NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA137 Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma (review of technology appraisal guidance 37)

This guidance was issued in February 2008.
The review date for this guidance is December 2010.

Recommendation

- A review of the guidance should be transferred to the 'static guidance list'. That we consult on the proposal.

Consideration of options for recommendation:

Options	Proposal	Comment
A review of the guidance should be planned into the appraisal work programme.	No	There is currently not enough new evidence to recommend that a review of the guidance should be planned into the appraisal work programme.
The decision to review the guidance should be deferred [to a specified date].	No	There is no reason to defer the review.
A review of the guidance should be combined with a review of a related technology and conducted at the scheduled time for the review of the related technology.	No	No related technology appraisals are due for review at present.
A review of the guidance should be combined with a new appraisal that has recently been referred to the Institute.	No	No relevant technology appraisals have recently been referred.
A review of the guidance should be incorporated into an on-going clinical guideline.	No	No relevant on-going clinical guidelines have been identified.
A review of the guidance should be updated into an on-going clinical guideline.*[1]	No	No relevant on-going clinical guidelines have been identified.

[1] See Appendix A on page 4

A review of the guidance should be transferred to the 'static guidance list'.	**Yes**	There is no new compelling evidence to suggest a review should be undertaken and no new evidence is anticipated.

Original remit(s)

To appraise the clinical and cost effectiveness of rituximab for recurrent or refractory stage III or IV follicular non-Hodgkin's lymphoma.

Current guidance

NOTE: This guidance replaces NICE technology appraisal guidance 37 issued in March 2002. The Institute reviews each piece of guidance it issues. The review and reappraisal of the use of rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma has resulted in a change in the guidance. In people with relapsed stage III or IV follicular non-Hodgkin's lymphoma, rituximab is now an option in combination with chemotherapy to induce remission or alone as maintenance therapy during remission. Rituximab monotherapy is also an option for people with relapsed or refractory disease when all alternative treatment options have been exhausted.

1 Guidance

1.1 Rituximab, within its marketing authorisation, in combination with chemotherapy, is recommended as an option for the induction of remission in people with relapsed stage III or IV follicular non- Hodgkin's lymphoma.

1.2 Rituximab monotherapy as maintenance therapy, within its marketing authorisation, is recommended as an option for the treatment of people with relapsed stage III or IV follicular non- Hodgkin's lymphoma in remission induced with chemotherapy with or without rituximab.

1.3 Rituximab monotherapy, within its marketing authorisation, is recommended as an option for the treatment of people with relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma, when all alternative treatment options have been exhausted (that is, if there is resistance to or intolerance of chemotherapy).

Relevant Institute work

Published

Rituximab for the treatment of follicular lymphoma. TA110. Issued: September 2006. Review date: June 2009 (Guidance Executive decided to update the guidance to include the extension to the licence covering a wider range of chemotherapy regimens).

Rituximab for aggressive non-Hodgkin's lymphoma. TA65. Issued: September 2003. Review date: August 2006 (Guidance Executive decided that the guidance should be placed on the static list).

Bendamustine for the treatment of indolent (low grade) non-Hodgkin's lymphoma that is refractory to rituximab (terminated appraisal). TA206. Issued: October 2010.

Improving outcomes in haemato-oncology cancer. Cancer service guidance CSGHO. Issued: October 2003.

In progress

Rituximab for the maintenance treatment of follicular non-Hodgkin's lymphoma following response to first-line chemotherapy. Referral date: March 2009. Expected date of publication: April 2011.

Rituximab for the treatment of follicular lymphoma (review of TA110). Expected date of publication: December 2011.

Suspended/terminated

None

In topic selection

Safety information

Summary of Product Characteristics updated May 2010. Respiratory System: cases of interstitial lung disease, some with fatal outcome have been reported.

Summary of Product Characteristics updated September 2007 with special warnings and precautions for use as very rare cases of Progressive Multifocal Leukoencephalopathy have been reported during post-marketing use of MabThera/Rituxan in NHL.

Details of changes to the indications of the technology

Drug (manufacturer)	Details
Rituximab (Roche)	The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMEA) has adopted (September 2010) a positive opinion recommending that the licensed indications for rituximab (MabThera) be extended to include the treatment of follicular lymphoma patients responding to induction therapy. [redacted] Licence extension added 2009: MabThera in combination with chemotherapy is indicated for the treatment of patients with previously untreated and relapsed/refractory chronic lymphocytic leukaemia. In Phase III Clinical Trials for ANCA-associated Vasculitis. In Phase III Clinical Trials for Systemic lupus erythematosus (SLE). [redacted] In Phase II Clinical Trials for Type 1 diabetes mellitus.

Details of new products

Drug (manufacturer)	Details
Afutuzumab (RG7159, GA101, RO5072759, Roche)	Proposed licence extension in Phase III clinical trials for indolent Non-Hodgkin's lymphoma (NHL). Estimated Primary Completion Date: January 2015.
BiovaxID (B cell lymphoma vaccine, Biovest International)	In Phase III clinical trials for Non-Hodgkin's lymphoma (NHL).
Bendamustine Hydrochloride (Levact in EU, Treanda in US,	Launched in EU, September 2010. Non-Hodgkins lymphoma second line.

Napp/Cephalon)	Approved in the EU as monotherapy for indolent NHL in patients who have progressed during or within 6 months following treatment with rituximab or a rituximab containing regimen.
Bortezomib (Velcade, Janssen-Cilag)	In Phase III clinical trials for relapsed or refractory follicular NHL comparing bortezomib plus rituximab with rituximab alone (trial completed June 2010). [redacted]
Iodine 131 Tositumomab (Bexxar, GlaxoSmithKline)	Licensed in US for Non-Hodgkin's lymphoma (NHL) July 2003.
Ofatumumab (Arzerra, GlaxoSmithKline)	In Phase III clinical trials for second-line therapy for Non-Hodgkin's lymphoma (NHL). [redacted]
Pixantrone (Pixuvri, Cell Therapeutics)	Marketing Authorisation application submitted to the European Medicines Agency on 1 November 2010 for pixantrone dimaleate as monotherapy for the treatment of adult patients with multiply relapsed or refractory aggressive non-Hodgkin's lymphoma. [redacted]

On-going trials

Trial name and contact	Details
Rituximab in Treating Patients With Follicular Non-Hodgkin's Lymphoma (SAKK 35/03) NCT00227695 Phase III Sponsor: Swiss Group for Clinical Cancer Research	Status: Ongoing, not recruiting Enrolment: 270 Study start date: June 2004 Completion date: September 2016 Purpose: This randomized phase III trial is studying rituximab to see how well it works when given over a short period of time compared to when given over a long period of time in treating patients with follicular non-Hodgkin's lymphoma.
MAXIMA Study: A Study of Maintenance Therapy With MabThera (Rituximab) in Patients With Non-Hodgkin's Lymphoma NCT00430352 Phase IV Sponsor: Hoffmann-La Roche	Status: Ongoing, not recruiting Enrolment: 540 Study start date: September 2006 Completion date: October 2010 Purpose: This single arm study will evaluate the safety and efficacy of MabThera maintenance therapy following a MabThera-containing induction regimen in first line or relapsed patients with follicular non-Hodgkin's lymphoma.

New evidence

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline(R) In-Process and Embase. References from April 2007 onwards were reviewed. The results of the literature search are discussed in the 'Appraisals comment' section below.

Implementation

A submission from Implementation is attached at the end of this paper. The use of rituximab has increased since the publication of TA 137, although important to note that rituximab is licensed for a number of indications

Equality and diversity issues

No equality and diversity issues have been identified.

Appraisals comment:

There is an anticipated license extension for rituximab. Positive CHMP opinion for the following was issued in September 2010: "for the treatment of follicular lymphoma patients responding to induction therapy". However, this is currently an ongoing appraisal and no further license extensions are planned.

There are a number of technologies that are expected to be licensed for the treatment of NHL that are in the topic selection process. Many of these are in combination with rituximab and compared with rituximab. There are a number of other technologies undergoing clinical trials for the treatment of NHL; however these are not likely to affect the guidance in TA137.

Bendamustine has a license "for the treatment of indolent NHL in patients who have progressed during or within 6 months following treatment with rituximab or a rituximab containing regimen." An appraisal for this indication was terminated because the manufacturer of bendamustine did not provide a submission (TA206). Combining a review of TA206 and TA137 is not feasible however as the licensed indications are for different points in the treatment pathway of NHL.

Only 2 relevant ongoing trials of rituximab were identified. One trial is studying the effects of rituximab treatment duration and is not due to report until 2016. As the guidance in TA137 recommended rituximab treatment then it is unlikely that the results of this study would change the guidance. The other study is a single-arm extension study of rituximab and is also unlikely to change the results of the guidance.

In summary, no new evidence has been identified to indicate that a review of TA137 is necessary at this time.

[redacted]

Key issues

No new evidence has been identified to indicate a need for review of Technology Appraisal No.137. Therefore it would be suitable to propose that the appraisal is transferred to the 'static guidance list'. The Centre for Health Technology Evaluation should continue to track whether it is suitable to reconsider this static status if and when related technology appraisals are being considered for the work programme. If a Clinical Guideline on the treatment of NHL were to be planned, the Technology Appraisals programme should be alerted at that time. Until then, it cannot be determined how the status of Technology Appraisal No.137 would relate to such a guideline.

GE paper sign off: Helen Chung, 29 November 2010

Contributors to this paper:

Information Specialist: Paul Levay
Technical Lead: Helen Tucker
Technical Adviser: Rebecca Trowman
Implementation Analyst: Mariam Bibi
Project Manager: Andrew Harding

NATIONAL INSTITUE FOR HEALTH AND CLINICAL EXCELLANCE
IMPLEMENTATION DIRECTORATE

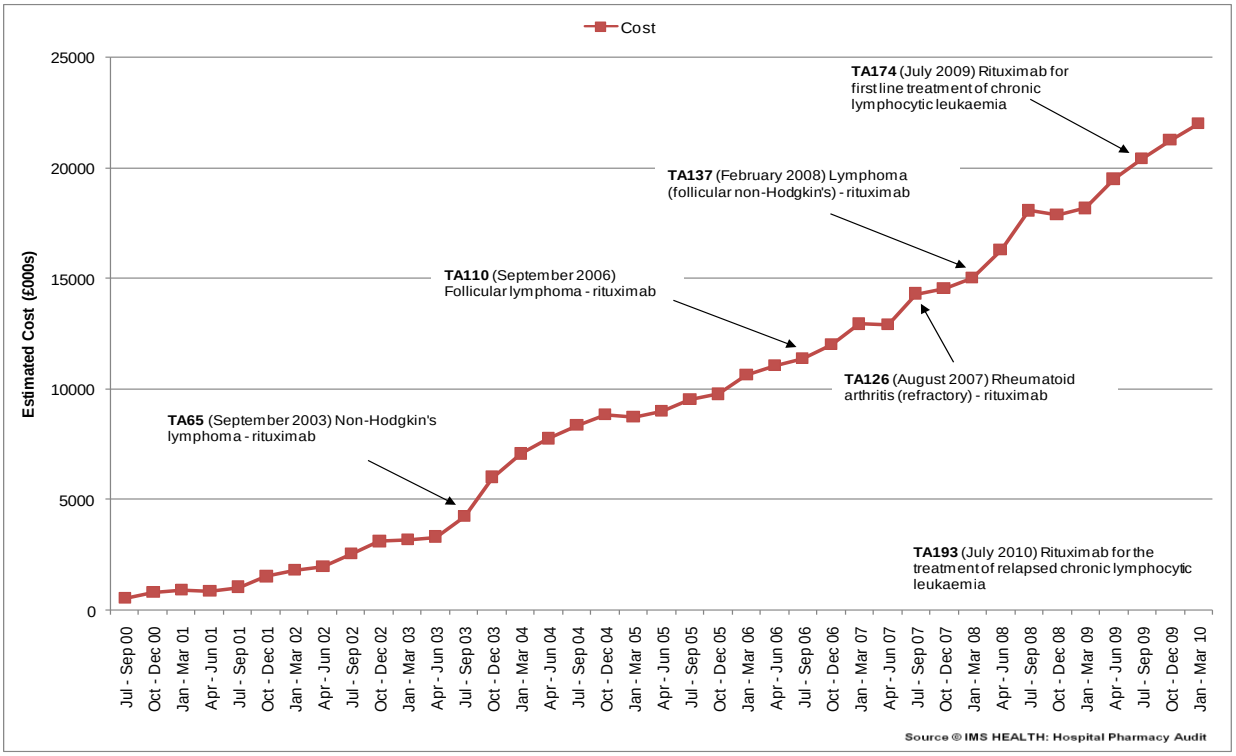
Guidance Executive Review

Technology appraisal TA 137: Rituximab for the treatment of relapsed of refractory stage III or IV follicular non-Hodgkin's lymphoma

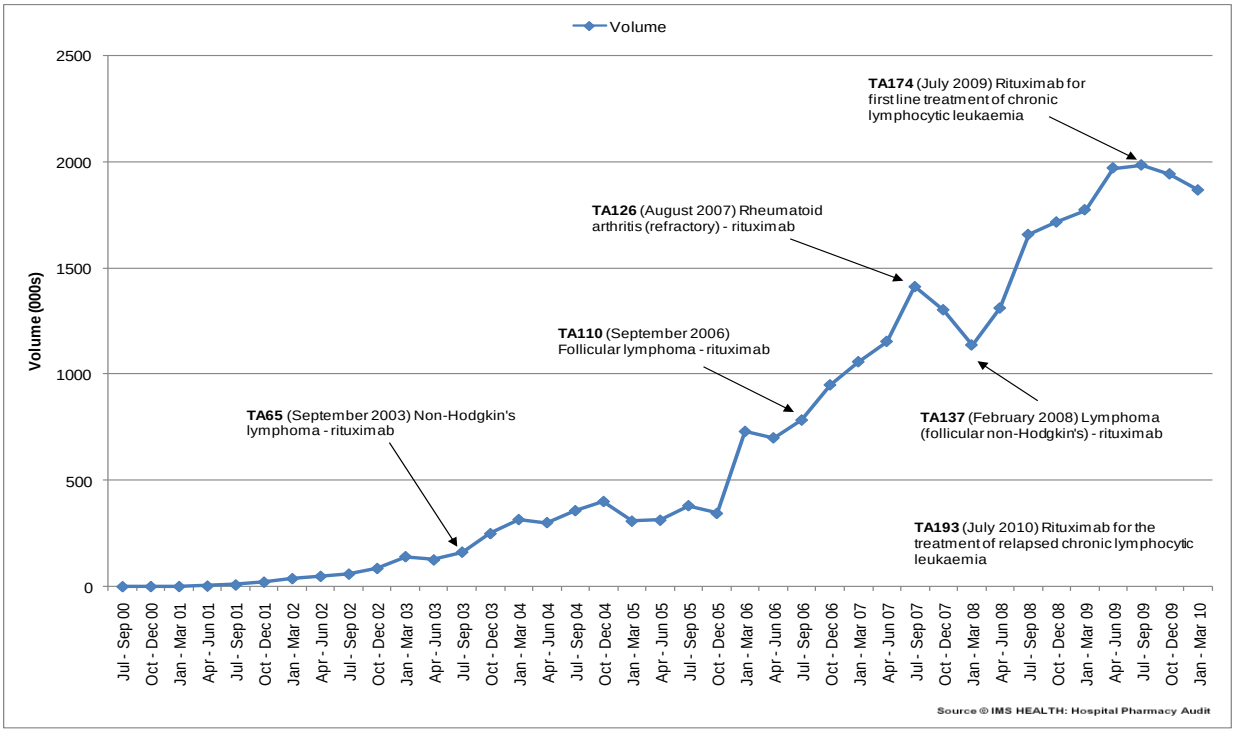
1. Routine healthcare activity

Data showing trends in prescribing costs and volume are presented below. Unfortunately this data does not link to diagnosis or stage of cancer so needs to be treated cautiously in relation to the specific recommendations of the guidance. Rituximab has multiple indications which are not reflected in the data presented below. Additionally, the Hospital Pharmacy Audit Index database measures volume in packs and a drug may be available in different pack sizes and pack sizes can vary between medicines. 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.

Estimated cost



Volume



2. Implementation studies from published literature

Information if taken from the ERNIE website

Richard M (2009) Uptake of NICE approved cancer drugs 2007/2008. Department of Health: London.

Headline findings
Analysis of prescribing data across cancer networks. Data show a 44% increase in prescribing of rituximab from 2005 to 2007/08 and a 24% reduction in variation across networks (NB data is not linked to diagnosis).