

## 1. NAME OF THE MEDICINAL PRODUCT

**VITAMINE B1 STEROP 100mg/2ml solution for injection**

**VITAMINE B1 STEROP 250mg/2ml solution for injection**

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

VITAMINE B1 STEROP is a thiamine (vitamin B1)-containing monovitamin product.

VITAMINE B1 STEROP 100mg/2ml: Each ml solution contains 50mg thiamine hydrochloride.

VITAMINE B1 STEROP 250mg/2ml: Each ml solution contains 125mg thiamine hydrochloride.

Excipient with known effect: sodium.

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Solution for injection.

Aqueous, clear, colourless to slightly yellow sterile solution, free of visible particles.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

VITAMINE B1 STEROP is indicated for the prevention and the treatment of vitamin B1 deficiencies like beriberi, deficiency related to chronic alcoholism and Wernicke-Korsakoff syndrome.

### 4.2 Posology and method of administration

#### Posology

#### Adults

- Mild thiamine deficiency of non-alcoholic causes (ex. malnutrition):
  - 100mg orally daily.Dilute the content of the ampoule in a glass water.
- Beriberi:
  - Starting dose: 10mg - 20mg by intramuscular injection or slow intravenous infusion (over 30 minutes) 3 times/day for up to 2 weeks.
  - Maintenance dose: this treatment is continued by an oral maintenance with 5mg-10mg thiamine hydrochloride daily for 1 month.

If severe life threatening deficiency (e.g. *shoshin* beriberi): 100mg to 300mg/day by intramuscular injection or slow intravenous infusion.

- Wernicke-Korsakoff syndrome associated with alcohol use disorder:
  - Lower risk patients with mild deficiency (e.g. alcoholic patients without malnutrition): 200mg orally (diluted in a glass water).
  - Prophylaxis in patients with a high risk (e.g. hospitalized patients managed for alcohol withdrawal in presence of malnutrition): 250mg by intramuscular or intravenous route 1 time/day for 3 to 5 days.
  - Treatment: 500mg to 750mg by intravenous route 3 times/day for at least 2 days (up to 1000mg/dose during the first 12 hours has been used). In case of favorable response the treatment

will be continued with 250mg by intramuscular or intravenous route 1 time/day for 5 days or until there is no further improvement. Followed with thiamine 100mg orally 3 times daily for 1 to 2 weeks, then 100mg orally once daily.

Treatment duration should not exceed 6 months.

Patients with marginal thiamine status to whom glucose is being administered should receive 100mg thiamine hydrochloride in each of the first few liters of IV fluid to avoid precipitating heart failure (see section 4.4).

#### Paediatric population

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

Beriberi:

- Starting dose: 10mg to 25mg/day by intramuscular injection or slow intravenous infusion or 10mg-50mg/day orally for 2 weeks.
- Maintenance dose: this treatment is continued by 5mg-10mg/day orally for 1 month.
- Mild: 10mg/day orally.

IV and oral doses of 100mg/day or even higher may be needed in severe cases (IV doses up to 500mg three times a day have been described in a 13 years old boy).

#### 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

VITAMINE B1 STEROP should be administered by slow intravenous or intramuscular route or by oral route. The oral route is also used for supporting or/and continuing ongoing injection therapy.

**For slow intravenous administration, the drug solution must be first diluted into 50ml to 250ml of 5% glucose or 0.9% sodium chloride sterile solutions. The injection is administered slowly over 30 minutes.**

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

For intramuscular administration, use the undiluted drug solution. Deep intramuscular injection must be given into a big muscular mass (upper outer quadrant of the buttock or the lateral part of the thigh). Before injection of the dose, suck up to be sure that the needle is not into a vein. If blood appears, take the needle out and inject into another site. Change the injection site in case of repeated doses.

For oral use, the drug solution should be diluted in a glass water.

### **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).
- Anaphylactic reactions leading to shock have been reported **mainly** after thiamine hydrochloride parenteral administration (see section 4.8). Nevertheless, this risk increases in case of repeated doses. An intradermal test dose is recommended prior parenteral administration in patients suspected to be drug sensitive. **The emergency medical equipment useful 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 100mg thiamine hydrochloride is associated with immediate burning in the arm after injection with 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 with patients suffering from an underlying thiamine deficiency. It is consequently recommended to administer intravenously thiamine before or simultaneously to an 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 medicinal product contains less than 1mmol sodium (23mg) per 2ml ampoule, i.e. essentially “sodium free”.

### Precautions for use

- Do not use this medicine if you notice visible particles in the solution, if the solution is not clear or if it contains a precipitate.
- This drug solution and any syringe containing this medicine are destined for single and individual use (see section 6.3).

## **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.

### Other forms of interaction

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.

## **4.6 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 outweighs 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 immediate burning in the arm have been reported after a fast intravenous administration.

The frequency of the possible side effects is defined as following:

- 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.

<b>Table: Known undesirable effects</b>		
<b>Organ system</b>	<b>Undesirable effects</b>	<b>Frequency</b>
Immune system disorders	Allergic or anaphylactic reactions (with respiratory depression, pruritus, shock and abdominal pain) <sup>1</sup>	Unknown
Skin and subcutaneous tissue disorders	Contact dermatitis (which can appear after an oral or parenteral administration to sensitized individuals)	Unknown
General disorders and administration site conditions	Injection site reactions (pain, burning in the arm) <sup>2</sup>	Unknown

<sup>1</sup> Reaction observed whatever the administration way, generally after repeated injections of high doses from 25mg to 100mg 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.

<sup>2</sup> Fast intravenous administration of 100mg thiamine hydrochloride is associated with immediate burning in the arm after injection with 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

### **België**

Federaal agentschap voor geneesmiddelen en gezondheidsproducten  
Afdeling Vigilantie  
EUROSTATION II  
Victor Hortaplein, 40/ 40  
B-1060 Brussel  
Website: [www.fagg.be](http://www.fagg.be)  
e-mail: [adversedrugreactions@fagg-afmps.be](mailto:adversedrugreactions@fagg-afmps.be)

### **Belgique**

Agence fédérale des médicaments et des produits de santé  
Division Vigilance  
EUROSTATION II  
Place Victor Horta, 40/ 40  
B-1060 Bruxelles  
Site internet: [www.afmps.be](http://www.afmps.be)  
e-mail: [adversedrugreactions@fagg-afmps.be](mailto:adversedrugreactions@fagg-afmps.be)

### **Belgien**

Föderalagentur für Arzneimittel und Gesundheitsprodukte  
Abteilung Vigilanz  
EUROSTATION II  
Victor Hortaplein, 40/40  
B-1060 BRUSSEL  
Website: [www.fagg-afmps.be](http://www.fagg-afmps.be)  
E-Mail: [adversedrugreactions@fagg-afmps.be](mailto:adversedrugreactions@fagg-afmps.be)

### **Česká republika**

Státní ústav pro kontrolu léčiv  
Šrobárova 48  
100 41 Praha 10  
Webové stránky: [www.sukl.cz/nahlasit-nezadouci-ucinek](http://www.sukl.cz/nahlasit-nezadouci-ucinek)

### **Danmark**

Lægemiddelstyrelsen  
Axel Heides Gade 1  
DK-2300 København S  
Websted: [www.meldenbivirkning.dk](http://www.meldenbivirkning.dk)  
E-mail: [dkma@dkma.dk](mailto:dkma@dkma.dk)

### **Norge**

Statens legemiddelverk  
Nettside: [www.legemiddelverket.no/meldeskjema](http://www.legemiddelverket.no/meldeskjema)

### **Suomi/Finland**

www-sivusto: [www.fimea.fi](http://www.fimea.fi)  
Lääkealan turvallisuus- ja kehittämiskeskus Fimea  
Lääkkeiden haittavaikutusrekisteri  
PL 55  
00034 FIMEA

webbplats: [www.fimea.fi](http://www.fimea.fi)  
Säkerhets- och utvecklingscentret för läkemedelsområdet Fimea  
Biverkningsregistret  
PB 55

00034 FIMEA

## **Sverige**

Läkemedelsverket

Box 26

751 03 Uppsala

Webbplats: [www.lakemedelsverket.se](http://www.lakemedelsverket.se)

## **4.9 Overdose**

### Symptoms and signs

Thiamine is widely used; serious toxicity is not expected.

Single parenteral doses of 100mg to 500mg have been given with no toxic effects reported. Toxicity is uncommon following oral supplementation; excessive doses are usually excreted rapidly in the urine.

Long-term supplementation of doses greater than 3000mg daily has been known to produce toxicity.

Severe toxicity has not been reported.

### Treatment

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

In case of mild or moderate anaphylaxis: antihistamines are given (with or without inhaled beta agonists), corticosteroids or epinephrine.

In case of severe anaphylaxis occurs: oxygen, aggressive airway management, antihistamines, epinephrine, corticosteroids, ECG monitoring, and IV fluids.

## **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.

Thiamine combined with adenosine triphosphate (ATP) is converted to the active coenzyme thiamine pyrophosphate (thiamine diphosphate) by the enzyme thiamine diphosphokinase. Thiamine pyrophosphate is a coenzyme in carbohydrate metabolism (in the decarboxylation of pyruvic and alpha-ketoglutaric acids) and in transketolation reactions. Thiamine diphosphate is also a coenzyme in the utilisation of pentose in the hexose monophosphate shunt.

Thiamine pyrophosphate would also have a neurotransmitter function.

### Pharmacodynamics

Thiamine deficiency results in beriberi and Wernicke-Korsakoff syndrome. Clinical signs of thiamine deficiency become evident after 2-3 weeks of inadequate thiamine intake. The organ systems principally affected by thiamine deficiency are the nervous system, cardiovascular system, and GI tract.

Administration of thiamine completely reverses the cardiovascular and gastro-intestinal symptoms of thiamine deficiency; however the degree of improvement in neurologic symptoms depends on the duration and severity of the lesions.

Fatal deficiency can develop as rapidly as within 3-4 weeks in the absence of thiamine intake.

Several cases of fatal, acute beriberi developed within 5 weeks in patients receiving thiamine-deficient total parenteral nutrition solutions have been observed.

### 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. And the improvement of symptoms is also 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).

Thiamine has a good safety profile. The only adverse events observed with parenteral administration include injection site pain, contact dermatitis, and mild to anaphylactic allergic reactions. More of these events are easy to manage, though there have been reports of severe anaphylaxis following IV thiamine (see sections 4.4 and 4.8). In case of anaphylaxis it is agreed that standard anaphylaxis care and interruption of administration should be sufficient to manage the patient.

In contrast, no safety reports on oral thiamine use could be identified and likely this route of administration is thus perfectly safe.

## 5.2 Pharmacokinetic properties

### Absorption

Thiamine is well absorbed by the small intestine, mainly from the upper part of the duodenum.

At low doses, free thiamine is absorbed by a saturable active transport system and at high doses by a slower nonsaturable passive process.

Absorption of thiamine appears to be independently affected by ethanol and malnutrition.

According to some authors, in alcoholics without encephalopathy, oral thiamine hydrochloride, when given over a 5-days period, produces blood levels that approach those obtained by intramuscular and intravenous administration.

Thiamine is rapidly and completely absorbed after intramuscular administration.

### Distribution

Thiamine is nonspecifically bound to several proteins, especially albumin, in the plasma.

It is widely distributed to most body tissues. It is not known if thiamine crosses placenta. Supplementation did not significantly affect thiamine concentration in breast milk of healthy, well-nourished women and appears in breast milk in lactating women with poor nutritional status. The authors supposed that absorptive capacity of the mammary gland may be saturable.

Within the cell, it is mostly present as diphosphate.

Thiamine is a water-soluble vitamin and therefore the quantity of thiamine reserves in the lipid structures of body cells is quite low, with the maximum storage capacity being 30mg.

### Biotransformation and elimination

Thiamine is metabolised in the liver in animals. 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.

In thiamine deficiency, thiamine is generally absent from the urine. However, a patient can be clinically (or subclinically) thiamine-deficient despite a "normal" serum and urinary thiamine excretion level.

### Specific groups of patients

#### Renal impairment

The influence of renal impairment on the pharmacokinetics of thiamine has not been evaluated. No data is available suggesting that dosing changes are necessary for patients with renal issues. Thus no dose adjustment is required in patients with renal impairment. But, as elimination through the urine is the main excretion pathway, it is conceivable that patients with disturbed urinary function may build up high systemic doses of thiamine and its metabolites. Though no knowledge nor proof on potential toxicity

exists, given the anaphylactic potential of the compound, 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. These patients may also have a resistance to vitamin activity. The results may show normal concentrations of thiamine but low or marginal ETKo levels.

#### Hepatic impairment

The influence of hepatic impairment on the PK of thiamine has not been evaluated, although vitamin B1 supplementation is highly recommended in patients with end-stage liver failure of either alcoholic or non-alcoholic etiologies (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.

#### Elderly

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

#### **Paediatric population**

There is only limited experience with therapy in paediatric 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 5% w/v solution (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

For single use only. Discard any unused product at the end of each operating session. VITAMINE B1 STEROP does not contain any antimicrobial preservative. Therefore the growth of microorganisms in the solution cannot be prevented. After first opening the medicinal product should be used immediately (see section 4.4).

#### 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, the diluted product in an infusion fluid should be used immediately and would normally not be longer than 24 hours at 2-8°C, unless dilution has taken place in controlled and validated aseptic conditions. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

#### **6.4 Special precautions for storage**

Do not store above 25°C. Do not freeze.

Keep the ampoules in the outer carton in order to protect from light.

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**

2ml uncoloured glass ampoules.

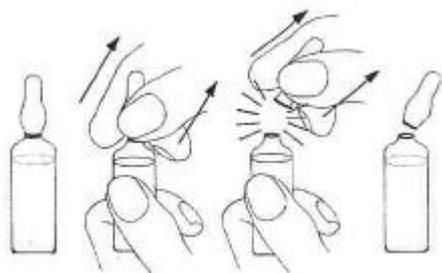
Pack sizes containing 3, 10 or 100 ampoules. Not all pack sizes may be marketed.

#### **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.

##### Opening of the ampoules

- Before using the ampoule, roll it briefly between both hand palms to warm up the product.
- Locate the short score mark on the thin part of the neck. This score is the breaking point of the ampoule.
- Hold the bottom of the ampoule between the thumb and index finger, leaving the tip of the ampoule free.
- With the other hand, hold the tip of ampoule putting the index finger against the neck of ampoule and the thumb on the other side above the coloured ring.
- Sharply break the tip of ampoule while holding firmly the other part of the ampoule in the hand.
- Carefully dispose of the tip of the ampoule in a “Sharps” bin.
- Once opened VITAMINE B1 STEROP ampoules should be used immediately.



##### Dilution for infusion

VITAMINE B1 STEROP can be administered by slow intravenous injection after dilution in 50ml to 250ml of a 50mg/ml glucose (5%) or a 9mg/ml sodium chloride (0.9%) sterile solution for up to 8 hours without protection from light.

The solution after dilution remains clear, colourless to slightly yellow and free of visible particles.

The prepared diluted solution should be made up immediately before use.

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

## **7. MARKETING AUTHORISATION HOLDER**

LABORATOIRES STEROP NV  
Scheutlaan 46-50

THIAMINE HCl STEROP

Summary of product characteristics

1070 Brussels  
Belgium.

## **8. MARKETING AUTHORISATION NUMBERS**

VITAMINE B1 STEROP 100mg/2ml: BE271695  
VITAMINE B1 STEROP 250mg/2ml: BE271704

## **9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 11/04/2005  
Date of latest renewal: 28/10/2010

## **10. DATE OF REVISION OF THE TEXT**

Date of revision of the text: 01/2019  
Date of approval of the text: 12/2016