

Response from Dr M J D Cassidy on behalf of the Renal Association

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Appraisal Consultation Document

Cinacalcet hydrochloride for the treatment of secondary hyperparathyroidism in patients with end-stage renal disease on maintenance dialysis therapy

Appraisal Committee's preliminary recommendations

Cinacalcet hydrochloride is not recommended for the routine treatment of secondary hyperparathyroidism in patients with end-stage renal disease on maintenance dialysis therapy.

Response

While it is clear that treatment with cinacalcet hydrochloride leads to significant improvement in the biochemical parameters of secondary hyperparathyroidism I would agree that until additional randomised trials become available the benefits of this drug on patient based end points are uncertain. This concurs with the recently published meta-analysis of biochemical and patient level effects of calcimimetic therapy by the Cochrane Renal Group ¹. It is very likely that treatment with cinacalcet hydrochloride will demonstrate clinical benefits in terms of reduction in adverse events but the evidence is not conclusively there yet.

I would be grateful however if the Committee would review their recommendations in 4.3.6 which states:-

4.3.6 The Committee heard from the experts that there may be a very small subgroup of people with refractory or 'tertiary' hyperparathyroidism for whom cinacalcet hydrochloride may be an alternative to surgical parathyroidectomy. This option may be particularly useful where surgical risk is considered to be high. However, there was insufficient clinical evidence on the effectiveness of cinacalcet hydrochloride in this subgroup, and there was no evidence on the clinical effectiveness of cinacalcet hydrochloride compared with surgical parathyroidectomy. In addition, cost-effectiveness analysis suggested that cinacalcet hydrochloride was less cost effective in people with very uncontrolled hyperparathyroidism, although the extent to which this analysis reflected the population with refractory disease was not clear. The Committee therefore concluded that there was insufficient evidence to enable it to recommend cinacalcet hydrochloride in this group.

I agree that this small sub-group of patients has not been specifically investigated to assess the benefits of cinacalcet. That cinacalcet significantly improves the biochemical

parameters of hyperparathyroidism however is acknowledged by all and while we await out-come data it is clear that some patients that fall into this small sub-group, including those with calciphylaxis will benefit from treatment as shown in case reports 2. The evidence currently is only at case report level and it is unlikely that large trials will be able to show benefit in calciphylaxis as the prevalence of this condition is very low. I do not think that a cost-effective analysis is valid here. I do think that a stopping rule could be included for this sub-group of patients for non-responders after 3 months of treatment.

Therefore, while aware that the evidence base is limited as mentioned above, I would urge the Committee to reconsider its recommendation for the use of cinacalcet hydrochloride in this sub-group of patients.

- 1) Strippoli G.F.M., Palmer S., Tong A., Elder G., Messe P., Craig J.C. Meta-Analysis of Biochemical and Patient-Level Effects of Calcimimetic Therapy. *Am J Kidney Dis* 2006; 47: 715-726.
- 2) Nestor Velasco, Mark S. MacGregor, Andrew Innes and Ian G. MacKay. Successful treatment of calciphylaxis with cinacalcet—an alternative to parathyroidectomy? *Nephrology Dialysis Transplantation* 2006; 21:1999-2004.

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