AWTTC
All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

Arsenic trioxide (TRISENOX®) in combination with all-trans retinoic acid for the first-line treatment of acute promyelocytic leukaemia in adult patients unsuitable for anthracycline-based therapy

October 2016

ONE WALES INTERIM COMMISSIONING DECISION

Arsenic trioxide (TRISENOX®) in combination with all-trans retinoic acid for the first-line treatment of acute promyelocytic leukaemia in adult patients unsuitable for anthracycline-based therapy

Date of advice: October 2016

The following Interim Pathways Commissioning Group (IPCG) recommendation has been endorsed by health board Chief Executives.

Arsenic trioxide (TRISENOX®) can be made available within NHS Wales to be used in combination with all-trans retinoic acid for the first line treatment of acute promyelocytic leukaemia, characterised by the presence of the t(15;17) translocation and/or the presence of the Pro-Myelocytic Leukaemia/Retinoic-Acid-Receptor-alpha gene, in adult patients unsuitable for anthracycline-based therapy.

The risks and benefits of the off-label use of arsenic trioxide for this indication should be clearly stated and discussed with the patient to allow informed consent.

Providers should consult the General Medical Council Guidelines on prescribing unlicensed medicines before any off-label medicines are prescribed.

This advice will be reviewed after 12 months or earlier if new evidence becomes available.

One Wales advice promotes consistency of access across NHS Wales.

KEY FINDINGS: This is an abbreviated summary of the evidence provided to IPCG

Report background
Acute promyelocytic leukaemia (APL) is a distinct subtype of acute myeloid leukaemia and presents clinically with coagulation disorders, which are associated with life-threatening haemorrhages. All-trans retinoic acid (ATRA) in combination with anthracycline-based chemotherapy is the mainstay treatment for APL in patients deemed suitable for intensive therapy. For patients unsuitable for anthracycline-based therapy, arsenic trioxide (ATO) in combination with ATRA may offer a treatment option. ATO is licensed for induction of remission and consolidation in adult patients with relapsed/refractory APL, however, ATO is not licensed for the first-line treatment of this indication and therefore its use is off-label. A cohort of patients has been identified through data from individual patient funding request (IPFR) panels; based on unmet need within the service this medicine was considered to be suitable for assessment via the One Wales process. The marketing authorisation holder is pursuing a licence for the first line treatment of APL in low to intermediate risk APL. If licensing is successful, the company have agreed to submit to AWMSG for appraisal. Treatment of patients with high-risk disease will remain an off-label indication.

Efficacy/Effectiveness
Published results from two phase III trials demonstrates that ATRA plus ATO is at least not inferior and may be superior to ATRA plus chemotherapy in the treatment of patients with APL; no significant difference in the quality of life was reported. These trials were analysed in a meta-analysis together with a third trial. The results of which support the trial findings.

Safety
No new safety signals have been observed for ATO in combination with ATRA for the first-line treatment of APL in patients unsuitable for anthracycline-based therapy.

Patient factors
ATO should only be considered for patients deemed unsuitable for anthracycline-based therapy due to frailty or co-morbidities.

Cost effectiveness
One study was identified assessing the cost-effectiveness of ATRA plus ATO versus ATRA plus idarubicin and ATRA plus cytarabine and chemotherapy from a US payer perspective. Cost effectiveness estimates have been calculated by the All Wales Therapeutics and Toxicology Centre (AWTTC) but are subject to large uncertainty due to the assumptions made in calculating these estimates. With this caveat, the estimated incremental cost-effectiveness ratio per quality-adjusted life-year gained was £3,669 versus ATRA plus idarubicin and £3,368 versus ATRA plus cytarabine and chemotherapy.

Budget impact
The addition of ATO to ATRA for the first line treatment of APL in patients unable to receive chemotherapy is likely to result in an additional cost of £185,645 per annum. This is based on five patients being eligible for treatment in Wales each year.

Commercial Access Agreement
This medicine is currently not licensed for the indication under consideration (off-label) and therefore a commercial access agreement cannot be offered by the company.

Impact on health and social care services
Minimal increased use of existing services.

Innovation and/or advantages
Arsenic trioxide offers a treatment choice for APL in patients unsuitable for anthracycline-based therapy.