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Welsh Health Specialised Services Committee (WHSSC)

Specialised Services Policy Position PP195

Lutetium (^{177}Lu) oxodotreotide for treating unresectable or metastatic neuroendocrine tumours

September 2020

Version 1.0

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Author	Welsh Health Specialised Services Committee
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Description	NHS Wales will routinely commission this specialised service in accordance with the criteria described in this policy
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Contents

Policy Statement

Welsh Health Specialised Services Committee (WHSSC) will commission Lutetium (^{177}Lu) oxodotreotide for people with neuroendocrine tumours (NETs) in accordance with the criteria outlined in this document.

In creating this document WHSSC has reviewed the relevant guidance issued by National Institute of Health and Care Excellence (NICE) and has concluded that Lutetium (^{177}Lu) oxodotreotide should be made available.

Disclaimer

WHSSC assumes that healthcare professionals will use their clinical judgment, knowledge and expertise when deciding whether it is appropriate to apply this policy position statement.

This policy may not be clinically appropriate for use in all situations and does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

WHSSC disclaims any responsibility for damages arising out of the use or non-use of this policy position statement.

1. Introduction

This Policy Position Statement has been developed for the planning and delivery of Lutetium (^{177}Lu) oxodotreotide for people resident in Wales. This service will only be commissioned by the Welsh Health Specialised Services Committee (WHSSC) and applies to residents of all seven Health Boards in Wales.

1.1 Plain language summary

Neuroendocrine tumours (NETs) or Neuroendocrine Neoplasms (NENs) are uncommon cancers and can arise from cells of the neuroendocrine system. The neuroendocrine system consists of cells which are spread through organs of the body e.g. gastrointestinal tract, or form some glands. These cells can produce hormones and releases them into the bloodstream.

NETs are tumours (abnormal growths) that develop from cells of the neuroendocrine system. NETs can arise from different parts of the body, most commonly gastrointestinal tract and lung. They are considered malignant but the behaviour can vary with some slow growing cancers and some that are very aggressive. There are a number of different types of NET, depending on the specific cells affected.

Gastroenteropancreatic neuroendocrine tumours (GEP NETs) are tumours that develop in the gut or pancreas. Gastrointestinal neuroendocrine tumours (GI NETs) develop in the digestive system, which includes the bowel, stomach or oesophagus. Pancreatic neuroendocrine tumours (pNETs) develop in the pancreas[1].

Lutetium (^{177}Lu) oxodotreotide is a type of radionuclide used in a therapy known as a targeted radionuclide therapy or peptide receptor radionuclide therapy (PRRT). PRRT is a type of internal radiotherapy. Internal radiotherapy means giving radiotherapy to the cancer from inside the body. The treatment is to control the growth of the tumour (delay progression) and/or for symptoms control but is generally not curative. It gives a high dose of radiation to the cancer, but little to surrounding tissues. PRRT is also called targeted radiotherapy, radiolabelled treatment, targeted radionuclide therapy or molecular radiotherapy.

Some neuroendocrine cells have proteins (receptors) on the outside of them called somatostatin receptors. The somatostatin hormone attaches to these receptors and causes changes in the cell. For example, they may tell the cell to slow down growth and slow down the production of hormones.

Special scans such as PET scans or octreotide scans can check whether the NET has these receptors. If the NET has somatostatin receptors, doctors can use them to target radiotherapy.

[1] NHS Inform Scotland

In the laboratory, doctors attach a radioactive substance to a man-made form of the hormone somatostatin (a somatostatin analogue). This radioactive treatment circulates through the body in the bloodstream and attaches to the somatostatin receptors on the NET cells. It then enters the cell and kills it from the inside[2].

1.2 Aims and Objectives

This Policy Position statement aims to define the commissioning position of WHSSC on the use of Lutetium (^{177}Lu) oxodotreotide for people with NETs.

The objectives of this policy are to:

- ensure commissioning for the use of Lutetium (^{177}Lu) oxodotreotide is evidence based
- ensure equitable access to Lutetium (^{177}Lu) oxodotreotide
- define criteria for people with NETs to access treatment
- improve outcomes for people with NETs

1.3 Epidemiology

Although NETs affect only a small percentage of the general population at any one time, the number of people being newly diagnosed with NETs overall is believed to be rising.

This is mainly due to increased awareness of the condition and improved diagnostic testing. NETs are now the fastest growing class of cancers worldwide, accounting for around 2% of all cancers at any one time.

Depending on the type of tumour, most NETs occur in people aged 50 to 60 years old but they can affect anyone of any age, and generally affect the same number of women and men.[3]

1.4 Current Treatment

Treatment for a NET depends on a number of things including where the cancer is, its size and whether it has spread. Current treatment options include:

- Surgery
- Active monitoring
- Somatostatin analogues
- Targeted cancer drugs
- Chemotherapy
- Radiotherapy
- Transarterial embolisation
- Radiofrequency ablation

[2] Cancer Research UK
[3] Living with NETs

- Microwave ablation

1.5 Proposed Treatment

In PRRT, a cell-targeting protein (or peptide), similar to the natural circulating hormone somatostatin, is combined with a small amount of radioactive material, or radionuclide, creating a special type of radiopharmaceutical called a radiopeptide. When injected into the patient's bloodstream, this radiopeptide travels to and binds to neuroendocrine tumour cells, delivering a targeted high dose of radiation directly to the cancer cells. The mechanism by which this radiopeptide can target the tumour cell is the abundance (called an overexpression) of a specific type of surface receptor, a protein that extends from the cell's surface that binds to somatostatin[4].

1.6 What NHS Wales has decided

WHSSC has carefully reviewed the relevant guidance issued by the National Institute of Health and Care Excellence (NICE). We have concluded that there is enough evidence to fund the use of Lutetium (^{177}Lu) oxodotreotide, within the criteria set out in section 2.1.

[4] Kwekkeboom DJ, Kam BL, van Essen M, et al. Somatostatin-receptor-based imaging and therapy of gastroenteropancreatic neuroendocrine tumors. *Endocr Relat Cancer.* 2010;17:R53-73 quoted in "What is Peptide Receptor Radionuclide Therapy (PRRT)?" factsheet, Society of Nuclear Medicine & Molecular Imaging

2. Criteria for Commissioning

The Welsh Health Specialised Services Committee approve funding of Lutetium (^{177}Lu) oxodotreotide for adults with NETs, in-line with the criteria identified in the policy.

2.1 Inclusion Criteria

Lutetium (^{177}Lu) oxodotreotide is recommended, within its marketing authorisation, as an option for treating unresectable or metastatic, progressive, well-differentiated (grade 1 or grade 2), somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumours (NETs) in adults. It is recommended only if the company provides it according to the commercial arrangement[5].

2.2 Exclusion Criteria

- Yttrium (90Y) and other radiolabels are not included in this policy.

- The marketing authorisation states that Lutetium is administered as an intravenous infusion. A single course consists of 4 infusions of 7.4 gigabecquerels (GBq). The recommended interval between infusions is 8 weeks. Anything more than 4 infusions (i.e. 5 or 6) would be considered an off label use of Lutetium and would therefore require an IPFR request.

- Retreatment with Lutetium[6].

2.3 Continuation of Treatment

Healthcare professionals are expected to review a patient's health at regular intervals to ensure they are demonstrating an improvement to their health due to the treatment being given.

If no improvement to a patient's health has been recorded then clinical judgement on the continuation of treatment must be made by the treating healthcare professional.

[5] NICE TA539 Recommendations

[6] When preparing the guidance, the NICE TA assessment group included retreatment with Lutetium in a sensitivity analysis at the time of the first appraisal committee meeting. In response to consultation on the assessment report, the company stated that retreatment with Lutetium was not recommended clinical practice. The committee noted that there was no mention of retreatment after disease progression in the Lutetium summary of product characteristics (SPC) or any evidence supporting retreatment from the clinical trials that underpinned the marketing authorisation. It also noted that previous treatment with peptide receptor radionuclide therapy at any time before randomisation was an exclusion criterion in NETTER 1. Also, none of the company's analyses or the assessment group's revised analyses included Lutetium retreatment. The committee concluded that it was not appropriate to include retreatment with Lutetium after disease progression in its consideration of the clinical and cost effectiveness of Lutetium.

2.4 Acceptance Criteria

The service outlined in this specification is for patients ordinarily resident in Wales, or otherwise the commissioning responsibility of the NHS in Wales. This excludes patients who whilst resident in Wales, are registered with a GP practice in England, but includes patients resident in England who are registered with a GP Practice in Wales.

2.5 Patient Pathway (Annex i)

- Patients with NETs being considered for PRRT should be referred by their regional NETs MDT to the Royal Free Hospital in London or the Royal Liverpool Hospital.

- All patients should be discussed at the regional NET MDT prior to referral for PRRT to ensure they are appropriate for referral and have had all the required diagnostic tests and investigations completed.

- Patients are reviewed by the consultant in the NET clinic following PRRT.

- Follow up blood tests should be carried out locally by the GP and feedback provided to the place of PRRT treatment, under instruction by the PRRT administering centre.

- Some complications from PRRT should be managed locally such as blood transfusion and haematology and renal medical opinions.

- Although hormonal excretion by NETs is uncommon (most are non-functional), in the event of neuroendocrine hormonal crisis - rarely seen a few days after PRRT - the patient should be admitted locally.

- A dedicated Wales NET specialist nurse should liaise with the PRRT provider's specialist nurses who coordinate care, informing and supporting the patient when appropriate.

2.6 Exceptions

If the patient does not meet the criteria for treatment as outlined in this policy, an Individual Patient Funding Request (IPFR) can be submitted for consideration in line with the All Wales Policy: Making Decisions on Individual Patient Funding Requests. The request will then be considered by the All Wales IPFR Panel.

If the patient wishes to be referred to a provider outside of the agreed pathway, and IPFR should be submitted.

Further information on making IPFR requests can be found at: Welsh Health Specialised Services Committee (WHSSC) | Individual Patient Funding Requests

2.7 Clinical Outcome and Quality Measures

The Provider must work to written quality standards and provide monitoring information to the lead commissioner.

The centre must enable the patient's, carer's and advocate's informed participation and to be able to demonstrate this. Provision should be made for patients with communication difficulties.

PRRT therapy should be conducted in recognised centres equipped with the required expertise.

2.8 Responsibilities

Referrers should:

- inform the patient that this treatment is not routinely funded outside the criteria in this policy, and
- refer via the agreed pathway.

Clinicians considering treatment should:

- discuss all the alternative treatment with the patient
- advise the patient of any side effects and risks of the potential treatment
- inform the patient that treatment is not routinely funded outside of the criteria in the policy, and
- confirm that there is contractual agreement with WHSSC for the treatment.

In all other circumstances an IPFR must be submitted.

3. Documents which have informed this policy

The following documents have been used to inform this policy:

- **National Institute of Health and Care Excellence (NICE) guidance**
  - Lutetium (177Lu) oxodotreotide for treating unresectable or metastatic neuroendocrine tumours, TA539, August 2018

This document should be read in conjunction with the following documents:

- **NHS Wales**
  - All Wales Policy: Making Decisions in Individual Patient Funding requests (IPFR).

4. Date of Review

This document will be reviewed when information is received which indicates that the policy requires revision.

5. Putting Things Right:

5.1 Raising a Concern

Whilst every effort has been made to ensure that decisions made under this policy are robust and appropriate for the patient group, it is acknowledged that there may be occasions when the patient or their representative are not happy with decisions made or the treatment provided.

The patient or their representative should be guided by the clinician, or the member of NHS staff with whom the concern is raised, to the appropriate arrangements for management of their concern.

If a patient or their representative is unhappy with the care provided during the treatment or the clinical decision to withdraw treatment provided under this policy, the patient and/or their representative should be guided to the LHB for NHS Putting Things Right. For services provided outside NHS Wales the patient or their representative should be guided to the NHS Trust Concerns Procedure, with a copy of the concern being sent to WHSSC.

5.2 Individual Patient Funding Request (IPFR)

If the patient does not meet the criteria for treatment as outlined in this policy, an Individual Patient Funding Request (IPFR) can be submitted for consideration in line with the All Wales Policy: Making Decisions on Individual Patient Funding Requests. The request will then be considered by the All Wales IPFR Panel.

If an IPFR is declined by the Panel, a patient and/or their NHS clinician has the right to request information about how the decision was reached. If the patient and their NHS clinician feel the process has not been followed in accordance with this policy, arrangements can be made for an independent review of the process to be undertaken by the patient's Local Health Board. The ground for the review, which are detailed in the All Wales Policy: Making Decisions on Individual Patient Funding Requests (IPFR), must be clearly stated

If the patient wishes to be referred to a provider outside of the agreed pathway, an IPFR should be submitted.

Further information on making IPFR requests can be found at: Welsh Health Specialised Services Committee (WHSSC) | Individual Patient Funding Requests

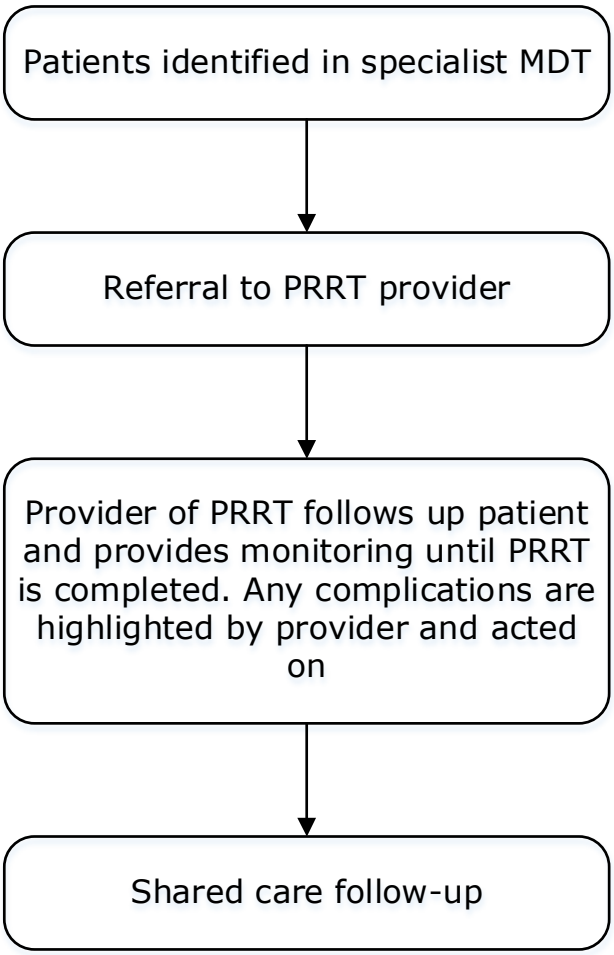
6. Equality Impact Assessment

The Equality Impact Assessment (EQIA) process has been developed to help promote fair and equal treatment in the delivery of health services. It aims to enable Welsh Health Specialised Services Committee to identify and eliminate detrimental treatment caused by the adverse impact of health service policies upon groups and individuals for reasons of race, gender re-assignment, disability, sex, sexual orientation, age, religion and belief, marriage and civil partnership, pregnancy and maternity and language (Welsh).

This policy has been subjected to an Equality Impact Assessment.

The Assessment demonstrates the policy is robust and there is no potential for discrimination or adverse impact. All opportunities to promote equality have been taken.

Annex i Patient Pathway



Annex ii Neuroendocrine Tumour (NET) Prior Approval

Details of clinician making the referral:
Name:
Designation:
Address:
Postcode:
Telephone number:
Email:

Patient Details	
First Name:	Last Name:
Address:	Date of birth:
	NHS number:
Postcode:	Hospital number:
GP Name and address:	

Clinical details
Medical history and current clinical status: (**Please provide a copy of the latest clinical report**)
Additional information to support the referral: (e.g. relevant clinical letters/reports)

I confirm that as the patient's Consultant, I have discussed this application and consent has been provided to obtain further clinical information pertinent to this funding request if required.

Clinicians signature: **Date:**

Please return this form with a copy of the supporting information to:

Patient Care Team
Welsh Health Specialised Services
Unit G1, Treforest Industrial Estate
Pontypridd
CF37 5YL

Email: whssc.ipc@wales.nhs.uk or whssc.ipc@nhs.net

If you have any questions, please telephone 01443 443443 ext.78123