FLUORESCEIN- fluorescein injection
Nexus Pharmaceuticals LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use FLUORESCEIN INJECTION safely and effectively. See full prescribing information for FLUORESCEIN INJECTION.
FLUORESCEIN injection, for intravenous use
Initial U.S. Approval: 1976

INDICATIONS AND USAGE

Fluorescein Injection, USP is indicated in diagnostic fluorescein angiography or angioscopy of the retina and iris vasculature. (1)

DOSAGE AND ADMINISTRATION

- The normal adult dose of Fluorescein Injection 10%, is 5 mL (500 mg) and of Fluorescein Injection 25%, is 2 mL (500 mg) via intravenous administration. (2.1)
- 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). (2.2)
- Do not mix or dilute with other solutions or drugs. (2.2)

DOSAGE FORMS AND STRENGTHS

- Fluorescein Injection 10%, 100 mg/mL in a 5 mL single dose vial (3)
- Fluorescein Injection 25%, 250 mg/mL in a 2 mL single dose vial (3)

CONTRAINDICATIONS

- Hypersensitivity to any component of this product. (4.1)

WARNINGS AND PRECAUTIONS

- Respiratory reactions. (5.1)
- Severe local tissue damage. (5.2)

ADVERSE REACTIONS

The most common adverse reactions include skin discoloration, urine discoloration, nausea, vomiting, and gastrointestinal distress. (6)
To report SUSPECTED ADVERSE REACTIONS, contact Lambda Therapeutics Limited at 1-855-642-2594or email: safety.nexuspharma@lambda-cro.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch (6)

USE IN SPECIFIC POPULATIONS

Caution should be exercised when fluorescein sodium is administered to a nursing woman. (8.3)
See 17 for PATIENT COUNSELING INFORMATION.

Revised: 10/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1. INDICATIONS & USAGE

Fluoresecin Injection 10%, , (100 mg/mL) and Fluorescein Injection 25% (250 mg/mL) is indicated in diagnostic fluorescein angiography or angioscopy of the retina and iris vasculature.

2. DOSAGE & ADMINISTRATION

2.1 Dosing

Adult Dose

The recommended dosage of Fluorescein Injection 10% (100 mg/mL) and of Fluorescein Injection 25% (250 mg/mL) is 500 mg via intravenous administration.

Pediatric Dose

For children, the dose is 7.7 mg/kg (actual body weight) up to a maximum of 500 mg, via intravenous infusion calculated on the basis of 35 mg for each 10 lbs. (4.54 kg) of body weight.

2.2 Preparation for Administration

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. Discard unused portion.

2.3 Administration

Inject the dose (over 5-10 seconds is normally recommended) into the antecubital vein, after taking precautions to avoid extravasation. A syringe, fi led with Fluorescein, 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 500 mg to 200 mg Fluorescein Injection, 10% may be appropriate in cases when a highly sensitive imaging system e.g., scanning laser ophthalmoscope is used.

3. DOSAGE FORMS & STRENGTHS

Fluorescein Injection 10%, 100 mg/mL in a 5 mL single-dose vial.

Fluorescein Injection 25%, 250 mg/mL in a 2 mL single-dose vial.

4. CONTRAINDICATIONS

4.1 Hypersensitivity

Fluorescein Injection, USP is contraindicated in patients with known hypersensitivity to fluorescein sodium or any other ingredients in this product. Rare cases of death due to anaphylaxis have been reported *[see WARNINGS AND PRECAUTIONS (5.1) and ADVERSE REACTIONS (6.2)]*.

5. WARNINGS AND PRECAUTIONS

5.1 Respiratory Reactions

Caution should be exercised in patients with a history of allergy or bronchial asthma. An emergency tray should always be available.

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.

5.2 Severe local tissue damage

Extravasation during injection can result in severe local tissue damage due to high pH of fluorescein solution. 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 nerve in the antecubital area. Complications resulting from extravasation can cause severe pain in the arm for up to several hours. When extravasation occurs, the injection should be discontinued and conservative measures to treat damaged tissue and to relieve pain should be implemented. *[see ADMINISTRATION (2.3) and ADVERSE REACTIONS (6.6)]*.

6. ADVERSE REACTIONS

6.1 Skin and urine discoloration

The most common reaction is discoloration of the skin and urine. Skin will attain a temporary ye lowish discoloration. Urine attains a bright ye llow color. Discoloration of the skin usually fades in 6 to 12 hours and usually fades in urine in 24 to 36 hours.

6.2 Gastrointestinal Reaction

The next most common adverse reaction is nausea. Vomiting, and gastrointestinal distress have also occurred. A strong taste may develop after injection.

6.3 Hypersensitivity Reactions

Symptoms and signs of hypersensitivity have occurred. Generalized hives and itching, bronchospasm and anaphylaxis have been reported. *[see CONTRAINDICATIONS (4.1) and WARNINGS AND PRECAUTIONS (5.1)]*.

6.4 Cardiopulmonary Reactions

Syncope and hypotension may occur. Cardiac arrest, basilar artery ischemia, severe shock and death may occur rarely *[see WARNINGS AND PRECAUTIONS (5.1)]*.

6.5 Neurologic Reactions

Headache may occur. Convulsions may rarely occur following injection.

6.6 Thrombophlebitis

Thrombophlebitis at the injection site has 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 ADMINISTRATION (2.3) and WARNINGS AND PRECAUTIONS (5.2)]*.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

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.

8.3 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.

8.4 Pediatric Use

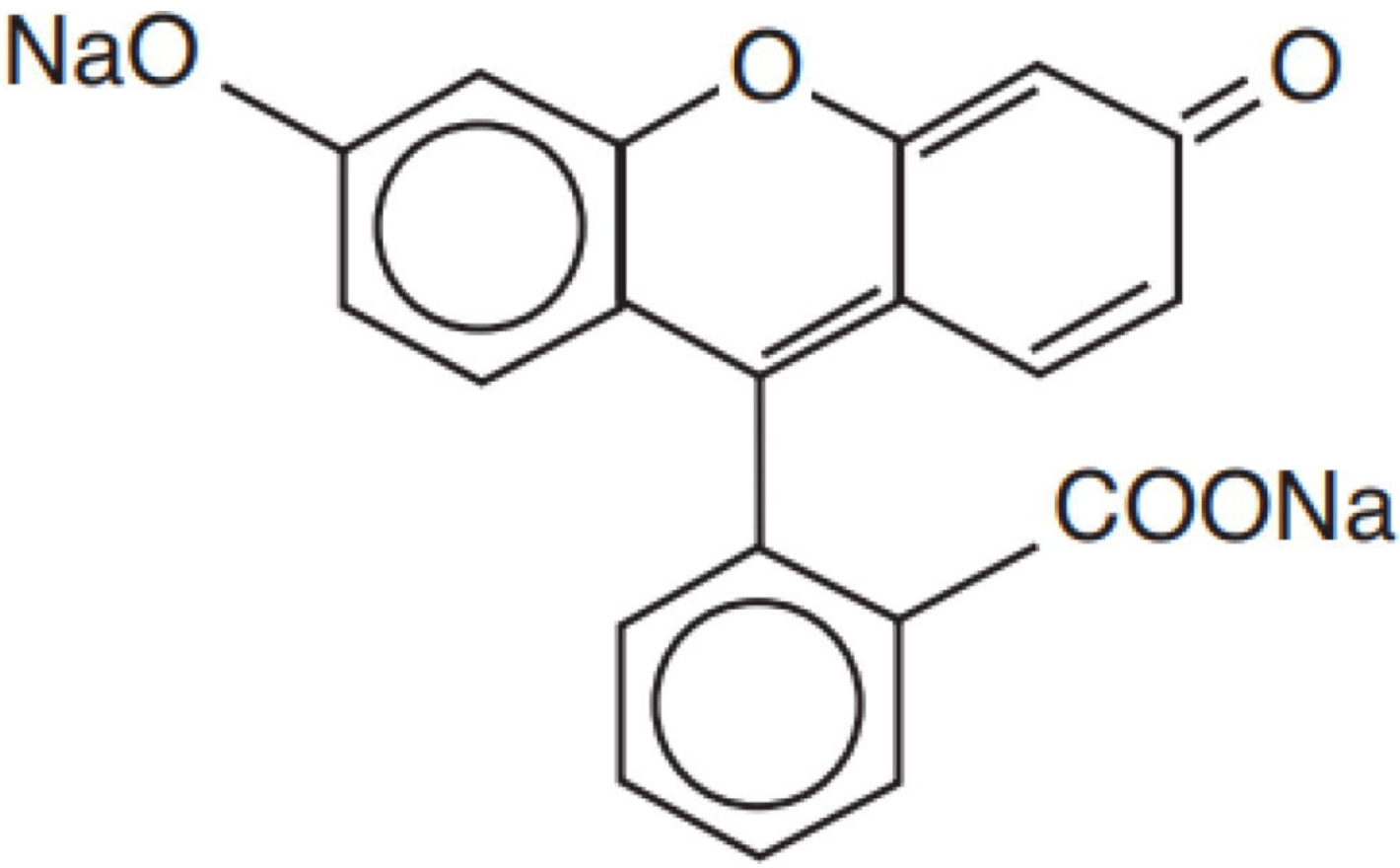
Pediatric patients have been included in clinical studies. No overall differences in safety or effectiveness have been observed between pediatric and adult patients.

8.5 Geriatric Use

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

11. DESCRIPTION

Fluorescein Injection, is a sterile solution for use intravenously as a diagnostic aid. It is a dark reddish orange solution with a pH of 8.3 to 9.8 and an osmolality of 572 to 858 mOsm/kg for the 10% and 1800 to 2200 mOsm/kg for the 25%. 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:



MW = 376.27

Fluorescein Injection 10% contains:

Active: fluorescein sodium (equivalent to fluorescein 10 % w/v, 100 mg/mL)

Inactives: Sodium Hydroxide and/or Hydrochloric Acid may be used to adjust pH (8.3 to 9.8), and Water for Injection.

Fluorescein Injection 25% contains:

Active: fluorescein sodium (equivalent to fluorescein 25% w/v, 250 mg/mL)

Inactives: Sodium Hydroxide and/or Hydrochloric Acid may be used to adjust pH (8.3 to 9.8), and Water for Injection.

12. CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Fluorescein sodium responds to electromagnetic radiation and light between the wavelengths of 465 to 490 nm and fluoresces, i.e., emits light at wavelengths of 520 to530 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 ye lowish 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.

12.3 Pharmacokinetics

Distribution.

Within 7 to 14 seconds after IV administration into the antecubital vein, fluorescein usually appears in the central retinal artery of the eye. Within a few minutes of IV administration of fluorescein sodium, a ye lowish discoloration of the skin occurs, which begins to fade 6 to 12 hours after dosing. Various estimates of volume of distribution indicate that fluorescein distributes into interstitial space (0.5 L/kg).

Metabolism.

Fluorescein is metabolized 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.

Excretion.

Fluorescein and its metabolite 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 essentia ly complete by 48 to 72 hours after administration of 500 mg fluorescein.

13. NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

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

16. HOW SUPPLIED

Fluorescein Injection 10%, is supplied in a single-dose 5 mL glass vial with a gray bromobutyl serum siliconized stopper and orange flip-off cap. It contains a sterile dark reddish orange solution of fluorescein sodium.

(NDC 14789-122-05) 5 mL, single dose vials in a package of 10.

Fluorescein Injection 25%, is supplied in a single-dose 2 mL glass vial with a gray bromobutyl serum siliconized stopper and orange flip-off cap. It contains a sterile dark reddish orange solution of fluorescein sodium.

(NDC 14789-123-05) 2 mL, single dose vials in a package of 10.

Fluorescein Injection, USP should be stored at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]. Protect from freezing.

17. PATIENT COUNSELING INFORMATION

After administration of Fluorescein sodium, 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. *[see WARNINGS AND PRECAUTIONS AND ADVERSE REACTIONS (6.1)]*.

Rx only

Manufactured in Italy for:
Nexus Pharmaceuticals LLC.
400 Knightsbridge Parkway
Lincolnshire, IL 60069

FLRPI01ITR01 Rev. 05/2023

Principal Display Panel – 5 mL Carton Label

Rx Only

NDC 14789-122-05

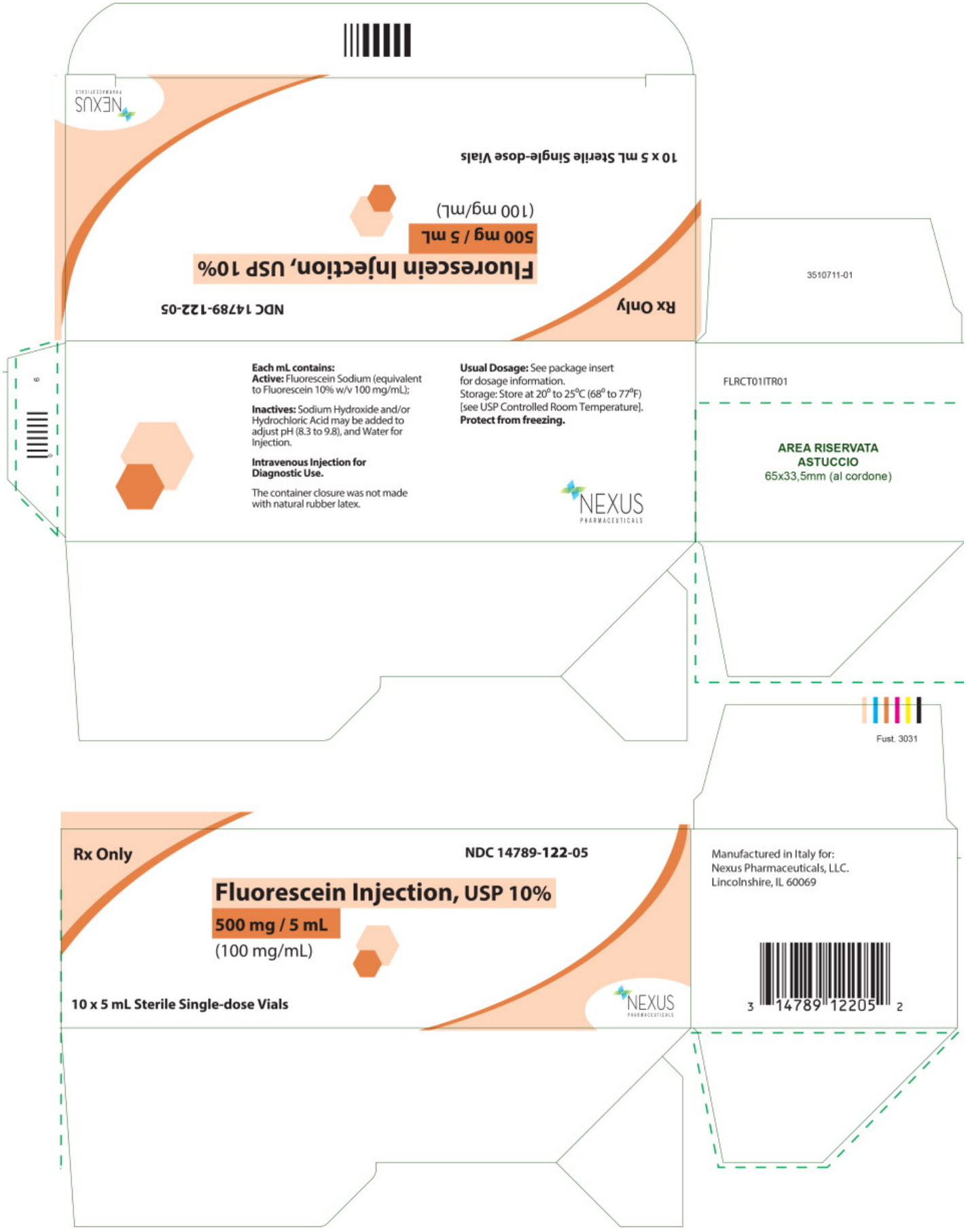
Fluorescein Injection, USP 10%

500 mg / 5 mL

(100 mg/mL)

10 x 5 mL Sterile Single-dose Vials

NEXUS
PHARMACEUTICALS



Principal Display Panel – 5 mL Vial Label

NDC 14789-122-07

Rx Only

Fluorescein
Injection, USP 10%

500 mg/5 mL

(100 mg/mL)

5 mL Sterile Single-dose Vial

For Intravenous Injection.

Discard unused portion

NEXUS
PHARMACEUTICALS

FLUORESCEIN
fluorescein injection

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:14789-122
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
Fluorescein (UNII: TPY09G7XIR) (Fluorescein - UNII:TPY09G7XIR)	Fluorescein	500 mg in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
Hydrochloric Acid (UNII: QTT17582CB)	
Water (UNII: 059QF0KO0R)	
Sodium Hydroxide (UNII: 55X04QC32I)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:14789-122-05	10 in 1 CARTON	10/24/2023	
1	NDC:14789-122-07	5 mL in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information			
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA215709	10/24/2023	

FLUORESCEIN

fluorescein injection

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:14789-123
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	Basis of Strength	Strength
Fluorescein (UNII: TPY09G7XIR) (Fluorescein - UNII:TPY09G7XIR)	Fluorescein	250 mg in 1 mL

Inactive Ingredients	
Ingredient Name	Strength
Hydrochloric Acid (UNII: QTT17582CB)	
Water (UNII: 059QF0KO0R)	
Sodium Hydroxide (UNII: 55X04QC32I)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:14789-123-05	10 in 1 CARTON	10/24/2023	
1	NDC:14789-123-07	2 mL in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information			
Marketing	Application Number or Monograph	Marketing Start	Marketing End

Category	Citation	Date	Date
ANDA	ANDA215709	10/24/2023	

Labeler - Nexus Pharmaceuticals LLC (620714787)

Establishment

Name	Address	ID/FEI	Business Operations
Nexus Pharmaceuticals LLC		620714787	ANALYSIS(14789-122, 14789-123)

Revised: 10/2023 Nexus Pharmaceuticals LLC