swissmedic

Date: 3 July 2025
Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

Radelumin

International non-proprietary name: [^{18}F]PSMA-1007
Pharmaceutical form: solution for injection
Dosage strength(s): 200 - 4500 MBq/ml
Route(s) of administration: intravenous
Marketing authorisation holder: Posimed Radiopharm AG
Marketing authorisation no.: 67400
Decision and decision date: approved on 11 June 2024

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

Table of contents

1 Terms, Definitions, Abbreviations

1L	First-line
2L	Second-line
ADA	Anti-drug antibody
ADME	Absorption, distribution, metabolism, elimination
AE	Adverse event
ALT	Alanine aminotransferase
ASCO	American Society of Clinical Oncology
AST	Aspartate aminotransferase
API	Active pharmaceutical ingredient
ATC	Anatomical Therapeutic Chemical Classification System
AUC	Area under the plasma concentration-time curve
$AUC_{0\text{-}24h}$	Area under the plasma concentration-time curve for the 24-hour dosing interval
BCP	Biochemical persistence
BCR	Biochemical recurrence
CI	Confidence interval
C_{max}	Maximum observed plasma/serum concentration of drug
CT	Computed tomography
CYP	Cytochrome P450
DDI	Drug-drug interaction
DOR	Duration of response
DMSO	Dimethyl sulfoxide
EAU	European Association of Urology
ECOG	Eastern Cooperative Oncology Group
EMA	European Medicines Agency
EOS	End of synthesis
ERA	Environmental risk assessment
ESMO	European Society for Medical Oncology
FDA	Food and Drug Administration (USA)
FCH	[^{18}F]fluorocholine
GLP	Good Laboratory Practice
HPLC	High-performance liquid chromatography
IC/EC_{50}	Half-maximal inhibitory/effective concentration
ICH	International Council for Harmonisation
Ig	Immunoglobulin
INN	International non-proprietary name
ITT	Intention-to-treat
LoQ	List of Questions
MAH	Marketing Authorisation Holder
Max	Maximum
Min	Minimum
MRHD	Maximum recommended human dose
MRI	Magnetic resonance imaging
MTD	Maximum tolerated dose
N/A	Not applicable
NCCN	National Comprehensive Cancer Network
NO(A)EL	No observed (adverse) effect level
ORR	Objective response rate
OS	Overall survival
PBPK	Physiology-based pharmacokinetics

PD	Pharmacodynamics
PET	Positron emission tomography
PET/CT	Positron emission tomography / computed tomography
PFS	Progression-free survival
PIP	Paediatric Investigation Plan (EMA)
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
PSA	Prostate-specific antigen
PSMA	Prostate-specific membrane antigen
PSP	Pediatric study plan (US FDA)
RMP	Risk management plan
SAE	Serious adverse event
SwissPAR	Swiss Public Assessment Report
TEAE	Treatment-emergent adverse event
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)
TRUS	Transrectal ultrasound

2 Background information on the procedure

2.1 Applicant's request(s)

New active substance status

The applicant requested new active substance status for [^{18}F]PSMA-1007 in the above-mentioned medicinal product.

Diagnostic or therapeutic radiopharmaceutical

This application for a diagnostic radiopharmaceutical has been reviewed by Swissmedic and the Expert Commission for Radiopharmaceuticals.

2.2 Indication and dosage

2.2.1 Requested indication

This medicinal product is intended for diagnostic purposes only.
Radelumin is indicated for use with positron emission tomography (PET).
A PET scan in a patient is indicated when a biological recurrence of a prostate cancer that was originally treated with radical therapy reveals a new increase in serum prostate specific antigen (PSA) concentration.

2.2.2 Approved indication

Radelumin ([^{18}F]PSMA-1007) is a radioactive diagnostic agent indicated for the imaging of prostate-specific membrane antigen (PSMA)-positive lesions by positron emission tomography (PET) in adult patients with prostate cancer.

2.2.3 Requested dosage

Summary of the requested standard dosage:

The standard dosage for adults is 3 - 4 MBq/kg body weight, with a maximum dose not to be exceeded of 450 MBq.
The medicinal product has not been tested in children or adolescents.
No dose adjustment is necessary for elderly persons (> 65 years) or for persons with renal dysfunction and/or hepatic impairment.
A table of radiation exposures for the organs is available.

2.2.4 Approved dosage

(see appendix)

2.3 Regulatory history (milestones)

Application	5 December 2022
Formal objection	20 December 2022
Response to formal objection	24 January 2023
Formal control completed	20 February 2023
List of Questions (LoQ)	13 July 2023

Response to LoQ	9 October 2023
Preliminary decision	12 January 2024
Response to preliminary decision	2 April 2024
Final decision	11 June 2024
Decision	approval

3 Medical context

Diagnostic work-up of prostate cancer includes PSA testing, digital rectal palpation, transrectal ultrasound (TRUS), prostate biopsy, and histopathological examination. Additionally, further imaging techniques such as magnetic resonance imaging (MRI), bone scintigraphy, computed tomography (CT), and positron emission tomography (PET)/CT with different PET tracers are used.
Before March 2023, [^{18}F]fluorocholine was the only radioactive PET diagnostic agent authorised for the indication of prostate cancer in Switzerland.

Given the limitations of the most widely investigated PET tracers, targeting PSMA with molecular imaging agents has been increasingly investigated. PSMA is a transmembrane protein with an extracellular binding site. PSMA tissue expression is high on the cell surface of prostatic tissues affected by prostate cancer. However, despite the name, PSMA is not specific to prostate tissue. The PSMA protein can be found in low concentrations in many other organs[1]. Most adenocarcinomas of the prostate gland express high levels of PSMA in primary and metastatic lesions[2].
Since March 2023, [^{68}Ga]PSMA-11 has been authorised as a PSMA-specific PET tracer for the detection of PSMA-positive lesions in patients with prostate cancer in Switzerland.
Currently, several guidelines highlight the superior accuracy of PSMA-ligand PET/CT for the staging of primary disease in prostate cancer (European Association of Urology [EAU], European Society for Medical Oncology [ESMO], National Comprehensive Cancer Network [NCCN]), or consider additional value in this setting (American Society of Clinical Oncology [ASCO]). PSMA-ligand PET/CT evaluation of biochemical recurrence (BCR) or biochemical persistence (BCP) of prostate cancer is recommended in documents produced by the EAU, ASCO, and NCCN.

[1] Fendler WP et al., PSMA PET/CT: joint EANM procedure guideline/SNMMI procedure standard for prostate cancer imaging 2.0, Eur J Nucl Med Mol Imaging. 2023 Apr;50(5):1466-1486
[2] Mannweiler S et al., Heterogeneity of prostate-specific membrane antigen (PSMA) expression in prostate carcinoma with distant metastasis. Pathol Oncol Res. 2009;15:167–72; Bostwick DG et al. Prostate-specific membrane antigen expression in prostatic intraepithelial neoplasia and adenocarcinoma: a study of 184 cases. Cancer. 1998;82:2256–61

4 Quality aspects

4.1 Drug substance

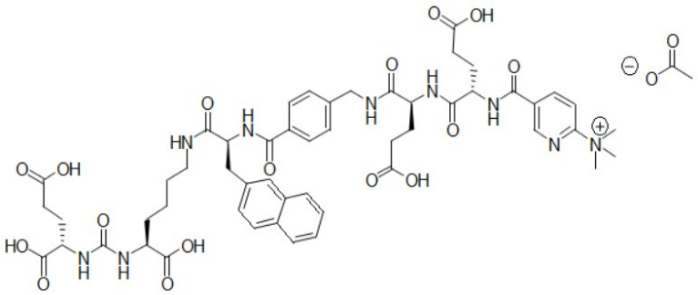
Precursor (non-radioactive): PSMA-1007

Chemical name: 5-((S)-4-carboxy-1-((S)-4-carboxy-1-(4-((S)-1-((S)-5-carboxy-5-(3-((S)-1,3-dicarboxypropyl)ureido)pentylamino)-3-(naphthalen-2-yl)-1-oxopropan-2-ylcarbamoyl)benzylamino)-1-oxobutan-2-ylamino)-1-oxobutan-2-ylcarbamoyl)-*N*,*N*,*N*-trimethylpyridin-2-aminium acetate

Molecular formula: $C_{52}H_{64}N_9O_{16} \cdot x\ CH_3COOH$

Molecular mass: 1071.12 g/mol

Molecular structure:



Physicochemical properties:
White to off-white solid, slightly soluble in water and soluble in dimethyl sulfoxide.

Synthesis:
PSMA-1007 precursor is obtained by adopting solid-phase synthesis starting from 2-CTC resin. After coupling the amino acid derivatives and, finally, the building block with the quaternary amine moiety to the resin, the crude product is cleaved from the solid support and deprotected, followed purification by preparative HPLC. Salt exchange is then performed by preparative HPLC using a mobile phase containing acetic acid, and PSMA-1007 precursor is finally isolated by concentration and lyophilisation. Pre-defined amounts of the solid bulk material are transferred into the final vials and flushed with argon before stoppers and caps are placed on the vials and crimped.

Specification:
In order to ensure a consistent quality of PSMA-1007 precursor, the specifications include all relevant test parameters as recommended by the relevant ICH guidelines. The analytical methods are adequately described and the non-compendial methods are fully validated in accordance with the ICH guidelines.

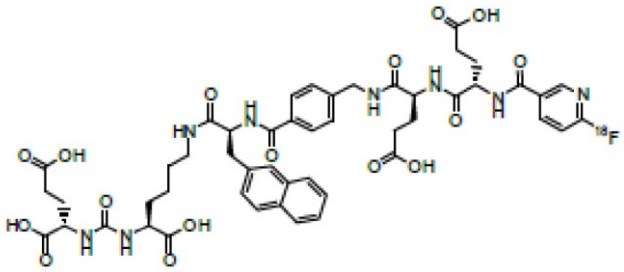
Stability:
Appropriate stability data have been presented. Based on the results, a satisfactory shelf-life has been established when stored at −20 °C ± 5°C in the hydrolytic type I glass vials, closed by a chlorobutyl rubber stopper with a FluroTec™ barrier film and capped with a tear-off crimp.

Drug Substance (radioactive): [^{18}F]PSMA-1007

Chemical name: (3S,10S,14S)-1-(4-(((S)-4-carboxy-2((S)-4-carboxy-2-(6[^{18}F]fluoronicotinamido)butanamido)butanamido)methyl)-phenyl)-3-(naphthalen-2-ylmethyl) 1,4,12-trioxo-2,5,11,13-tetraazahexadecane-10,14,16-tricarboxylic acid

Molecular formula: $C_{49}H_{55}{}^{18}FN_8O_{16}$

Molecular mass: 1030.01 g/mol
Molecular structure:



Physicochemical properties:
[^{18}F]PSMA-1007 is a radioactive drug substance with a half-life of 110 minutes (rounded). The decay mode is β^+ (96.7%) and electron capture (3.3%).

Synthesis:
The Drug Substance is manufactured in a radiosynthesis from non-radioactive precursor material, PSMA-1007 precursor, and the 18F-fluoride-radionuclide (generated by means of an accelerated cyclotron proton beam via the nuclear reaction: ^{18}O(p,n)^{18}F). The radiosynthesis of [^{18}F]PSMA-1007 is a nucleophilic aromatic substitution reaction performed by heating the precursor in DMSO in the presence of a base. The reaction is carried out in an automated radiosynthesis module and takes place in a disposable cassette with reagent kits. The radiolabelling reaction is stopped by diluting the reaction mixture with an ethanol solution and then by loading it on a silica C18-cation cartridge. The resulting trapped Drug Substance is rinsed with a washing solution and then eluted with an ethanolic solution, diluted with a PBS-sodium ascorbate solution and sterilised via a 0.22 μm sterile filter. Next, the product is formulated by adding phosphate-buffered saline through the sterile filter.

Specification and Stability: see next paragraph.

4.2 Drug product

Description and composition:
Radelumin is a radiopharmaceutical used for PET diagnostic imaging. It contains 18F-fluorine and is administered intravenously. It is provided as a sterile, clear and colourless solution in a multi-dose vial. Following the synthesis process, the bulk product solution is filled into a single container with approximately 18 ml. This bulk solution (200 – 4500 MBq/ml) can be diluted with sterile isotonic sodium chloride solution (0.9%) to reach a consistent volume of 25 ± 1 ml at the activity reference time (ART), defined as the end of synthesis (EOS). It includes various components such as [^{18}F]PSMA-1007 as active substance, the excipients of disodium hydrogen phosphate, potassium dihydrogen phosphate, sodium chloride, potassium chloride, water for Injections, ethanol, and sodium ascorbate, and the diluent sterile isotonic sodium chloride solution. The maximum injectable volume is 10 ml.

Pharmaceutical development:
The drug product Radelumin underwent improvements in its composition. The formulation aims to achieve product stabilisation and minimise radiolysis, ensuring the drug's effectiveness and stability over time. Several experiments for stabilisation of the product with sodium ascorbate were carried out. In the development process, the formulation of the drug substance was examined with both 0.9% NaCl and PBS buffer. The formulation using PBS buffer demonstrated a more stable pH for the resulting Radelumin solution, leading to the selection of PBS and ethanol as solvents for the Drug Product formulation. Ethanol and sodium ascorbate serve as scavenger and stabiliser.

Manufacture:
All development steps in the manufacturing process have been described. The necessary information on the batch formula is provided.

Specification:
Radelumin solution for injection has a radioactivity concentration of [^{18}F]PSMA-1007 of 200-4500 MBq/mL at EOS. Release specifications for the Radelumin solution for injection include appearance of the solution, radioactivity concentration, identity tests (such as gamma emission energy, half-life, and retention time of [^{18}F]PSMA-1007), microbiological tests (including sterility, bacterial endotoxins), purity tests (radiochemical purity, radionuclide purity, chemical purity, tetrabutylammonium carbonate, ethanol, dimethyl sulfoxide, sodium ascorbate) and pH value. These criteria ensure the quality and compliance of the Radelumin solution for injection.

Container Closure System:
Radelumin solution is supplied in a pyrogen-free sterile borosilicate glass vial closed with a rubber stopper and sealed with a flip-off crimp cap and with a volume 15 ml or 20 ml, intended for multi-dose use. The maximum injectable volume is 10 ml.

Stability:
Stability studies have been performed, demonstrating that the composition of the Radelumin solution for injection does not undergo significant changes in radiochemical identity and purity (including radiochemical impurities), appearance, pH, stabiliser effectiveness and chemical purity. Undiluted and diluted batches were tested. Based on the obtained results, it has been determined that the Radelumin solution for injection has a recommended shelf-life of 10 hours after the EOS. All results obtained during the test period, conducted at a temperature of 30°C and with filling volumes of 0.3 ml and 15 ml, met the specified shelf-life requirements.

4.3 Quality conclusions

Satisfactory and consistent quality of the drug substance and drug product has been demonstrated.

5 Nonclinical aspects

5.1 Pharmacology

[^{19}F]PSMA-1007 bound with high affinity to the prostate-specific membrane antigen in a competitive binding assay in the nanomolar range of 4.2 and 6.7 nM in two independent experiments. [^{18}F]PSMA-1007 had a high internalisation rate of 68.9% *in vitro*. This high rate of internalisation, in addition to the high binding affinity, supports its use as a radioimaging ligand. [^{18}F]PSMA-1007 was taken up rapidly by tumour cells in nu/nu mice bearing lymph node carcinoma of the prostate (LNCaP) tumours, reaching a maximum within a few minutes and remained stable over time (140 min). The absolute uptake of [^{18}F]PSMA-1007 in PSMA-positive tumours was significantly higher than that of comparable radioimaging agents.
No secondary off-target activity of [^{18}F]PSMA-1007 is expected. Due to the low radiation intensity, a direct cytotoxic effect induced by the radiation of [^{18}F]PSMA-1007 is unlikely, as both, the type of radiation (positron emission) and the radiation dose are optimised for imaging purposes.
No dedicated safety pharmacology studies have been conducted. In a GLP-compliant extended single dose toxicity study, rats did not show any adverse clinical signs when treated with intravenous injections of up to 1430 µg/kg [^{19}F]PSMA-1007. This corresponded to 1000-fold exposure of the highest intended human mass dose (100 µg single dose, in a patient with body weight of 70 kg). [^{18}F]PSMA-1007 at 10^{-8} to 10^{-4} M had no effect on the hERG channel.

5.2 Pharmacokinetics

After intravenous administration, [^{18}F]PSMA-1007 exposure declined rapidly within 10 minutes in mice. Concomitantly, tissue concentrations were highest at 10 minutes post-injection. Plasma concentration reached about 5% of the injected dose after 60 minutes.
[^{18}F]PSMA-1007 was highly bound to serum albumin. It distributed to the whole body where it rapidly accumulated in cells with high PSMA expression, i.e. tumour cells and kidneys. [^{18}F]PSMA-1007 was highly stable in human plasma with no degradation observed over a period of 4 h at 37°C. *In vivo*, only very low levels of metabolites were observed, amounting to 2% of the total activity in the urine and 4% in the kidneys at 1 h post injection. Urine was the major route of elimination in mice whilst the hepatobiliary clearance was the main elimination route in humans.

5.3 Toxicology

Toxicity and the toxicokinetic profile of PSMA-1007 was investigated in a GLP extended single-dose toxicity study in rats with intravenous administration up to 1430 µg/kg body weight. PSMA-1007 treatment was well tolerated and no toxicological effects were observed. No repeat-dose toxicity studies have been conducted in accordance with the ICH M3 guideline on microdose trials. PSMA-1007 was not genotoxic *in vitro*. No carcinogenicity or reproductive toxicity studies were conducted.

5.4 Nonclinical conclusions

The toxicological profile of [^{18}F]PSMA-1007 is considered to be sufficiently characterised. The submitted nonclinical data support its use as a radiodiagnostic agent. The relevant information has been included in the Information for healthcare professionals, although some revision is needed.

6 Clinical aspects

6.1 Clinical pharmacology

A summary of the clinical pharmacology is provided in the Information for healthcare professionals in the appendix of this report.

6.2 Dose finding and dose recommendation

No particular dose-finding studies were conducted by the Applicant or were reported in the literature either.
The currently available published studies demonstrated that a sufficient signal intensity could be reached with the application of a total radioactivity dose between approximately 100 MBq and 450 MBq.
The proposed dose of [^{18}F]-PSMA-1007 solution for injection is 3-4 MBq/kg bodyweight (210-280 MBq for a 70kg patient), with a maximum dose of 450 MBq. This is within the reported radioactivity doses reported in the literature on comparable human studies.

6.3 Efficacy

The main efficacy data were derived from the controlled, randomised, phase 3, pivotal study ABX-CT-301.
This study investigated [^{18}F]PSMA-1007 vs [^{18}F]fluorocholine (FCH) PET in patients with biochemical recurrence (BCR) after previous definitive treatment of localised prostate cancer. The comparator arm was considered acceptable given that FCH was the only PET tracer specifically authorised for prostate cancer in Switzerland at that time.
The study was initiated in March 2019 and completed in October 2020 at six study sites in France. A total of 200 patients were enrolled, and 195 of them received at least one study drug.
The primary objective of the study was to show superiority of [^{18}F]PSMA-1007 vs FCH PET based on the patient-based detection rate of all lesions compared with an expert panel assessment (standard of truth) as determined in an independent image read by three readers blinded to clinical data and tracer. The expert panel, consisting of a urologist, a radiologist, and a nuclear physician, had access to all imaging assessments from the clinical side (except the study PET examinations) together with clinical information (medical history, concomitant medications, procedures, results).
The detection rate was tested using a z-test based on generalised estimation equations (GEEs) at a one-sided level of significance of 2.5% each. Secondary endpoints included sensitivity, specificity, accuracy, positive and negative predictive value of [^{18}F]PSMA-1007 and FCH, which were analysed only descriptively. No target value was defined prospectively for specificity and sensitivity, and no superiority hypothesis was defined for the respective differences.

Patients with BCR after initial radical treatment were randomised to either [^{18}F]PSMA-1007 PET followed by FCH PET or to FCH PET followed by [^{18}F]PSMA-1007. The second PET examination was performed between 24 hours and 240 hours (10 days) after the first PET. Safety follow-up was 24h after the second PET CT. Patients were to be followed for 6 months for diagnostic and therapeutic procedures.
[^{18}F]PSMA-1007 was administered as a single intravenous injection of 3-4 MBq/kg (corresponding to a dose of 210-280 MBq for a 70 kg adult). FCH was similarly administered with an activity of 200-400 MBq.

Of the 195 patients with at least one dose of study drug, 190 underwent PET imaging with both study drugs.

Median age was 69 years. Most of the patients had a Gleason score of 7 (124/195). The median PSA level was slightly lower in the “FCH first” group (1.27 ng/ml vs. 2.05 ng/ml).

The sensitivity in detecting prostate cancer lesions was 77% (95% 69-84%) with [^{18}F]PSMA-1007 and 57% (95%CI 48-67%) with FCH. The positive predictive values were similar, at 0.95 and 0.97 for [^{18}F]PSMA-1007 and FCH, respectively.
The proportion of patients with correct detection rate of prostate cancer lesions was analysed descriptively according to baseline PSA level (categories <0.5 ng/ml, 0.5 < 1.0 ng/ml; ≥1.0 ng/ml < 2.0 ng/ml, ≥ 2.0 ng/ml). For both study drugs, the proportion of patients for whom prostate cancer recurrence was correctly identified was higher when the category with higher PSA values was assessed, but for all subgroups examined, more patients were correctly identified using [^{18}F]PSMA-1007 than with FCH.

6.4 Safety

The safety population of study ABX-CT-301 included 195 patients who received at least one of both radiotracers. Median injected activity in study ABX-CT-301 was 322.5 MBq (range 134.1-461.5).
Adverse events (AE) as reported in the safety follow-up period (24h after the second PET examination) were observed in 2.0% of patients with [^{18}F]PSMA-1007 injected first and in 0.5% of patients with FCH injected first. The AEs by preferred term were toothache, diarrhoea, chest discomfort and arterial hypertension in the [^{18}F]PSMA-1007 first group (in n=1 patient each) and shoulder pain in the FCH first group.
No serious adverse events or events of death occurred during the safety follow-up period.

In addition, the Applicant provided an overview of literature reports on the clinical use of [^{18}F]PSMA-1007. Safety information was available for 198 subjects (195 patients, 3 healthy volunteers) in a total of 1093 subjects. No adverse events or other drug-related symptoms were reported.

6.5 Final clinical benefit risk assessment

Based on the efficacy and safety data provided, the benefit risk balance is considered positive for the visualisation of PSMA-positive lesions in adult patients with prostate cancer.

7 Risk management plan summary

The RMP summaries contain information on the medicinal products′ safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.

The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

8 Appendix

Approved Information for healthcare professionals

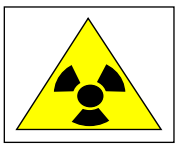
Please be aware that the following version of the Information for healthcare professionals for Radelumin was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo.ch).

Note:

The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

Radioactive pharmaceutical



Radelumin

This medicinal product is subject to additional monitoring. This enables rapid identification of new safety findings. Healthcare professionals are encouraged to report suspected new or serious adverse reactions. For information on reporting adverse reactions, see the "Adverse reactions" section.

Composition

Active ingredients

Active substance:	[18F]F-PSMA-1007
Nuclide:	[18F]Fluorine

Excipients (per ml water for injection)

Sodium chloride	6.60 mg
Sodium ascorbate	16 mg
Di-sodium-hydrogen-phosphate	0.69 mg
Potassium-dihydrogen-phosphate	0.12 mg
Potassium chloride	0.12 mg
Ethanol	≤ 10% v/v
The sodium content is	4.67 mg/mL

Specifications:	
Radionuclide purity:	[18F]Fluorine ≥ 99.9%
Radiochemical purity:	[18F]PSMA-1007 ≥ 93% (HPLC, at calibration), [18F]PSMA-1007 ≥ 91% (HPLC, at end of shelf life)
Free [18F]fluoride	≤ 5% (TLC)
PSMA-1007:	0.01 mg/ml
Other impurities (total):	≤ 0.05 mg/ml
Activity concentration:	200- 4500 MBq/ml

Dosage form and amount of active substance per unit

Radelumin is a ready-to-use radiodiagnostic agent for intravenous injection. It is suitable for multiple use.

Nuclide:	[18F]fluorine
Galenical form:	pyrogen-free injection solution; pH 4.5 - 8.5
Activity concentration:	200 - 4500 MBq/ml
Calibration time:	time of filling
Expiry date:	10 hours after calibration time

Indications/possible applications

Radelumin ([18F]PSMA-1007) is a radioactive diagnostic agent indicated for the imaging of prostate-specific membrane antigen (PSMA)-positive lesions by positron emission tomography (PET) in adult patients with prostate cancer.

Dosage/application

Radiopharmaceutical products may only be used by or under the supervision of qualified healthcare professionals who have undergone appropriate training and who know how to use and handle radionuclides safely and whose experience and training have been recognised by federally recognised government authorities authorised to issue licences for the use of radionuclides.

Usual dosage

The recommended radioactivity dose is 2-4 MBq per kg body weight depending on the exposure protocol and equipment. A maximum dose of 360 MBq should not be exceeded. The maximum injection volume is 10 ml.

Special dosing instructions

Patients with kidney dysfunction

The use of PSMA-1007 has not been studied in patients with renal impairment.
In patients with impaired kidney function, no adjustment of the injected activity compared to the recommended activity in persons with normal renal function is required, since the urinary excretion of PSMA-1007 in healthy persons is very low and hardly affects the radiation exposure.

Patients with liver dysfunction

The use of PSMA-1007 has not been investigated in patients with liver dysfunction. Due to the delayed biliary excretion, there is a prolonged non-specific distribution in the body, with possibly a worse tumour to background ratio in the accumulation, which can possibly impair the diagnostic safety. An increase in the effective dose is possible in patients with impaired liver function.

Older patients

A dose adjustment is not necessary.

Children and young people

Radelumin is not approved for use in the paediatric population. The safety and efficacy of [18F]PSMA-1007 have not been evaluated in children and adolescents under 18 years of age.

Type of application

For intravenous use
The activity of Radelumin must be measured with an activimeter immediately before injection.
The recommended maximum injection volume of Radelumin is 10 mL. The medicinal product may only be diluted with physiological saline solution.

Image acquisition

The patient should be positioned supine, if possible with arms above the head. A CT or MRI scan should be taken for attenuation correction and anatomical correlation. The PET scan should begin 90 to 120 minutes after completion of the injection. It is recommended to start the scan from the centre of the thigh and continue to the top of the skull.

Evaluation of Radelumin images
The images generated using [18F]PSMA-1007 must be analysed by a nuclear medicine specialist with an FMH title or federally recognised equivalent who is appropriately trained in the field of PET in prostate cancer.
The PET images obtained using [18F]PSMA-1007 must be interpreted visually. Tumour tissue is suspected at typical sites of prostate cancer recurrence if an accumulation of [18F]PSMA-1007 is observed at these sites compared to background activity, whereby information from the corresponding CT and/or MRI image must be included. The known physiological fixation of tracers targeting PSMA must be taken into account.
Using [18F]PSMA-1007, prostate cancer recurrences were detected in the prostate analogue, regional and distant lymph nodes, skeleton, soft tissue and visceral organs.
The significance of the quantitative/semiquantitative measurement of [18F]PSMA-1007 enrichment for the purpose of image interpretation was not assessed.

Radiation exposure

Average absorbed radiation doses for adult patients after intravenous injection of Radelumin are shown in the table below. The values were calculated from distribution data in humans using the software OLINDA/EXM (Organ Level Dose Assessment/Exponential Modelling) Version 2.1. The effective dose was calculated according to the organ assessment factors defined in the publication 103 of the International Commission on Radiological Protection (ICRP-103).

Table 1: Estimated absorbed radiation doses for prostate cancer patients receiving Radelumin

Organ	Averaged absorbed radiation dose [mGy/MBq]
brain	0,003
Eyes	0,0072
Testicles	0,0074
Osteogenic cells	0,0101
Muscles	0,0103
Whole body	0,0103
Thymus	0,0106
Red bone marrow	0,013
Rectum	0,0145
Lung	0,0147
Thyroid	0,0151
Stomach	0,0170
Upper large intestine	0,0176
Oesophagus	0,0187
Bladder	0,0212
Lower large intestine	0,0239
Heart wall	0,0259
Small intestine	0,0334
Adrenal	0,0349
Salivary glands	0,0642
Pankreas	0,0677
Spleen	0,0851
Liver	0,0883
Kidneys	0,1030
Gallbladder wall	0,1400
Effective dose [mSv/MBq] (ICRP-103)	0,0191

The effective dose resulting from the administration of the recommended activity of 280 MBq (for an adult with a body weight of 70 kg) is approximately 5.3 mSv.
The effective dose resulting from the administration of the maximum recommended activity of 360 MBq is approximately 6.9 mSv.
With an administered activity of 280 MBq, the typical radiation dose for the critical organs: gall bladder, kidneys and liver is about 39 mGy, 29 mGy and 25 mGy respectively.

Contraindications

Hypersensitivity to the active substance or to one of the excipients mentioned.

Warnings and precautions

Limitations of applicability
Interactions between newer generation anti-hormonal therapy and PSMA PET have been described in the literature and should be taken into account accordingly when analysing PSMA PET/CT (see "Interactions").

Individual benefit/risk assessment

For each patient, the radiation exposure must be justified by the expected diagnostic benefit. The administered activity should always be kept as low as possible and must not be higher than is necessary to obtain the diagnostic information.

Risk of misinterpretation
Errors can occur when interpreting PET images using [18F]PSMA-1007. The [18F]PSMA-1007 enrichment is not specific for prostate carcinoma, which is why false positive findings in other types of cancer, prostatitis and benign prostatic hyperplasia cannot be ruled out.
Other false positive results have also been described in active inflammatory processes in the lymph nodes, benign thyroid diseases, benign bone diseases, liver inflammation and in the consolidation of rib fractures.
If necessary, further investigations should be considered, such as a histopathological assessment of suspected recurrent foci.

Radiation risk
Radioactive preparations must be handled with special care and under strict radiation protection measures in order to minimise the radiation exposure of both patients and personnel. [18F]-PSMA-1007 contributes to the total long-term cumulative radiation exposure of the patient. Long-term cumulative radiation exposure is associated with an increased risk of cancer. Any use of radiopharmaceuticals on patients is the exclusive competence and responsibility of officially authorised nuclear medicine physicians. In any case, administration must be carried out in accordance with the rules of radiation protection.

After the procedure

Close contact with infants and pregnant women should be restricted for the first 12 hours after the injection.

Special warnings

This medicinal product contains up to 50 mg sodium per injection (10 mL), which corresponds to 2.5 % of the maximum daily dose of 2 g sodium recommended by the WHO for an adult. This should be taken into account for patients on a low sodium diet.
This medicinal product contains up to 800 mg ethanol per injected activity (8 % w/v). This amount in 10 mL of this medicine is equivalent to ≤ 20 mL of beer or ≤ 8 mL of wine. This must be taken into account in patients with known alcohol dependence.

Interactions

The interaction potential of radelumin has not been investigated in vitro or in clinical studies. Since radelumin is mainly eliminated via the hepatobiliary route, interactions with liver enzymes and/or drug transporters are potentially possible. The clinical significance is not known.

Pregnancy, breastfeeding

Pregnancy
Radelumin is not indicated for use in women.
No animal studies have been conducted to investigate the reproductive toxicity of [18F]-PSMA-1007.

Lactation
Radelumin is not indicated for use in women.

Fertility
No fertility studies have been conducted.

Effect on the ability to drive and operate machinery

No studies have been conducted on the effects on the ability to drive and use machines.

Undesirable effects

No adverse effects have been observed to date. The main safety data come from 190 patients (see also Clinical efficacy).

Exposure to ionising radiation is associated with the development of cancer and the possibility of hereditary damage. Since the effective dose is 6.9 mSv when the maximum recommended activity of 360 MBq radelumin is administered, these adverse effects are unlikely to occur.
As in the case of other injection preparations, allergic and anaphylactic reactions cannot be ruled out, but have not been reported to date.
The reporting of suspected adverse reactions after authorisation is of great importance. It enables continuous monitoring of the risk-benefit ratio of the medicinal product. Healthcare professionals are

requested to report any suspicion of a new or serious side effect via the online portal ElViS (Electronic Vigilance System). Information on this can be found at www.swissmedic.ch.

Overdosage

The activity must be measured before each intravenous application to determine the dosage. An overdose in the pharmacological sense is not to be expected with the quantities of substance used for diagnosis.

Treatment

Risk profile-adapted hydration can increase the clearance of the radiopharmaceutical.

Properties/effects

ATC-Code
V09IX17

Mechanism of action

Radelumin is a synthetic prostate-specific membrane antigen (PSMA peptidomimetic) that contains the building block Glu-NH-CO-NH-Lys. It binds with high affinity to the PSMA enzyme site, which is overexpressed in most prostate cancer cells and is internalised after binding. Internalisation leads to increased accumulation of radelumin in prostate cancer cells.

The nuclide fluorine-18 decays with a half-life of 109.77 minutes into stable oxygen-18 under positron emission with a maximum energy of 634 keV, followed by a positron/electron pair annihilation of 511 keV.

Pharmacodynamics

At the molar concentration corresponding to the recommended activities for diagnostic tests, [18F]PSMA-1007 does not appear to have any pharmacodynamic activity.

Clinical efficacy

At the molar concentrations corresponding to the recommended activities, radelumin does not appear to have a pharmacodynamic effect.

The main efficacy data come from 190 patients who were examined as part of the ABX-CT-301 study at six different centres in France. The patients were adult and elderly men with suspected recurrence of prostate cancer due to elevated serum PSA levels after initial curative treatment of localised prostate cancer.

The study was an active comparative study: PET/CT with [18F]PSMA-1007 (radelumin) was compared with PET/CT with fluorcholine (18F).

The PET/CT images obtained from each patient with the two radiopharmaceuticals were interpreted by blinded independent reviewers, and the observed results were compared to a composite reference standard (SOR), with the extent of disease determined by a panel of experts blinded to both PET/CT scans.

The diagnostic performance of [18F]PSMA-1007 and fluorcholine (18F) PET/CT was characterised as correct detection rates (agreement of the observed results with the standard of truth (SOT)) and is shown in Table 1.

The overall detection rate for all detectors was 77% for [18F]PSMA-1007 and 57% for fluorcholine (18F), with the difference being statistically significant. Detection rates stratified by serum PSA concentration are also shown in Table 1.
At the molar concentrations corresponding to the recommended activities, [18F]PSMA-1007 does not appear to have a pharmacodynamic effect.

Table 1: Correct detection rate of prostate cancer lesions, blinded reading with SOT as Reference, Patientenebene[18F]PSMA-1007

	N	[^{18}F]PSMA-1007 (Radelumin)	Fluorcholin (^{18}F)	Odds Ratio [^{18}F]PSMA-1007/ Fluorcholin (^{18}F)	p-value*
Overall recognition rate	179	77,0 %	56,5 %	2,61	< 0,001
Detection rate by PSA serum level					
PSA < 0,5 ng/mL	43	56,6 %	38,8 %	2,10	
0,5 <= PSA <1.0 ng/mL	25	82,7 %	42,7 %	6,88	
1 <= PSA < 2.0 ng/mL	33	80,8 %	49,5 5	4,31	
PSA<2.0 ng/mL	78	84.6 %	73,5 %0031	2,01	

*Chi-square test based on generalised estimating equations

Pharmacokinetics

Absorption

[18F]PSMA-1007 is administered intravenously.

Distribution

[18F]PSMA-1007 is distributed through the bloodstream immediately after intravenous administration. In healthy volunteers, the blood compartment contained an average of 76%, 22%, 12% and 8% of the injected activity 2 minutes, 1 hour, 2 hours and 3 hours after injection, respectively.
[18F]PSMA-1007 is preferentially taken up in prostate cancer cells compared to the surrounding normal tissues. One hour after injection, tumour lesions become visible and uptake increases up to 3 hours after injection. The mean SUVmax in prostate cancer lesions in patients with biochemical recurrence has been reported to be approximately 4-40.

Highest uptake of [18F]PSMA-1007 in non-target organs was reported for kidneys, salivary glands, lacrimal glands, liver, spleen and gall bladder up to 3 hours after injection (mean SUVmean ca.12 - 30). The activity in the brain is negligible.

Metabolism

The metabolism of [18F]PSMA-1007 has not been investigated.

Elimination

It is assumed that hepatobiliary excretion is the most important route of elimination for [18F]PSMA-1007. However, this has not been quantitatively characterised and it is not known which enzymes and drug transporters are potentially involved.

The most important excretion route is the hepatobiliary route.
In a study of 3 healthy volunteers, only minimal excretion via the urine was observed, and on average 2.4 % of the administered radioactivity was excreted within 6 hours of the injection.

Kinetics of special patient groups

Liver dysfunction

The pharmacokinetics and biodistribution in patients with impaired liver function have not been investigated.
Since the hepatobiliary route of excretion probably determines the excretion from the body, there is an increased, prolonged non-specific distribution in the body with impaired liver function.

Kidney dysfunction

The pharmacokinetics and biodistribution in patients with renal dysfunction have not been investigated.
Renal excretion is very low compared to hepatobiliary excretion.

Further information

The influence of ethnic origin or body weight on the pharmacokinetics and biodistribution of [18F]PSMA-1007 has not been investigated.

Preclinical data

Safety pharmacology
[18F]PSMA-1007 has been evaluated in single dose safety pharmacology and toxicity studies. Based on the conventional safety pharmacology and single-dose toxicity studies, the preclinical data do not indicate any particular hazard to humans.

Carcinogenicity and reproductive toxicity
No studies on mutagenic or carcinogenic potential and reproductive toxicity have been conducted with [18F]PSMA-1007.

Other information

Incompatibilities
As no compatibility studies have been carried out, Radelumin must not be mixed with other medicinal products apart from 0.9 % saline solution.

Radiation protection notice

Radioactive medicinal products may only be received, handled and administered by authorised persons in specially designated clinical areas. Handling and use are subject to the provisions of the Radiation Protection Ordinances and the corresponding authorisations in Switzerland. Contamination by radioactivity excreted by patients must be avoided.

Shelf life

Radelumin should be used within 10 hours after the end of synthesis (time of calibration), which is indicated on the container label.

Special storage information

Until the first use, the radioactive medicinal product can be stored upright at room temperature (15-25°C) in the original container and lead or tungsten pot.

Method of preparation
Radelumin is a ready-to-use injection solution. However, the injection solution can be diluted with physiological saline solution.

Legal regulations

When using radioactive substances on humans, the Radiation Protection Ordinance must be observed by law. A licence from the Federal Office of Public Health is required for handling radioactive substances. When handling radioactive substances and disposing of all radioactive waste, the safety precautions of the above-mentioned ordinance must be observed in order to avoid any unnecessary exposure of patients and staff to radiation. Unused radioactive solutions and objects contaminated with them must be stored in a decay room set up for this purpose until the activity of the radionuclide has decayed to the exemption limit.

Authorisation number

67400

Packages

Product vials with a volume of 15 ml or 20 ml are used. The activity concentrations of the injection solutions are between 200 - 4500 MBq/ml. The activity is filled according to the ordered activity in MBq ± 10 %. The calibration time (ART) is the time of filling and is indicated on the label of the outer packaging.

Sales category A.

Marketing authorisation holder

Posimed Radiopharm AG, Spitalgasse 4, 3011 Bern

Status of the information

January 2024