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

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

ONE WALES INTERIM COMMISSIONING DECISION

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

Date of original advice: October 2016
Date of review: July 2020

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

Arsenic trioxide in combination with all-trans retinoic acid can continue to be made available within NHS Wales for the first line treatment of high-risk 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.

Arsenic trioxide is not licensed to treat this indication and is therefore off-label. Each provider organisation must ensure all internal governance arrangements are completed before this medicine is prescribed.

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.

Clinician responsibility
Clinicians will be obliged to collect and monitor patient outcomes. Evidence of clinical outcomes will be taken into consideration when reviewing the One Wales Interim Commissioning decision.

Health board responsibility
Health boards will take responsibility for implementing One Wales Interim Commissioning decisions and ensuring that a process is in place for monitoring clinical outcomes.

One Wales advice promotes consistency of access across NHS Wales.

This is a summary of new evidence available and patient outcome data collected, to inform the review.

Background
Acute promyelocytic leukaemia (APL) is a distinct subtype of acute myeloid leukaemia (AML) and presents clinically with coagulation disorders, which are associated with life threatening haemorrhages. Arsenic trioxide was licensed in November 2016 for the induction of remission, and consolidation in adult patients with newly diagnosed low-to-intermediate risk APL (white blood cell count ≤ 10 x 10^9/L) in combination with all-trans retinoic acid (ATRA), characterised by the presence of the t(15;17) translocation and/or the presence of the pro-myelocytic leukaemia/retinoic acid receptor-alpha (PML-RARA) gene[1]. Arsenic trioxide is recommended for use in this indication by the National Institute for Health and Care Excellence (NICE)[2]. Treatment of high-risk APL remains off-label and is currently supported by One Wales Interim Commissioning advice[3]. Clinicians in Wales consider treatment to meet an unmet need and is a potentially curative option for a very small patient group.

Current One Wales Interim Commissioning Decision
Arsenic trioxide in combination with all-trans retinoic acid can continue to be made available within NHS Wales for the first line treatment of high-risk 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. Reviewed March 2019[3].

Licence status
Arsenic trioxide in combination with ATRA for the first-line treatment of high-risk APL in adult patients remains off-label.

Guidelines
There have been no new guidelines or updates to existing guidelines identified that would affect the current One Wales Interim Commissioning decision.

Licensed alternative medicines/Health Technology Appraisal advice for alternative medicines
There remain no alternative licensed medicines or health technology appraisal advice for this indication.

Efficacy/Effectiveness
A repeat literature search identified no new efficacy/effectiveness data for the indication and treatment regimen under review. One ongoing randomised clinical trial (n = 280) was identified (NCT02688140) and is due to complete in January 2022[4]. The regimens used within this trial, specifically idarubicin as part of the induction regimen, do not align with the treatment regimen under review.

Safety
No new significant safety issues were identified.

Cost effectiveness
A repeat literature search found no new cost-effectiveness evidence to that provided in the original evidence status report.

Budget impact
In both Cardiff and Vale and Betsi Cadwaladr University Health Boards in the last 12 months, no patients received arsenic trioxide in combination with ATRA for the treatment of high-risk APL in line with the One Wales decision. Clinicians in Wales indicate that only about 10% of newly diagnosed APL cases are high risk and, with about 5–8 newly diagnosed APL cases in Wales each year, it is feasible that there were no patients with high-risk APL who were unsuitable for anthracycline-based therapy in Wales in the last 12 months. For younger, fitter patients with high-risk APL, clinicians state that they would use ATRA plus idarubicin while patients unsuitable for anthracyclines-based therapy would be started on arsenic trioxide plus ATRA. All responding clinicians commented on the usefulness of having this medicine combination funded for this rare cohort of patients in Wales.

A generic preparation of arsenic trioxide is now available. The list price of this generic is 7.5% lower than the reference medicine, Trisenox®.[5] Since the original assessment in 2016, the list price of ATRA has increased by 22%[5]. Together, since 2016 the price of arsenic trioxide in combination with ATRA has reduced by around £2,000 per patient. These prices exclude VAT and do not take into account any contract prices which may be significantly different to the list prices.

Impact on health and social care services
This remains minimal.

Patient outcome data
In both Cardiff and Vale and Betsi Cadwaladr University Health Boards, no patients received arsenic trioxide in combination with ATRA for the treatment of high-risk APL in the last 12 months. Data from the remaining health boards have not been provided.

Next review date: July 2021

References

1. European Medicines Agency. Trisenox®. Procedural steps taken and scientific information after the authorisation. May 2017. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Procedural_steps_taken_and_scientific_information_after_authorisation/human/000388/WC500042843.pdf. Accessed Feb 2020.
2. National Institute for Health and Care Excellence. Technology Appraisal 526. Arsenic trioxide for treating acute promyelocytic leukaemia. Jun 2018. Available at: https://www.nice.org.uk/guidance/ta526. Accessed Feb 2020.
3. All Wales Therapeutics and Toxicology Centre. One Wales Interim Commissioning Decision. Arsenic trioxide in combination with all-trans retinoic acid is supported for the first-line treatment of high-risk acute promyelocytic leukaemia in adult patients unsuitable for anthracycline-based therapy. Mar 2019. Available at: https://www.awttc.org/pams/current-one-wales-interim-commissioning-decisions. Accessed Feb 2020.
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5. Haymarket Publications. Monthly Index of Medical Specialities (MIMS). Available at: http://www.mims.co.uk/. Accessed Feb 2020.