דצמבר 2020

רופא/ה, רוקח/ת נכבד/ה,

הנדון: עדכון עלון לרופא של התכשיר
Stamicis 1mg KIT for Radiopharmaceutical Preparation

מרכיב פעיל:

Tetrakis Copper (I) Tetrafluoroborate 1mg/Vial

צורת מינון ומתן: Lyophilized powder for solution for injection, IV

התוויה מאושרת:
טקסט המסומן בקו תחתי מסמן עדכון שבוצע בהתוויה:

This medicinal product is for diagnostic use only. This is indicated for adults. For paediatric population see section 4.2.

After radiolabelling with sodium pertechnetate (99mTc) solution, the solution of technetium (99mTc) sestamibi obtained is indicated for:

Myocardial perfusion scintigraphy
For the detection and localisation of coronary artery disease (angina pectoris and myocardial infarction).

Assessment of global ventricular function
First-pass technique for determination of ejection fraction and/or ECG-triggered, gated SPECT for evaluation of left ventricular ejection fraction, volumes and regional wall motion.

Scintimammography for the detection of suspected breast cancer
When mammography is equivocal, inadequate or indeterminate.

Localisation of hyperfunctioning parathyroid tissue
In patients with recurrent or persistent disease in both primary and secondary hyperparathyroidism, and in patients with primary hyperparathyroidism scheduled to undergo initial surgery of the parathyroid glands.

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חברת איזוטופיה מולקיולר אימג'ינג מבקשת להודיעכם על העדכונים הבאים בעלון לרופא של התכשיר:
- סעיף 4.2 עודכן (משטר המינון של התכשיר), להלן הסעיף המעודכן במלואו.
- ביתר הסעיפים מצוינים שינויים המהווים החמרה בלבד - מסומנים בקו תחתי.

4.2 Posology and method of administration

Posology

Adults and elderly population
Posology may vary depending on gamma camera characteristics and reconstruction modalities. The injection of activities greater than local DRLs (Diagnostic Reference Levels) should be justified. The activity range for intravenous administration to an adult patient of average weight (70 kg) is for:

Diagnosis of reduced coronary perfusion and myocardial infarction: 400-900 MBq.

The recommended activity range for diagnosis of ischaemic heart disease according to the European procedural guideline is:

– Two-day protocol: 600–900 MBq/study
– One-day protocol: 400–500 MBq for the first injection, three times more for the second injection.

Not more than a total of 2000 MBq should be administered for a one-day protocol and 1800 MBq for a two-day-protocol. For a one-day protocol, the two injections (stress and rest) should be done at least two hours apart but may be performed in either order. After the stress injection, exercise should be encouraged for an additional one minute (if possible).

For diagnosis of myocardial infarction one injection at rest is usually sufficient.

For diagnosis of ischaemic heart disease two injections (stress and rest) are required in order to differentiate transiently from persistently reduced myocardial uptake.

Assessment of global ventricular function: 600-800 MBq injected as a bolus.

Scintimammography: 700-1000 MBq injected as a bolus usually in the arm opposite to the lesion.

Localisation of hyperfunctioning parathyroid tissue: 200-700 MBq injected as a bolus. The typical activity is between 500-700 MBq.

Posology may vary depending on gamma camera characteristics and reconstruction modalities.

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The injection of activities greater than local DRLs (Diagnostic Reference Levels) should be justified.

Renal impairment
Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in these patients.

Hepatic impairment
In general, activity selection for patients with a decreased hepatic function should be cautious, usually starting at the low end of the dosing range.

Paediatric population
The use in children and adolescents has to be considered carefully, based upon clinical needs and assessing the risk/benefit ratio in this patient group. The activities to be administered to children and adolescents may be calculated according to the recommendations of the European Association of Nuclear Medicine (EANM) paediatric dosage card; this activity administered to children and to adolescents may be calculated by multiplying a baseline activity (for calculation purposes) by the weight-dependent multiples given in the table below.

A[MBq]Administered = Baseline Activity X Multiple:

The baseline activity is 63 MBq as a cancer seeking agent. For cardiac imaging, the minimum and maximum baseline activities are 42 and 63 MBq, respectively, for the two-day protocol cardiac scan both at rest and stress. For the one-day cardiac imaging protocol, the baseline activity is 28 MBq at rest and 84 MBq at stress. The minimum activity for any imaging study is 80 MBq.

Weight (kg)	Multiple	**Weight (kg)**	Multiple	**Weight (kg)**	Multiple
3	1	**22**	5.29	**42**	9.14
4	1.14	**24**	5.71	**44**	9.57
6	1.71	**26**	6.14	**46**	10.00
8	2.14	**28**	6.43	**48**	10.29
10	2.71	**30**	6.86	**50**	10.71
12	3.14	**32**	7.29	**52-54**	11.29
14	3.57	**34**	7.72	**56-58**	12.00
16	4.0	**36**	8.00	**60-62**	12.71
18	4.43	**38**	8.43	**64-66**	13.43
20	4.86	**40**	8.86	**68**	14.00

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Method of administration

For intravenous use.
Because of potential tissue damage, extravasal injection of this radioactive product has to be strictly avoided.
For multidose use.

Precautions to be taken before handling or administration of the medicinal product
This medicinal product should be reconstituted before administration to the patient. For instructions on reconstitution and control of the radiochemical purity of the medicinal product before administration, see section 12.

For patient preparation, see section 4.4.

Image acquisition
Cardiac imaging
Imaging should begin approximately after 30-60 min after injection to allow for hepatobiliary clearance. Longer delay can be required for resting images and for stress with vasodilatators alone because of the risk of higher subdiaphragmatic technetium (^{99m}Tc) activity. There is no evidence for significant changes in myocardial tracer concentration or redistribution, therefore imaging for up to 6 hours post injection is possible. Test may be done in a one-day or two-days protocol.

Preferably tomographic imaging (SPECT) with or without ECG gating should be performed.

Scintimammography
Breast imaging is optimally initiated 5 to 10 minutes post injection with the patient in the prone position with breast freely pendant.

The product is administered in an arm vein contralateral to the breast with the suspected abnormality. If the disease is bilateral, the injection is ideally administered in a dorsal vein of the foot.

Conventional gamma camera
The patient should then be repositioned so that the contralateral breast is pendant and a lateral image of it should be obtained. An anterior supine image may then be obtained with the patient's arms behind her head.

Detector dedicated to breast imaging
In case a detector dedicated to breast imaging is used, a relevant machine-specific protocol must be followed to obtain the best possible imaging performance.

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Parathyroid imaging

Parathyroid image acquisition depends on the protocol chosen. The most used studies are either the subtraction and/or the dual-phase techniques, which can be performed together.

For the subtraction technique either sodium iodide (^{123}I) or sodium pertechnetate (^{99m}Tc) can be used for imaging for the thyroid gland since these radiopharmaceuticals are trapped by functioning thyroid tissue. This image is subtracted from the technetium (^{99m}Tc) sestamibi image, and pathological hyperfunctioning parathyroid tissue remains visible after subtraction.

When sodium iodide (^{123}I) is used, 10 to 20 MBq are orally administered. Four hours after the administration, neck and thorax images may be obtained. After sodium iodide (^{123}I) image acquisition, 200 to 700 MBq of technetium (^{99m}Tc) sestamibi are injected and images are acquired 10 minutes post injection in double acquisition with 2 peaks of gamma energy (140 keV for technetium (^{99m}Tc) and 159 keV for iodide (^{123}I)). When sodium pertechnetate (^{99m}Tc) is used, 40-150 MBq are injected and neck and thorax images are acquired 30 minutes later. Then 200 to 700 MBq of technetium (^{99m}Tc) sestamibi are injected and a second acquisition of images is acquired 10 minutes later.

When the dual-phase technique is used, 400 to 700 MBq of technetium (^{99m}Tc) sestamibi are injected And the first neck and mediastinum image is obtained 10 minutes later. After a wash-out period of 1 to 2 hours, neck and mediastinum imaging is again performed.

The planar images may be complemented by early and delayed SPECT or SPECT/CT.

4.4 Special warnings and precautions for use

…
Renal or hepatic impairment
Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible (see section 4.2).
…
After the procedure
Close contact with infants and pregnant women should be restricted during the initial 24 hours following the injection.
…

4.5 Interaction with other medicinal products and other forms of interaction

Medicinal products which affect myocardial function and/or blood flow may cause false negative results in the diagnosis of coronary arterial disease. Particularly beta-blockers

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and calcium antagonists reduce oxygen consumption and thus also affect perfusion and beta-blockers inhibit the increase of heart frequency and blood pressure under stress. For this reason, concomitant medicinal product should be taken into consideration when interpreting the results of the scintigraphic examination. The recommendations of the applicable guidelines on ergometric or pharmacological stress tests should be followed.

When the subtraction technique is used for imaging of hyperfunctioning parathyroid tissue, recent use of iodine containing radiologic contrast media, medicinal products used to treat hyper- or hypothyroidism or of several other medicinal products is likely to decrease the quality of thyroid imaging and even makes subtraction impossible. For a complete list of possibly interacting medicinal products refer to the SmPCs of sodium iodide (123I) or sodium pertechnetate (99mTc).

5.3 Preclinical safety data

…
Neither rats nor dogs exhibited treatment related effects at reconstituted kit doses of 0.42 mg/kg (30 times MHD) and 0.07 mg/kg (5 times MHD) respectively for 28 days. At repeated dose administration, the first toxicity symptoms appeared during the administration of 150 times the daily dose during 28 days.
Extravasation administration in animals showed acute inflammation with oedema and haemorrhages at the injected site.
…

6.6 Special precautions for disposal

General warnings
Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the competent official organisation.
….
Contents of the vial are intended only for use in the preparation of technetium (99mTc) sestamibi and are not to be administered directly to the patient without first undergoing the preparative procedure.
…
Administration procedures should be carried out in a way to minimize risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.

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The content of the kit before extemporary preparation is not radioactive. However, after sodium pertechnetate (99mTc), is added, adequate shielding of the final preparation must be maintained.

…

11. DOSIMETRY

…

Cardiac imaging

The effective dose resulting from the administration of a maximal recommended activity of 2,000 MBq of technetium (99mTc) sestamibi for an adult weighing 70 kg is about 16.4 mSv if implementing the one-day protocol with administration of 500 MBq at rest and 1,500 MBq at exercise.

For this administered activity of 2,000 MBq the typical radiation dose to the target organ heart is 14 mGy and the typical radiation doses to the critical organs gall bladder, kidneys and upper large intestine are 69, 57 and 46.5 mGy, respectively.

The effective dose resulting from the administration of a maximal recommended activity of 1,800 MBq (900 MBq at rest and 900 MBq at exercise) of technetium (99mTc) sestamibi for a two-day protocol for an adult weighing 70 kg is about 15.2 mSv.

For this administered activity of 1,800 MBq the typical radiation dose to the target organ heart is 12.2 mGy and the typical radiation doses to the critical organs gall bladder, kidneys and upper large intestine are 64.8, 55.8 and 44.1 mGy, respectively.

…

Scinti-mammography

The effective dose resulting from the administration of a maximal recommended activity of 1,000 MBq of technetium (99mTc) sestamibi for an adult weighing 70 kg is about 9 mSv.

For an administered activity of 1,000 MBq the typical radiation dose to the target organ breast is 3.8 mGy and the typical radiation doses to the critical organs gall bladder, kidneys and upper large intestine are 39, 36 and 27 mGy, respectively.

Parathyroid imaging

The effective dose resulting from the administration of a maximal recommended activity of 700 MBq of technetium (99mTc) sestamibi for an adult weighing 70 kg is about 6.3 mSv.

For an administered activity of 700 MBq the typical radiation dose to the target organ thyroid is 3.7 mGy and the typical radiation doses to the critical organs gall bladder, kidneys and upper large intestine are 27.3, 25.2 and 18.9 mGy, respectively.

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12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Withdrawals should be performed under aseptic conditions. The vials must not be opened before disinfecting the stopper, the solution should be withdrawn via the stopper using a single dose syringe fitted with suitable protective shielding and a disposable sterile needle or using an authorised automated application system.

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העלון המאושר נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות www.health.gov.il וניתן לקבלו מודפס על ידי פנייה לבעל הרישום, איזוטופיה מולקיולר אימג'ינג, טלפון: 03-9130314.

בברכה,
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