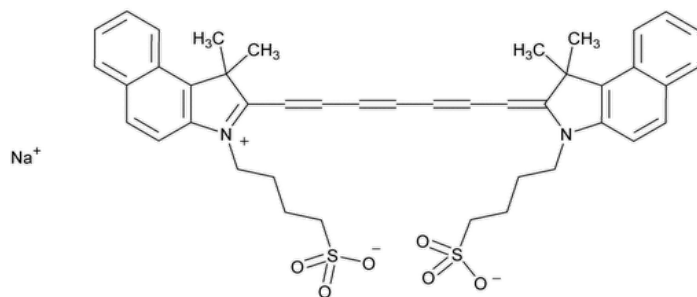


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Indocyanine Green

Change to read:



$C_{43}H_{47}N_2NaO_6S_2$ ▲774.97▲ (USP 1-Aug-2022)

1*H*-Benz[e]indolium, 2-[7-[1,3-dihydro-1,1-dimethyl-3-(4-sulfobutyl)-2*H*-benz[e]indol-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-3-(4-sulfobutyl)-, hydroxide, inner salt, sodium salt;

2-[7-[1,1-Dimethyl-3-(4-sulfobutyl)benz[e]indolin-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-3-(4-sulfobutyl)-1*H*-benz[e]indolium hydroxide, inner salt, sodium salt CAS RN®: 3599-32-4; UNII: IX6J1063HV.

Change to read:

DEFINITION

Indocyanine Green contains NLT 89.0% and NMT 100.0% of indocyanine green ($C_{43}H_{47}N_2NaO_6S_2$), calculated on the dried basis. It contains

NMT 5.0% of sodium iodide ▲(NaI),▲ (USP 1-Aug-2022) calculated on the dried basis.

IDENTIFICATION

• **A. IDENTIFICATION TESTS—GENERAL** (191), [Chemical Identification Tests, Sodium](#) and [Sulfate](#)

Analysis: Incinerate a portion of Indocyanine Green and use the residue.

Acceptance criteria: Meets the requirements

Change to read:

• **B.**

Sample solution: 0.05 mg/mL of Indocyanine Green in [water](#)

Analysis: Add 10 drops of ▲[sodium hydroxide TS](#)▲ (USP 1-Aug-2022) to the *Sample solution* and heat to about 60°. Add 10 drops of [hydrogen peroxide TS](#) and mix.

Acceptance criteria: A red color develops within 4 min, which on standing, fades to a pale orange.

ASSAY

Change to read:

• **PROCEDURE**

Standard solution: 2 µg/mL of [USP Indocyanine Green RS](#) in [methanol](#)

Sample solution: 2 µg/mL of Indocyanine Green in [methanol](#)

Instrumental conditions

▲(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)▲ (USP 1-Aug-2022)

Mode: UV-Vis

Analytical wavelength: 785 nm

Cell: 1 cm

Blank: [Methanol](#)

Analysis**Samples:** *Standard solution* and *Sample solution*Calculate the percentage of indocyanine green ($C_{43}H_{47}N_2NaO_6S_2$) in the portion of Indocyanine Green taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

 A_U = absorbance of the *Sample solution* A_S = absorbance of the *Standard solution* C_S = concentration of [USP Indocyanine Green RS](#) in the *Standard solution* (µg/mL) C_U = concentration of Indocyanine Green in the *Sample solution* (µg/mL)**Acceptance criteria:** 89.0%–100.0% on the dried basis**OTHER COMPONENTS****Change to read:**• **SODIUM IODIDE****Sample:** 200 mg of Indocyanine Green**Titrimetric system**▲(See [Titrimetry \(541\)](#).) ▲ (USP 1-Aug-2022)**Mode:** Direct titration**Titrant:** 0.01 N silver nitrate VS**Electrode system:** Silver-glass**Endpoint detection:** Potentiometric**Analysis:** Dissolve the *Sample* in 100 mL of [water](#). Add 1 mL of [nitric acid](#) and mix. Titrate with *Titrant* to a potentiometric endpoint.

Calculate the percentage of sodium iodide (NaI) in the portion of Indocyanine Green taken:

$$\text{Result} = [(V \times N \times F)/W] \times 100$$

 V = volume of *Titrant* consumed by the *Sample* (mL) N = *Titrant* concentration, in normality (mEq/mL) F = equivalency factor of sodium iodide, 149.9 mg/mEq W = weight of *Sample* taken (mg)**Acceptance criteria:** NMT 5.0% on the dried basis**Delete the following:**▲ **IMPURITIES**• [ARSENIC \(211\), Procedures, Method II](#): NMT 8 ppm• [LEAD \(251\)](#)**Sample solution:** A 5-mL portion of the solution prepared for the test for [Arsenic \(211\), Procedures, Method II](#)**Analysis:** Proceed as directed for the limit test of [Lead \(251\)](#). Use 3 mL of *Ammonium Citrate Solution*, 1 mL of *Potassium Cyanide Solution*, and 0.5 mL of *Hydroxylamine Hydrochloride Solution*.**Acceptance criteria:** NMT 10 ppm ▲ (USP 1-Aug-2022)**SPECIFIC TESTS**• [STERILITY TESTS \(71\)](#): Where the label states that Indocyanine Green is sterile, it meets the requirements.**Change to read:**• [BACTERIAL ENDOTOXINS TEST \(85\)](#): Where the label states that Indocyanine Green is sterile or must be subjected to further processing during the preparation of injectable dosage forms, ▲the level of bacterial endotoxins is such that the requirement under the relevant dosage form monograph(s) in which Indocyanine Green is used can be met. ▲ (USP 1-Aug-2022)• [LOSS ON DRYING \(731\)](#)**Analysis:** Dry under vacuum at 50° for 3 h.**Acceptance criteria:** NMT 6.0%

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at 25°, excursions permitted between 15° and 30°.

Change to read:

• **LABELING:** Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms ▲to ensure acceptable levels of bacterial endotoxins.▲ (USP 1-Aug-2022)

• **USP REFERENCE STANDARDS (11).**
[USP Indocyanine Green RS](#)

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
INDOCYANINE GREEN	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: [Chromatographic Database](#)

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