety data

There are insufficient data to exclude genotoxicity, carcinogenicity or reproductive toxicity. There are no other non-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SmPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

Before opening
3 years.

After first opening
After first opening the medicinal product should be used immediately.

After dilution for infusion
Chemical and physical in-use stability has been demonstrated for up to 8 hours at a temperature between 15 and 25°C when the product is diluted in 50ml and 250ml of sodium chloride 0.9% and glucose 5%. The diluted solutions need not to be stored protected from light (see section 6.6).

From a microbiological point of view, unless the method of opening/dilution precludes the risks of microbial contamination, the diluted product in an infusion fluid should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Do not store above 30°C.

For storage conditions after opening of the ampoule and dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

2 ml clear glass ampoules.
Pack sizes containing 5, 10 or 100 ampoules.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal <and other handling>

The solution is to be visually inspected prior to use (also after dilution). Only clear solutions free from visible particles should be used. For single use only. Discard any unused product at the end of each operating session.

Dilution for infusion
For slow intravenous administration, the drug solution must be first diluted into 50 ml to 250 ml of 5% glucose or 0.9% sodium chloride sterile solutions. It can be administered for up to 8 hours without protection from light. The solution after dilution remains clear, colourless or almost colourless, and free of visible particles.

Any unused medicinal product, waste material or remaining medicinal solution should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

2026-05-28