NICE National Institute for Health and Care Excellence

NICE guidance

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

Technology appraisal guidance
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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do 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.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

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1 Recommendations

1.1 Lutetium (177Lu) 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.

Why the committee made these recommendations

NETs can affect the pancreas and gastrointestinal tissue and are difficult to diagnose and treat. Current treatment options include everolimus, sunitinib and best supportive care.

Clinical trial evidence shows that lutetium (177Lu) oxodotreotide (referred to as lutetium) is effective for treating somatostatin receptor-positive gastrointestinal and pancreatic NETs. Indirect comparison with everolimus, sunitinib and best supportive care suggests lutetium is effective for treating gastrointestinal and pancreatic NETs in people with progressive disease.

For treating pancreatic NETs, lutetium meets NICE's end-of-life criteria. Compared with everolimus, sunitinib and best supportive care, the cost-effectiveness estimates are within the range NICE normally considers acceptable. So lutetium can be recommended for treating pancreatic NETs.

For treating gastrointestinal NETs, lutetium does not meet the end-of-life criteria because life expectancy for this form of the disease is between 5 and 6 years. But it can be recommended because the most plausible cost-effectiveness estimate is within what NICE normally considers acceptable and treatment options for gastrointestinal NETs are limited.

2 Information about lutetium (177Lu) oxodotreotide

Information about lutetium (177Lu) oxodotreotide

Marketing authorisation indication	Lutetium (177Lu) oxodotreotide (Lutathera, AAA, referred to as lutetium) is indicated for 'unresectable or metastatic, progressive, well-differentiated (G1 and G2), somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumours (GEP NETs) in adults'.
Dosage in the marketing authorisation	Lutetium is administered as an intravenous infusion. A single cycle consists of 4 infusions of 7.4 gigabecquerels (GBq). The recommended interval between infusions is 8 weeks.
Price	£71,500.00 for 4 administrations of 7.4 GBq (excluding VAT; company submission). The company has a commercial arrangement. This makes lutetium available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The appraisal committee (section 5) considered evidence from a number of sources. See the committee papers for full details of the evidence.

Clinical need and current practice

People with NETs will welcome new treatment options because of high unmet need

3.1 The committee understood that neuroendocrine tumours (NETs) can affect the pancreas and gastrointestinal tissue. They are difficult to diagnose and treat, can significantly affect emotional health and often mean that people are unable to work. The patient expert explained that lutetium (177Lu) oxodotreotide (referred to as lutetium) is a very effective treatment with tolerable side effects, which allowed people to live a relatively normal life. The committee concluded that there is a recognised need for treatment for NETs at different sites.

Everolimus, sunitinib and best supportive care are appropriate comparators for lutetium for pancreatic NETs

3.2 The clinical experts explained that managing NETs in the NHS follows the European Neuroendocrine Tumor Society's (ENETs) guidelines. For treating pancreatic NETs causing symptoms (functional NETs) in people with progressive disease, options include everolimus and lutetium. For non-functional pancreatic NETs, the guidelines suggest lutetium or chemotherapy for progressive disease after offering everolimus or sunitinib. The clinical experts stated that although most centres would use lutetium after everolimus or sunitinib, there is no evidence to show that this is more effective than using it instead of everolimus or sunitinib. They further explained that chemotherapy is sometimes used if people have symptoms because of the bulk of their disease (mainly people with high disease burden with a Ki-67 proliferative index of around 20% or more, that is, grade 3 tumours). The committee agreed that

chemotherapy was not a relevant comparator because lutetium is indicated for grade 1 and 2 tumours. The committee concluded that everolimus, sunitinib and best supportive care were appropriate comparators.

Everolimus and best supportive care are appropriate comparators for lutetium for gastrointestinal NETs

3.3 For treating functional and non-functional advanced gastrointestinal NETs in people with progressive disease, the ENETs guidelines suggest lutetium as an option with everolimus, and interferons. The committee agreed that everolimus may be a relevant comparator for lutetium but noted that its marketing authorisation is for non-functional gastrointestinal NETs only. The clinical experts explained that although interferons may be considered in people with progressive disease, they are not routinely used in England because of their toxicity. The committee agreed that interferons were not relevant comparators for lutetium. It therefore concluded that the relevant comparators for lutetium for gastrointestinal NETs were everolimus (non-functional disease only) and best supportive care.

Clinical trial evidence (ERASMUS)

Lutetium is effective for treating gastroenteropancreatic NETs

3.4 ERASMUS is a phase 1 and 2 single-arm study, which evaluated the efficacy of lutetium in people with different somatostatin receptor-positive tumour types, including pancreatic, foregut, midgut, hindgut and bronchial NETs. However, because bronchial NETs are not covered by the marketing authorisation for lutetium, these results were not considered by the committee. The committee was concerned that ERASMUS was a single-arm open-label study but acknowledged that it was the largest study of NETs currently available. It noted that the company only presented results for the Dutch population (n=360) in the trial (see table 1). This was because of the high percentage of non-Dutch patients lost to follow-up, which resulted in a substantial amount of missing data.

Table 1 Survival results from ERASMUS

Type of neuroendocrine tumours (NETs)	Median progression-free survival in months (95% confidence interval)	Median overall survival in months (95% confidence interval)
Gastroenteropancreatic (n=360, includes bronchial NETs)	28.5 (24.8 to 31.4)	61.2 (54.8 to 67.4)
Pancreatic (n=133)	30.3 (24.3 to 36.3)	66.4 (57.2 to 80.9)
Midgut (n=183)	28.5 (23.9 to 33.3)	54.9 (47.5 to 63.2)
Foregut (n=12)	43.9 (10.9 to not reached)	Not reached
Hindgut (n=13)	29.4 (18.9 to 35.0)	Not reached

The committee concluded that lutetium was clinically effective for people with gastroenteropancreatic NETs.

Clinical trial evidence (NETTER-1)

Lutetium is effective for treating midgut gastrointestinal NETs

3.5 NETTER-1 is a phase 3, open-label, randomised controlled trial, which recruited people with inoperable, progressive, somatostatin receptor-positive, midgut gastrointestinal NETs. The trial compared lutetium plus long-acting release octreotide 30 mg (n=116) with long-acting release octreotide 60 mg (n=113). The results from the June 2016 data-cut were:

- Progression-free survival: hazard ratio (HR) 0.21 (95% confidence interval [CI] 0.14 to 0.33).
- Overall survival: HR 0.54 (95% CI 0.33 to 0.86), median overall survival not reached in the lutetium arm.
- Overall survival, adjusted for crossover from octreotide 60 mg to lutetium: HR 0.49 (95% CI 0.30 to 0.80).

The committee considered whether these results were relevant to clinical

practice in England given that the dose of the comparator, octreotide 60 mg, is higher than the licensed dose of 30 mg. The clinical experts confirmed that the results were relevant because some centres would increase the dose of octreotide for progressive disease. The clinical experts explained that octreotide 60 mg was actually more effective than best supportive care, therefore underestimating the results for lutetium. Although NETTER-1 only recruited people with midgut gastrointestinal NETs, the clinical experts explained that they would not expect much difference in the efficacy of lutetium across the different tumour sites. The committee considered that the results were relevant and supported the conclusions from ERASMUS. It concluded that lutetium was clinically effective for people with midgut gastrointestinal NETs compared with octreotide 60 mg.

Indirect and mixed treatment comparisons

The company's matched adjusted indirect treatment comparisons are very uncertain

3.6 The company did matched adjusted indirect treatment comparisons (MAICs) for pancreatic NETs and gastrointestinal NETs using lutetium data from ERASMUS. Data for the comparators were taken from 3 randomised controlled trials (A6181111, RADIANT-3 and RADIANT-4). For pancreatic NETs, lutetium was compared with sunitinib from A6181111 and with everolimus and best supportive care from RADIANT-3. For gastrointestinal NETs, lutetium was compared with everolimus and best supportive care from RADIANT-4. The assessment group highlighted several limitations in the company's MAICs:

- The company only included the Dutch population from the ERASMUS study, which resulted in very small sample sizes after the selected baseline covariates were matched.
- The approach to selecting baseline covariates for matching meant that the most important prognostic factors and treatment effect modifiers, such as tumour functionality and grade and stage of disease, were excluded.
- Relative treatment effects were modelled after assuming proportional hazards, without any statistical testing for that assumption.

- For the pancreatic NETs MAIC, the company could not carry out a closed network because individual patient data from A6181111 and RADIANT-3 were not available to them. Also, the single-arm ERASMUS trial was being compared with 2 randomised controlled trials (A6181111 and RADIANT-3) and the inclusion criteria (such as tumour functionality, grade and stage of disease, presence of somatostatin receptors) among the 3 trials differed.
- For gastrointestinal NETs, the company was only able to do a MAIC for progression-free survival because overall survival data from RADIANT-4 were not available to them.

  The committee acknowledged these limitations. Therefore it concluded that the results of the company's MAICs for pancreatic NETs and gastrointestinal NETs were associated with uncertainty, which needed to be accounted for in its decision-making.

The company's network meta-analysis for gastrointestinal NETs is inappropriate for decision-making

3.7 The committee noted that the company also did a network meta-analysis for gastrointestinal NETs comparing lutetium with everolimus and best supportive care, using data from NETTER-1 and RADIANT-4. However, it noted that there were important differences between the 2 trials:

- The control arm of RADIANT-4 (placebo plus best supportive care) was assumed to be equivalent to the control arm of NETTER-1 (octreotide 60 mg).
- The population from RADIANT-4 (non-functional gastrointestinal and lung NETs) was assumed to be equivalent to the population from NETTER-1 (functional and non-functional somatostatin receptor-positive midgut-only NETs).

  The committee concluded that because of these differences, the trials may not be fully comparable and results from any indirect comparison would not be robust. It therefore agreed that it would not consider the network meta-analysis further.

The assessment group's MAICs are preferred for decision-making

3.8 Having established that the company's MAICs for the pancreatic and gastrointestinal NETs populations were limited, the committee considered the assessment group's revisions to the analyses. It noted that the assessment group had done 3 MAICs based on the NETs location (using ERASMUS), which included revisions to the company's preferred assumptions:

- Including additional baseline covariates for matching.
- Including both the Dutch and non-Dutch populations from ERASMUS to increase the sample size for matching.
- Building a complete network for the pancreatic NETs population; the sunitinib arm by Bucher indirect comparison and the ERASMUS arm by MAIC were matched to RADIANT-3 as a whole.
- Doing a MAIC for overall survival for the gastrointestinal NETs population based on additional data from Novartis (for everolimus).
- Doing a MAIC of midgut-only NETs by matching the midgut-only NETs population from ERASMUS to the whole gastrointestinal NETs population in RADIANT-4.
- Estimating relative treatment effects by fitting separate curves to each arm using proportional hazards and accelerated failure time functions.

The committee acknowledged that the assessment group's analyses addressed most of the limitations highlighted in the company's MAICs (see section 3.6). It therefore accepted the assessment group's MAICs as the preferred analyses for decision-making. But because the MAIC analysis for midgut-only NETs used the whole gastrointestinal NETs population in RADIANT-4, the committee considered it inappropriate to consider the midgut NETs population separately. It therefore concluded that it would consider only the MAIC analyses for pancreatic and gastrointestinal NETs for decision-making.

Lutetium improves progression-free survival and overall survival

for people with pancreatic and gastrointestinal NETs

3.9 The results of the assessment group's MAICs and Bucher indirect comparisons showed that lutetium was statistically significantly more effective in improving progression-free survival than current treatment (everolimus, sunitinib and best supportive care for pancreatic NETs and everolimus and best supportive care for gastrointestinal NETs). For pancreatic NETs, lutetium was statistically significantly more effective in prolonging overall survival than everolimus (HR 0.54; 95% CI 0.33 to 0.88) and best supportive care (HR 0.22; 95% CI 0.10 to 0.50) but not sunitinib (HR 0.65; 95% CI 0.16 to 2.54). For gastrointestinal NETs, a statistically significant improvement in overall survival was seen only when lutetium was compared with best supportive care (HR 0.34; 95% CI 0.16 to 0.69). The difference in overall survival between lutetium and everolimus was not statistically significant (HR 0.55; 95% CI 0.27 to 1.11), but the committee considered it reasonable to assume that both drugs have similar effectiveness in prolonging survival. The committee concluded that lutetium was effective for people with pancreatic and gastrointestinal NETs compared with current treatment.

Economic models

The assessment group's economic model is the most appropriate for decision-making

3.10 The company and the assessment group's models were partitioned survival models with health states corresponding to pre-progression, post-progression and death. Both models included data for lutetium and the comparators (everolimus, sunitinib and best supportive care) from the MAIC analyses. The company also included separate analyses comparing lutetium with best supportive care (octreotide 60 mg) using data from NETTER-1 and analyses using the network meta-analysis of lutetium and everolimus for gastrointestinal NETs. Given the concerns with the population in NETTER-1 (see section 3.5) and the concerns with the company's indirect treatment comparisons (see section 3.6 and section 3.7), the committee concluded that the assessment group's economic model was the most appropriate for decision-making.

Applying background mortality in the gastrointestinal NETs analyses is appropriate

3.11 The committee noted that in the assessment group's base-case analysis for gastrointestinal NETs, an adjustment in the survival analysis for background mortality was made. It understood that this was applied because of the short follow-up period in the indirect comparison of progression and mortality. It agreed that this approach was appropriate to minimise the effect of death from other causes on relative health benefit.

Health-related quality of life

The assessment group's estimates are acceptable for decision-making

3.12 For pancreatic NETs, the assessment group used EQ-5D valuations from A6181111 and assumed that the utilities for lutetium, everolimus and sunitinib were equal. The committee had previously accepted this assumption in NICE's technology appraisal guidance on everolimus and sunitinib for treating unresectable or metastatic neuroendocrine tumours in people with progressive disease following the comment from clinical experts that it was reasonable to assume that health-related quality of life would be similar. For gastrointestinal NETs, the assessment group used values estimated from RADIANT-4 for everolimus, best supportive care and lutetium (progressed disease only) and from ERASMUS for lutetium (stable disease). The committee noted that using alternative sources reduced the incremental cost-effectiveness ratios (ICERs) slightly, more so for pancreatic NETs than for gastrointestinal NETs. The company used values from ERASMUS in its base case for pancreatic and gastrointestinal NETs. The committee understood that new data from NETTER-1, which showed statistically significant improvement in quality of life for lutetium compared with octreotide, had become available. The company stated that it did not use these data because the model is primarily based on effectiveness data from ERASMUS. Based on the data presented to it, the committee concluded that the assessment group's estimates were acceptable for decision-making.

Resource use and costs

None of the analyses reflect the use of somatostatin receptor agonists in clinical practice

3.13 The company's definition of best supportive care was based on the design of NETTER-1, in which all patients had a high dose of octreotide (60 mg) before progression and a lower dose (30 mg) after progression. The committee noted that the company's estimates of somatostatin receptor agonist use were substantially different to the assessment group's estimates, which were based on the observed rates in RADIANT-3 (pancreatic NETs) and RADIANT-4 (gastrointestinal NETs). However, the clinical experts explained that the assessment group's estimates were lower than would be seen in clinical practice, particularly for gastrointestinal NETs. The clinical experts stated that for progressive disease, most people with pancreatic or gastrointestinal NETs (approximately 85% and 95%, respectively) would continue having a somatostatin receptor agonist. On further progression, about 10% would stop treatment or reduce their dose. The committee noted the comment from 1 of the experts that about 20% of people would have a somatostatin receptor agonist at a higher dose. The assessment group also presented 3 separate best supportive care scenario analyses:

- Scenario 1: octreotide 60 mg in 40% of people in the progression-free health state, best supportive care arm only.
- Scenario 2: octreotide 60 mg in 100% of people in the progression-free health state, best supportive care arm only.
- Scenario 3: octreotide 30 mg in 90% of people in the progression-free health state, regardless of the treatment arm of the model, reducing to 85% after progression (based on expert opinion).

  The clinical experts explained that concomitant use of somatostatin receptor agonists with targeted treatments varied in clinical practice. The company emphasised that the marketing authorisation for lutetium is for monotherapy and that only about half of the patients in ERASMUS had octreotide with lutetium. The committee noted that none of the analyses presented completely

reflected the views of the clinical experts. However, it agreed that the most reasonable estimate for its decision-making would lie between the assessment group's best supportive care scenarios 2 and 3.

The dose intensity estimate for lutetium should be based on ERASMUS

3.14 The committee noted that the dose intensity estimate for lutetium in the company's model was based on NETTER-1 instead of ERASMUS, which is the source trial for the lutetium effectiveness data used in the indirect comparisons for pancreatic and gastrointestinal NETs. The assessment group explained that this potentially overestimated the cost effectiveness of lutetium because the dose intensity increased from 86.4% to between 94.4% and 97.8%. However, it stated that when the figures from ERASMUS were implemented in the model, the dose intensity reduced to about 86% to 88%. The committee agreed that the dose intensity should be based on the source trial and concluded that relative dose intensity based on ERASMUS was more appropriate.

Retreatment with lutetium is not considered

3.15 The 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 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.

All relevant administration costs for lutetium are included in the

assessment group's model

3.16 The committee questioned whether there would be additional costs for administering lutetium because it is a radionuclide. The clinical experts explained that the initial scans needed to identify somatostatin receptor-positive tumours are part of standard care. They also stated that although most people having lutetium usually stay overnight in hospital (over 90%), some are discharged the same day. The assessment group's base case assumed that 90% of patients stay overnight. It also used the national average cost of an elective inpatient excess bed day instead of the national average cost of a non-elective inpatient short stay to reduce potential double counting of resources. In a scenario analysis, the assessment group explored lutetium being administered in a day-case setting in 65% of patients. The effect of this assumption on the assessment group's base-case ICERs was minimal. The clinical experts agreed with the company that although a nuclear medicines consultant needs to be present on site, they do not necessarily administer the treatment. Also, the committee noted that the expert evidence submissions stated that no additional resources would be needed for lutetium because several centres in England have been providing it for some time. The committee was satisfied that all relevant costs associated with lutetium had been captured in the assessment group's model.

Cost-effectiveness results

There are confidential patient access scheme discounts for lutetium and everolimus

3.17 The assessment group's base-case results, which were used in the committee's decision-making, included the confidential patient access scheme discounts for lutetium and everolimus. So the exact cost-effectiveness results cannot be reported here.

The ICERs for lutetium for pancreatic NETs are less than £30,000 per QALY gained

3.18 The committee considered the cost effectiveness of lutetium compared with everolimus, sunitinib and best supportive care for pancreatic NETs. All the deterministic and probabilistic ICERs were below £30,000 per quality-adjusted life year (QALY) gained.

The ICER for lutetium for gastrointestinal NETs is less than £30,000 per QALY gained

3.19 The committee considered the cost effectiveness of lutetium compared with everolimus and best supportive care for gastrointestinal NETs. It recalled that everolimus was only licensed for non-functional NETs, therefore it agreed that best supportive care was the most appropriate comparator. The most plausible ICER for lutetium using the committee's preferred somatostatin receptor agonist scenarios (see section 3.13) was below £30,000 per QALY gained when compared with best supportive care.

Innovation

All significant health-related benefits are captured in the analyses

3.20 The patient and clinical experts explained that lutetium is an important new treatment option that represents a major change in managing NETs. The company commented that lutetium addresses a significant unmet need for people with inoperable NETs whose disease has progressed on somatostatin analogues. However, the committee concluded that there were no additional health benefits that had not been captured in the QALY calculations.

End of life

Lutetium meets NICE's end-of-life criteria for pancreatic NETs

3.21 The committee considered the advice about life-extending treatments for people with a short life expectancy in NICE's final Cancer Drugs Fund technology appraisal process and methods. For pancreatic NETs, the committee noted that the extrapolated survival for best supportive care was 41.6 months. However, the clinical experts stated that they would expect people with pancreatic NETs to have a life expectancy of less than 24 months (the first end-of-life criterion). The committee recalled that in NICE's technology appraisal guidance on everolimus and sunitinib, these drugs met the short life expectancy criterion based on the clinical experts' views that life expectancy for people with pancreatic NETs was closer to 20.5 months (from A6181111) than to 41.6 months (from RADIANT-3). It also understood from the assessment group that the choice of parametric extrapolation could be the reason for the different results, so the estimates were very uncertain. Based on the clinical experts' views and previous conclusions from the guidance on everolimus and sunitinib, the committee accepted that life expectancy for people with pancreatic NETs was less than 24 months. The committee noted that the extrapolated survival benefit for lutetium compared with best supportive care, everolimus and sunitinib was over 3 months (64.2, 49.5 and 29.1 months, respectively), meaning that the second end-of-life criterion, of extending life by at least 3 months, was met. The committee therefore concluded that lutetium met the end-of-life criteria for somatostatin receptor-positive pancreatic NETs in people with progressive disease.

Lutetium does not meet NICE's end-of-life criteria for gastrointestinal NETs

3.22 The clinical experts explained that the average life expectancy for people with advanced gastrointestinal NETs was around 5 to 6 years. Survival of less than 24 months, as would be necessary to meet NICE's first end-of-life criterion, was not seen in practice. The committee noted that the extrapolated survival was 58.8 months for best supportive care, meaning

that the criterion for short life expectancy of 24 months was not met. For the second criterion, of extension to life of at least 3 months, the difference in extrapolated survival for lutetium compared with best supportive care was 36.1 months. The committee considered that the second criterion was met. However, because the criterion for short life expectancy was not met, the committee concluded that lutetium did not meet the end-of-life criteria for somatostatin receptor-positive gastrointestinal NETs in people with progressive disease.

Recommendations

Lutetium is recommended for treating pancreatic NETs

3.23 For pancreatic NETs, lutetium met the end-of-life criteria (see section 3.21) and all the ICERs were below £30,000 per QALY gained (see section 3.18). Therefore, the committee concluded that it could be recommended as a cost-effective use of NHS resources for treating somatostatin receptor-positive pancreatic NETs in people with progressive disease.

Lutetium is recommended for treating gastrointestinal NETs

3.24 The committee had concluded that lutetium did not meet the end-of-life criteria for gastrointestinal NETs (see section 3.22). However, it noted that the most plausible ICER was below £30,000 per QALY gained (see section 3.19). The committee understood that the treatment options for this group of people were limited, particularly for people with functional NETs. Based on the ICER estimate and the limited treatment options available, the committee concluded that it could recommend lutetium as a cost-effective use of NHS resources for treating somatostatin receptor-positive gastrointestinal NETs in people with progressive disease.

4 Implementation

4.1 Section 7(6) of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.

4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal document.

4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has unresectable or metastatic, progressive, well-differentiated (grade 1 or grade 2), somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumours and the doctor responsible for their care thinks that lutetium (177Lu) oxodotreotide is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee D.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

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Accreditation