

# NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

## GUIDANCE EXECUTIVE (GE)

### Review of TA177; Alitretinoin for the treatment of severe chronic hand eczema

This guidance was issued in August 2009

The review date for this guidance is August 2012

#### 1. Recommendation

The guidance should be transferred to the 'static guidance list'. That we consult on this proposal.

#### 2. Original remit(s)

To appraise the clinical and cost effectiveness of oral alitretinoin within its licensed indication for the treatment of severe chronic hand eczema.

#### 3. Current guidance

1.1 Alitretinoin is recommended, within its licensed indication, as a treatment option for adults with severe chronic hand eczema that has not responded to potent topical corticosteroids if the person has:

- severe disease, as defined by the physician's global assessment (PGA) **and**
- a dermatology life quality index (DLQI) score of 15 or more.

1.2 Alitretinoin treatment should be stopped:

- as soon as an adequate response (hands clear or almost clear) has been achieved **or**
- if the eczema remains severe (as defined by the PGA) at 12 weeks **or**
- if an adequate response (hands clear or almost clear) has not been achieved by 24 weeks.

1.3 Only dermatologists, or physicians with experience in both managing severe chronic hand eczema and the use of systemic retinoids, should start and monitor treatment with alitretinoin.

1.4 When using the DLQI, healthcare professionals should take into account any physical, sensory or learning disabilities, or other communication difficulties that could affect the responses to the DLQI. In such cases, healthcare professionals should ensure that the DLQI continues to be a sufficiently accurate measure.

#### **4. Rationale<sup>1</sup>**

No new evidence has emerged since the publication of TA177 and there are no changes in the marketing authorisation or price. There are very few ongoing trials and the results of these are not expected to change the recommendations.

#### **5. Implications for other guidance producing programmes**

There is no proposed or ongoing guidance development within the Centre for Clinical Practice that overlaps with this review proposal.

#### **6. New evidence**

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from November 2007 onwards were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section below. See Appendix 2 for further details of ongoing and unpublished studies.

#### **7. Summary of evidence and implications for review**

The UK marketing authorisation for alitretinoin (Toctino, Basilea) for use in adults who have severe chronic hand eczema that is unresponsive to treatment with potent topical corticosteroids has not changed from when TA177 was issued in 2009. The comparators in the original guidance (ultraviolet light therapies [PUVA] and immunosuppressive therapies [azathioprine and ciclosporin]) have stayed the same and no new comparators have emerged. The costs for alitretinoin and the comparators have not significantly changed.

Since the BAP0003, BAP00089 and BAP00091 trials, which were reviewed during the development of TA177, no new evidence has been published that is directly relevant to the population described in TA177 as eligible for treatment with alitretinoin. No trials have been conducted that directly compare alitretinoin with PUVA or immunosuppressant therapies. There was one registered and unpublished trial and one poster identified during this review.

Wootton et al. 2012 presented a poster demonstrating that alitretinoin and PUVA had similar efficacy within one dermatology department. Additionally, there is a Phase IV trial registered that is not yet recruiting that will compare ciclosporin with alitretinoin for severe atopic hand dermatitis (TocyDD trial). The HANDEL trial is an ongoing Phase III study examining alitretinoin compared with placebo in patients with severe hand eczema, due to end in 2012. None of this evidence is currently available or expected to lead to a change in the recommendations in the future.

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<sup>1</sup> A list of the options for consideration, and the consequences of each option is provided in Appendix 1 at the end of this paper

## **8. Implementation**

A submission from Implementation is included in Appendix 3. Figures 1, 2 and 3 show that the volume and cost of alitretinoin dispensed in in the community and in hospitals rose considerably after the introduction of TA177 in 2009. Given that alitretinoin does not have any other licensed indications, these figures suggest that the NICE guidance has been implemented.

## **9. Equality issues**

The original guidance noted that the dermatology life quality index (DLQI) includes aspects that depend on physical activity, such as shopping, working in the home or garden, and sport. The guidance therefore specified that the DLQI should be used judiciously in people with a physical disability to take account of a lower baseline activity level, and to ensure that sensory or learning disabilities did not affect the response to the DLQI.

**GE paper sign off:** Elisabeth George, 12 07 12

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## Appendix 1 – explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	Consequence	Selected – ‘Yes/No’
A review of the guidance should be planned into the appraisal work programme.	A review of the appraisal will be planned into the NICE’s work programme.	No – as no new evidence or significant trial activity has been found
The decision to review the guidance should be deferred to [specify date or trial].	NICE will reconsider whether a review is necessary at the specified date.	No – as no significant trial activity has been found that is expected to affect the recommendations.
A review of the guidance should be combined with a review of a related technology appraisal.	A review of the appraisal(s) will be planned into NICE’s work programme as a Multiple Technology Appraisal, alongside the specified related technology.	No – as no related TA has been identified
A review of the guidance should be combined with a new technology appraisal that has recently been referred to NICE.	A review of the appraisal(s) will be planned into NICE’s work programme as a Multiple Technology Appraisal, alongside the newly referred technology.	No - as no related TA has been identified
The guidance should be incorporated into an on-going clinical guideline.	<p>The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review.</p> <p>This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.</p>	No as no - ongoing guideline has been identified

Options	Consequence	Selected – ‘Yes/No’
The guidance should be updated in an on-going clinical guideline.	<p>Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn.</p> <p>Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).</p>	No – as no ongoing guideline has been identified
The guidance should be transferred to the ‘static guidance list’.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.	Yes – no new evidence and no significant trial activity has been found

NICE would typically consider updating a technology appraisal in an ongoing guideline if the following criteria were met:

- i. The technology falls within the scope of a clinical guideline (or public health guidance)
- ii. There is no proposed change to an existing Patient Access Scheme or Flexible Pricing arrangement for the technology, or no new proposal(s) for such a scheme or arrangement
- iii. There is no new evidence that is likely to lead to a significant change in the clinical and cost effectiveness of a treatment
- iv. The treatment is well established and embedded in the NHS. Evidence that a treatment is not well established or embedded may include;
  - Spending on a treatment for the indication which was the subject of the appraisal continues to rise
  - There is evidence of unjustified variation across the country in access to a treatment
  - There is plausible and verifiable information to suggest that the availability of the treatment is likely to suffer if the funding direction were removed

- The treatment is excluded from the Payment by Results tariff
- v. Stakeholder opinion, expressed in response to review consultation, is broadly supportive of the proposal.

## Appendix 2 – supporting information

### Relevant Institute work

#### *Published*

Clinical Guideline CG57 Atopic eczema in children. Issued December 2007, with a review decision in August 2011 not to update. The next review decision date is July 2014.

Technology Appraisal TA82 Atopic dermatitis (eczema): pimecrolimus and tacrolimus. Issued August 2004, and placed on the static list June 2009.

Technology Appraisal TA81 Atopic dermatitis (eczema): topical steroids. Issued August 2004, with a review decision to place on the static list December 2007.

### Details of changes to the indications of the technology

Indication considered in original appraisal	Proposed indication (for this appraisal)
Oral alitretinoin (Toctino, Basilea Pharmaceuticals) is indicated for use in adults who have severe chronic hand eczema that is unresponsive to treatment with potent topical corticosteroids.	The indication is the same.

### Registered and unpublished trials

Trial name and registration number	Details
Ciclosporin Versus Alitretinoin for Severe Atopic Hand Dermatitis. A Randomized Controlled Investigator-initiated Double-blind Trial NCT01231854	Phase IV study, not yet open for recruiting. Estimated enrollment: 78 Study start date: November 2010. Estimated study completion date: July 2013.
	Alitretinoin is: <ul style="list-style-type: none"><li>• In phase II for SLE: NCT01407679</li><li>• In phase II for lichen planus: NCT01538732</li><li>• In phase II for pustular psoriasis: NCT01245140</li></ul>

## References

Wootton C, English J (2012) Hand dermatitis: Alitretinoin versus PUVA. *Journal of the American Academy of Dermatology*. Conference (var.pagings): April-

## Appendix 3 – Implementation submission

### Implementation feedback: review of NICE technology appraisal guidance 177

NICE Technology Appraisal 177 Alitretinoin for the treatment of severe chronic hand eczema
Implementation input required by 13/06/2012
Please contact Rebecca Lea regarding any queries <a href="mailto:rebecca.lea@nice.org.uk">rebecca.lea@nice.org.uk</a>

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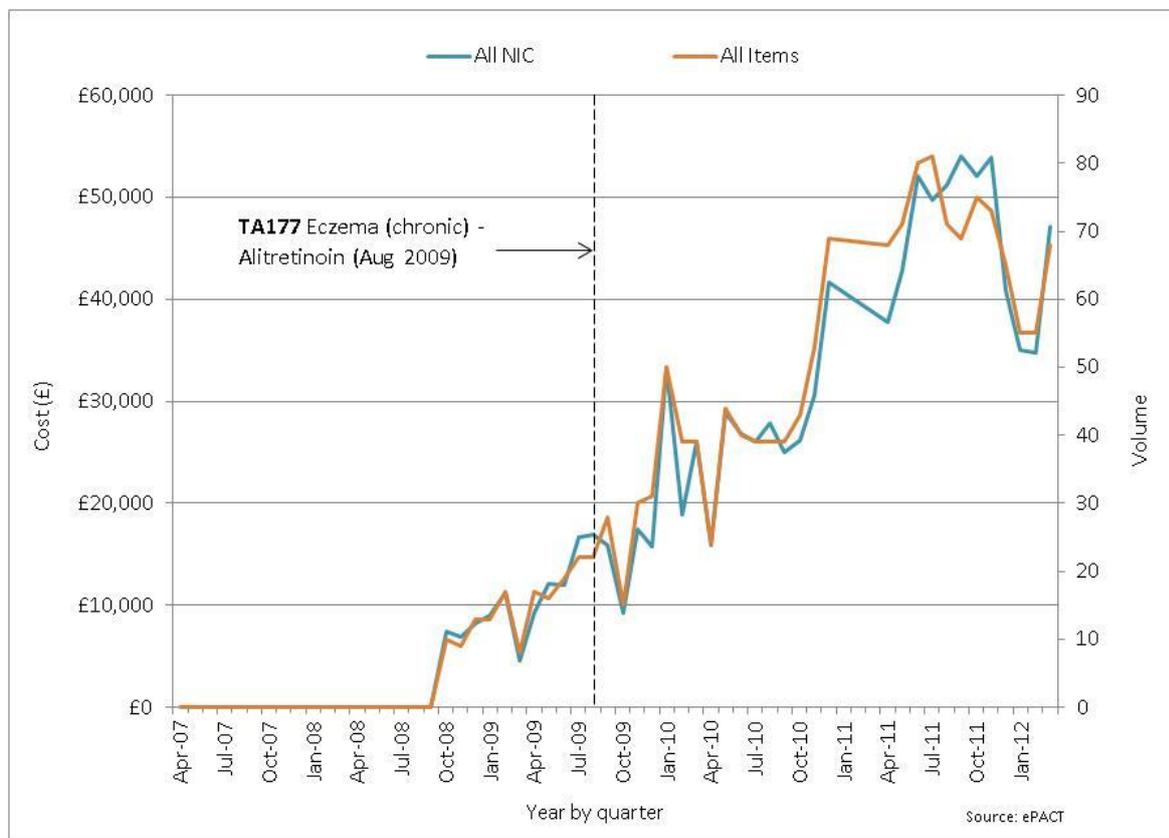
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# 1 Routine healthcare activity data

## 1.1 ePACT and Hospital ePACT data

This section presents ePACT and hospital ePACT data on the net ingredient cost (NIC) and volume of Alitretinoin prescribed in primary care and hospitals that has been dispensed in the community in England between April 2007 and March 2012.

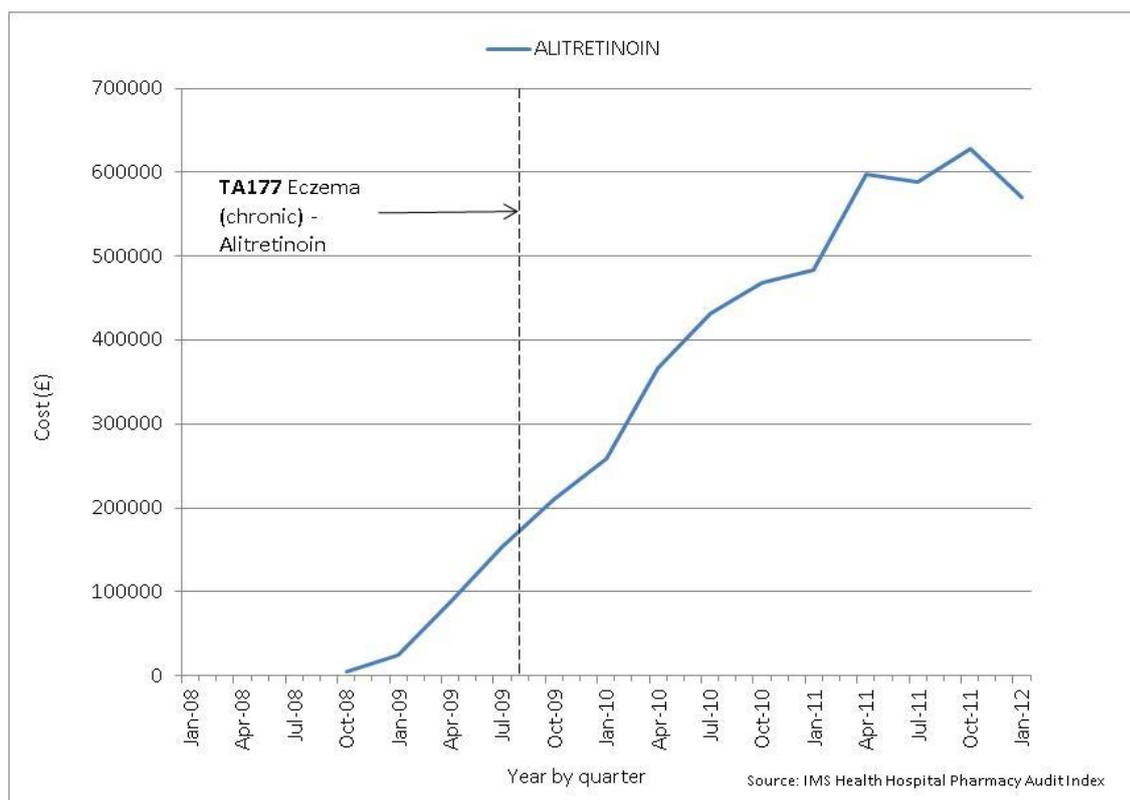
**Figure 1 Net ingredient cost and volume of Alitretinoin dispensed in the community**



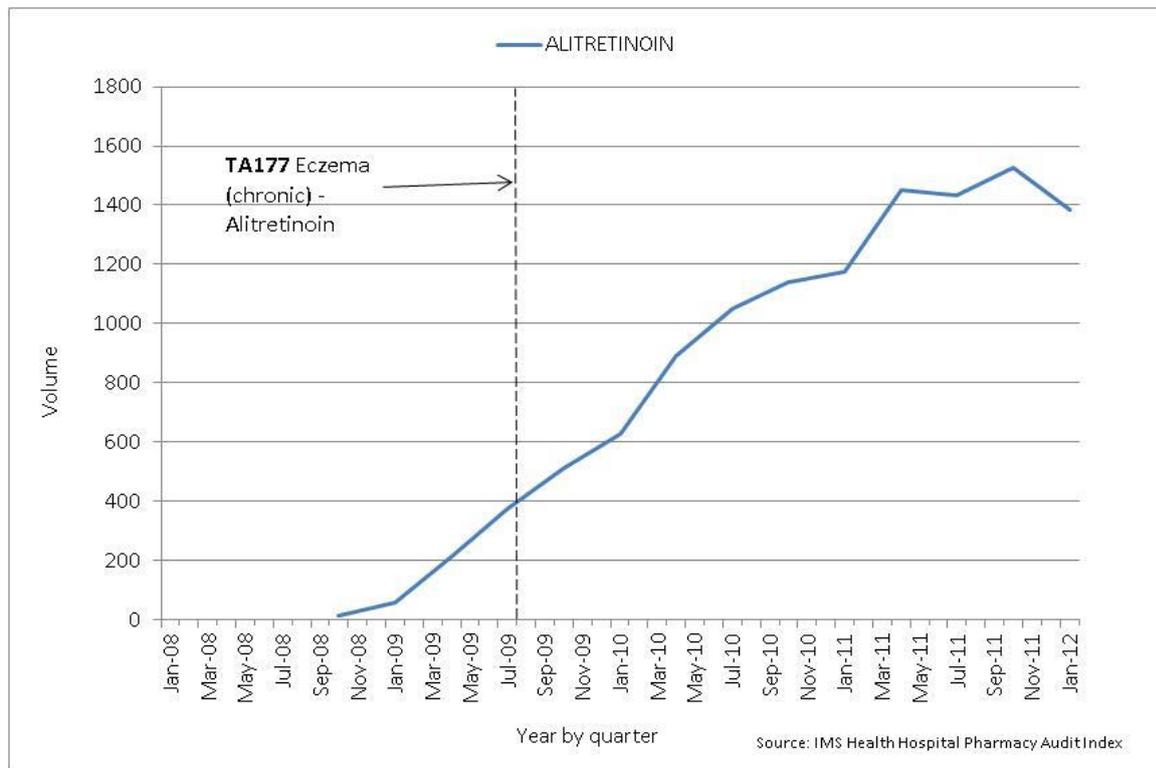
## 1.2 Hospital Pharmacy Audit Index Data

This section presents Hospital Pharmacy Audit Index (HPAI) data on the cost and volume of Alitretinoin prescribed and dispensed in hospitals in England between January 2008 and March 2012.

**Figure 2 Cost of Alitretinoin prescribed and dispensed in hospitals in England**



**Figure 3 Volume of Alitretinoin prescribed and dispensed in hospitals in England**



## 2 Implementation studies from published literature

Information is taken from the uptake database ([ERNIE](#)) website.

### 2.1 The NHS Information Centre for Health and Social Care (2011) [Use of NICE-appraised medicines in the NHS in England-2009, Experimental Statistics](#)

This is the second report commissioned by the Metrics Working Group to look at the variation in use of positively appraised medicines in relation to the expected use as predicted by NICE. In all, 47 medicines in 18 groups, relating to 29 technology appraisals were considered. Out of the 12 groups where a comparison could be made (these are presented in Section 1 of the technology section results), observed use by the NHS in England was higher than the predicted use for eight and lower for three.

### 3 Qualitative input from the field team

***The implementation field team have recorded the following feedback in relation to this guidance:***

Nothing to add at this time.

#### **Appendix A: Healthcare activity data definitions**

##### ***Prescribing analysis and cost tool system***

This information comes from the electronic prescribing analysis and cost tool (ePACT) system, which covers prescriptions by GPs and non-medical prescribers in England and dispensed in the community in the UK. The Prescription Services Division of the NHS Business Services Authority maintains the system. PACT data are used widely in the NHS to monitor prescribing at a local and national level. Prescriptions written in hospitals but dispensed in the community (FP10 [HP]) are not included in PACT data. Prescriptions dispensed in hospitals or mental health units, and private prescriptions, are not included in PACT data.

##### ***Measures of prescribing***

**Prescription Items:** Prescriptions are written on a prescription form. Each single item written on the form is counted as a prescription item. The number of items is a measure of how many times the drug has been prescribed.

**Cost:** The net ingredient cost (NIC) is the basic price of a drug listed in the drug tariff, or if not in the drug tariff, the manufacturer's list price.

##### ***Data limitations (national prescriptions)***

PACT data do not link to demographic data or information on patient diagnosis.

Therefore the data cannot be used to provide prescribing information by age and sex or prescribing for specific conditions where the same drug is licensed for more than one indication.

### *IMS HEALTH Hospital Pharmacy Audit Index (IMS HPAI)*

IMS HEALTH collects information from pharmacies in hospital trusts in the UK. The section of this database relating to England is available for monitoring the overall usage in drugs appraised by NICE. The IMS HPAI database is based on issues of medicines recorded on hospital pharmacy systems. Issues refer to all medicines supplied from hospital pharmacies: to wards; departments; clinics; theatres; satellite sites and to patients in outpatient clinics and on discharge.

#### ***Measures of prescribing***

**Volume:** The HPAI database measures volume in packs and a drug may be available in different pack sizes and pack sizes can vary between medicines.

**Cost:** Estimated costs are also calculated by IMS using the drug tariff and other standard price lists. Many hospitals receive discounts from suppliers and this is not reflected in the estimated cost.

Costs based on the drug tariff provide a degree of standardization allowing comparisons of prescribing data from different sources to be made. The costs stated in this report do not represent the true price paid by the NHS on medicines. The estimated costs are used as a proxy for utilization and are not suitable for financial planning.

#### ***Data limitations***

IMS HPAI data do not link to demographic or to diagnosis information on patients. Therefore, it cannot be used to provide prescribing information on age and sex or for prescribing of specific conditions where the same drug is licensed for more than one indication.