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 \(^{123}\)I 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\textsuperscript{®} 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, \(^{123}\)I-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 \(m\)-iodophippuric 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**
\(^{123}\)I-Iobenguan injection (MIBG\textsuperscript{®}) has a shelf life of 20 h after activity reference time.
$^{123}$I-Jobenguan 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 ($^{123}$I) injection; $^{123}$I-Jobenguane.