NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Cinacalcet HCl for the treatment of hyperparathyroidism secondary to impaired renal function

Draft scope

Draft remit / appraisal objective:
To appraise the clinical and cost effectiveness of cinacalcet HCl for the treatment of hyperparathyroidism secondary to impaired renal function.

Background:
People with chronic renal disease, particularly those on dialysis, often suffer from secondary hyperparathyroidism. This disorder is characterised by persistently elevated levels of parathyroid hormone (PTH) and complicated by disturbances in phosphate and calcium metabolism, which in turn are associated with increased long-term morbidity and possibly mortality. Clinical manifestations include vascular calcification and renal osteodystrophy with symptoms including bone, joint and muscle pain. There is an increased risk of fracture, tendon rupture and cardiovascular disease.

In 2001 there were approximately 30,000 people in England and Wales receiving renal replacement therapy including approximately 15,500 on dialysis. The incidence and prevalence of renal impairment and established renal failure is expected to increase as the population ages and the prevalence of diabetes increases. Between 40 and 50% of patients on dialysis have PTH or phosphate levels outside the recommended range.

The goal of current therapies is to re-establish homeostasis of serum phosphate, PTH and calcium levels. Conventional therapy includes dietary modification, the use of phosphate binders or vitamin D analogues, adjustments to the dialysis regimen, and calcium supplementation. The optimum combination of therapies for individuals changes over time and varies between patients. Some patients require sub-total parathyroidectomy.

The technology:
Cinacalcet HCl is an orally administered calcimimetic compound that increases the sensitivity of calcium-sensing receptors in the parathyroid gland. It inhibits the release of PTH within a few hours of administration, thus reducing serum calcium and phosphate. Patients who receive cinacalcet may need additional monitoring for calcium, phosphate and PTH levels compared with people who receive current standard treatments for renal failure.

Cinacalcet HCl is not currently licensed in the UK. Amgen submitted a licensing application to the EMEA for the treatment of hyperparathyroidism secondary to renal failure in October 2003. The FDA approved cinacalcet for

the treatment of secondary hyperparathyroidism in patients with chronic kidney disease on dialysis, and for the treatment of hypercalcaemia in patients with parathyroid carcinoma in March 2004.

Intervention(s)	Cinacalcet HCl (Sensipar) as an adjunct to current standard treatments
Population(s)	Adults with hyperparathyroidism secondary to renal failure
Current standard comparators	Standard management strategies not including cinacalcet
Outcomes	Outcomes should include: • survival • morbidity – incidence of fractures and tendon ruptures related to renal osteodystrophy – incidence of cardiovascular events related to vascular calcification – need for sub-total parathyroidectomy • in the absence of directly measured mortality and morbidity outcomes, biochemical markers may be considered as potential surrogate outcomes • health-related quality of life • adverse effects of treatment
Economic analysis	The reference case stipulates that the cost effectiveness of treatments of cinacalcet should be expressed in terms of incremental cost per quality-adjusted life year. Treatment duration is unknown, but may be for life. The time horizon of the economic analysis should reflect the life expectancy of people with renal failure. Costs will be considered from an NHS and Personal Social Services perspective.

Other considerations	Conventional therapy includes dietary modification, alteration of the dialysis regimen and drugs such as phosphate binders and vitamin D analogues. These treatments may be used concomitantly with cinacalcet. Therefore, the addition of cinacalcet to conventional management strategies will be compared to conventional management strategies alone. The intervention will be appraised according to its anticipated licensed indication. Guidance will only be issued in accordance with marketing authorisation. EMEA licence approval for cinacalcet is anticipated within an appropriate time frame for this appraisal. Price and specific indications are currently not known.