NHS ENGLAND SPECIALISED SERVICES

CLINICAL PANEL REPORT

Date: 17th January 2024

Intervention: Bedaquiline, Pretomanid, Linezolid, +/- Moxifloxacin (BPaLM/BPaL)

Indication: patients aged ≥14 years with suspected, functional or confirmed rifampicin resistant (RR) tuberculosis (TB), multi-drug resistant (MDR) TB or pre-extensively drug resistant (pre-XDR) TB

URN: 2310

Gateway: 2, Round 1

Programme: Blood and Infection

CRG: Infectious Diseases

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 (EtD) Summary

Equalities and Health Inequalities (EHIA) Assessment

Patient Impact Assessment

Blueteq™ Form

Policy Working Group (PWG) Appendix

This Policy Proposition recommends the off-label use of Bedaquiline, Pretomanid, Linezolid, +/- Moxifloxacin (BPaLM/BPaL) for patients aged ≥14 years with suspected, functional or confirmed rifampicin resistant (RR) tuberculosis (TB), multi-drug resistant (MDR) TB or pre-extensively drug resistant (pre-XDR) TB. The current standard treatment for patients with RR-TB, MDR-TB and pre-XDR TB involves an individualised treatment regimen consisting of at least seven agents, with an average duration of 18-24 months. A six-month 3-4 agent BPaLM/BPaL treatment regimen is recommended in the updated WHO (2022) guidelines for defined patients with RR-TB, MDR-TB or pre-XDR TB. It represents a shorter treatment regimen for patients and a reduced polypharmacy burden so would help increase concordance and compliance. This proposition includes an option to extend from 6 to 9 months should it be felt clinically appropriate.

The different categories of TB resistance and the sub-categorisation of patients were explained to Panel members.

The proposition and the supporting evidence review were presented to Panel members. Five papers were included in the evidence review - one randomised controlled trial (RCT), one uncontrolled randomised trial, one prospective case series, and two economic evaluation studies. No studies were conducted in the UK.

The critical outcomes for clinical effectiveness were sputum culture conversion rates, unfavourable treatment outcome, and treatment completion rates. Important outcomes identified were treatment failure and disease recurrence, amplification of drug resistance, and quality of life (QoL). The presentation to Panel members covered all elements of the evidence.

A higher sputum culture conversion rate was reported in BPaLM and BPaL compared with standard of care (SOC) across the studies. For BPaLM, one RCT provided moderate certainty evidence of a statistically significant lower risk of unfavourable treatment outcome compared to SOC at 108 weeks. This was reported for BPaL also at 108 weeks. One RCT provided low certainty evidence of a higher completion rate at 72 weeks in people with RR who received either BPaLM or BPaL, compared with SOC. For people with pre-XDR or MDR TB treated with BPaL, amplification of drug resistance was reported in 1/109 (0.9%) of patients at 6 months. Fewer/less severe adverse events were reported across some studies. The main adverse event reported was prolonged QT interval. QoL was not reported.

The evidence presented across all critical and important outcomes was reported as very low to moderate, using modified GRADE.

The economic evaluation studies were not completed in the UK and so may not be generalisable to the UK. There was also large variation in costs across different countries.

Panel members agreed that a clear clinical benefit can be seen across the studies reported. This proposition is proposing treatment options into an already mature service.

The proposition and supporting documents were considered and some amendments requested. The criteria for inclusion, exclusion and stopping were considered appropriate.

EHIA – no amendments requested.
PIA – no amendments requested.

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 agreed that a clinical benefit can be seen across the studies reported and this proposition is important for public health considerations. This draft proposition has been endorsed by the Respiratory National Clinical Director.

Documentation amendments required

Policy Proposition:

- Consider whether this would be suitable for access via the Medicines for Children Policy. The Summary of Product Characteristics for each drug should be checked in relation to the safety profiles.
- This proposition is a mix of licensed and off-label drug use. Off-label use should be stated earlier in the proposition under the section ‘About BPaLM/BPaL’ on page 4.

- Stopping criteria – this needs to include a discussion with the patient.

Declarations of Interest of Panel Members: None received.

Panel Chair: Anthony Kessel, Deputy Medical Director, Specialised Services

Post Panel Amendments

Panel Comment	Amendment	Page number (if applicable)
Policy Proposition		
Consider whether this would be suitable for access via the Medicines for Children Policy. The Summary of Product Characteristics for each drug should be checked in relation to the safety profiles.	This has been considered discussed with the PWG. It is the clinical consensus of the PWG that this proposition should be restricted to individuals 14 years old and older only, in line with the evidence review, international consensus and with the updated WHO guidance. Therefore, a Medicines for Children Blueteq form has not been completed.	N/A
This proposition is a mix of licensed and off-label drug use. Off-label use should be stated earlier in the proposition under the section 'About BPaLM/BPaL' on page 4.	Added.	pp. 2, 4
Stopping criteria – this needs to include a discussion with the patient.	Added	p.6
Additional request from pharmacy colleagues to include link to updated MHRA guidance on the use of fluroquinolone antibiotics.	This was discussed with the PWG who confirmed that the updated MHRA advice did not impact on the policy proposition. A link to the updated advice has been added on page 3 of the proposition for clarity.	p. 3