FLUORESCITE™

SCHEDULING STATUS:
S3

PROPRIETARY NAME
(and dosage form):

FLUORESCITE™
(fluorescein injection, USP) 10%

COMPOSITION:
FLUORESCITE™ (fluorescein injection, USP) 10% contains 500 mg fluorescein per 5 mL in a sterile, unpreserved, pyrogen free, buffered unit dose aqueous solution that has a pH of 8.0 - 9.8 and an osmolality of 572-858 mOsm/kg. Excipients: Sodium hydroxide and/or hydrochloric acid (for pH adjustment) and water for injection.

PHARMACOLOGICAL CLASSIFICATION:
A28 Contrast media
ATC Code: S01JA01

PHARMACOLOGICAL ACTION
Mechanism of Action
Fluorescein sodium responds to electromagnetic radiation or light between the wavelengths of 465-490 nm and fluoresces, i.e., emits light at wavelengths of 520-530 nm. Thus, the hydrocarbon is excited by blue light and emits light that appears yellowish-green.

Distribution:
Within a few minutes of IV administration of fluorescein sodium, a yellowish discoloration of the skin occurs, which begins to fade after 6 to 12 hours of dosing.

INDICATIONS
FLUORESCITE™ Injection 10% is indicated in diagnostic fluorescein angiography or angioscopy of the retina and iris vasculature.

CONTRA-INDICATIONS
FLUORESCITE™ Injection 10% is contraindicated in patients with known hypersensitivity to fluorescein sodium or any other ingredients in this product.

NOT FOR INTRatheCAL OR INTRA-ARTERIAL USE

FOR OPHTHALMIC DIAGNOSTIC USE ONLY.

WARNINGS
Special Warnings and Precautions for Use
Fluorescein sodium can induce serious intolerance reactions. These reactions of intolerance are always unpredictable but they are more frequent in patients who have previously experienced an adverse reaction after fluorescein injection (symptoms other than nausea and vomiting) or in patients with history of allergy, such as food or drug induced urticaria, asthma, eczema, allergic rhinitis.
The benefit to risk of the angiography procedure should be considered in elderly patients with pre-existing conditions such as cardiovascular disease, diabetes mellitus and multiple concomitant drug therapies.
Detailed questioning of each patient must be carried out before the angiography to evaluate any prior history of cardiopulmonary disease or allergy or concomitant medications.
In the event of serious intolerance reactions during a first angiography, the benefit of an additional fluorescein angiography should be balanced with the risk of severe hypersensitivity reactions (with fatal outcome in some cases).

The risk of hypersensitivity reactions with fluorescein sodium requires:

- Close monitoring of the patient by the ophthalmologist performing the examination, throughout the examination and for at least 30 minutes thereafter;
- Maintaining the infusion line for at least 5 minutes, to treat a possible severe adverse reaction without delay;
- To have at one’s disposal appropriate material for emergency resuscitation which is based first on the installation of a 2nd intravenous line, allowing the restoration of the plasma volume (aqueous solution polyionic or colloidal substitute of plasma) and the intravenous injection of adrenaline at the recommended dosage (see section “INTERACTIONS”).

This medicinal product contains up to 3.15 mmol (72.45 mg) sodium per dose. This should be taken into consideration by patients on a controlled sodium diet.

Care must be taken to avoid extravasation during injection as the high pH of fluorescein solution can result in severe local tissue damage. The following complications resulting from extravasation of fluorescein have been noted to occur: Sloughing of the skin, superficial phlebitis, subcutaneous granuloma, and toxic neuritis along the median curve in the antecubital area. Complications resulting from extravasation can cause severe pain in the arm for up to several hours. When significant extravasation occurs, the injection should be discontinued and conservative measures to treat damaged tissue and to relieve pain should be implemented. Do not mix or dilute with other solutions or drugs. Flush intravenous cannulas before and after drugs are injected to avoid physical incompatibility reactions.

Rare cases of death due to anaphylaxis have been reported (See precautions).

Precautions

General
Caution is to be exercised in patients with a history of allergy or bronchial asthma. An emergency tray including such items as 0.1% epinephrine for intravenous or intramuscular use; an antihistamine, soluble steroid and aminophylline for IV use; and oxygen should always be available in the event of possible reaction to FLUORESCITE™ Injection 10%. Use only if the container is undamaged.

Information for Patients
Skin will attain a temporary yellowish discoloration. Urine attains a bright yellow colour. Discoloration of the skin fades in 6 to 12 hours and fades in urine in 24 to 36 hours.

Laboratory Information
If a potential allergy is suspected, an intradermal skin test may be performed prior to intravenous administration, i.e., 0.05 mL injected intradermally to be evaluated 30 to 60 minutes following injection. Given the sensitivity and specificity of skin testing, a negative skin test is not proof that a patient is not allergic to fluorescein.

Effects on Ability to Drive and Use Machines
The patient must be made aware that after application and until visual acuity returns to normal, driving a vehicle or operating dangerous machinery is not recommended.

INTERACTIONS
Fluorescein is a relatively inert dye and specific drug interaction studies have not been reported. There are few case reports on potential interactions with organic anion transporters and interference with certain laboratory tests. Compounds that inhibit or compete with the active transport of organic anions (e.g., probenicid) may affect the systemic profile of fluorescein.

The concomitant use of Fluorescite 100 mg/mL solution for injection with beta-blocking agents (including eye-drop solutions) may rarely provoke severe anaphylactic reactions. Beta-blocking agents could reduce the vascular compensation reactions to anaphylactic shock and also reduce the effectiveness of adrenaline in the presence of cardiovascular collapse. Concomitant intravenous injection of other solutions or the mixing of Fluorescite 100 mg/mL solution for injection with other solutions should be avoided as the possibility of interactions cannot be excluded.

PREGNANCY AND LACTATION

Pregnancy
Teratogenic Effects: Pregnancy Category C
There is insufficient data available concerning the use of Fluorescite 100 mg/mL solution for injection during pregnancy. Animal studies do not indicate teratogenic effects. However, due to limited experience, caution should be exercised when considering the use of Fluorescite 100 mg/mL solution for injection during pregnancy.

Lactation
Fluorescein sodium is excreted in human milk for up to 4 days. Following fluorescein angiography, breast-feeding should therefore be discontinued for at least 4 days and the milk should be pumped off and discarded during this period.
**DOSAGE AND DIRECTIONS FOR USE**

The normal adult dose of FLUORESCITE™ Injection 10% is 500 mg (100 mg/mL) via intravenous administration. For children, the dose should be calculated on the basis of 7.7 mg/kg body weight. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. Do not mix or dilute with other solutions or drugs. Flush intravenous cannulas before and after drugs are injected to avoid physical incompatibility reactions. Inject the dose rapidly (1 mL per second is normally recommended) into the antecubital vein, after taking precautions to avoid extravasation. A syringe, filled with FLUORESCITE™, is attached to transparent tubing and a 23 gauge butterfly needle for injection. Insert the needle and draw the patient’s blood to the hub of the syringe so that a small air bubble separates the patient’s blood in the tubing from the fluorescein. With the room lights on, slowly inject the blood back into the vein while watching the skin over the needle tip. If the needle has extravasated, the patient’s blood will be seen to bulge the skin and the injection should be stopped before any fluorescein is injected. When assured that extravasation has not occurred, the room light may be turned off and the fluorescein injection completed. Luminescence appears in the retina and choroidal vessels in 7 to 14 seconds and can be observed by standard viewing equipment.

**Paediatric Use**

Since children possess a small blood volume, the fluorescein dose is adjusted by body weight. To ensure a similar concentration of the dye in blood vessels as in adults, the recommended dose is 7.7 mg/kg body weight.

**Geriatric Use**

No overall differences in safety or effectiveness have been observed between elderly and other adult patients.

**SIDE EFFECTS AND SPECIAL PRECAUTIONS**

**Adverse Reactions (see Warnings and Precautions)**

Nausea, vomiting, gastrointestinal distress, headache, syncope, hypotension and symptoms and signs of hypersensitivity have occurred. Cardiac arrest, basilar artery ischemia, severe shock, convulsions, thrombophlebitis at the injection site and rare cases of death have been reported. Extravasation of the solution at the injection site causes intense pain at the site and a dull aching pain in the injected arm (see “WARNINGS”). Generalized hives and itching, bronchospasm and anaphylaxis have been reported. A strong taste may develop after injection.

The most frequently reported treatment related undesirable effects were nausea, vomiting, syncope and pruritus. Less frequent but more severe adverse reactions have been reported shortly after fluorescein injection such as respiratory disorders (bronchospasm, laryngeal oedema), anaphylactic shock, hypotension, loss of consciousness, convulsion, respiratory and cardiac arrest.

Additionally a yellowish discoloration of the skin could appear but usually disappears within 6 to 12 hours. Urine, which may also exhibit a bright yellow coloration, returns to its normal color after 24 to 36 hours. The following adverse reactions are classified according to the following convention: 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), or not known (cannot be estimated from the available data). Within each frequency-grouping, adverse reactions are presented in decreasing order of seriousness:

<table>
<thead>
<tr>
<th>System Organ Classification</th>
<th>MedDRA Term (v. 12.0)</th>
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</thead>
<tbody>
<tr>
<td>Immune system disorders</td>
<td>Uncommon: hypersensitivity</td>
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<tr>
<td></td>
<td>Rare: anaphylactic reaction</td>
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<tr>
<td></td>
<td>Very Rare: anaphylactic shock</td>
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<tr>
<td>Nervous system disorders</td>
<td>Common: syncope</td>
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<tr>
<td></td>
<td>Uncommon: dysphasia, paraesthesia, dizziness, headache</td>
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<tr>
<td></td>
<td>Very Rare: convulsion</td>
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<tr>
<td></td>
<td>Not Known: vertebrobasilar insufficiency, loss of consciousness, tremor, hypoaesthesia, dysgeusia</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td>Rare: cardiac arrest</td>
</tr>
<tr>
<td></td>
<td>Very Rare: angina pectoris, bradycardia, tachycardia</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td>Uncommon: thrombophlebitis</td>
</tr>
<tr>
<td></td>
<td>Rare: hypotension, shock</td>
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<tr>
<td></td>
<td>Very Rare: hypertension, vasospasm, vasodilatation, pallor, hot flush</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>Uncommon: cough, throat tightness</td>
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<tr>
<td></td>
<td>Rare: bronchospasm</td>
</tr>
<tr>
<td></td>
<td>Very Rare: respiratory arrest, pulmonary oedema, asthma, laryngeal oedema, dyspnoea, sneezing, nasal oedema</td>
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<tr>
<td>Gastrointestinal disorders</td>
<td>Very Common: nausea</td>
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<tr>
<td></td>
<td>Common: abdominal discomfort, vomiting</td>
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<tr>
<td></td>
<td>Uncommon: abdominal pain</td>
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<tr>
<td></td>
<td>Not Known: retching</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
</tr>
</tbody>
</table>
KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT
No case of overdose has been reported.

IDENTIFICATION
A sterile clear red orange solution.

PRESENTATION
Single use 5 mL glass vial with a grey chlorobutyl rubber (latex free) stopper and aluminium seal with a purple flip-off cap.

STORAGE INSTRUCTIONS
Store at 2º-25ºC
Do Not Freeze
Keep out of reach and sight of children

REGISTRATION NUMBER
A40/28/0679

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