NICE STA

Alitretinoin for the treatment of chronic eczema of the hand, refractory to steroids

Comments on the ACD from the British Association of Dermatologists

i) We do consider that all of the relevant evidence has been taken into account.

iv) We do not feel that there are any equality related issues that need special consideration that are not covered in the ACD.

ii) and iii) See comments below:

1) We feel that too much emphasis is being placed on the DLQI as a severity assessment tool in this condition. This condition, being limited to a specific body site is very different to a generalised disease like psoriasis although the impact on quality of life is often large, given that it affects the hands. If DLQI is to be used then what is the evidence for a score of 15 as opposed to 10 for the biologics? This high score could exclude a significant number of deserving patients and it would make more sense to use the same DLQI as for the biologics, bearing in mind also that Alitretinoin is significantly less expensive than the biologics. This would demonstrate a consistent approach by NICE to the impact of differing dermatological diseases and might be perceived as "fairer" by external observers such as our patient groups.

2) We also have concerns regarding the ranking of Alitretinoin relative to its conparators. Alitretinoin is licensed for this indication and the comparators of PUVA, Azathioprine and Ciclosporin are not. Although it is not always better to use a licensed product, by placing Alitretinoin after these comparators, it appears that NICE is actively advising unlicensed in preference to licensed treatment. In addition, there is more evidence to support the use of Alitretinoin however, without the comparative studies that have not yet been performed, there is no evidence that Alitretinoin is clinically superior to the other treatments.
Given that the risks associated with the use of immunosuppressant drugs (especially infection and malignancies) are higher than with a retinoid, we would suggest that Alitretinoin would be better placed after PUVA and before Azathioprine and Ciclosporin or after the patient has failed on any one of the comparators.

3) The ACD states that treatment should be discontinued as soon as an adequate response has been achieved. Should there be guidance about when to restart Alitretinoin and whether the same thresholds apply? There would be an argument for reintroducing at a lower level of disease severity to avoid patients relapsing to pre-treatment levels.

4) See executable model proforma for comments on the economic case. The financial calculations here are very dependent on whether patients are attending to see a dermatologist every 4, 6 or 12 weeks for either support or monitoring of treatment. The reality in the NHS is that there is no spare capacity for additional follow up patients. It is therefore hypothetical to make these comparisons. The appraisal should consider the capacity that would have to be put in place in order for any option to be

considered. This is likely to be dermatology nurse monitoring clinics which have different costs to dermatologist clinics and thus will alter the calculation.

Issue 1 Unlicensed therapies lacking in evidence must be used before licensed therapy

Description of problem	Description of proposed amendment	
According to GMC, use of unlicensed medicines should be considered where the clinician takes responsibility for an assessment that there is not a licensed more effective therapy. (Good practice in prescribing medicines 2008). This was raised by the clinical experts but not recorded in the ACD. According to GMC, the clinician prescribing off label must be satisfied that an "alternative licensed medicine would not meet the patients needs." "Be satisfied that it would better serve the patients needs than an appropriate licensed alternative" And "Be satisfied that there is a sufficient evidence base and experience of using the medicine to demonstrate its safety and efficacy and document the reasons for choosing the therapy in the patients' notes" and must discuss this with the patient. In a guideline development process alitretinoin would be more highly recommended than the comparators because the level of evidence for its use	We suggest that the clinician be given latitude to choose the most appropriate therapy for the patient based on his knowledge of the alternative therapies and considering that the alternatives are much cheaper than alitretinoin. A compromise might be to require that a single second line therapy (azathioprine, ciclosporin or PUVA) has been ineffective or contraindicated.	

is exceeded. Put another way, the positioning alitretinoin after failure of azathioprine, ciclosporin and PUVA does not have an evidence base.		

Issue 2 Related to 1 clinical and economic case for positioning of alitretinoin

Description of problem	Description of proposed amendment	
That the appraisal will make this treatment available to patients with high need disabling hand dermatitis who have failed other therapies is welcomed. Clinical experts recognised the need to restrict the use of this treatment which would have a large budget impact. However, a typical patient will have to fail a line of therapy including potent topical steroids, azathioprine, ciclosporin and PUVA which could mean a long road with much resource use before alitretinoin is used and this was not the model used in the economic assessment. Patients would typically require 12 months of ineffective therapy with loss of earnings before gaining access to alitretinoin. Receiving an effective treatment early in the algorithm of therapy will have	The cost benefit of about 18-20 months of repeated therapeutic failures attended with side effects followed finally by alitretinoin could be compared to that of intermittent alitretinoin as first line therapy. There are uncertainties around the benefit of current therapies that make such assessment challenging but with sensitivity analysis based on uncertainty of the manufacturers model an estimate of saving by earlier introduction of alitretinoin in the algorithm could be decisive.	

cost, quality of life and societal benefits. Insisting on failure of all of these treatments will inevitably lead to greater use of the first line therapies which are not currently favoured because of their toxicity.		

Issue 3 Choice DLQI threshold

Description of problem	**Description of proposed amendment**	
In earlier appraisals for anti-TNF therapy in psoriasis a DLQI >10 was accepted as evidenced by Prof A Finlay as indicative of severe QOL impairment for psoriasis requiring admission or secondary drug therapies. We have no doubt that patients with severe hand dermatitis would have DLQIs of this order but question the evidence supporting the choice of this threshold which could deny therapy to a patient with DLQI for example of 13 which would represent quite disabling disease.	Give details of any amendments/corrections made in sufficient detail to allow these to be reproduced	