

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Arsenic trioxide for the first line treatment of acute promyelocytic leukaemia

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of arsenic trioxide within its licensed indication for the first line treatment of acute promyelocytic leukaemia.

Background

Acute promyelocytic leukaemia (APL) is a subcategory of acute myeloid leukaemia (AML) a form of bone marrow cancer characterised by malignant transformation and uncontrolled proliferation of abnormally differentiated precursor cells of the bone marrow that results in a high number of circulating immature blood cell forms.

There were 1,878 new cases of AML in England and Wales in 2002 and 1,776 deaths in 2003. One in every ten adult cases of AML is APL. APL differs from other categories of AML as APL affects on average younger adults with a median age of 40 years with 80% of patients between the ages of 15 and 55 years. APL is equally common in men and women.

In 95% of cases of APL, there is an underlying change in genetic constitution involving reciprocal translocation of the retinoic acid receptor-alpha (RAR α) gene on chromosome 17 with the promyelocytic leukemia gene (PML) on chromosome 15. The resulting fusion protein (PML/RAR α) exerts oncogenic effects by disrupting and blocking normal formation of precursor cells of the bone marrow.

Symptoms of APL include: fatigue; bleeding and/or bruising; and infections and/or fevers. The difference between APL and AML is that there is a greater frequency with which patients present with a serious bleeding abnormality. Patients with APL can develop disseminated intravascular coagulation requiring emergency intensive management.

The treatment of APL differs from that for all other forms of AML. Current first line treatment for most APL patients involves the use of all-trans-retinoic acid (tretinoin or ATRA therapy). ATRA activates the retinoid receptor RAR and causes the promyelocytes (blasts) to differentiate (to mature) and this deters them from proliferating. ATRA can induce a complete remission in most patients with APL by causing the APL-blasts to mature. However, ATRA cannot eliminate the leukaemic clone. ATRA is therefore used in combination

National Institute for Health and Clinical Excellence

Draft scope for the proposed appraisal of arsenic trioxide for first line acute promyelocytic leukemia

Issue Date: August 2008

Page 1 of 3

with an anthracycline-based chemotherapy. Maintenance treatment with ATRA, and possibly with low-dose chemotherapy, further reduces the incidence of relapse.

The technology

Arsenic trioxide (Trisenox, Cephalon UK) is a form of naturally occurring arsenic believed to have multiple mechanisms of action including inducing cell death (apoptosis) by damaging or degrading the PML/RAR α fusion protein in APL.

Arsenic trioxide does not have a UK marketing authorisation for first-line treatment of APL. It has been studied in clinical trials comparing arsenic trioxide monotherapy and arsenic trioxide in combination with ATRA and chemotherapy with ATRA and chemotherapy in newly diagnosed APL

Arsenic trioxide is already licensed for the treatment of patients with APL who are refractory to or have relapsed from previous treatment with retinoid and anthracycline chemotherapy.

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| Intervention(s) | Arsenic trioxide (alone or in combination with ATRA and chemotherapy) |
| Population(s) | Patients with newly diagnosed acute promyelocytic leukemia |
| Standard comparators | Tretinoin (ATRA therapy) in combination with anthracycline-based chemotherapy |
| Outcomes | The outcome measures to be considered include: <ul style="list-style-type: none"> • overall survival • progression-free survival • response rates • adverse effects of treatment • health-related quality of life. |

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| Economic analysis | <p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> |
| Other considerations | Guidance will only be issued in accordance with the marketing authorisation |
| Related NICE recommendations | None. |

Questions for consultation

Have the most appropriate comparators for the treatment of APL been included in the scope? Which chemotherapy agents are most commonly used with ATRA therapy?

Are there any subgroups of patients in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

Which process would be the most suitable for appraising this technology, the single technology or multiple technology process? (Information on these processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)