https://doi.org/10.30895/2312-7821-2025-13-3-247-262-tabl

Table 1. Drug profile of SomaKit TOC
Таблица 1. Характеристика препарата SomaKit TOC

Parameters *Характеристика*	**Description** *Описание*
Trade name	SomaKit TOC
International non-proprietary name	Edotreotide is a cold chemical precursor designed for radiolabelling with ^{68}Ga radionuclide allowing to obtain clinically significant radioactive substance [^{68}Ga] edotreotide used as a diagnostic radiopharmaceutical for positron emission tomography (PET)
Article 10(a), Directive 2001/83/EC, is a legal base for an application that concerns medicines with well-established use confirmed in the scientific literature. The application includes executive information, full quality parameters, preclinical and clinical data collected from the scientific literature that replaces (pre)clinical trials	
Indications	The medicine is designed for diagnostic use. After radiolabelling with gallium chloride (^{68}Ga) solution, the active substance is a peptide including eight (8) amino acids and a covalently bound chelator (DOTA). The resulting gallium edotreotide (^{68}Ga) solution is indicated for PET assessment of somatostatin receptor overexpression in adults with differentiated gastroenteropancreatic neuroendocrine tumours (GEP-NET), to assess primary tumours and metastases
Preclinical (non-clinical) aspects	
Pharmacokinetics	Literature data on edotreotide biodistribution are provided for healthy rodents and tumour models using both therapeutic and diagnostic radionuclides
Pharmacology studies	***Primary pharmacodynamics:*** literature data were found classifying *in vitro* and *in vivo* by coupling with the target tissues. ***Secondary pharmacodynamics:*** studies not performed. ***Safety pharmacology:*** data not available. ***Pharmacodynamic interactions:*** data not available
Toxicology studies	Extended toxicity study for ***single*** intravenous administration: literature data. Unlabelled edotreotide in healthy rats (2 mg/kg, maximum tolerated dose equal to 500 therapeutic doses); labelled edotreotide in rats with tumours (0.010–0.014 mg/kg). Toxicity studies not available for ***repeated*** edotreotide administration. ***Genotoxicity:*** data not available. ***Carcinogenicity:*** data not available. ***Reproductive toxicity:*** data not available. ***Toxicokinetic study:*** not performed. ***Local tolerance:*** literature data on ^{68}Ga edotreotide study in rabbits. ***Other toxicity studies:*** literature data on preclinical studies of similar precursors and preparations. Safety of a new excipient, 1,10-phenanthroline, was justified. ***Ecotoxicity / environmental risk:*** literature data were calculated for ^{68}Ga-edotreotide

The table is adapted by the authors from[30] / Таблица составлена авторами по данным[30]

[30] SomaKit TOC. International non-proprietary name: edotreotide. Assessment report. EMA/734748/2016. EMA; 2016. https://www.ema.europa.eu/en/documents/assessment-report/somakit-toc-epar-public-assessment-report_en.pdf

Table 2. Profile of LUTATHERA
Таблица 2. Характеристика препарата LUTATHERA

Parameters *Характеристика*	**Description** *Описание*
Trade name	LUTATHERA
International non-proprietary name	Lutetium (^{177}Lu) oxodotreotide
The applicant requested radiopharmaceutical Lutetium (^{177}Lu) oxodotreotide to be considered as a new active substance, since this component was not previously approved as a medicinal product in the European Union, neither was ligand-radionuclide coupling mechanism authorised within the European Union	
Indications	Progressive unresectable or metastatic well-differentiated (G1 и G2) gastroenteropancreatic neuroendocrine tumours positive to somatostatin receptors (GEP-NETs) in adults
Preclinical (non-clinical) aspects	
Pharmacokinetics	Octreotide pharmacokinetics was studied in preclinical experiments in mice and cynomolgus macaques after a single intravenous administration. ^{177}Lu-oxodotreotide: biodistribution in intact rats and rats with tumours; excretion. ^{175}Lu-oxodotreotide: binding to plasma proteins, metabolism. Data analysis on biodistribution of ^{177}Lu-DOTA peptides and free ^{177}Lu
Pharmacology studies	***Primary pharmacodynamics:*** literature data and in-house *in vitro / in vivo* studies (in rat tumour model, doses of 4 to 20 mCi/kg, 3 doses with an interval of 30 days). ***Secondary pharmacodynamics:*** the applicant did not provide any data; according to EMA expert, no additional studies of ^{177}Lu-oxodotreotide are required considering the established bioactivity targets of somatostatin analogues. ***Safety pharmacology (GLP):*** after a single intravenous administration, effect of ^{175}Lu-oxodotreotide kit was studied on hERG-channel current, blood pressure, electrocardiogram, heart rate, body temperature in dogs, and respiration in anaesthetised rats. ***Pharmacodynamic interactions:*** data not available
Toxicology studies	Toxicity for ***single*** intravenous administration of novel ^{175}Lu-oxodotreotide in rats (up to 20,455 μg/kg, maximum tolerable dose) and dogs (up to 10,000 μg/kg, maximum tolerable dose). Toxicity for ***repeated*** intravenous administration, with toxicokinetic study (GLP) of novel ^{175}Lu-oxodotreotide every two weeks: test in rats (up to 20,000 μg/kg for 42 days, NOEL 1,250 μg/kg, equal to 40 therapeutic doses) and dogs (up to 3,200 μg/kg for 43 days). ***Genotoxicity (GLP):*** ^{175}Lu-oxodotreotide (Ames test, gene mutations in murine lymphoma test). ***Carcinogenicity:*** data not available. ***Reproductive toxicity:*** data not available. ***Toxicokinetic study:*** performed using ^{175}Lu-oxodotreotide (when studying systemic toxicity). ***Local tolerance:*** data not available; when discussing preclinical results, effects at the injection site were not described. ***Other toxicity studies:*** data not available. ***Ecotoxicity / environmental risk:*** results of in-house studies are available

The table is adapted by the authors from[31] / Таблица составлена авторами по данным[31]

[31] LUTATHERA. International non-proprietary name: lutetium (^{177}Lu) oxodotreotide. Assessment report. EMA/506460/2017. EMA; 2017. https://www.ema.europa.eu/en/documents/assessment-report/lutathera-epar-public-assessment-report_en.pdf

Table 3. Profile of Locametz
Таблица 3. Характеристика препарата Locametz

Parameters *Характеристика*	**Description** *Описание*
Trade name	Locametz
International non-proprietary name	Gozetotide Gozetotide (PSMA-11) is a cold chemical precursor designed for radioactive labelling with ^{68}Ga radionuclide allowing to obtain clinically significant radioactive substance [^{68}Ga] gozetotide used as a diagnostic radiopharmaceutical for positron emission tomography
The applicant applied to register active pharmaceutical ingredient [^{68}Ga] gozetotide as a new active substance; according to the applicant, the substance is not included in medicinal products that have been authorised within the European Union	
Indications	An approved indication for Locametz after labelling with ^{68}Ga is determining prostate specific membrane antigen (PSMA)-positive foci using PET in adults with prostate cancer under preset clinical conditions
Preclinical (non-clinical) aspects	
Pharmacokinetics	Pharmacokinetic properties (absorption, distribution, metabolism, and excretion) and pharmacokinetic interactions were studied for PSMA-11
Pharmacology studies	***Primary pharmacodynamics:*** literature data and results of in-house studies. ***Secondary pharmacodynamics:*** results of in-house studies for binding with 87 targets (receptors, ion channels, enzymes, and transporters). ***Safety pharmacology:*** PSMA-11 effect on hERG-channel current was studied. Effect on central nervous system, cardiovascular and respiratory systems was studied in vivo in rats (up to 0.75 mg/kg intravenously) and pygmy hogs (up to 0.29 mg/kg intravenously). ***Pharmacodynamic interactions:*** studies not performed due to the established high specificity and selectivity of gallium gozetotide toward PSMA
Toxicology studies	Extended toxicity study for ***single*** intravenous administration (GLP) not labelled with PSMA-11 in rats at 0.67 mg/kg and 1.33 mg/kg. Toxicity studies for ***repeated*** injection of ^{68}Ga-PSMA-11 or PSMA-11 precursor not performed. ***Genotoxicity:*** studies not performed. ***Carcinogenicity:*** studies of ^{68}Ga-PSMA-11 and PSMA-11 precursor not performed. ***Reproductive toxicity:*** studies of ^{68}Ga-PSMA-11 and PSMA-11 precursor not performed. ***Toxicokinetic studies:*** performed for PSMA-11. ***Local tolerance:*** assessed in an extensive toxicity study with a single administration. ***Other toxicity studies:*** SAR analysis (structure–activity relationship) for PSMA-11 mutagenicity in silico. ***Ecotoxicity / environmental risk:*** results of in-house studies were presented

The table is adapted by the authors from[32] / Таблица составлена авторами по данным[32]

[32] Locametz. International non-proprietary name: gozetotide. Assessment report. EMA/CHMP/954737/2022. EMA; 2022. https://www.ema.europa.eu/en/documents/assessment-report/locametz-epar-public-assessment-report_en.pdf

Table 4. Profile of Pluvicto
Таблица 4. Характеристика препарата Pluvicto

Parameters *Характеристика*	**Description** *Описание*
Trade name	Pluvicto
International non-proprietary name	Lutetium (^{177}Lu) vipivotide tetraxetan
The applicant applied to register active pharmaceutical ingredient Lutetium (^{177}Lu) vipivotide tetraxetan, as a new active substance; according to the applicant, the substance is not included in medicines that have been authorised within the European Union	
Indications	Pluvicto is indicated in adults with prostate specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) whoc have been treated androgen receptor (AR) pathway inhibitors and taxane-based chemotherapy
Preclinical (non-clinical) aspects	
Pharmacokinetics	Pharmacokinetic parameters (absorption, distribution, metabolism, excretion) were studied, as well as biodistribution and pharmacokinetic interaction of ^{175}Lu-PSMA-617 kit and PSMA-617 precursor. Binding of ^{177}Lu-PSMA-617 active substance to tumour cells in mice
Pharmacology studies	***Primary pharmacokinetics:*** results of in-house *in vitro* and *in vivo* studies. ***Secondary pharmacokinetics:*** results of in-house studies of ^{175}Lu-PSMA-617 binding with 87 targets (receptors, ion channels, enzymes, and transporters). ***Safety pharmacology:*** effect of medicine and precursor kit ^{175}Lu-PSMA-617/PSMA-617 on hERG-channel current was studied. *In vivo* studies were performed in rats and pygmy hogs (effect on central nervous system, cardiovascular and respiratory systems). ***Pharmacodynamic interactions:*** studies not performed. Lutetium vipivotide tetraxetan binds to PSMA expressed specifically in prostate cancer
Toxicology studies	Extended studies for ***single*** intravenous administration of a non-radioactive compound of medicine kit ^{175}Lu-PSMA-617 and PSMA-617 precursor were performed in rats (up to 4 mg/kg, maximum tolerable dose equal to 150 therapeutic doses) and pygmy hogs (up to 1,8 mg/kg, maximum tolerable dose equal to 400 therapeutic doses). Toxicity studies for ***repeated*** intravenous administration of unlabelled PSMA-617 performed in rats (4 injections once a week at doses 0.04 to 0.4 mg/kg, NOAEL, 15 times succeeding equal therapeutic dose in patients, 275 μg). ***Genotoxicity:*** unlabelled PSMA-617 was studied in Ames test. ***Carcinogenicity:*** studies of ^{177}Lu-PSMA-617, ^{175}Lu-PSMA-617 or unlabelled PSMA-617 precursor were not performed. ***Reproductive toxicity:*** studies of ^{177}Lu-PSMA-617, ^{175}Lu-PSMA-617 or unlabelled PSMA-617 precursor were not performed. ***Toxicokinetic studies:*** performed in rats and pygmy hogs using non-radioactive ^{175}Lu-PSMA-617 and unlabelled PSMA-617. ***Local tolerance:*** assessed in extended toxicity study for single administration and toxicity study for repeated administration. ***Ecotoxicity / environmental risk:*** inexpedience of the study was justified

The table is adapted by the authors from[33] / Таблица составлена авторами по данным[33]

[33] Pluvicto. International non-proprietary name: Lutetium (^{177}Lu) vipivotide tetraxetan. Assessment report. EMA/871459/2022. EMA; 2022. https://www.ema.europa.eu/en/documents/assessment-report/pluvicto-epar-public-assessment-report_en.pdf