**NEW ZEALAND DATA SHEET**

## 1. PRODUCT NAME

FLUORESCITE™ (fluorescein) Injection 10%

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Fluorescite™ injection 10% contains 100 mg/mL fluorescein (equivalent to 113.2 mg/mL fluorescein sodium).

## 3. PHARMACEUTICAL FORM

Solution, sterile pyrogen-free injection.

Unpreserved with a pH of 8.0 to 9.8.

## 4. CLINICAL PARTICULARS

### 4.1. Therapeutic indications

Indicated in diagnostic fluorescein angiography or angioscopy of the fundus and of the iris vasculature.

### 4.2. Dose and method of administration

The usual adult dose is the contents of one Fluorescite™ injection 10% vial (5 mL of 10% solution) via intravenous administration.

For children, the dose is calculated on the basis of 8 mg/kg of body weight.

Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration. Do not mix or dilute with other solutions or drugs. Flush intravenous cannulae before and after drugs are injected to avoid physical incompatibility reactions.

Product is for single use in one patient only. Discard any residue. Contains no antimicrobial agent.

Inject the contents of the vial rapidly into the antecubital vein after taking precautions to avoid extravasation. A syringe filled with Fluorescite™ injection 10% 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 Fluorescite™ injection 10%. 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 immediately before any Fluorescite™ injection 10% is administered. When assured that extravasation has not occurred, the room light may be switched off and the Fluorescite™ injection 10% administration completed. Luminescence appears in the retina and choroidal vessels in 7 to 14 seconds and can be observed by standard viewing equipment. An emergency tray and oxygen should be present when administering this product (see 4.4. Special warnings and precautions for use).

### 4.3. Contraindications

Fluorescite™ injection 10% should not be injected intrathecally or intraarterially.

It is contraindicated in those persons who have shown hypersensitivity to fluorescein or any component of this preparation. See Section 6.1. List of excipients.

### 4.4. Special warnings and precautions for use

NOT FOR INTRATHECAL USE – FOR OPHTHALMIC DIAGNOSTIC USE ONLY.

Hypersensitivity Reactions

Fluorescein sodium can induce serious hypersensitivity and 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 or in patients with history of bronchial asthma.

Intradermal skin tests have limited predictive value for serious intolerance reactions to fluorescein. Fluorescein intolerance reactions can occur following a negative intradermal skin test.

The benefit to risk of the angiography procedure should be considered in patients with pre-existing conditions such as cardiovascular disease, diabetes mellitus, and multiple concomitant drug therapies (in particular beta blockers).

Fluorescein Angiography (FA) may cause contrast-induced Nephropathy (CIN) based on increased serum creatinine. CIN is a possible risk factor for end-stage renal disease progression.

In the event of serious hypersensitivity and 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 at 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.

−In addition, in patients identified as being at risk of hypersensitivity reactions, but in whom a fluorescein angiography is considered to be essential, it is recommended to carry out the procedure with the equipment and personnel trained in emergency resuscitation in the treatment room.

Extravasation should be avoided 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. The correct intravenous position of the needle tip must be ascertained. When extravasation occurs, the injection should immediately be discontinued and conservative measures to treat damaged tissue and relieve pain should be implemented. Do not mix or dilute Fluorescite™ injection 10% with other solutions or drugs.

Flush intravenous cannulae before and after drugs are injected to avoid physical incompatibility reactions.

Anaphylaxis

Rare cases of death due to anaphylaxis have been reported with sodium fluorescein injection (see 4.8. Undesirable effects).

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.

Cardiovascular Disease

Patients with a history of cardiovascular disease require careful evaluation before undergoing an elective procedure with sodium fluorescein. Rarely, severe cardiovascular complications such as chest pain, myocardial infarction and death have occurred following administration of sodium fluorescein.

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.

Other considerations

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.

Special instructions

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.

Paediatric use

Safety and effectiveness in children have not been established.

Use in the elderly

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

Other patient populations

*Renal Impairment*

Limited experience in renally-impaired subjects suggests that no dose adjustment is necessary in renal impaired patients.

*Hepatic Impairment*

Fluorescein undergoes hepatic metabolism to fluorescein glucuronide. Dose adjustment is not necessary in hepatic impaired patients.

## 4.5 Interactions with other medicinal products and other forms of interactions

Fluorescein is a relatively inert dye and specific drug interaction studies are not reported. There are few case reports on potential interactions with organic anion transporters and interference with certain laboratory tests. The fluorescence may interfere with the analysis of blood and urinary parameters for a period of 3 to 4 days. Caution is advised when performing therapeutic drug monitoring for drugs with a narrow therapeutic window, e.g. digoxin, quinidine. Compounds that inhibit or compete with the active transport of organic anions (e.g. Probenecid) may affect the systemic profile of fluorescein.

The concomitant use of Fluorescite™ 100 mg/mL solution for injection with beta-blocking agents (including eye-drops 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 or drugs should be avoided as the possibility of interactions cannot be excluded.

## 4.6 Fertility, pregnancy and lactation

Pregnancy

Category B2

Avoid angiography on patients who are pregnant, especially those in the first trimester. There have been no adequate and well-controlled human studies on the safety of Fluorescite™ injection 10% during pregnancy. Fluorescite™ injection 10% should be used in pregnancy only if clearly needed.

See Section 5.3. Preclinical safety studies for reproduction studies in animals.

Breast-feeding

Fluorescein has been demonstrated to be excreted in human milk for up to 7 days. Following fluorescein angiography, breast-feeding should therefore be discontinued for at least 7 days and the milk should be pumped off and discarded during this period. Because of the potential for serious reactions in breastfed infants from fluorescein, a decision should be made whether to discontinue breast-feeding or to discontinue the drug, taking into account the importance of the drug to the mother.

Fertility

No studies investigating the effect of fluorescein on fertility have been conducted.

## 4.7 Effects on ability to drive or 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.

## 4.8 Undesirable effects

The safety and diagnostic utility of Fluorescite™ injection 10% were clinically investigated in patients with various ocular pathologies requiring fluorescein angiography including macular degeneration, diabetic retinopathy, macular oedema, intraocular tumors and vascular occlusions.

A summary of treatment emergent adverse events based on 4 clinical trials with Fluorescite™ injection 10% and 25% (N=735) and their estimate of frequencies (very common, common, uncommon, rare, very rare, and not known) in accordance with preferred term and system organ classes (SOC) of any severity are listed below.

Nervous system disorders

Common (> 1% to < 10%): syncope.

Uncommon (> 0.1% to ≤ 1%): dizziness, paresthesia.

Respiratory, thoracic and mediastinal disorders

Uncommon (> 0.1% to ≤ 1%): cough, throat tightness.

Gastrointestinal disorders

Very Common (≥ 10%): nausea.

Common (> 1% to < 10%): vomiting.

Uncommon (> 0.1% to ≤ 1%): abdominal pain.

Skin and subcutaneous tissue disorders

Uncommon (> 0.1% to ≤ 1%): urticarial.

General disorders and administration site conditions

Common (> 1% to < 10%): extravasation.

Uncommon (> 0.1% to ≤ 1%): dysphasia, feeling hot, pain.

**Postmarketing Experience**

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 colouration, returns to its normal colour after 24 to 36 hours

A summary of treatment emergent adverse events based on literature and postmarketing experience and their estimate of frequencies (very common, common, uncommon, rare, very rare, and not known) in accordance with preferred term and system organ classes (SOC) of any severity are listed below.

Immune system disorders

Uncommon (> 0.1% to ≤ 1%): hypersensitivity.

Rare (> 0.01% to ≤ 0.1%): anaphylactic reaction.

Very Rare (≤ 0.01%): anaphylactic shock, anaphylactoid reaction, anaphylactoid shock, hypersensitivity.

Nervous system disorders

Common (> 1% to < 10%): dysgeusia, syncope.

Uncommon (> 0.1% to ≤ 1%): headache, paraesthesia, dizziness.

Very Rare (≤ 0.01%): convulsion.

Not Known: vertebrobasilar insufficiency, loss of consciousness, tremor, hypoaesthesia, cerebrovascular accident.

Cardiac disorders

Rare (> 0.01% to ≤ 0.1%): cardiac arrest.

Very Rare (≤ 0.01%): angina pectoris, bradycardia, tachycardia.

Not Known: myocardial infarction.

Vascular disorders:

Uncommon (> 0.1% to ≤ 1%): thrombophlebitis.

Rare (> 0.01% to ≤ 0.1%): hypotension, shock.

Very Rare (≤ 0.01%): hot flush, hypertension, intermittent claudication, pallor, peripheral vascular disorder, vasodilation, vasospasm.

Respiratory, thoracic and mediastinal disorders

Uncommon (> 0.1% to ≤ 1%): cough, throat tightness.
Rare (> 0.01% to ≤ 0.1%): bronchospasm.
Very Rare (≤ 0.01%): asthma, cough, dyspnoea, hypoventilation, laryngeal oedema, nasal oedema, pulmonary oedema, respiratory arrest, sneezing.
Not Known: throat irritation.

Gastrointestinal disorders

Very Common (≥ 10%): nausea.
Common (> 1% to < 10%): abdominal discomfort, vomiting.
Uncommon (> 0.1% to ≤ 1%): abdominal pain.
Not Known: retching, diarrhoea.

Skin and subcutaneous tissue disorders

Common (> 1% to < 10%): pruritus, urticarial.
Not Known: rash, cold sweat, eczema, erythema, hyperhidrosis, skin discolouration.

General disorders and administration site conditions

Common (> 1% to < 10%): extravasation.
Uncommon (> 0.1% to ≤ 1%): pain, feeling hot.
Very Rare (≤ 0.01%): death.
Not Known: oedema, malaise, asthenia, chills.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/.

### 4.9 Overdose

Each vial of Fluorescite™ injection 10%, is considered to be a complete adult dose of fluorescein. An emergency tray (see Section 4.4. Special warnings and precautions for use) should always be available when administering Fluorescite™ injection 10%. No case of overdose has been reported. In the event that an unexpected reaction occurs appropriate supportive therapy should be instituted.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764 766).

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic Group – Diagnostic, Colouring Agents, ATC Code: SO1JA01.

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 fluorescein dye 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 captured on film. In the fundus, the fluorescence of the dye demarcates the retinal and/or choroidal vasculature under observation, distinguishing it from adjacent areas/structures.

Some factors that affect the quality of a fluorescein angiogram (i.e. the intensity of fluorescence light) are the intravascular fluorescein concentration, the injection technique, and the status of blood circulation.

Pharmacodynamic effects

Not available.

Clinical efficacy and safety

Not available.

## 5.2 Pharmacokinetic properties

Absorption

Following IV and oral administration of 188mg fluorescein sodium in a crossover design using 10 healthy subjects, the mean plasma $C_{max}$ values were 10.9 µg/mL (IV) and 3.5 µg/mL (oral), and the mean AUC values were 1350 µg.min/mL (IV) and 1480 µg.min/mL (oral). Peak blood fluorescein concentrations are typically observed within an hour after oral administration. Within 7 to 14 seconds of intravenous administration into the antecubital vein, fluorescein appears in the central artery of the eye. The mean peak concentration of fluorescein sodium in the retinal artery is amounted to 0.5 mg/mL.

Distribution

Fluorescein binds to albumin and red blood cells in a reversible fashion and the binding is moderate (~70-80%) during the first hour.

Within a few minutes of intravenous 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 to 0.8 L/kg).

Biotransformation

Fluorescein undergoes rapid metabolism to fluorescein monoglucuronide. After intravenous administration of fluorescein sodium (14 mg/kg) to 7 healthy subjects, approximately 80% of fluorescein in plasma was converted to glucuronide after a period of 1 hour post dose, indicating relatively rapid conjugation. Fluorescein monoglucuronide is about 1/3 to 1/4 as fluorescent as fluorescein, depending on the wavelength of excitation of the blue light.

Elimination

Fluorescein and its metabolites are mainly eliminated via renal excretion. After intravenous 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.

## 5.3 Preclinical safety data

Pregnancy

Embryofetal toxicity studies in animals showed that doses of sodium fluorescein associated with exposure levels approximately 9-times higher (rats) or the same (rabbits) as the human dose (on relative mg/m$^2$ body surface area basis) caused no fetal harm when administered IV during organogenesis.

Carcinogenicity

No long-term studies in animals to evaluate the carcinogenic potential of fluorescein have been conducted

Mutagenicity

The genotoxicity of fluorescein has not been investigated.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1. List of excipients

Sodium hydroxide and/or hydrochloric acid to adjust pH

Water for Injections.

### 6.2 Incompatibilities

Do not mix or dilute Fluorescite™ injection 10% with other solutions or drugs.

### 6.3 Shelf life

36 months.

### 6.4 Special precautions for storage

Store below 25°C. Do not freeze. Protect from light.

### 6.5 Nature and contents of container

5 mL glass vial with a gray butyl (latex free) stopper and aluminium flip-off cap.

### 6.6 Special precautions for disposal

Not available.

## 7. MEDICINE SCHEDULE

Prescription Only Medicine.

## 8. SPONSOR

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## 9. DATE OF FIRST APPROVAL

11 June 1992.

## 10. DATE OF REVISION OF THE TEXT

17 March 2025.

Summary Table of Changes

| | |
|---|---|
| 4.8 | Add “Diarrhoea” to Gastrointestinal Disorders section under Postmarketing Experience.<br>Update link to report adverse events based on the latest Medsafe Data Sheet template. |