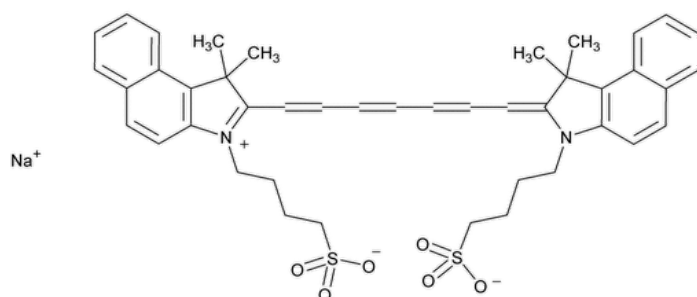


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Indocyanine Green

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%