General Recommendations for Radiopharmacy

The individual monographs of this Chapter are structured as follows:

1. Indications
2. Preparation
3. Quality control
4. Interactions, contraindications & adverse reactions
5. Biodistribution & pharmacokinetics
6. Stability
7. Literature

1. Indications

The most important indications, as described in the summary of product characteristics (SmPC), are set out. If there is no SmPC available, the indications from literature apply and the application as described in the Chapters with diagnostic methods.

2. Preparation

The preparation paragraph describes the synthesis/preparation. If an SmPC is available, reference is made to the SmPC.

3. Quality Control

The quality control paragraph deals with quality control of the radiopharmaceutical. If an SmPC is available, reference is made to the SmPC.

4. Interactions, contraindications and adverse reactions

Interaction - Interaction refers to a change in the extent of the intended operation as a result of simultaneous use of medication and/or an illness. This may produce a significant change in the pharmacokinetics and distribution of radiopharmaceuticals. This paragraph deals with the most important interactions, using the SmPC, the Informatorium Medicamentorum and the reference work 'Radiofarmaca Medicatiebewaking'.
Contraindications - Rapidly growing tissues suffer more damage from ionising radiation. In children the risks must be weighed particularly carefully against the anticipated information from the investigation.
Adverse reactions - It is possible to distinguish between adverse reactions caused by the radiation load from the ionising radiation and those due to other properties of the radiopharmaceutical. For details about the dosimetry see part V pag.751
A number of publications, including Sampson (1993) and Hesslewood (1997), demonstrate that the adverse reactions of radiopharmaceuticals are relatively seldom. Hesslewood reported a prevalence of 11 per 100.000 administrations, which is a factor 1000 less than for contrast agents and medicinal products. The frequency at which adverse reactions occur is highest for administering albumin and colloidal preparations (frequency of 1-10 per 1000 administrations). Adverse reactions can also occur due to a

poor radiochemical purity (distribution over organs other than the intended organs) and due to poor radionuclide purity (higher than inevitable radiation load).
Reports from the Task Group on Radiopharmaceuticals of the European Association of Nuclear Medicine demonstrate that adverse reactions of radiopharmaceuticals are generally of a minor nature. The symptoms can be categorized in allergic, vasovagal, local and other reactions.
Allergic reactions have been reported repeatedly for labelled leucocytes. In many cases plasma-replacement agents (dextrans, hydroxyethyl starch) are used to promote the erythrocyte sedimentation. It is probable that such plasma replacement agents are responsible for the allergic reactions. For details about the reported adverse reactions, please refer to literature, the reports of the EANM, that are published annually in the European Journal of Nuclear Medicine and Molecular Imaging, and to individual monographs. They note the adverse reactions of the radiopharmaceutical or one of the following two statements:
Not observed to date: to date the manufacturer is not aware of any reported adverse reactions.
No details: details are not known.

In the case of suspected adverse reactions caused by administering a radiopharmaceutical, please report this to the company and to:
Stichting LAREB
Antwoordnummer 10670
5200 WB 's-Hertogenbosch
www.lareb.nl
The Task Group on Radiopharmaceuticals of the European Association of Nuclear Medicine

5. Biodistribution and pharmacokinetics
The Chapter biodistribution and pharmacokinetics describes the normal distribution and pharmacokinetic parameters of the radiopharmaceutical, information comes from literature and if available from the SmPC. Abnormal distribution, distribution over organs other than the intended organs may be caused by the patient's pathology or by the patient's medication (please refer also to interaction).

6. Stability
The Chapter stability deals with information about the shelf-life. Generally speaking radiopharmaceuticals are prepared or prepared for administration on the day of administration. Stability is therefore often limited to a few hours.

Miscellaneous
Child doses: The doses for children are preferably in function of body weight. It is not recommended to administer less than the minimum dose, as this produces a poor quality investigation. The minimum dose is generally noted in the product information. The European Association of Nuclear Medicine (EANM) has issued guidelines for the nuclear medical application in children. For more information about the dose of radiopharmaceuticals for children see part V pag.751.

Pregnancy and lactation

The risk of applying ionising radiation to pregnant women must be weighed up extremely carefully against the expected benefits of the information from the investigation. Radiopharmaceuticals often enter the breast milk. It may be necessary to stop breastfeeding temporarily. Iodides are concentrated selectively in breast milk, which means the concentration in breast milk may be approximately 40x the concentration in the mother's plasma. For the technetium compounds, the excretion of sodium pertechnetate ^{99m}Tc is the highest in breast milk.

Breastfeeding may generally be resumed when the level in the breast milk does not produce a higher radiation dose than 1 mSv. Part V, Radiation Dosimetry in Nuclear Medicine contains a table with the periods when breastfeeding must be stopped, assuming a dose equivalent for the child of maximum 0,5 mSv.

7. Literature

- British Institute of Radiology; British Nuclear Medicine Society; UK Radiopharmacy Group. Guidelines for the provision of radiopharmacy support to nuclear medicine. Nucl Med Commun 2003;24:429-33.
- EANM. Draft guidelines for radiopharmacy. Eur J Nucl Med Mol Imaging 2003;30:63-72.
- European system for reporting of adverse reactions to and defects in radiopharmaceuticals. Annual report: 1997. Eur J Nucl Med 1998;25:45-50.
- European system for reporting of adverse reactions to and defects in radiopharmaceuticals. Annual report: 1998. Eur J Nucl Med 1999;26:33-8.
- Hesslewood S.R., Keeling D.H. Frequency of adverse reactions to radiopharmaceuticals in Europe. Eur J Nucl Med 1997;24:1179-82.
- Hesslewood SR. European system for reporting adverse reactions to and defects in radiopharmaceuticals: annual report 1999. Eur J Nucl Med 2001;28:2-8.
- Hesslewood SE. European system for reporting adverse reactions to and defects in radiopharmaceuticals: annual report 2000. Eur J Nucl Med Mol Imaging 2002;29:13-9.
- Hesslewood S. European system for reporting adverse reactions to and defects in radiopharmaceuticals: annual report 2001. Eur J Nucl Med Mol Imaging 2003;30:87-147.
- Informatorium Medicamentorum, 's Gravenhage. KNMP.
- Martens HJM, van Dam JG, Hollander JMR, et al. Kwaliteitscontrole van radiofarmaca. Nucl Geneeskd Bull 1989;11:81-8.
- Product-informaties (SmPC) van GE Healthcare, CIS bio international, Cygne, Du Pont, IRE, Isotopen Dienst Benelux, Mallinckrodt Medical, Sorin (Solco).
- Radiopharmacy and Quality Control Pharmacists Subcommittees of the Regional Pharmaceutical officers Committee. Nucl Med Comm 1994;15:886-9.
- Richtlijn Radionucliden Laboratoria 1994, Ministeries van VROM, Sociale Zaken en VWS.
- Richtlijn GMP-ziekenhuisfarmacie, NVZA/KNMP.
- Richtlijn GMP-ziekenhuisfarmacie, hoofdstuk Z3 Aseptische handelingen, NVZA.
- Sampson CB. Adverse reactions and drug interactions with radiopharmaceuticals. Drug Safety 1993;8:280-94.