

¹⁵O-water

¹⁵O-H₂O

1. Indications

¹⁵O-H₂O injection kit is used for the imaging of blood flow in the greater circulation (larger vessels, heart, kidneys).

2. Preparation

¹⁵O-water will be formed by radiation of the ¹⁵O target with protons in an N₂-15 gas area. The new formed O₂-15 gas will be transported to the module where the radioactive gas will be mixed with N₂/H₂. The total gas mix then will be headed over a palladium pipe at 150°C.

The nuclear reaction: ¹⁵N (p,n) ¹⁵O

The formed ¹⁵O-H₂O comes into a physiological salt solution and will be filled with a prepared 25 ml sterile vial into a 10 ml syringe.

3. Quality control

¹⁵ O-H ₂ O	In house requirement	Release requirement?	Ph Eur 8,7
Appearance	Clear, colorless	Yes	Clear, colorless
pH	5,5-8,5	Yes	5,5-8,5
Pressure hold test GP-filter 1 (bar)	<20%	No	-
Pressure hold test GP-filter 2 (bar)	<20%	Yes	-
Radiochemical purity (%) impurities: O ₂ -15 Fixed via O ₂ -15 trap efficiency	>99	No (only during validation)	>99
Radionuclidic purity(%): gammaspectrum (keV) t _{1/2} (min)	>99 511, evt 1022 1,9-2,2 min	No	>99 511, evt 1022 1,9-2,2 min
Ammonia Nitrate	<10 ppm <10 ppm	No	<10 ppm <10 ppm
Osmolarity (mosmol/kg)	<400	No	-

Sterility	Sterile	No	Sterile
Endotoxins (EU/ml)	<2,5	No	<5,82
Plate count after 1 time gp filtration 3	Max 1 kve/ml	No	-
Plate count after 2 times gp filtration	0	No	-
Al (ig/l)4	<2000	No	<2000

4. Interactions

At this moment, no cross reactions with other drug substances have been described. When the drug product is administered via a catheter, some retention of the drug substance in the catheter may occur. Lines should be as short as possible.

5. Contraindications

No contraindications have been observed nor reported yet.

6. Adverse reactions

In the UMCG, many clinical studies with ¹⁵O-H₂O have been performed in both healthy volunteers and different patient groups. No adverse effects have been seen in these groups, nor have adverse events been reported in the international literature. Based on all these data, one may conclude that human exposure to ¹⁵O-H₂O is safe.

7. Biodistribution & pharmacokinetics

As stated in the introduction, ¹⁵O-H₂O is identical to plain water. The only difference is the physical properties of the oxygen-atom, making the molecule a positron-emitting substance. Since the chemical properties are not altered, ¹⁵O-H₂O behaves identical to its non-radioactive counterpart.

The radioactive half-life of the isotope ¹⁵O, and thus the tracer ¹⁵O-H₂O, is 2 min. A bolus of water injected intravenously will spread through the body through the vascular system and readily diffuse from the capillaries into the surrounding tissues. Because of the freely moving capacities of the molecule, the distribution over the body is blood flow dependent. Because of the high percentage of the heart-minute volume of blood that is transported towards the brain, ¹⁵O-H₂O can be used to estimate cerebral blood flow (CBF) and changes in CBF under the influence of different tasks offered to the brain.

8. Stability

Physical half-life of ¹⁵O-H₂O is 2,03 min. The injection takes place as soon as possible after production. Therefore there is no use of stability testing.

9. Literature

- UMCG, investigational medicinal product dossier ¹⁵O-H₂O.
- Production protocol UMCG ¹⁵O-H₂O.