

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Proposed Health Technology Appraisal**

**Etelcalcetide for treating secondary hyperparathyroidism**

**Draft scope (pre-referral)**

**Draft remit/appraisal objective**

To appraise the clinical and cost effectiveness of etelcalcetide within its marketing authorisation for treating secondary hyperparathyroidism in people with chronic kidney disease.

**Background**

The parathyroid glands are located in the neck behind the thyroid gland and produce parathyroid hormone, which controls the levels of calcium and phosphate in the blood. Excessive production of parathyroid hormone is called hyperparathyroidism and it causes serum calcium levels to increase and serum phosphate levels to fall. Clinical manifestations include deposition of calcium in the blood vessels and the kidneys, pruritus, bone, joint and muscle pain. There is an increased risk of fracture and cardiovascular disease.

When hyperparathyroidism is caused by another condition, it is called secondary hyperparathyroidism. Secondary hyperparathyroidism is a common complication of chronic kidney disease. In chronic kidney disease, insufficient filtering of phosphate from the blood in the urine, results in abnormally elevated phosphate levels. High serum phosphate levels can directly and indirectly lead to over activity of the parathyroid glands, leading to the development of secondary hyperparathyroidism.

Secondary hyperparathyroidism may develop in the early stages of chronic kidney disease and almost all people who require renal replacement therapy (dialysis or renal transplantation) have secondary hyperparathyroidism. In 2013, approximately 48,000 people were receiving renal replacement therapy in England including approximately 23,500 receiving haemodialysis<sup>1</sup>.

The aim of treatment for secondary hyperparathyroidism is to manage levels of parathyroid hormone, phosphate, and calcium. NICE clinical guideline 157 recommends dietary modification to reduce phosphate intake and the use of phosphate binders to control serum phosphate level in people with advanced chronic kidney disease (stage 4 or 5). Other treatments include hydroxylated vitamin D sterols (calcitriol, alfacalcidol) or the synthetic vitamin D analogue paricalcitol, and modification of the dialysis regimen. In severe hyperparathyroidism, total or partial surgical removal of the parathyroid glands may be needed. NICE technology appraisal guidance 117 does not recommend routine use of cinacalcet in people with end-stage renal disease on maintenance dialysis therapy. It recommends cinacalcet for treating

refractory secondary hyperparathyroidism only in those who have plasma levels of 'intact parathyroid hormone' greater than 85 pmol/litre and a normal or high adjusted serum calcium level, and in whom surgical parathyroidectomy is contraindicated.

**The technology**

Etelcalcetide (brand name unknown, Amgen) is a short peptide that acts on the calcium-sensing receptors present on the hormone producing cells of the parathyroid gland. It acts like calcium (calcimimetic) on the receptors and inhibits parathyroid hormone production and secretion. It is given intravenously.

Etelcalcetide does not currently have a marketing authorisation in the UK for treating secondary hyperparathyroidism. It has been studied in clinical trials, compared with cinacalcet or placebo, for treating secondary hyperparathyroidism in adults with chronic kidney disease receiving haemodialysis. It has also been studied, in a single-arm study, in adults with chronic kidney disease receiving haemodialysis who have higher levels of parathyroid hormone despite having had cinacalcet.

<b>Intervention(s)</b>	Etelcalcetide
<b>Population(s)</b>	People with secondary hyperparathyroidism with chronic kidney disease, receiving haemodialysis
<b>Comparators</b>	<ul style="list-style-type: none"> <li>• Established clinical practice without etelcalcetide (which may include dietary modification to restrict phosphate, phosphate binders, vitamin D and its analogues)</li> <li>• Surgery (parathyroidectomy)</li> <li>• Cinacalcet (only if parathyroidectomy is contraindicated)</li> </ul>

<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• survival</li> <li>• incidence of fractures</li> <li>• incidence of cardiovascular events</li> <li>• need for sub-total parathyroidectomy</li> <li>• symptoms such as bone pain and itching or mobility</li> <li>• hospitalisation</li> <li>• health-related quality of life</li> <li>• adverse effects of treatment</li> </ul> <p>In the absence of directly measured mortality and morbidity outcomes, biochemical markers may be considered as potential surrogate outcomes, such as changes in serum levels of;</p> <ul style="list-style-type: none"> <li>• parathyroid hormone</li> <li>• calcium, and</li> <li>• phosphate</li> </ul>
<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p>
<b>Other considerations</b>	<p>Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.</p>
<b>Related NICE recommendations and NICE Pathways</b>	<p>Related Technology Appraisals:</p> <p>Cinacalcet for the treatment of secondary hyperparathyroidism in patients with end-stage renal disease on maintenance dialysis therapy (January 2007). NICE Technology Appraisal 117. Transferred to 'static guidance list' June 2013.</p>

	<p>Related Guidelines:</p> <p>Chronic kidney disease in adults: assessment and management (July 2014). NICE guideline 182</p> <p>Chronic kidney disease (stage 4 or 5): management of hyperphosphatemia (March 2013). NICE guideline 157. Review date TBC.</p> <p>Related Quality Standards:</p> <p>Renal replacement therapy services for adults (November 2014). NICE quality standard 72.</p> <p>Chronic kidney disease in adults (March 2011). NICE quality standard 5.</p> <p><a href="http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp">http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp</a></p> <p>Related NICE Pathways:</p> <p>Chronic kidney disease (August 2015) NICE pathway</p> <p><a href="http://pathways.nice.org.uk/pathways/chronic-kidney-disease#content=view-info-category%3Aview-about-menu">http://pathways.nice.org.uk/pathways/chronic-kidney-disease#content=view-info-category%3Aview-about-menu</a></p>
<p><b>Related National Policy</b></p>	<p>Manual for Prescribed Specialised Services 2013/14 Adult specialist endocrinology services (Chapter 9). Parathyroidectomy</p> <p><a href="http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf">http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf</a></p> <p>Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 1a, 1b, 2.1, 2.2, 2.3, and 2.7.</p> <p><a href="https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf">https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf</a></p>

### Questions for consultation

Have all relevant comparators for etelcalcetide been included in the scope?  
Which treatments are considered to be established clinical practice in the NHS for treating secondary hyperparathyroidism in people with chronic kidney disease?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom etelcalcetide is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider etelcalcetide will fit into the existing NICE pathway, '[Chronic kidney disease](#)'?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which etelcalcetide will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider etelcalcetide to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of etelcalcetide can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at <http://www.nice.org.uk/article/pmg19/chapter/1-Introduction>)

### References

1. Rao A, Casula A, Casteldine C (2014) UK Renal Replacement Therapy Prevalence in 2013: National and Centre-specific Analyses, UK Renal Registry 17th Annual Report (Chapter 2): 39-64  
<https://www.renalreg.org/wp-content/uploads/2014/12/02-Chap-02.pdf>  
(accessed November 2015)