

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

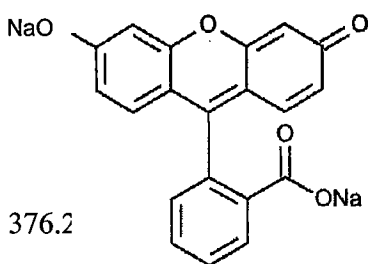
APPLICATION NUMBER:

21-980

LABELING

**FLUORESCITE® (fluorescein injection, USP) 10%****Sterile****DESCRIPTION**

FLUORESCITE® (fluorescein injection, USP) 10% contains fluorescein sodium (equivalent to fluorescein 10% w/v). It is a sterile solution for use intravenously as a diagnostic aid. Its chemical name is spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-3-one, 3'6'-dihydroxy,disodium salt. The active ingredient is represented by the chemical structure:



FLUORESCITE® (fluorescein injection, USP) 10% is supplied as a sterile, unpreserved, unit dose aqueous solution, that has a pH of 8.0 - 9.8 and an osmolality of 572-858 mOsm/kg.

Active ingredient: fluorescein sodium

Inactive Ingredients

Sodium hydroxide and/or hydrochloric acid (to adjust pH), and water for injection.

CLINICAL PHARMACOLOGY**Mechanism of Action**

Fluorescein sodium responds to electromagnetic radiation and 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. Following intravenous injection of fluorescein sodium in an aqueous solution, the unbound fraction of the fluorescein can be excited with a blue light flash from a fundus camera as it circulates through the ocular vasculature, and the yellowish green fluorescence of the dye is captured by the camera. In the fundus, the fluorescence of the dye demarcates the retinal and/or choroidal vasculature under observation, distinguishing it from adjacent areas/structures.

Pharmacokinetics**Distribution:**

Within 7 to 14 seconds after IV administration into antecubital vein, fluorescein usually appears in the central artery of the eye. 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. Various estimates of volume of distribution indicate that fluorescein distributes well into interstitial space (0.5 L/kg).

Metabolism:

Fluorescein undergoes rapid metabolism to fluorescein monoglucuronide. After IV administration of

fluorescein sodium (14 mg/kg) to 7 healthy subjects, approximately 80% of fluorescein in plasma was converted to glucuronide conjugate after a period of 1 hour post dose, indicating relatively rapid conjugation.

Excretion:

Fluorescein and its metabolites are mainly eliminated via renal excretion. After IV administration, the urine remains slightly fluorescent for 24 to 36 hours. A renal clearance of 1.75 mL/min/kg and a hepatic clearance (due to conjugation) of 1.50 mL/min/kg have been estimated. The systemic clearance of fluorescein was essentially complete by 48 to 72 hours after administration of 500 mg fluorescein.

INDICATIONS AND USAGE:

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

CONTRAINDICATIONS

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

WARNINGS

FOR INTRAVENOUS USE

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. 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 should 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 color. Discoloration of the skin usually fades in 6 to 12 hours and usually 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.

Carcinogenesis, Mutagenesis, Impairment of Fertility

There have been no long-term studies done using fluorescein in animals to evaluate carcinogenic

potential.

Pregnancy

Teratogenic Effects: Pregnancy Category C

Adequate animal reproduction studies have not been conducted with fluorescein sodium. It is also not known whether fluorescein sodium can cause fetal harm when administered to a pregnant woman. Fluorescein sodium should be given to a pregnant woman only if clearly needed.

Nursing Mothers

Fluorescein sodium has been demonstrated to be excreted in human milk. Caution should be exercised when fluorescein sodium is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in pediatric patients have been established.

Geriatric Use

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

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.

DOSAGE AND ADMINISTRATION

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 35 mg for each ten pounds of body weight (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®, may be 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 usually appears in the retina and choroidal vessels in 7 to 14 seconds and can be observed by standard viewing equipment.

Reduction in dose from 5 ml to 2 ml of FLUORESCITE Injection 10% may be appropriate in cases when a highly sensitive imaging system e.g., scanning laser ophthalmoscope is used.

HOW SUPPLIED

FLUORESCITE® (fluorescein injection, USP) 10% is supplied in a single use 5 mL glass vial with a gray FluroTec coated chlorobutyl (latex free) stopper and purple flip-off aluminum seal. It contains a sterile, red-orange solution of fluorescein sodium.

NDC 0065-0092-05

Storage

Store at 2°- 25°C (36°- 77°F).

Do Not Freeze

RX Only

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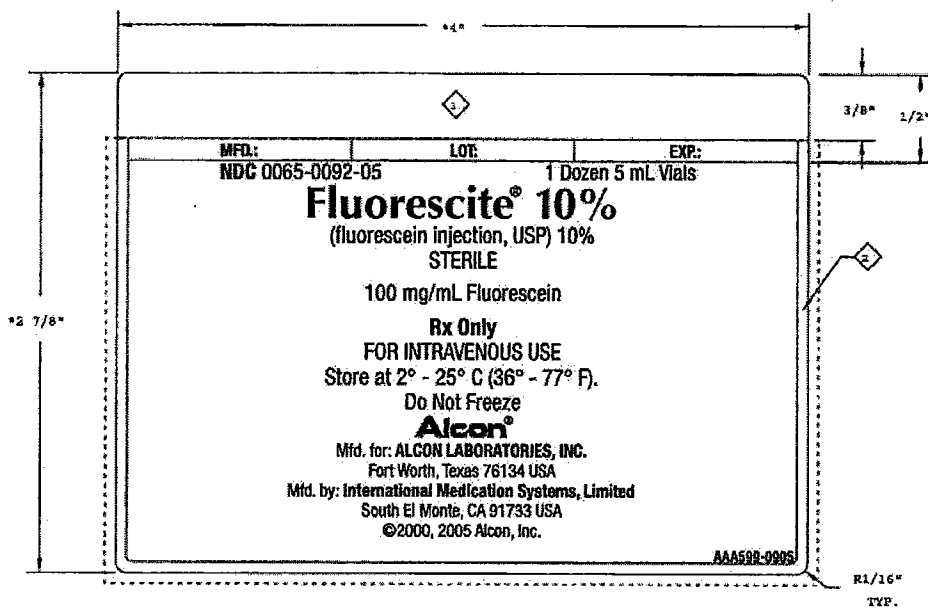
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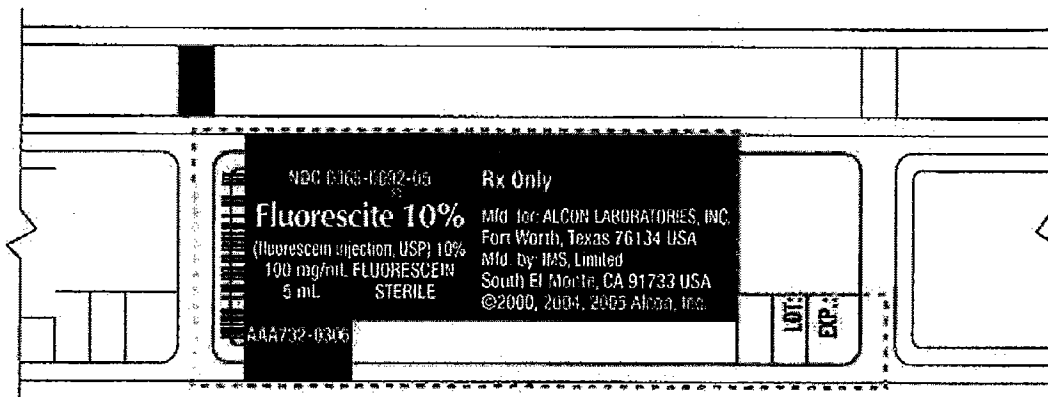
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Carton Labeling



Container Labeling



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