SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Kaliumjodid SERB 65 mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 tablet contains 65 mg of potassium iodide (corresponding to 50 mg iodide).

Excipient with known effect: Lactose 176 mg.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.
White to off-white, round, flat bevelled tablet, with a cross line on one side, diameter 9 mm.

The tablet can be divided into two or four equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Prevention of the uptake of radioactive iodine by the thyroid gland in case of a nuclear accident.

The use of this antidote should be in accordance with official national recommendations of competent authorities.

4.2 Posology and method of administration

This medicinal product should only be taken after explicit instructions of the national competent authorities.

The protocol of administration is in line with the latest WHO recommendations for Iodine Prophylaxis following Nuclear Accidents (2017).

Posology

People living in iodine deficient areas are more likely to be affected by exposure to radioactive iodine. In such places, national or regional programmes targeting iodine deficiency should be considered.

Time of administration
- The optimal period of administration of potassium iodide is less than 24 hours prior to, and up to 2 hours after, the expected onset of exposure. It would still be reasonable to administer potassium iodide up to 8 hours after the estimated onset of exposure. See also section 4.4.
- Potassium iodide should not be administered later than 24 hours following exposure.

Recommended single dosage by age
- *Adults including pregnant and breastfeeding women.*

The standard dose is detailed below:

	Potassium iodide dose	Potassium iodide 65 mg tablet
Adults	130 mg	2

- *Paediatric population*

The standard dose is defined according to the age of the patient:

	Potassium iodide dose	Potassium iodide 65 mg tablet
Adolescents (above 12 years old)	130 mg	2
Children (from 3 to 12 years old)	65 mg	1
Infants (from 1 month to 3 years old)	32 mg	1/2
Newborns (<1 month)	16 mg	1/4

Repeated doses in case of prolonged exposure
A single administration of stable iodine is usually sufficient. In case of prolonged exposure, additional doses may be administered following explicit instructions of the competent authorities.
New-borns (<1 month), pregnant and breastfeeding women and older adults (over 60 years) should not receive repeated doses of potassium iodide.

Renal impairment
There are no available information that suggests that a dose reduction is necessary.
However, due to the decrease in renal excretion, there is a risk of accumulation of drug in the body.

Hepatic impairment
There are no available information that suggests that a dose reduction is necessary.
However, due to the decrease in liver detoxification, there is a risk of accumulation of drug in the body.

Elderly population
There are no available information that suggests that a dose reduction is necessary.
However, because this population is at higher risk of liver and/or renal impairment, there is a risk of accumulation of drug in the body.
Due to an increased risk of pre-existing thyroid diseases in the elderly population, repeated doses should not be given.

Method of administration
The tablets are provided with cross lines in order to facilitate the dosage for children.
The tablet can be chewed, swallowed or crushed and mixed with fruit juice, jam, milk or similar substance.
In case of dissolution, the solution must be taken immediately.
Food in the stomach may delay absorption; therefore, it is preferable to take tablet away from food intake.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Dermatitis herpetiformis (Duhring-Brocq disease)
- Hypocomplementaemic urticarial vasculitis (Mac Duffie syndrome)

4.4 Special warnings and precautions for use

This medicinal product should be taken immediately after explicit instructions of the competent authorities (see section 4.2).

The late intake of potassium iodide tablets (24 hours after exposure) may be harmful as it would prolong the half-life of radioactive iodine that has accumulated in the thyroid leading to possible hypothyroidism by thyroid-cell destruction and to thyroid cancer.

Precautions for use

- The groups most likely to benefit from treatment with iodine tablets after exposure to radioactive iodine are children, adolescents, and pregnant and lactating women, as well as those living in iodine-poor areas (who are more likely to be affected by exposure to radioactive iodine). If the supply of stable iodine is limited, preference should be given to children and young adults.
- Adults over 40 years of age are less likely to benefit from treatment with iodine tablets after exposure to radioactive iodine. However, persons at risk of exposure to high doses of radioactive iodine (e.g. workers involved in rescue or cleaning operations) are more likely to benefit from treatment regardless of age and should be given priority.
- Prophylaxis with iodine protects against inhaled or ingested radioiodine, but has no effect on other ingested radionuclides.
- An enlargement of the thyroid gland i.e. goitre can be observed following potassium iodide administration (see section 4.8). It can subsequently lead to difficulties to breath or to swallow by pressure on adjacent tissues.
- Potassium iodide must be administered with caution in persons with thyroid disorders as they have higher risk of developing thyroid related side effects (e.g. hyperthyroidism) especially with repeated administration. Patients should continue their thyroid therapy and regularly undergo medical examinations and biological tests at short intervals.
- The administration of iodine interferes with radioiodine therapy and thyroid diagnostics.
- In the presence of known or suspected thyroid cancer, iodine should generally not be administered.

Paediatric population
- The risk of thyroid carcinoma after exposure to radiations is higher in younger children at the time of exposure. As their thyroid gland is still growing, new-borns and children are more susceptible to the dangerous effects of radioactive iodide than adults and should be treated with potassium iodide in priority.
- Hypothyroidism can be observed following potassium iodide administration (see section 4.8). As transient hypothyroidism during brain development in this early period can result in a decrease in intellectual abilities, neonates (birth to 1 month of age) given potassium iodide should be monitored for the potential development of hypothyroidism by measuring thyrotropin (thyroid-stimulating hormone, TSH) and, if indicated, free thyroxine (free T4) and thyroid replacement therapy should be instituted if hypothyroidism occurs . In addition, repeated administration of potassium iodide should be avoided in neonates to minimize the risk of hypothyroidism during a period of critical brain development.
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Lactose
- Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

The risk of interactions is low when the medicinal product is used in accordance with the recommended posology.

+ Angiotensin-converting enzyme (ACE) inhibitors

Use of ACE inhibitors with potassium iodide may result in hyperkaliaemia and cardiac arrhythmias or cardiac arrest; serum potassium concentrations should be monitored to avoid potassium toxicity.

+ Potassium-sparing diuretics (such as amiloride, triamterene or aldosterone antagonists)

Use of potassium-sparing diuretics with potassium iodide may result in hyperkaliaemia and cardiac arrhythmias or cardiac arrest; serum potassium concentrations should be monitored to avoid potassium toxicity.

+ Lithium

Use of lithium with potassium iodide may potentiate the hypothyroid and goitrogenic effects of either medication; baseline thyroid status should be determined at periodic intervals to detect changes in the thyroid-pituitary response.

+ Antithyroid agents

Use of antithyroid agents with potassium iodide may potentiate the hypothyroid and goitrogenic effects of both drugs; baseline thyroid status should be determined at periodic intervals to detect changes in the thyroid-pituitary response.

+ Iodine-containing drugs

Use of iodine-containing drugs (e.g. amiodarone) increases the overall iodine dose and thus the risk of toxic side effects.

4.6 Fertility, pregnancy and lactation

Pregnancy

- No dosage adjustments are required during pregnancy.
- Pregnant women should be given potassium iodide for their own protection and for that of the foetus, as iodine (whether stable or radioactive) readily crosses the placenta.
- Potassium iodide intake during pregnancy may result in abnormal thyroid function and/or goiter in the neonate. If potassium iodide is used during pregnancy or if the patient becomes pregnant while receiving the drug, the patient should be informed of the potential risks to the foetus.
- Pregnant women should not receive repeated administration of potassium iodide.

Breast-feeding

- No dosage adjustments are required in breastfeeding women.
- Lactating females should be administered potassium iodide for their own protection and to potentially to reduce the radioiodine content of the breast milk.
- Breastfeeding women should not receive repeated administration of potassium iodide.

Fertility.

- No data is available on potassium iodide effect on fertility in human.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

The undesirable effects are listed by MedDRA System Organ Classes.
Assessment of undesirable effects is based on the following frequency groupings:
Very common: ≥1/10
Common: ≥1/100 to <1/10
Uncommon: ≥1/1,000 to <1/100
Rare: ≥1/10,000 to <1/1,000
Very rare: <1/10,000
Not known: cannot be estimated from the available data

Systeme Organ class	**Undesirable effect**	**Frequency**
Immune system disorders	Hypersensitivity reactions	Not known*

Endocrine disorders	Hyperthyroidism Goitre Hypothyroidism	Not known
Gastrointestinal disorders	Vomiting Diarrhoea Gastric pain	Common
	Metallic taste Thirst Abdominal pain Bloody diarrhoea	Not known
Skin disorders	Skin rash	Common

*Hypersensitivity reactions to iodides are exceptional. Those may include bronchospasm, urticaria, angioedema, cutaneous haemorrhage or purpuras, fever, arthralgia, lymphadenopathy, and eosinophilia.

Paediatric population
Endocrine disorders: a transient increase in serum TSH and decreased free serum thyroxine has been observed in 0.37% of newborns who received potassium iodide prophylaxis on the second day of life (uncommon).

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
Large doses of iodides may lead to a range of adverse effects, often called `iodism', some of which resemble hypersensitivity reactions, including:
- Metallic taste, increased salivation, burning or painful mouth;
- Coryza-like symptoms: swelling and inflammation of the throat and salivary glands. Eyes may be irritated and swollen and there may be increased lachrymation.
- Pulmonary oedema, dyspnoea, and bronchospasm may develop.
- Skin reactions include mild acneiform eruptions or, more rarely, severe eruptions (iododerma).

Management of overdose
In case of drug overdose, it is advised to contact the anti-poison center nearby.
Hemodialysis can be performed. The management can include as well the treatment of symptoms, activated charcoal and gastric lavage as per the doctor’s decision.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: ANTIDOTES. ATC code: V03AB21.

Mechanism of action
In the event of a nuclear accident, a large amount of radioactive iodine may be released in the environment. Because of its high volatility, it can be easily inhaled and resorbed by the lungs. The radioactive iodine is found in large quantities in the thyroid gland, which become exposed to very strong local radiations. This is the origin of the occurrence of thyroid lesions that may induce late disorders such as thyroid cancer.

Radioactive iodine uptake by the thyroid can be effectively blocked by a single, high and timely appropriate dose administration of potassium iodide. An adequate dose of potassium iodide (as recommended by the local health authority), administered less than 24 hours before the expected exposure and up to 2 hours after the exposure, results in an almost complete saturation of the thyroid, blocking radioactive iodine entering the thyroid gland for the next 24 hours.

5.2 Pharmacokinetic properties

Absorption
Potassium iodide administered orally is rapidly absorbed by the gastrointestinal tract.
Absorption is complete within 2 hours after administration.
The food causes an absorption delay of 10-15 minutes.

Distribution
After absorption, iodide enters the systemic circulation and is exchanged rapidly between erythrocytes and extracellular fluid.
Then, iodide follows two main and competitive routes of distribution: absorption by the thyroid gland or renal excretion. Iodide is also distributed in a minor way in tissues other than the thyroid.

Thyroid
Thyroid uptake begins rapidly and then in euthyroid patients reaches a plateau of 10% to 40% of the dose in 24 to 48 hours. The time required to reach half of total thyroid absorption ranges from 3 to 6.5 hours with significant interindividual variation.
Thyroid clearance depends on the volume and activity of the gland. It is adaptive and depends on plasma concentration and dietary intake. As a result, when dietary iodine intake is low, thyroid uptake increases. Thyroid absorption also depends on the physiological age; it is higher in adolescents than in adults and decreases gradually with age.

Extrathyroidal tissues
In addition to the thyroid gland, active iodine transport also occurs in extrathyroidal tissues such as salivary glands, gastric mucosa, choroid plexus and in the mammary glands during lactation, but to a lesser extent.
Iodine also crosses the placental barrier and is absorbed by the fetal thyroid, which begins to concentrate iodine and synthesize thyroid hormones after 12 weeks of pregnancy.

Biotransformation
In the thyroid, iodide is incorporated and oxidized to iodine and then bound to thyroglobulin (organification).
Thyroid hormones thyroxine (T4) and triiodothyronine (T3) are then synthesized by oxidative condensation of iodinated intermediates (monoiodotyrosine (MIT) and diiodotyrosine (DIT)).

Elimination
Iodide is eliminated mainly by the kidneys (> 95%) by rapid filtration and partial reabsorption, with a clearance of 30 to 36 mL / min. The half-life of iodide in the systemic circulation is about 6 hours.
The renal elimination rate is not influenced by iodine intake or serum iodine levels.
Only small amounts of iodide are excreted in the faeces (about 1%), saliva and sweat.
In breastfeeding women, there is an increased elimination of iodide, which is excreted in large amounts in breast milk, which gradually decreases during the first 6 months of lactation.

5.3 Preclinical safety data

Effects in non-clinical acute and repeated oral dose toxicity, carcinogenotoxicity, and reproductive and developmental studies were observed, but only at exposures considered sufficiently in excess of the maximum human dosage, indicating little relevance to clinical use for this single dose therapy.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Microcrystalline cellulose
Magnesium stearate (E 572)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

10 years.
During storage, the tablets may become off-white. This discolouration will not affect the efficiency of prevention.

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage conditions.
Store in the original package in order to protect from light.

6.5 Nature and content of container

Blister (OPA/Al/PVC/Al) containing 10 tablets each.
Pack sizes: 10 and 20 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

8 MARKETING AUTHORISATION NUMBER

<[To be completed nationally]>

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<Date of first authorisation: {DD month YYYY}>
<Date of latest renewal: {DD month YYYY}>

10 DATE OF REVISION OF THE TEXT

2023-06-30