RETINOFLUOR™ INJECTION
(FLUORESCEIN SODIUM)

1 NAME OF THE MEDICINE

Fluorescein sodium

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Fluorescein sodium 10% injection contains 100 mg in 1 mL (available in 5 and 10 mL vials) and fluorescein sodium 25% injection contains 250 mg in 1 mL (5 mL vials) in water for injection.

For the full list of excipients, see Section 6.1 List of Excipients.

3 PHARMACEUTICAL FORM

Retinofluor is an orange/red sterile solution for intravenous administration.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Diagnostic: Intravenous injection of fluorescein sodium dye followed by multiframe photography (angiography) or ophthalmoscopic evaluation (angioscopy). It is used in evaluation of a wide range of retinal and choroidal diseases. It is less commonly used to evaluate abnormalities of the optic nerve and iris. It may be used in diagnosis and management of macular and vascular (including diabetic) diseases.

4.2 DOSE AND METHOD OF ADMINISTRATION

Product is for single use in one patient only. Discard any residue.

After taking precautions to avoid extravasation (e.g. checking with the lights on) 10% or 25% fluorescein sodium injection is rapidly injected in the antecubital vein and then the room lights turned off.

A recommended dose is 500 mg but this dose may be varied depending on the patient and the camera used in the diagnostic procedure and the individual experience of the operator. It is recommended that the dose be kept as low as possible.

About ten minutes after the injection, very little of the fluorescein sodium dye remains in the eye. The retina and choroidal vessels are stained within 15 seconds and the optic disc will normally fluoresce for several hours after injection.

4.3 CONTRAINDICATIONS

Sensitivity to fluorescein sodium or any components in the injection. Concomitant use of contact lenses.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

General

Fluorescein sodium contains no iodine. A yellowish discolouration of the skin and conjunctiva may occur. This usually subsides after several hours. This product is only to be used intravenously in ophthalmic diagnostic procedures. Do not mix or dilute with any other solutions or medicines. If a catheter is used, flush pre and post use to avoid any drug incompatibility reactions. Don't use if container or closure is damaged in any way.

Extravasation at the injection site

There is a possibility of extravasation at the injection site. This may cause discomfort, severe pain, subcutaneous granuloma, phlebitis, necrosis of the skin and/or neuritis. Therefore, care must be taken to avoid extravasation. If extravasation occurs, cease injection and take corrective action to minimise tissue damage and control pain.

Cardiovascular disease

Patients with a history of cardiovascular disease require careful evaluation before undergoing an elective procedure with fluorescein sodium. Rarely, severe cardiovascular complications such as chest pain, myocardial infarction and death have occurred following administration of fluorescein sodium. Yannuzzi (1986) reports an incidence of 1 in 5,300 for these complications. In such cases there is often a history of cardiovascular disease (Karhunen 1986). It is, therefore, advisable that patients with a history of cardiovascular disease be carefully evaluated before receiving fluorescein sodium injection.

Anaphylaxis

Fluorescein sodium injection, may, rarely, cause life-threatening or fatal anaphylaxis. A protocol for management of anaphylaxis, and appropriate resuscitation equipment such as adrenaline for intravenous or intramuscular use, intravenous fluids and oxygen must always be available in case of such a reaction.

Diabetes mellitus

In some cases in patients with non-insulin dependent diabetes mellitus there has been an increase in whole blood viscosity, erythrocyte elongation index, blood pH, carboxyhaemoglobin and methaemoglobin levels and a sudden reduction of red cell acetylcholinesterase activity. These findings suggest that fluorescein interferes with the red cell membrane and with microcirculatory blood flow. The clinical relevance of these findings is uncertain.

Bronchial asthmatic patients and patients with any history of allergy

Bronchial asthmatic patients and patients with any history of allergy must be treated with special caution. This may involve treatment with antihistamines and steroids, respectively. Acute pulmonary oedema has been reported in 2 patients following administration of fluorescein sodium.

Patient aftercare

Patients should be escorted by a responsible adult from the testing site.

Special instructions

Patients should expect temporary decrease in vision and red-after image secondary to flash photography.

The skin and urine may be coloured yellow but this is transient. Fluorescein sodium can stain skin, clothing and soft contact lenses on contact. Intraocular fluorescein can produce transient blurring of vision.

Use in the elderly

No data available.

Paediatric use

Safety and effectiveness in children has not been established.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No data available.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

There have been no long-term studies using fluorescein sodium in animals to evaluate impairment of fertility.

Use in pregnancy

Australian Pregnancy Category B3

Neither human nor animal reproduction studies have been done with fluorescein sodium. It is also not known whether fluorescein sodium can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity. Fluorescein sodium should therefore not be given to a pregnant woman.

Use in lactation

Fluorescein sodium has been shown to be present in breast milk in lactating women. It is therefore not advisable to administer to a nursing woman.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

A summary of treatment of emergent adverse effects and their estimate of frequencies (common, rare, very rare) in accordance with preferred term and system organ classes (SOC) of any severity are listed below*. All of these events and their frequencies are extracted from the uncontrolled studies of fluorescein safety.

Cardiovascular

Common: Hypotension.
Uncommon: Syncope.
Rare: Arterial ischaemia basilar, cardiac arrest, shock (severe).

Dermatologic

Uncommon: Injection site thrombophlebitis. Skin eruptions, urticaria, and pruritus occur in about 1% of patients.

Gastrointestinal

Common: Drug induced gastrointestinal disturbance, nausea, vomiting.

Immunologic

Common: Generalised pruritus, hives, generalised hypersensitivity reaction.
Rare: Anaphylaxis.

Neurologic

Common: Headache.
Rare: Seizure.

Respiratory

Uncommon: Bronchospasm, dyspnea and breathlessness.

**The CIOMS (Council for International Organisation of Medical Sciences) III standard categories are used for classification of frequencies:*

Very common:	10% or more
Common: (frequent)	1 to < 10%
Uncommon: (infrequent)	0.1 to < 1%
Rare:	0.01 to < 0.1%
Very rare:	0.01% or less

Other adverse effects reported in the literature include: vasovagal reaction with or without collapse; dyspnoea; convulsions; intense lower back pain; local complications such as paraesthesia, pain, thrombophlebitis and inadvertent intra-arterial injection; paraesthesia of tongue and lips; abdominal cramping; excessive sneezing and more serious reactions referred to under Section 4.4 Special Warnings and Precautions for Use.

Severe reactions (0.1 to 0.2%) such as anaphylactic reaction or respiratory and cardiac arrest (requiring medical treatment see under Section 4.4 Special Warnings and Precautions for Use), severe shock and rare cases of death have been reported. Fluorescein sodium dye will turn a patient's urine orange for a brief period. Extravasation (see under Section 4.4 Special Warnings and Precautions for Use) can lead to severe pain at the injection site. Paraesthesia has occurred after administration of intravenous fluorescein sodium.

594,687 angiographic procedures reported in the literature indicated that the incidence of serious reactions was 1 in 18,020 and 1 in 49,557 fatal reactions. Reactions included anaphylactic shock, cardiac arrest, myocardial infarction and shock with hypotension or respiratory distress.

A USA survey of 221,781 fluorescein angiograms reported frequency rates of 1 in 63 for a moderate reaction (urticaria, syncope, thrombophlebitis, pyrexia, tissue necrosis, or nerve palsy) and 1 in 1,900 for severe reactions (respiratory or cardiac events or tonic-clonic seizures); there was one death.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at http://www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Fluorescein sodium has a green-yellow fluorescence which may be used to highlight the vascular perfusion and its abnormalities.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

No data available.

Distribution

No data available.

Metabolism

No data available.

Excretion

No data available.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

There have been no long-term studies using fluorescein sodium in animals to evaluate mutagenicity.

Carcinogenicity

There have been no long-term studies using fluorescein sodium in animals to evaluate carcinogenic potential.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Retinofluor contains water for injection, with the pH adjusted using sodium hydroxide and/or hydrochloric acid. Contains no antimicrobial agent.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG)[1]. The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C. Protect from light.

6.5 NATURE AND CONTENTS OF CONTAINER

Retinofluor (Fluorescein Sodium Injection) is a sterile single use injection supplied in cartons of 10 rubber capped vials.

It is presented as:

Retinofluor, Fluorescein Sodium 10% - 5 mL in a 7 mL vial. Pack of 10 vials.
Phebra product code - INJ140

Retinofluor, Fluorescein Sodium 10% - 10 mL in a 10 mL vial. Pack of 10 vials.
Phebra product code - INJ028

Retinofluor, Fluorescein Sodium 25% - 5 mL in a 7 mL vial. Pack of 10 vials.
Phebra product code - INJ030

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

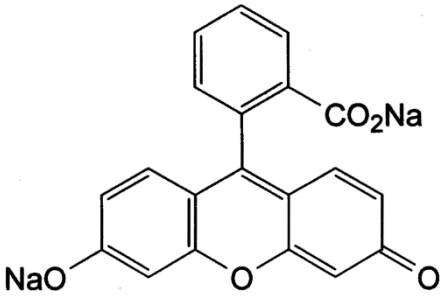
Non-proprietary name: Fluorescein Sodium 10% and Fluorescein Sodium 25% for injection.

Chemical name: Disodium 2-(6-oxido-3-oxo- 3*H*-xanthen-9-yl) benzoate.

The molecular weight of the compound is 376.3. The molecular formula is $C_{20}H_{10}Na_2O_5$.

[1] AUST R 23130; AUST R 121873; AUST R 23138

Chemical structure



CAS number

518-47-8

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule S4 - Prescription Only Medicine

8 SPONSOR

Phebra[2] Pty Ltd, 19 Orion Road, Lane Cove West, NSW 2066, Australia.
Phone 1800 720 020.

9 DATE OF FIRST APPROVAL

Jun 1999

10 DATE OF REVISION

6 May 2019

TBA SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
NA	PI reformatted to align with new form

[2] Retinofluor, Phebra and the Phi symbol are trademarks of Phebra Pty Ltd, 19 Orion Road, Lane Cove West, NSW 2066, Australia.