

EANM Response to the EMA Consultation on the Union List of Critical Medicines

Scientific Rationales for Proposed Amendments

European Association of Nuclear Medicine (EANM)

PART I — PROPOSED ADDITIONS TO THE UNION LIST

The EANM recommends the inclusion of the following six radiopharmaceuticals in the Union List of Critical Medicines, on the grounds that they are indispensable to patient care across Europe, have no suitable alternatives, and are vulnerable to supply disruptions. Full rationales are provided below.

1. ¹⁷⁷Lutetium-vipivotide tetraxetan

V10XX05 (ATC code) — Intravenous use

¹⁷⁷Lutetium-vipivotide tetraxetan (¹⁷⁷Lu-PSMA-617) is a therapeutic radiopharmaceutical used for the treatment of metastatic prostate cancer. ¹⁷⁷Lutetium-vipivotide tetraxetan (7.4 GBq) is administered approximately every 6 weeks for a total of up to 6 doses. ¹⁷⁷Lutetium-vipivotide tetraxetan, in combination with androgen deprivation therapy (ADT) with or without androgen receptor pathway inhibition (ARPI), provides an overall survival and imaging progression-free survival (PFS) benefit compared to best standard-of-care treatment in patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have progressed on ARPI and taxane-based chemotherapy (Phase III VISION trial; Sartor et al., *NEJM*, 2021). Based on its high efficacy and favourable toxicity profile, ¹⁷⁷lutetium-vipivotide tetraxetan has been awarded the highest possible score of 5 on the EMA-endorsed ESMO-MCBS scale (European Society for Medical Oncology — Magnitude of Clinical Benefit Scale), indicating substantial clinical benefit in a non-curative setting. Ensuring the timely administration of this life-prolonging treatment through sustained availability is therefore essential. ¹⁷⁷Lutetium-vipivotide tetraxetan provides a PFS benefit compared to ARPI switch in patients with PSMA-positive mCRPC who have progressed following initial ARPI treatment (Phase III PSMAfore trial; Morris et al., *Lancet Oncology*, 2024). ¹⁷⁷Lutetium-vipivotide tetraxetan also provides a PFS benefit when administered in combination with ADT and ARPI compared to ADT and ARPI alone in patients with PSMA-positive metastatic hormone-sensitive prostate cancer (Phase III PSMAddition trial; Tagawa et al., *Annals of Oncology*, 2025).

2. ²²³Radium-dichloride

V10XX03 (ATC code) — Intravenous use

²²³Radium-dichloride is a therapeutic radiopharmaceutical used for the treatment of metastatic prostate cancer. ²²³Radium-dichloride (55 kBq per kg body weight) is administered at 4-week intervals for a total of up to 6 injections. ²²³Radium-dichloride in combination with best standard-of-care improves overall survival and prolongs the time to first symptomatic skeletal event compared to placebo plus best standard-of-care in patients with metastatic castration-resistant prostate cancer (mCRPC), symptomatic bone metastases, and no visceral metastases, who have progressed after a minimum of 2 prior lines of systemic therapy for mCRPC (Phase III ALSYMPCA trial; Sartor et al., *NEJM*, 2013). Based on its high efficacy and favourable toxicity profile, ²²³radium-dichloride has been awarded a high score of 4 on the EMA-endorsed ESMO-MCBS scale

(European Society for Medical Oncology — Magnitude of Clinical Benefit Scale), indicating substantial clinical benefit in a non-curative setting. Ensuring the timely administration of this life-prolonging treatment through sustained availability is therefore essential.

3. ¹⁷⁷Lutetium-oxodotreotide

V10XX04 (ATC code) — Intravenous use

¹⁷⁷Lutetium-oxodotreotide (¹⁷⁷Lu-DOTATATE) is a therapeutic radiopharmaceutical used for the treatment of metastatic neuroendocrine tumours. ¹⁷⁷Lutetium-oxodotreotide (7.4 GBq) is administered as a single infusion approximately every 8 weeks for a total of up to 4 injections. ¹⁷⁷Lutetium-oxodotreotide in combination with best supportive care, including long-acting repeatable (LAR) octreotide, provides a progression-free survival (PFS) benefit compared to octreotide LAR alone in patients with unresectable or metastatic, progressive, well-differentiated (G1 and G2), somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumours (GEP-NETs) (Phase III NETTER-1 trial; Strosberg et al., *NEJM*, 2017). Based on its high efficacy and favourable toxicity profile, ¹⁷⁷Lutetium-oxodotreotide has been awarded a high score of 4 on the EMA-endorsed ESMO-MCBS scale (European Society for Medical Oncology — Magnitude of Clinical Benefit Scale), indicating substantial clinical benefit in a non-curative setting. ¹⁷⁷Lutetium-oxodotreotide in combination with octreotide LAR also provides a PFS benefit compared to octreotide LAR alone in patients with newly diagnosed higher-grade 2 (Ki67 ≥10% and ≤20%) and grade 3 (Ki67 >20% and ≤55%), somatostatin receptor-positive, advanced GEP-NETs (Phase III NETTER-2 trial; Singh et al., *Lancet Oncology*, 2024). Ensuring the timely administration of this well-established GEP-NET treatment through sustained availability is therefore essential.

4. Fludeoxyglucose ([¹⁸F]FDG)

V09IX04 (ATC code) — Intravenous use

2-[¹⁸F]fluoro-2-deoxy-D-glucose ([¹⁸F]FDG) is a diagnostic radiopharmaceutical used for positron emission tomography (PET). It is a glucose analogue that accumulates intracellularly in various cell types, including neurones, cancer cells, and cells associated with infection and inflammation. PET imaging with [¹⁸F]FDG is used for the diagnosis and staging of a wide range of tumours, the evaluation of therapy response, and prognostication. It is also used for the accurate detection of infectious and inflammatory conditions, and for the assessment of cerebral glucose metabolism in neurodegenerative disorders and epilepsy. [¹⁸F]FDG is a cornerstone radiopharmaceutical for PET imaging, widely available at reasonable cost across Europe, and has no alternative for PET imaging.

5. Sodium iodide (Na[¹³¹I])

V10XA01 (ATC code) — Oral use

Sodium iodide (Na[¹³¹I]) is a therapeutic radiopharmaceutical used for the treatment of benign thyroid disorders and differentiated thyroid carcinoma. Sodium iodide (Na[¹³¹I]) is selectively taken up by the follicular epithelial cells of the thyroid gland (thyrocytes). When administered at activities between 185 and 555 MBq, it can treat a variety of benign thyroid disorders, including Graves' disease, toxic adenoma, and multinodular goitre. In differentiated thyroid cancer, higher activities (1,110–7,400 MBq) are used for ablation of remnant thyroid tissue following total thyroidectomy, adjuvant therapy after surgery, and the treatment of metastatic disease with curative intent.

6. Technetium (^{99m}Tc) generator

V09FX01 (ATC code) — Intravenous use

The molybdenum-99/technetium-99m ($^{99}\text{Mo}/^{99m}\text{Tc}$) generator enables the decentralised, on-site elution of technetium-99m (^{99m}Tc ; half-life: 6 hours) from its parent radionuclide molybdenum-99 (^{99}Mo). Sodium pertechnetate ($\text{Na}[^{99m}\text{Tc}]\text{TcO}_4$) can be used for the radiolabelling of a wide range of cold kits, enabling the assessment of numerous physiological functions, including myocardial perfusion, bone metabolism, renal and hepatic function, and lymphatic drainage, using planar gamma scintigraphy or single-photon emission computed tomography (SPECT). This generator provides a versatile range of molecules that can be readily radiolabelled on-site (extemporaneously) and has no alternative. Major worldwide shortages have already occurred over the past 20 years, resulting in significant disruption to and delays in patient management, particularly for the assessment of myocardial perfusion, bone studies, and sentinel lymph node procedures.

PART II — PROPOSED REMOVALS FROM THE UNION LIST

The EANM recommends the removal of the following two radiopharmaceuticals from the Union List of Critical Medicines, on the grounds that suitable alternatives exist and that they are not considered essential or critical to patient care.

7. Human serum albumin — ^{99m}Tc (^{99m}Tc]Tc-HSA)

V09GA04 (ATC code) — Intravenous use

Human serum albumin radiolabelled with ^{99m}Tc (^{99m}Tc]Tc-HSA) is used for the assessment of ventricular ejection fraction and for various rare indications in blood pool imaging. The former can readily be obtained using transthoracic echocardiography or ^{99m}Tc -radiolabelled autologous red blood cells. This radiopharmaceutical is therefore not considered essential or critical.

8. Human serum albumin — ^{125}I (^{125}I]I-HSA)

V09GB02 (ATC code) — Intradermal, intratumoral, intravenous, and subcutaneous use

Human serum albumin radiolabelled with ^{125}I (^{125}I]I-HSA) is used for the measurement of plasma volume. While it has utility in clinical practice — in particular for the diagnosis of pseudopolycythaemia due to haemoconcentration — it is not considered essential or critical.