## 1. NAME OF THE MEDICINAL PRODUCT

Fluoresceine SERB

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Fluorescein sodium 10g/100 ml of solution for injection

One 5 mL ampoule contains 0.5g of fluorescein sodium

One 5 mL ampoule contains 5.58 mg of sodium

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Solution for injection

## 4. CLINICAL PARTICULARS

### 4.1. Therapeutic indications

For examination of the retina by fluorescent angiography.

### 4.2. Posology and method of administration

**Posology**

One 5-ml ampoule (10%) injected intravenously

**Patients with renal insufficiency**

The limited experience with use of Fluorescein sodium in patients with renal insufficiency suggests that dose adjustment is not necessary in these patients (see section 5.2)

**Patients with hepatic insufficiency**

No studies have been performed in patients with hepatic insufficiency

**Paediatric population**

The safety of Fluorescein SERB in children has not been established.

**Geriatrics (65 years old and over)**

There is no indication that dosage needs to be modified for the elderly.

**Method of administration**

Intravenous use

### 4.3. Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Use by intrathecal or intra-arterial routes.

### 4.4. Special warnings and precautions for use

**Special warnings**

**Hypersensitivity**

Fluorescein sodium may induce severe hypersensitivity reactions.

The benefit of Fluorescein angiography must be carefully weighed against the risk of severe hypersensitivity reactions (sometimes with a fatal outcome).

A detailed medical history of each patient must be carried out before examination including any history of allergy, history of cardiopulmonary disease, diabetes mellitus or concomitant treatments (in particular beta-blocking drugs, including eye drops solutions). Beta-blocking agents can reduce the vascular compensation reactions to anaphylactic shock and reduce the effectiveness of adrenaline in the case of cardiovascular collapse.

These hypersensitivity reactions are always unforeseeable, but they occur more frequently in patients who have poorly tolerated a previous injection of fluorescein sodium (other than by nausea and vomiting) and in patients who have displayed a history of allergy such as food-induced or drug-induced urticaria, asthma, eczema or allergic rhinitis. These hypersensitivity reactions may not be detected by carrying out a specific intradermal skin allergy fluorescein test, whose results are unreliable and sometimes possibly dangerous. A specialised allergy consultation may provide a more precise diagnosis.

Premedication is proposed. However, it does not prevent the occurrence of severe accidents:

- premedication mainly includes H1 antihistamines administered orally, followed by corticosteroids before fluorescein injection
- it is not currently considered necessary to administer the premedication to all patients given the low percentage of accidents

The risk of hypersensitivity reactions to fluorescein sodium means that throughout the examination:

- fluorescein angiography must be performed only in facilities with staff trained in emergency resuscitation with the appropriate materials and equipment,
- close patient monitoring must be ensured by the ophthalmologist carrying out the examination throughout the duration of the examination and for at least 30 minutes following completion of the examination,
- the venous infusion line must be maintained for at least 5 minutes in order to treat any potential accident without delay,
- the materials required for emergency resuscitation must be available. This involves inserting a second intravenous line to enable vascular filling (polyionic solution or colloidal plasma substitute) and the intravenous injection of adrenaline at an appropriate dose.

**Extravasation:**

Due to the alkaline pH of the solution, care must be taken not to inject the fluorescein solution outside the vein. It is important to make sure that the needle is inserted properly into the vein before beginning to inject the fluorescein. If the product passes into the surrounding tissues (extravasation), the injection must be stopped immediately.

**This medicinal product contains 58.5 mg of sodium per ampoule, equivalent to 2.93% of the maximum daily amount recommended by the WHO which is 2 g of sodium per adult.**

## 4.5 Interaction with other medicinal products and other forms of interaction

- Solutions for injection with an acid pH (in particular antihistamines) may induce precipitation of fluorescein due of their alkaline pH. For this reason they are contraindication for use via the same intravenous line (see section 6.1). It is recommended that concomitant use of Fluorescein sodium with other solutions be avoided. Physico-chemical incompatibility cannot be ruled out.
- Analytical interferences with blood parameters (particularly serum digoxin and serum cortisol levels) and urinary parameters are possible 3 to 4 days due to the fluorescence. Caution should be used when interpreting serum concentrations for drugs with narrow therapeutic range (e.g. quinidine, digoxin).

## 4.6. Fertility, pregnancy and lactation

**Pregnancy**

Animal studies do not indicate any direct or indirect harmful effect with reproductive (see section 5.3). There are no data on the use of Fluorescein sodium in pregnant women. As precautionary measure, it is preferable to avoid the use of Fluorescein sodium during pregnancy.

**Breast-feeding**

Fluorescein sodium is excreted in breast milk. The effect of fluorescein sodium on infants/newborns is unknown.

Breast-feeding should be discontinued for 7 days after treatment with fluorescein sodium.

**Fertility**

No studies have been performed to evaluate the effects on fertility of intravenously-administered fluorescein.

## 4.7. Effects on ability to drive and use machines

Due to the mydriasis induced by the angiography examination, patients should not drive or use machines while still experiencing visual disorders (glare, blurred vision).

## 4.8. Undesirable effects

Minor intolerance reactions can occur. They can be isolated or associated with others. Transient nausea and vomiting are commonly reported (>1 % and <10 %). Uncommon adverse reaction (>0.1% and <1%) include feeling of malaise and skin reactions such as pruritus, rash, urticaria. More severe adverse reactions can follow these minor signs or occur directly after the injection: rarely (>1/10,000 and<1/1,000) angioedema, hypotension, respiratory symptoms (bronchospasm, laryngeal oedema, respiratory distress) and very rarely (<1/10,000) anaphylactic shock that can lead to cardiovascular collapse, heart failure or even death.

**Immune system disorders**

Hypersensitivity reactions (liable to be accompanied by hypoaesthesia and dysgeusia), potentially fatal anaphylactic or anaphylactoid shock

**Nervous system disorders**

Loss of consciousness, convulsions, stroke, headache, dizziness, paraesthesia

**Cardiac disorders**

Cardiac arrest, acute myocardial infarction, bradycardia, tachycardia

**Vascular disorders**

Shock, thrombophlebitis, hypotension, hypertension, pallor, hot flush

**Respiratory, thoracic and mediastinal disorders**

Respiratory arrest, pulmonary oedema, asthma, dyspnoea, laryngeal oedema, cough, feeling of throat tightness, throat irritation, sneezing

**Gastrointestinal disorders**

Nausea, vomiting, abdominal pain

**Skin and subcutaneous tissue disorders**

Erythema, pruritus, urticaria, dermatitis, sweating, chills, temporary yellow coloring of the skin and conjunctiva which disappear within 6 to 12 hours after administration

**Renal and urinary disorders**

Light-yellow urine occurring 24 to 36 hours after administration

**General disorders and administration site conditions**

Injection site thrombophlebitis, extravasation of the solution which can involve intense pain and can be followed by tissue necrosis (see section 4.4), thoracic pain, oedema, malaise, asthenia.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form */https://sideeffects.health.gov.il*

### 4.9. Overdose

Not applicable.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1. Pharmacodynamic properties

Pharmacotherapeutic group: **DIAGNOSTIC AGENTS, COLOURING AGENTS;** ATC code: **S01JA01**.

Fluorescein exposed to blue light (465-490 nm) exhibits yellow-green fluorescence (520-530 nm). This fluorescence allows the detection of pathological changes in the retinal circulation.

### 5.2. Pharmacokinetic properties

**Distribution**

After intravenous injection, fluorescein is quickly distributed and appears in the retinal tissue within few seconds.

50 to 84% of fluorescein is bound to plasmatic proteins (mainly to albumin) and 15 to 17% to erythrocytes.

**Biotransformation**

After intravenous administration, fluorescein is quickly transformed into fluorescein glucuronide which also has fluorescent properties.

**Elimination**

Plasma elimination half-lives of fluorescein and fluorescein glucuronide are about 23.5 and 264 minutes.

After 4 to 5 hours, almost all plasma fluorescence is due to fluorescein glucuronide.

Plasma pharmacokinetics of fluorescein are the same in diabetic and non-diabetic patients.

Fluorescein and its metabolites are eliminated in bile and urine.

90% of elimination occurs within 48 hours.

Fluorescein is detectable in urine within 24 to 36 hours.

### 5.3. Preclinical safety data

In vitro and in vivo genotoxicity studies conducted with fluorescein sodium are negative in Ames test, in the chromosomal aberration test and in the micronucleus test in mice. In the mouse lymphoma assay, sister chromatid exchange test in vitro for CHO cells and in vivo for mouse bone-marrow cells are positive.

Fluorescein has not shown embryotoxic or teratogenic effects in rats and rabbits.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1. List of excipients

Sodium hydroxide, water for injection

### 6.2. Incompatibilities

In the absence of compatibility studies, this product must not be mixed with other medicinal products.

Solutions for injections with an acid pH (in particular antihistamines) can induce fluorescein precipitation and should not be injected simultaneously in the same intravenous line.

## 6.3. Shelf life

The expiry date of the product is indicated on the packaging materials.

## 6.4. Special precautions for storage

Store below 30ºC

## 6.5. Nature and contents of container

5 ml ampoule (colorless type I glass)

## 6.6. Special precautions for disposal and other handling

Check visually if there is any visible particulate matter or discoloration.

In the syringe, do not mix or dilute the solution with other solutions for medicinal products.

The venous infusion line must be rinsed before and after the injection in order to avoid incompatibility reactions.

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

## 7. MANUFACTURER

**SERB SAS**
40 AVENUE GEORGE V
75008 PARIS
FRANCE

## 8. MARKETING AUTHORISATION HOLDER

**Tradis Gat Ltd.**
32 Shacham St.
Petach Tikva.

## 9. MARKETING AUTHORISATION NUMBER(S)

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*Revised on November 2020*