

NICE appraisal – CINACALCET

Response from The British Renal Society

The council of the British Renal Society has considered the draft NICE appraisal of cinacalcet. We would like to make the following observations.

1. The main conclusion of this appraisal, that the committee does not recommend the use of cinacalcet for the routine treatment of secondary hyperparathyroidism, is reasonable. For routine management of SHPT, alfacalcidol together with calcium carbonate or acetate phosphate binders should provide adequate treatment.
2. For patients with tertiary hyperparathyroidism whose PTH and calcium remain high when all calcium containing phosphate binders have been stopped, there is no treatment available except cinacalcet or parathyroidectomy. The document suggests that parathyroidectomy is 'unsuccessful' in 8% of cases. What little long-term data on parathyroidectomy there is suggests that, in the long term, the success rate may be as low as 20%. These are cases in which the PTH level is in the desired range of 2-5 x normal. There is a high incidence of absent or low PTH levels post-PTX (as high as 65% after total parathyroidectomy) and a high incidence of recurrent severe hyperparathyroidism (15% or so after total parathyroidectomy). The document almost totally ignores problems associated with low PTH levels. The literature suggests that as well as there being an increased mortality at very high PTH levels – there is also a high mortality associated with very low levels. Very low levels are also associated with adynamic bone disease and enhanced vascular calcification. There are similar 'success' rates after subtotal and total with reimplantation, though in both these cases the incidence of chronic hypoparathyroidism is less and the incidence of severe recurrent hyperparathyroidism. There is a high early mortality after parathyroidectomy and a hugely increased complication profile of parathyroidectomy in patients with end-stage renal failure compared to that after primary parathyroidectomy. Cinacalcet is a potential alternative to parathyroidectomy and it will be difficult to recommend parathyroidectomy for a sizeable proportion of patients, especially if the increased risks related to end-stage renal disease are complicated by significant extra-renal co-morbidities.
3. The recommendations are based on the output of a complex modelling process. There are problems with the primary stratification, which is by PTH levels alone. A PTH level, unqualified by a serum calcium or calcium x phosphate product, is almost meaningless. In most individuals with end-stage renal failure and hyperparathyroidism, the PTH level can be manipulated from very low to very high depending on the level of serum calcium one is trying to achieve. A high PTH in the context of a serum calcium of 1.8mmol/l is a world away from the same PTH level with a serum calcium of 2.8mmol/l. It is necessary to define severe hyperparathyroidism appropriately – that is a high PTH in the context of a serum calcium at the upper levels of normal or even high, after appropriate 'standard therapy'. We suggest that had the

modelling been done in this group the outcome may have been different, especially if the points in paragraphs 1, 3 and 4 are also taken into account. . We appreciate that there is limited available evidence to base on which to base such modelling but point out that there are huge numbers of approximations in the model as presented, including the unsustainable assumption that a single PTH reading means very much at all.

4. The costs in the appraisal were based on the use of cinacalcet in a manner similar to its use in the clinical trials, in which the drug was essentially continued for the duration of the trial at maximum dose in poor or non-responders. This is not the appropriate basis on which to cost. It would be more appropriate to stop the drug in such cases after a reasonable trial period. We suggest that it would be reasonable to re-analyse the data with this rule.
5. There is reasonable evidence of an improvement of haemoglobin levels on resolution of severe hyperparathyroidism. There is reasonable evidence of a reduction in serum phosphate levels with cinacalcet. This may entail savings on EPO and phosphate binders, some of which are very expensive.
6. In summary, The British Renal Society maintains the view that Cinacalcet should be available for treatment of severe secondary hyperparathyroidism with hypercalcaemia especially where parathyroidectomy is deemed to have high surgical risk. Moreover, its use can also be justified in patients with calciphylaxis associated with SHPT which has devastating consequences although the evidence so far is anecdotal (Valesco et al, Nephrol Dial Transplant, 2006: 1999-2004).

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