NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Cinacalcet hydrochloride for the treatment of secondary hyperparathyroidism

Responses to comments via the NICE website on the Appraisal Consultation Document

Patient representatives and clinical experts

Profession	Section	Comment	Action/response
NHS Professional (1)	1	I agree, not for all or even most cases of SHPT	
	2	You are ignoring the abundant evidence that the existing therapies, calcium and vitamin D, while changing bone lesions, and leading to some reduction in PTH, have vascular calcification associated with them. So they are very far from perfect.	
	4	I can see your points. And I agree there are no trials of cinacalcet use in groups including people awaiting kidney transplants from living donors, people with calciphylaxis, people with recurrent hyperparathyroidism after parathyroidectomy, and people in whom surgical parathyroidectomy is contraindicated. But why trials can you expect here? It would not be ethical to conduct such trials. You can only expect case reports, and anecdotes. This drug for perhaps 1-3% of renal patients could be life-saving. It is this that disturbs me. To ""ban"" it completely will hinder its use. I completely agree more evidence is needed, but as a clinician I am sure some patients will die without access to it.	See 1.2 in new ACD – allows for prescribing in a subgroup of those with refractory disease in whom parathyroidectomy is contraindicated
	6	Hugely important.	
	8	I think for the Institute to have studied this therapy for SHPT in isolation makes little sense. You should have studied the whole area, including sevelamer and lanthanum. I do think you will need to return to this area sooner than 12/2009	Remit was for cinacalcet hydrochloride only.

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NHS Professional (2) – has acted as investigator on some trials and received honoraria from Amgen for educational events.	1	I believe that the committee should permit its use in selected cases - in particular dialysis patients with uncontrolled hyperparathyroidism who have a high co-morbid burden and for whom parathyroidectomy would be too risky. It would be reasonable to state that if there is not a sufficient effect after a trial period of the medication (eg 6 months) then its use should be terminated.	See new ACD sections 1.2 and 4.3.6
	2	Surgical parathyroidectomy is not an ideal treatment for these patients - depending on the technique (we use subtotal parathyroidectomy) it leads to a dramatic fall in pth levels - to a level associated with aedynamic bone disease in a large proportion of patients for a period. This is likely to be associated with an increased fracture risk. After a period of time the remaining parathyroid tissue can once again become hyperplastic - with pth levels running above the appropriate range. Some patients require repeat surgery eventually. Thus parathyroidectomy does not control secondary parathyroidism in an optimal sense - but is more or less ablative.	
	3	In the OPTIMA study - which has recently been completed - and presented in abstract form, most patients were on 60 mg per day or less.	The Committee considered a strategy that limited maximum dose
	4	Cinacalcet is certainly effective in many patients to lower pth levels - a condition which can be very difficult to manage in ESRD patients. This effect has been in addition to standard current therapies including active vitamin D. Untreated this condition is associated with severe morbidity, and there is associative data for pth, and Ca x P product of increased risk factors for mortality. We have experience of several dialysis patients for whom parathyroid surgery is not a possibility due to co-morbid burden and have uncontrolled secondary hyperparathyroidism despite maximal current medical therapy. Cinacalcet can have a beneficial effect in this group - and I believe that you should allow its use in such difficult cases. There is a significant risk for the NHS in subjecting unfit patients to surgery, or in allowing patients to deteriorate to a condition of dependency.	
	6	Some of these areas are problematic to study - such as calciphylaxis, which is rare and has an associated extremely high mortality.	See new ACD sections 1.2 and 4.3.6

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NHS Professional (3)	General	Disappointing conclusion. Agree with first comment on not recommending for routine treatment of SHPT but would wish to utilise in refractory SHPT or non-responders. Parathyoroidectomy is not without its complications and requires resources and skills which may not be informally available. Moreover surgical activity probably only tackles the tip of the demand iceberg in terms oc clinical need for good control of SHPT. Intervention is usually to little too late and should start earlier in the CKD cycle. Finally where does patient choice come in ?? Faced with medication or yet another surgical procedure many would choose the former.	See new ACD sections 1.2 and 4.3.6
NHS Professional – Consultant nephrologist (4)	1 2 4	This recommendation (routine treatment of secondary hyperparathyroidism) may put at risk patients for whom cinacalcet would be a much safer alternative to parathyroidectomy....unless direct reference is made to this subgroup. The anaesthetic risks to some patients for whom parathyroidectomy would have otherwise been recommended are not to be understimated and it is in this group that calcimimetics may have a particularly important role to play. It is one of the "dangers" of NICE that its "directives" based on evidence for a "population group (eg Dialysed patients)" are then used to prevent the use of a drug for a "subgroup (eg 4.3.6)" in whom there is a much more powerful clinical case. I suspect that all nephrologists will be looking after a few patients for whom they strongly suspect that cinacalcet would be of considerable benefit if they were able to prescribe it. Anaesthetic risk will often be the reason that prevents surgery...examples being 2 inpatients of mine at present both of whom are hypercalaemic as a result of hyperparathyroidism.....one has tight calcific aortic stenosis the other severe kyphoscoliosis as a result of spina bifida. I am unable to prescribe cinalcet for either but suspect that were I able to do so it would be of benefit. A NICE directive that "Cinacalcet is not to be used for the routine treatment of secondary hyperparathyroidism" will probably prevent its use under any circumstances unless appropriate qualifying remarks are made. Because of the nature of these sort of clinical situations "evidence" from randomised controlled trials is most unlikely to become available.	See new ACD sections 1.2 and 4.3.6 The Committee have reconsidered the issue of subgroups – section 4.3.6 is revised in the new ACD.

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NHS Professional – Consultant nephrologist (4 continued)	6	6.2 Identifies the "lack of evidence"...and by implication suggests that more information is required. However, because it is likely that its advice for "secondary hyperparathyroidism" will be interpreted by the "pursestrings" as Cinacalcet is "not recommended" those groups with particular needs will be deprived as well.	See new ACD section 1.2
NHS Professional – Consultant nephrologist (5)	2	There are factual errors in 2.6. Neither phosphate nor PTH are managed to re-establish normal values: target for phosphate in Renal Association guidelines is <1.8 mmol/l (NR 0.8 - 1.45), and target for PTH is "less than 4 times the upper limit of normal of the assay used", to avoid adynamic bone disease which is associated with increased development of vascular calcification, itself a marker of poor cardiovascular outcome.	Amended
	6	Studies of outcome and concomitant standard drug use in patients naive to treatments of renal bone disease would be useful: current studies show the effects of adding cinacalcet to standard therapy in patients biochemically defined to have failed that treatment. Thus, no evidence of effect of progression of bone disease in the ESRD cohort as a whole, only on worst-case patients. However, current therapies can be hypothesised to contribute to poor CV outcome due to their side effects (hypercalcaemia, hyperphosphataemia, elevated CaxPO4)even in patients who respond well, and thus this cohort may also benefit from cinacalcet if it has a favourable side effect profile and faciliatates reduction of other medication dosing.	
NHS Professional – Consultant nephrologist (6)	1	I agree that this should not be routine treatment, but I think that the NICE should look at the subgroup of patients with severe hyperparathyroidism in whom it is an effective and potentially cost saving therapy.	Comments noted
	2	agreed	
	3	agreed	

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NHS Professional – Consultant nephrologist (6 continued)	4	We have performed an observational study of the cost effectiveness of this drug in patients who would have otherwise been referred for parathyroidectomy. We have found that in this group the drug was effective and cost saving. We have presented this data in abstract form and are awaiting a publication of this data. Section 4.3.7 is very prescriptive in nature and this advice means that current recipients of this drug (even those in whom we can show that use of cinacalcet has resulted in an improved clinical state and a net saving on their drug costs) will need to be taken off the drug. Switching to an alternative (and probably inferior) strategy potentially harms patients. I think that NICE should reconsider this particular statement. Our data suggests that this difficult to manage group actually cost more to care for with inferior results without this drug(eg our data suggest that costs of expensive phosphate binders reduce and EPO doses are reduced).	The Committee considered the cost effectiveness of various strategies for use of cinacalcet. None was cost saving. NICE guidance is not retrospective so patients currently on treatment may continue if appropriate.
.	6	Agreed	
	8	This is an amazingly effective new drug with rapidly a evolving literature. Our experience with it is that it has transformed the life of some of our sickest patients. We believe that the guidance on this technology should be reviewed much sooner than 12/09 as data is rapidly accumulating for a specific role in a targeted population, that will prove not only clinically effective but might also show cost savings.	Consultees can request an early review if important new data become available
The National Kidney Federation	1	The National Kidney Federation represents 40,000 ERF patients of which 20,000 are on Dialysis. There is no satisfactory treatment yet available for secondary hyperparathyroidism and therefore we are seriously concerned at the preliminary recommendations as we believe that if used it may well be shown to be effective.	
	2	Surgical parathyroidectomy is a poor treatment. It is frequently not effective, exposes the patient to the very real risk of infection and leaves the patient without the parathyroid gland - a factor they will live to regret should they subsequently receive a transplant and wish to commence a normal life once more. Such unnecessary mutilation should be halted if there is an alternative.	See new ACD sections 1.2 and 4.3.6

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The National Kidney Federation (continued)	3	We have no comment about the cost of this treatment - it is not the patients major concern, - his health is.	The Committee is required to consider both clinical and cost effectiveness.