Australian Government
Department of Health
Therapeutic Goods Administration

Guidance 20: Radiopharmaceuticals

Previously ARGPM Appendix 20: Supplementary guidelines for radiopharmaceuticals

Version 1.0, July 2013

TGA Health Safety Regulation

Check the TGA website for up-to-date guidance

The most up-to-date information about prescription medicine registration in Australia is on the TGA website <http://www.tga.gov.au>. Now that guidance is presented in a series of web pages, updates are likely to be more common than in the past. If you subscribe to the TGA guidelines email alert service, you will be emailed every time the TGA web guidance is updated.

TGA web pages are dated, and can be printed.

A PDF format is being provided during the transition between the former version of the ARGPM (Australian Regulatory Guidelines for Prescription Medicines) and the new web format. Please note that information in the PDF should not be relied upon to be up-to-date.

About the Therapeutic Goods Administration (TGA)

- The Therapeutic Goods Administration (TGA) is part of the Australian Government Department of Health, and is responsible for regulating medicines and medical devices.
- The TGA administers the *Therapeutic Goods Act 1989* (the Act), applying a risk management approach designed to ensure therapeutic goods supplied in Australia meet acceptable standards of quality, safety and efficacy (performance), when necessary.
- The work of the TGA is based on applying scientific and clinical expertise to decision-making, to ensure that the benefits to consumers outweigh any risks associated with the use of medicines and medical devices.
- The TGA relies on the public, healthcare professionals and industry to report problems with medicines or medical devices. TGA investigates reports received by it to determine any necessary regulatory action.
- To report a problem with a medicine or medical device, please see the information on the TGA website <http://www.tga.gov.au>.

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	Office of Medicines Authorisation	1/07/2013

Contents

Introduction

This information is intended for sponsors applying to the TGA to enter a radiopharmaceutical in the Australian Register of Therapeutic Goods (ARTG).

20.1 What are radiopharmaceuticals

Radiopharmaceuticals contain a radioactive component or are intended to be combined with a radioactive component before use. They comprise of:

- ready-for-use radiopharmaceuticals, including Positron Emission Tomography (PET) radiopharmaceuticals
- nonradioactive components (kits and chemical precursors, including those for PET) for combination with a radioactive component (e.g. eluate from a radionuclide generator or a cyclotron-produced radionuclide)
- radionuclide generators
- radionuclide precursors used for radiolabelling other substances before administration.

Related information and guidance

- Guideline for radiopharmaceuticals (EMEA/CHMP/QWP/306970/2007)
- Guideline on clinical evaluation of diagnostic agents (CPMP/EWP/1119/98 rev. 1)
- Radiopharmaceuticals based on monoclonal antibodies (pp. 185–194 of Rules 1998 (3A)–3AQ21a)
- Concept paper on the revision of the guideline on radiopharmaceuticals based on monoclonal antibodies (EMEA/CHMP/CVMP/362268/2009)
- Note for guidance on specifications: test procedures and acceptance criteria for new drug substances and new drug products: chemical substances (CPMP/ICH/367/96 Corr)
  - Specifications for radiopharmaceuticals detailed in this note apply at all times up to product expiry. The radioactive content, or radioactive concentration, should be stated, along with the calibration date and time
  - In general, it will not be practical to apply a release specification of ±5per cent for the radioactive component of ready-to-use radiopharmaceuticals.

20.2 Product information for radiopharmaceuticals

Radiopharmaceuticals require a product information (PI) document. All changes to the PI must be consistent with the Minor variations to registered prescription medicines: chemical entities.

20.2.1 Units and calculations

Radioactivity should be expressed in SI units (becquerels).

Radiation dosimetry information should be based on the recommendations of the International Commission on Radiological Protection Publication 103 (ICRP 103).

The radiation doses provided in the radiation dosimetry table in the PI should be those delivered by administering the maximum recommended quantity of the radiopharmaceutical:

- Absorbed doses should be expressed in milligrays (mGy).
- The effective dose should be calculated using the weighting factors given by ICRP 103, and expressed in millisieverts (mSv).
- Where a radionuclidic impurity may make a significant contribution to the radiation dose, the additional contribution to the effective dose that results from the maximum allowable concentration of this impurity should be stated.
- If data based on ICRP 103 are not available at the time of application, radiation dosimetry estimates in the submission should be based on clinical trial information. When ICRP-based data become available, these should replace the clinical trial information in the PI.

20.2.2 Advice to users regarding disposal

Sponsors need to include a statement in the PI about waste disposal.

It is recommended that users are advised to observe the *Code of practice for the disposal of radioactive wastes by the user*. This code is published on the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) website as Radiation Health Series (RHS) No. 13.

20.3 Cyclotron-produced radiochemicals

Standard operating procedures (SOPs), together with an indication of how they have been validated, need to be included in an application to enter the medicine in the ARTG.

SOPs are required for:

- target preparation
- isotopic purity of target materials
- irradiation and processing.

It is not necessary to provide updated versions of these SOPs after the medicine has been entered in the ARTG.

Any changes to the method of manufacture are subject to the general and specific conditions outlined in Part 4 of Minor variations to registered prescription medicines: chemical entities.

20.4 Products based on monoclonal antibodies

Sponsors of new monoclonal antibody products that are intended to be labelled with ^{99m}Tc or other radionuclides do not need to demonstrate that their product is compatible with all sources of the radionuclide available in Australia.

It is sufficient for regulatory purposes for the sponsor to:

- demonstrate compatibility with one approved source of the radionuclide available in Australia (if possible, the market leader)

- mention the compatible brand in the PI
- mention in the PI if the product is incompatible with the market leader in Australia.

Any additional compatibility claims in the PI should be supported by data.

20.4.1 Restrictions on time intervals

Sponsors should state in the PI any restrictions on the time interval since a $^{99}Mo/^{99m}Tc$ generator has been previously eluted, including time after which sodium pertechnetate [^{99m}Tc] should not be used for labelling.

Related information and guidance

There are European Union guidelines specific to radiopharmaceuticals based on monoclonal antibodies.

All changes to the PI must be consistent with the information in the TGA guidance Minor variations to registered prescription medicines: biological medicines.

Therapeutic Goods Administration

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