

¹²³I iobenguane

Adreview[®], ¹²³I-MIBG, ¹²³I-metaiodobenzylguanidine

1. Indications

¹²³I-Iobenguane injection is approved for:

- Detection of tumours which originate from the neural crest. These are pheochromocytomas, paragangliomas, chemodectomas and ganglioneuromas.
- Detection, staging and follow-up of neuroblastomas.
- Assessment of sympathetic innervation of the myocardium.
- Test the function of the adrenal medulla (hyperplasia).

2. Preparation

Approved product, see summary of product characteristics (SmPC).

3. Quality control

Approved product, see summary of product characteristics (SmPC) and the European Pharmacopeia.

4. Interactions

Exogenous substances that affect the physiology of norepinephrine, either via enhancing or inhibiting uptake, release, metabolism or catabolism can have a significant effect upon the biodistribution of MIBG. In general medication has to be stopped for 4 biological half-lives.

Calcium channel blockers

Calcium channel blockers such as nifedipine, amlodipine and verapamil are responsible for an increase of uptake and retention ¹²³I-MIBG. An increase of the intracellular concentration of Ca²⁺ causes neurotransmitter release, and, as calcium channel blockers reduce influx of these ions, they reduce release of neurotransmitters and MIBG. Calcium channel blockers should be discontinued for tumour and adrenal gland imaging, not for cardiac MIBG imaging.

Caveat: slow release calcium channel blockers.

Labetalol

Labetalol is a beta-blocker with alpha blocker activity that has an inhibitory effect on cellular uptake of ¹²³I MIBG.

Tricyclic antidepressants (TCA)

TCA inhibit norepinephrine transporter function and inhibit uptake. Increasing the dose of ¹²³I iobenguane will not overcome any potential norepinephrine uptake inhibition by these drugs. Most commonly studied drugs are imipramine and desipramine.

Sympathomimetics (phenylephrine, ephedrine)

These compounds have structural similarities to the catecholamines and therefore

commonly have agonists effects on alpha and beta receptors.

Cocaine

Concomitant use of cocaine, which has the potential to decrease the uptake of norepinephrine, and ¹²³I iobenguane can cause false negative imaging results. Cocaine should be discontinued.

Reserpine

Reserpine is not commercially available anymore in The Netherlands, but it should be discontinued.

5. Contraindications

Adreview® contains 10,4 mg/ml benzylalcohol, 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 should be used. The CBG advises a maximum amount of 90 mg/kg body weight.

6. Adverse reactions

In rare cases adverse reactions have occurred: flushing, urticaria, nausea, chills and other symptoms of anaphylactic reactions. If the drug is administered too quickly adverse events like palpitations, shortness of breath, a feeling of heat, transient hypertension and abdominal cramps can occur. These events can happen during or immediately after administration. These symptoms normally disappear within one hour.

7. Biodistribution & pharmacokinetics

After intravenous administration, ¹²³I-MIBG is rapidly cleared from the blood and accumulates in adrenergically innervated tissues. Retention is especially prolonged in highly adrenergically innervated tissues, such as the adrenal medulla, heart, and salivary glands. 10-15% of the injected activity accumulates in cells with neuroendocrine receptors. During the first hour, it accumulates in the lungs and then in the heart, where the highest concentration value is reached after 2-3 h. Maximum accumulation in tumours and/or metastasis is reached after 24-96 h. The product builds up in the bladder, unblocked thyroid, and exhibits little affinity for the liver, heart, spleen, and salivary glands. Most of the iobenguane dose is excreted unaltered by the kidneys via glomerular filtration. In patients with normal renal function, about 50% of the injected radioactivity was recovered in urine during the first 24 h after the infusion. About 70-90% was recovered in the urine after 4 days, primarily as unchanged iobenguane.

In patients with normal renal function, the major metabolites that account for <10% of the administered dose are *m*-iodohippuric acid, *m*-iodobenzoic acid, and 4-hydroxy-3-iodobenzylguanidine and free radioiodide. The enzymatic process responsible for metabolism, however, has not been well-characterized, and the pharmacologic activity of these metabolites has also not been studied.

8. Stability

¹²³I-iobenguan injection (MIBG®) has a shelf life of 20 h after activity reference time.

¹²³I-Iobenguan injection (Adreview®) has a shelf life of about 26 h after activity reference time. The product has to be stored at 15-25°C.

9. Literature

- SmPC MIBG (I123) injection; ¹²³I-Jobenguane.
- Flotats A et al. Proposal for standardization of ¹²³I-metaiodobenzylguanidine (MIBG) cardiac sympathetic imaging by the EANM Cardiovascular Committee and the European Council of Nuclear Cardiology. *Eur J Nucl Med Mol Imaging* 2010.
- Vallabhajosula S et al. Radioiodinated metaiodobenzylguanidine (MIBG): radiochemistry, biology and pharmacology. *Seminars Nuc Med* 2011;4:324-33.
- Jacobson AF, Travin MI. Impact of medications on mIBG uptake, with specific attention to the heart: comprehensive review of the literature. *J Nucl Cardiology* 2015;22:980-93.
- Wafelman AR et al. Radioiodinated metaiodobenzylguanidine: a review of its biodistribution and pharmacokinetics, drug interactions, cytotoxicity and dosimetry. *Eur J Nucl Med* 1994;21(6):545-59.