NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA164; Febuxostat for the management of hyperuricaemia in people with gout

This guidance was issued in December 2008.

The review date for this guidance is August 2011.

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 febuxostat for the management of hyperuricaemia in adults with gout.

3. Current guidance

1.1 Febuxostat, within its marketing authorisation, is recommended as an option for the management of chronic hyperuricaemia in gout only for people who are intolerant of allopurinol (as defined in section 1.2) or for whom allopurinol is contraindicated.

1.2 For the purposes of this guidance, intolerance of allopurinol is defined as adverse effects that are sufficiently severe to warrant its discontinuation, or to prevent full dose escalation for optimal effectiveness as appropriate within its marketing authorisation.

1.3 People currently receiving febuxostat should have the option to continue therapy until they and their clinicians consider it appropriate to stop.

4. Rationale[1]

The new clinical evidence that has been published since TA164 was issued is consistent with the conclusions by the Appraisal Committee on the clinical effectiveness of febuxostat. There has been no change to the price of febuxostat, and no information is available about any changes to the marketing authorisation or any new or ongoing trials of the effectiveness of febuxostat. Based on this information it is proposed that the guidance is placed on the static list.

[1] A list of the options for consideration, and the consequences of each option is provided in Appendix 1 at the end of this paper

5. Implications for other guidance producing programmes

There is no proposed or ongoing guidance development 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 **December 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 See Appendix 2 for further details of ongoing and unpublished studies.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 manufacturers of the intervention and comparator did not respond to the request for information about their marketing authorisations and about the availability of new evidence. Therefore it is not known whether they anticipate any extension of their current marketing authorisations in the foreseeable future or if the manufacturers are planning any new studies.

Since the publication of TA164 (Dec 2008), neither the marketing authorisation nor the price for the intervention or comparator included in the previous guidance has changed.

Since Dec 2008, 2 new RCTs have been published. Both studies evaluate the efficacy and safety of febuxostat compared with fixed dose (300mg) allopurinol for the management of hyperuricaemia in people with gout. These studies are consistent with the Appraisal Committee's conclusion in the original guidance that febuxostat is more effective at reducing serum uric acid concentration than fixed-dose (300mg) allopurinol.

In TA164, the manufacturer provided interim data from the FOCUS study, in support of the clinical effectiveness of febuxostat in the treatment of gout. The final results of this study have now been published and are consistent with the conclusions about the effectiveness of febuxostat in TA164.

No new UK based studies evaluating the cost effectiveness febuxostat for the treatment of gout have been identified.

In 2010, a protocol for a Cochrane systematic review to evaluate the efficacy and safety of febuxostat for the treatment of chronic gout was published.

8. Implementation

No submission was received from Implementation.

9. Equality issues

No equality issues were raised in the original guidance.

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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
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
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
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
The guidance should be incorporated into an on-going clinical guideline.	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. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No
The guidance should be updated in an on-going clinical guideline.	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. 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).	No

Options	Consequence	Selected – 'Yes/No'
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

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

CG43 Early identification and management of chronic kidney disease in adults in primary and secondary care. Issued Sep 2008. Due for renewal: Sep 2011

In topic selection[2]

[redacted]

Details of changes to the indications of the technology

Indication considered in original appraisal	Proposed indication (for this appraisal)
Febuxostat has a marketing authorisation for the treatment of chronic hyperuricaemia in conditions where urate/uric acid deposition has already occurred (including a history or the presence of tophi and/or gouty arthritis).	Unchanged

Details of new products

Drug (manufacturer)	Details (phase of development, expected launch date)
Pegloticase (Savient)	UK launch date Q2 2012. FDA granted licence in US Sep 2010
Rilonacept (Regeneron)	UK: Phase III trials. Estimated launch date 2012

[2] Information held by the NICE Topic Selection Team is treated as being potentially commercially sensitive by default. Details of the topics considered by NICE's Consideration Panels may be available on the NICE website, providing the manufacturers of the technologies under discussion have consented to the release of this information.

Registered and unpublished trials

Trial name and registration number	Details
Cardiovascular Safety of Febuxostat and Allopurinol in Patients With Gout and Cardiovascular Comorbidities (CARES) NCT01101035	Phase III. Recruiting. Estimated enrolment 7500. Estimated completion date Apr 2015
An Assessment of Chronic Synovial-Based Inflammation and Its Role With Serum Urate Levels. NCT01112982	Phase IV. Recruiting. Estimated enrolment 76. Estimated completion date: May 2011. Primary endpoint: Presence of synovial pannus in index joint (by MRI) even in the absence of gouty attacks. Secondary endpoint: Effect of urate-lowering therapy (specifically with febuxostat [Uloric]) on synovial pannus
Febuxostat, Blood Pressure and the Intrarenal Renin-Angiotensin System (RAS) NCT01328769	Phase IV. Recruiting. Estimated enrolment: 70 Estimated completion date: Dec 2012 To test the effect of lowering uric acid with febuxostat on the activity of the intrarenal renin-angiotensin system.

References

Becker MA, Schumacher HR, Espinoza LR et al. (2010) **The urate-lowering efficacy and safety of febuxostat in the treatment of the hyperuricemia of gout: The CONFIRMS trial**. *Arthritis Research and Therapy* 12 (2).

Becker MA, Schumacher HR, MacDonald PA et al. (June 2009) **Clinical efficacy and safety of successful longterm urate lowering with febuxostat or allopurinol in subjects with gout**. *Journal of Rheumatology* 36 (6): 1273-1282.

Schumacher HR BMLEMPL (Feb. 2009) **Febuxostat in the treatment of gout: 5-yr findings of the FOCUS efficacy and safety study**. *Rheumatology* 48 (2): 188-194.