^{99m}Tc bicisate

^{99m}Tc Ethyl Cysteinate Dimer (ECD), Neurolite®

1. Indications

^{99m}Tc Bicisate is a brain imaging agent and is approved for localization of stroke in patients in whom stroke already has been diagnosed. ^{99m}Tc Bicisate is used for other indications such as detection of cerebral ischemia, seizures, brain trauma. See corresponding chapter Regional cerebral blood perfusion scan.

2. Preparation

The Bicisate kit consists of two vials. One vial (vial A) containing the chelating agent (bicisate) and a reducing agent and another vial (vial B) containing phosphate buffer to obtain a final pH value of 7.
Add 3,7 GBq ^{99m}Tc pertechnetate to the buffer vial in approximately 2,0 ml. Without withdrawing the needle, remove an equal volume of air to maintain pressure within the vial.
Add 3,0 ml of sodium chloride injection (0,9%) into vial A to dissolve the contents. Without withdrawing the needle, remove an equal volume of air to maintain pressure within the vial. Shake for a few seconds. With another sterile syringe, immediately (within 30 sec) withdraw 1,0 ml of vial A and inject it into vial B. Discard vial A immediately. Swirl the contents of the vial B for a few seconds, and allow this mixture to stand for 30 min at room temperature.

3. Quality control

Radiochemical purity by thin layer chromatography
Five potential impurities are formed through different mechanisms and therefore not likely to all be present at the same time.

Product information
Stationary Phase: Bakerflex Silica gel
Mobile phase: ethylacetate, freshly prepared and allow 15-30 min for solvent equilibration
Application: 5 µl, diameter of the spot not greater than 10 mm
Development over a path of 7 cm, about 15 min
Drying: in air
Retardation factors:
^{99m}Tc Technetium bicisate = 0,8-1,0
Radiochemical impurities = 0,0
Limit: radiochemical purity ≥ 90%

Literature[2]
Stationary phase: Whatman TLC
Mobile phase: acetone: ammonium acetate 0,5M: 60:40. Preequilibrate tank
Sample: 2µl, allowed to dry for 5-10 min

Development over a path of at least 6 cm, about 15 min
Drying: in air
Retardation factors:
99mTc Technetium bicisate = 0,25-0,4
Radiochemical impurities: at several places on the TLC
%99mTc Bicisate = *(Peak area of 99mTc Bicisate/ 100) /* Total area of all peaks.
Limit: radiochemical purity ≥90%

4. Interactions
No data.

5. Adverse events
Adverse event are rare and observed in ≤1% of the subjects.

Cardiovascular:	angina, hypertension, heart failure, syncope.
Dermatologic:	rash.
Metabolic:	inconsistent changes of serum phosphate and calcium levels, not requiring intervention.
Neurologic:	headache, dizziness, seizure, somnolence.
Gastrointestinal:	nausea
Psychiatric:	hallucinations, agitation, anxiety
Respiratory:	apnea, cyanosis
Other:	malaise, sense of smell altered (parosmia)

6. Biodistribution & pharmacokinetics
99mTc Bicisate is a neutral lipophilic complex that localizes in the brain by crossing the blood brain barrier via passive diffusion. In the brain, an anionic complex is formed by hydrolysation.
Brain uptake is rapid. Studies show cellular uptake of 4,8-6,5% of the injected dose at 5min after injection. Brain clearance is 12% per hour during the first hour, then 5% per hour thereafter.
Technetium 99mTc bicisate is metabolized by endogenous enzymes to the mono- and di-acids of Technetium 99mTc bicisate found in the blood and urine, metabolites are inactive. Neither 99mTc bicisate or the major metabolites are protein bound.
99mTc bicisate is primarily excreted by the kidneys with 50% of the injected dose excreted within 2 h of injection. By 24 h, 74% of the injected dose in recovered in the urine
Fecal excretion accounts for 12,5% of the injected dose after 48 h.

7. Stability
Reconstituted product should be use within 6 h.

8. Literature

- SmPC NEUROLITE®; Kit for preparation of Technetium Tc99m Bicisate for injection; june 2008
- Green JM et al. Thin-Layer chromatographic procedures for the characterization of Technetium-99m Bicisate; Journal of Nuclear Medicine Technology 1994;22:21-6.
- Holman BL, Hellman RS, Goldsmith SJ, et al: Biodistribution, dosimetry, and clinical evaluation of technetium-99m ethyl cysteinate dimer in normal subjects and in patients with chronic cerebral

infarction. J Nucl Med 1989;30:1018-24.

- Vallabhajosula S et al. Technetium-99m ECD: a new brain imaging agent: in vivo kinetics and biodistribution studies in normal human subjects. J Nucl Med 1989;30:599-604.