SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

SUCCICAPTAL 200 mg, capsule

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Succimer……200,00 mg

For one n°1 capsule of 350,00 mg.

Excipient with known effect: 139,58 mg of lactose monohydrate per capsule.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsule.

White capsule size n°1.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of lead and mercury poisoning.

4.2 Posology and method of administration

Posology

The posology for adults and children is:

- 10 mg/kg (or 350 mg/m^2) every 8 hours for 5 days (i.e. 30 mg/kg/day),
- followed by 10 mg/kg (or 350 mg/m^2) every 12 hours for 2 weeks (i.e. 20 mg/kg/day).

For adults, 1.80 g/day must generally not be exceeded.

Doses according to the bodyweight are therefore as follows:

Bodyweight	Dose
8 – 15 kg	100 mg / dose
16 – 23 kg	200 mg / dose
24 – 34 kg	300 mg / dose
35 – 44 kg	400 mg / dose
> 45 kg	500 mg / dose

Method of administration

Oral route.
In children, the capsule content can be mixed in fruit juice or soft food.

Frequency of administration

3 times per 24 hours every 8 hours for the first five days of the treatment, then every 12 hours for 2 weeks.

Treatment duration

19 days.
At the end of the treatment, monitor plasmatic concentrations of heavy metals during 10 days because a rebound rise may occur (due to redistribution of lead from bone) and multiple courses of treatment can be considered in the most severe cases (see section 5.1).

4.3 Contraindications

The medicinal product is contraindicated in case of hypersensitivity to the active substance or to one of the excipients.

4.4 Special warnings and precautions for use

Special warnings

This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose - galactose malabsorption syndrome (rare hereditary diseases) should not take this medicine.
Renal or hepatic insufficiency: in absence of data, caution should be exercised when treating patients suffering from renal or hepatic function impairment.

Precautions for use

Not applicable

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy
Animal studies revealed developmental toxicity (cleft palates, skeletal malformations, ocular abnormalities and fetal open neural tube defects). In humans, there is no clear clinical evidence.

The passage of succimer across the placental barrier is unknown.

Thus, succimer should be used during pregnancy only when there is a clear maternal benefit greater than the potential risk for the fetus.

Breastfeeding
Use of succimer during breast-feeding is not recommended.

Fertility
No fertility study has been performed.

4.7 Effects on ability to drive and use machines

No effect on the ability to drive or use machines is awaited with this medicinal product.

4.8 Undesirable effects

The most frequent undesirable effects (>5%) are digestive, cutaneous or biological disorders.

Gastro-intestinal disorders

- Nausea, vomiting.
- Diarrhoea.
- Decreased appetite.

Skin and subcutaneous tissue disorders

- rash, sometimes rash vesicular and possibly involved mucosa.

Biological abnormalities

- Transient transaminases increased
- Urine copper and zinc increased

Others

- **Urine odour** abnormal, breath odour

Rare cases of hypersensitivity reactions have been reported (urticaria,angioedema).

Most of the reactions described are of mild to moderate intensity. They resolved after cessation of the therapy.

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 : Agence nationale de sécurité du médicament et des produits de santé (ANSM) and Regional Pharmacovigilance Centres network - Website: www.signalement-sante.gouv.fr.

4.9 Overdose

The clinical experience concerning the consequences of an overdose is limited to the case of a 3 year-old child remaining clinically and biologically asymptomatic after the ingestion of 2,4 g succimer.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: **ANTIDOTE / CHELATOR OF HEAVY METALS**, ATC code: **V03AB**

Succimer increases the urinary excretion of heavy metals by forming stable hydrosoluble complexes.

Excretion is usually maximal on the first day of chelation and lead-induced symptoms usually alleviated within 2 days. However, the treatment must be adapted to avoid a rebound of blood lead levels and to achieve an effective and complete chelation therapy.

5.2. Pharmacokinetic properties

Absorption

After oral administration, the absorption of succimer from the gastrointestinal tract is rapid (Tmax from 1 to 4 hours) but incomplete (20%).

Distribution

In the blood stream, succimer is essentially bound to plasma proteins (mainly albumin) at 85%.

Succimer is primarily distributed within the extracellular space.

Metabolism

Succimer appears rapidly and extensively metabolised, probably in the liver mainly under succimer-cysteine disulfides that would play an active role in heavy metals chelation.

Succimer and/or its metabolites undergo enterohepatic circulation and storage of the metabolites into bile have been suggested.

Elimination

After oral administration, elimination of succimer is mainly by urinary excretion. Bile Excretion has been suggested.

90% of DMSA excreted in urine is found as mixed succimer-cysteine disulfide conjugates while 10% as unchanged drug.

The peak of urinary excretion appears between 2 and 4 hours after oral administration. Two different half-life of elimination have been reported: one initial half-life of less than 4 hours and one final half-life of 48 hours (explained by a storage in the gall-bladder).

The complex succimer with lead or mercury may be dialysed considering the theorical physico-chemical properties of the complex.

5.3 Preclinical safety data

The extracellular distribution of succimer may be responsible for its low toxicity compared to other dithiols. Toxic effects of succimer appear only at doses well in excess of the recommended doses for the treatment of the intoxication.

The median lethal single dose of DMSA in mice and rats exceeds 3000 mg/kg per os. In rats and dogs, significant signs of toxicity were observed with oral dose up to 200 mg/kg/day. In dogs, toxic effects have been observed at an oral dose of succimer greater than 300 mg/kg/day.

Thrombocytopenia was observed in dogs receiving succimer at 80 or 140 mg/kg/day after three months oral intake. Platelet counts remain normal after oral treatment of 10 mg/kg/day for three months.

No carcinogenicity study is available with this drug.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose, magnesium stearate, anhydrous colloidal silica.

Composition of the shell of the capsule: gelatin, titanium dioxide.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store at a temperature below 25°C, protect from light and humidity.

6.5 Nature and contents of container

15 capsules in a heat-sealed blister (PVC/Aluminium).

6.6 Special precautions for disposal <and other handling>

No special precaution for disposal.

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

7. MARKETING AUTHORISATION HOLDER

SERB
40 avenue George V
75008 Paris
FRANCE

8. MARKETING AUTHORISATION NUMBER(S)

34009 365 710 8 2 : 15 capsules in a heat-sealed blister (PVC/Aluminium) (marketed).

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01 February 1996
Date of latest renewal: 01 February 2011

10. DATE OF REVISION OF THE TEXT

11 March 2020 / V1

11. DOSIMETRY

Not applicable.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.

PRESCRIPTION AND DISPENSING CONDITIONS

List I.
The initial prescription of this medicine is restricted to a hospital setting.