^{131}I norcholesterol

^{131}I iodomethyl norcholesterol, ^{131}I-6b-Iodomethyl-19-Norcholesterol, NP-59

1. Indications

^{131}I iodomethyl norcholesterol is *not* approved in the Netherlands.

^{131}I iodomethyl norcholesterol is used for:

- Diagnostic evaluation of the functional state of adrenal cortical tissue.
- Differentiation between metastatic disease to the adrenals and non-malignant adrenal enlargement in cancer patients.
- Detection of remnants of functioning tissue in hypercortisonism after adrenalectomy or of ectopic endocrine tissue.
- Detection and follow-up of euadrenal tumours.

See chapter 'Adrenal scintigraphy'.

2. Preparation

^{131}I-norcholesterol is supplied as a solution for injection.

3. Quality control

^{131}I-norcholesterol is mentioned in the European Pharmacopeia.

pH: 3,5-8,5

Radiochemical purity

Thin-layer chromatography

	6ß-[^{131}I] Iodomethyl-19-norcholest-5(10)-en-3ß-ol	**Impurity C (^{131}I iodide)**
Test solution	Preparation to be examined	Preparation to be examined
Carrier solution	dissolve 10 mg of potassium iodide, 20 mg of potassium iodate and 0,1 g of sodium hydrogen carbonate in distilled water and dilute to 10 ml with the same solvent	dissolve 10 mg of potassium iodide, 20 mg of potassium iodate and 0,1 g of sodium hydrogen carbonate in distilled water and dilute to 10 ml with the same solvent
Plate	TLC silica gel GF_{254} plate	TLC silica gel GF_{254} plate
Mobile phase	Chloroform	Chloroform : anhydrous ethanol (50:50 V/V)
Application	5 µl of the test solution and 10 µl of the carrier solution on the same spot	10µl of the carrier solution and then up to 5 µl of the test solution on the same spot
Development	Over a path of 15 cm in about 60 min	Over a path of 15 cm in about 90 min
Drying	In air	In air

Detection	UV light at 254 nm and suitable detector	UV light at 254 nm and suitable detector
Rf value	Rf-value test solution = 0,5 Rf value impurity C (^{131}I iodide) =0,0	Rf value impurity C (yellow spot): 0,5 Principal peak of radioactivity is near to the solvent front
Limit	≥ 85% per cent of the total radioactivity	Impurity C: ≤ 5% of the total radioactivity

Radionuclidic purity
^{131}I minimum 99,9% of the total radioactivity.

4. Contraindications
^{131}I-norcholesterol contains 9,4 mg/ml benzylalcohol en 80 mg/l ethanol, which may cause serious reactions in premature and low birth-weight infants. The European Medicines Agency (EMA) and the Dutch College ter Beoordeling van Geneesmiddelen (CBG) have published guidelines on the maximum amount of benzylalcohol that can be used. The CBG advises a maximum amount of 90 mg/kg body weight.

5. Interactions
The uptake of ^{131}I iodomethyl norcholesterol is generally strongly influenced by concomitant medications which exert pharmacological influence at the level of the adrenal cortex. It is therefore necessary to withdraw the administration of the following drugs for a minimum of 48 h prior to administration of the radiopharmaceutical.

Oral contraceptives
Oral contraceptives have been found to increase the binding of adrenal cortex imaging agent ^{131}Iodomethyl-norcholesterol by increasing plasma renin activity. This results in adrenocortical stimulation; increased cortisol secretion and hyperplasia. They may cause false positives or just uninterpretable results complicating the interpretation of adrenal scintigrams.

Spironolactone
When the indication for the study is a possible aldosterone producing adenoma, eventual spironolactone medication must be withdrawn for at least 6 weeks before the start of the study.
Spironolactone affects the uptake of ^{131}Iodomethyl-nor-cholesterol by the adrenal cortex. It has been reported to both increase uptake as well as decrease uptake.

Inhibitors of the biosynthesis of adrenocortical steroids.
Ketoconazole, metyrapone, aminoglutethimide

Adrenocortical steroids, including their synthetic analogues.
Dexamethasone (see chapter Adrenal scintigraphy).

6. Adverse reactions

Intraveneus administration of ^{131}I norcholesterol can provoke an adverse reaction of an anaphylactoid nature. The symptoms are generally mild (hot flush, urticarial, nausea, hypotension), but serious symptoms (bronchospasm, hypotension, circulatory collapse) can occur. Generally, anaphylactoid reactions occur immediately after administration but the possibility of a delayed onset (15 min after intravenous administration) must be kept in mind.

It has been reported that ^{131}I norcholesterol can provoke hypertension, back pain and chest discomfort.

7. Biodistribution & pharmacokinetics

Less than 1% of a dose of ^{131}I iodomethyl norcholesterol accumulates in the adrenals. The majority of this uptake takes place within the first 48 h following administration. Part of the fraction that accumulates in the adrenals does so after one or more entero-hepatic circulation cycles.

The routes of elimination from the body are via urine and via the faeces (approx. 1/3 of the administered dose in 9 days for both routes).

At that time 1/3 is still retained in the body, mainly diffusely distributed but with approx. 2% in the liver. Invariably some thyroid uptake will occur notwithstanding adequate blockade.

8. Stability

The injection vials having a shelf life of 14 days from the date of its manufacture. After the first withdrawal, store in a refrigerator and use within 8 h.

9. Literature

- SmPC 131I iodomethyl norcholesterol CIS bio international 7.5-15 MBq/mL solution for injection.
- Kazerooni EA et al. Diagnostic Accuracy and Pitfalls of [Iodine-13 1] 6-Beta-Iodomethyl-19-Norcholesterol (NP-59) Imaging. J Nucl Med 1990;31:526-34.
- Santos-Oliveira R et al. Radiopharmaceuticals drug interactions: a critical review An Acad Bras Cienc 2008;80:665-75.
- European Pharmacopeia 8.0 volume 1.