**NHS England specialised services**

# Clinical panel report

Date: 21 February 2024

Intervention: Arsenic trioxide

Indication: high-risk acute promyelocytic leukaemia (age 12 months and over)

URN: 2320

Gateway: 2, Round 1

Programme: Cancer

CRG: Chemotherapy

## Information provided to the Panel

Policy Proposition

Evidence Review completed by Solutions for Public Health

Clinical Priorities Advisory Group (CPAG) Summary Report

Evidence to Decision Summary

Equalities and Health Inequalities (EHIA) Assessment

Patient Impact Assessment

Blueteq® Report

Policy Working Group (PWG) Appendix

This Policy Proposition recommends the off-label use of arsenic trioxide in combination with alltrans retinoic acid (ATRA) for patients with high-risk acute promyelocytic leukaemia (APML). APML is the most aggressive type of leukaemia with a severe bleeding tendency and potentially fatal course. APML is often associated with a severe disturbance in blood clotting which results in both bleeding and clot formation, resulting in an early mortality of up to 30%. Whilst APML can affect patients of all ages, the incidence tends to peak in children and elderly patients. There is a not for routine commissioning policy statement which was published in 2018. Positive NICE Technology Appraisal Guidance was also published in 2018 but for low-intermediate risk, which is in accordance with the marketing authorisation.

The proposition and the supporting evidence review were presented to Panel members. Three studies were included in the evidence review – a randomised controlled trial (RCT) and a nonRCT (non-inferiority), both from which only a subgroup of patients fitted the PICO, and a small retrospective case series. Therefore, evidence was non-comparative. No UK studies were included. No cost effectiveness studies were identified.

The critical outcomes for clinical effectiveness were overall survival (OS), event-free survival (EFS), and disease-free survival or remission. Identified important outcomes were hospitalisation, activities of daily living (ADLs), and quality of life (QoL). The presentation to Panel members covered all elements of the evidence. No studies reported QoL or ADLs.

Limitations of the studies presented were discussed which included non-comparative evidence and the applicability to patients seen in clinician practice in England. The evidence presented across all critical and important outcomes was reported as very low certainty using modified GRADE. Panel members discussed the low strength of the evidence but agreed that a clinical benefit can be seen particularly in relation to OS where between 85-100% of people within the specific population were still alive at 24 and 38 months follow up. EFS was reported as 8596.4% at 24 months follow up.

Adverse events (AEs) were reported, including prolonged QT interval. No studies reported long term AEs.

The proposition and supporting documents were considered and some amendments required. It was noted that the dosing reported in the evidence review was different to that within the proposition, however it was explained that paediatric guidelines had been followed for this. It was explained that, due to the nature of the condition, treatment must be commenced, and the treatment plan will then be agreed at the multi-disciplinary team (MDT) meeting at a later date.

EHIA – no amendments recommended.
PIA – no amendments recommended.

**Recommendation**

Clinical Panel agreed with the proposition and recommended this proceeds as a routine commissioning proposition.

**Why the panel made these recommendations**

The evidence and reported outcomes were considered carefully. Panel members discussed the low strength of the evidence but agreed that a clinical benefit can be seen particularly in relation to OS and EFS.

**Documentation amendments required Policy Proposition:**

- 'About current commissioned standard treatment' section – ATO is standard of care but is currently uncommissioned treatment and so there is an equity issue. Make sure this is clearer in proposition.
- Exclusion criteria – APL is referred to and needs amending to say APML.
- Dosing – include use of ATO and ATRA for completeness.
- Annex A outlines the treatment protocols and the treatment differences between people under and over 25 years old. There needs to be some narrative included in the proposition also as this is currently confusing.

**Blueteq® Form:**

- The differences in treatment protocols between people under 25 years and those over 25 years old needs to be clear. Two forms are required.
- Section 5 – the wording in bold relating to paediatrics needs including in the proposition also.

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Declarations of Interest of Panel Members: None received.

Panel Chair: James Palmer, Medical Director, Specialised Services