Auckland Regional Public Health Service
Rātonga Hauora ā Iwi o Tamaki Makaurau

Working with the people of Auckland, Waitemata and Counties Manukau

Auckland Regional Public Health Service
Cornwall Complex
Floor 2, Building 15
Greenlane Clinical Centre
Private Bag 92 605
Symonds Street
Auckland 1150
New Zealand
Telephone: 09-623 4600
Facsimile: 09-623 4633

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Caroline De Luca
Senior Therapeutic Group
Manager / Team Leader
PHARMAC
PO Box 10 254
WELLINGTON 6143

caroline.deluca@pharmac.govt.nz

PHARMAC consultation on proposal to list bedaquiline

1. Thank you for the opportunity for the Auckland Regional Public Health Service (ARPHS) to provide feedback on the proposal to list bedaquiline in the Pharmaceutical Schedule for treatment of extensively drug resistant tuberculosis (XDR-TB).

2. The following submission represents the views of ARPHS and does not necessarily reflect the views of the three District Health Boards it serves. Please refer to **Appendix 1** for more information on ARPHS.

3. The primary contact point for this submission is:

   Andrew Phillipps
   Policy Analyst
   Auckland Regional Public Health Service
   Private Bag 92 605
   Symonds Street
   Auckland 1150
   (09) 623 4600 (ext. 27105)
   aphillipps@adhb.govt.nz

Yours sincerely,

Dr Julia Peters
Clinical Director
Auckland Regional Public Health Service

Dr Cathy Pikholz
Medical Officer of Health
Auckland Regional Public Health Service

EXECUTIVE SUMMARY

4. The Communicable Disease Control Team at ARPHS has a key role in tuberculosis (TB) control in the Auckland region. The responsibility of ARPHS is to assist and supervise all Auckland residents with TB to complete their treatment and to follow up any close contacts who may need testing. Public health nurses supervise TB treatment in the community and meet regularly with patients.

5. We **recommend** the following:

   - Amend the proposal to enable the use of bedaquiline, where indicated, in the adult treatment regimen of any multidrug-resistant tuberculosis (MDR-TB).
   - The Tuberculosis Clinical Network (TBCN) should be the expert team that recommends the addition of bedaquiline to a regimen for MDR-TB.
   - Bedaquiline should only be prescribed by respiratory physicians and infectious diseases physicians, and only be dispensed from a hospital pharmacy.
   - There should be a requirement that every dose of bedaquiline must be given by directly observed therapy.

BACKGROUND

6. TB is a notifiable disease under the Tuberculosis Act 1948. Medical practitioners are required to notify TB cases to their local Medical Officer of Health.

7. The minimum duration of TB treatment is six months for drug susceptible TB cases i.e. in cases where there is no antibiotic resistance. However, the duration of treatment increases to 18-24 months for multidrug-resistant TB (MDR-TB) cases.

8. MDR-TB is defined as TB where the isolate is resistant to at least isoniazid and rifampicin (the two most important of the four first-line TB drugs, which are used for drug susceptible TB). XDR-TB is defined as MDR-TB with additional resistance to any fluoroquinolone and at least one of the second-line injectable drugs (amikacin, capreomycin or kanamycin). Therefore, XDR-TB is a more serious form of MDR-TB. All references to MDR-TB in this document should be interpreted as including XDR-TB.

9. In the ten years from 2005 to 2014, there were a total of 31 MDR-TB cases notified in New Zealand, including one XDR-TB case (in another region of New Zealand) notified in 2010.[1] There were a total of 20 MDR-TB cases notified in the greater Auckland region for the same ten year period. Thus 65% of MDR-TB cases over this period were notified in Auckland.

10. In late 2014 the Ministry of Health set up the Tuberculosis Clinical Network (TBCN), as a mechanism to strengthen and better utilise New Zealand's limited resource of specialist knowledge and experience around the clinical and public health aspects of the management and care of complex TB cases. The TBCN provides clinical advice and assists the case management team in developing a treatment and care plan for patients with MDR or XDR-TB, or other complex TB cases. It provides additional support for clinicians in centres where there may be less experience in treating TB. The TBCN is activated when a diagnosis of MDR-TB is made anywhere in New Zealand. The network operates via teleconferences convened and supported by the Ministry's Communicable Diseases Team. In addition to the TBCN members, teleconference participants include the clinician managing the case, and the Medical Officer of Health for the region in which the case resides.

11. In the greater Auckland region, Public Health Nurses (PHNs) from ARPHS are responsible for the follow up and support of all people diagnosed with TB. ARPHS PHNs are supported by ARPHS Medical Officers. ARPHS's support for people with TB includes:

    - assisting them to take their TB medicines for the full duration of their treatment;
    - monitoring them for medicine side effects, and;
    - assisting them to attend outpatient clinic appointments with the relevant DHB's specialist clinical service (which is responsible for prescribing their TB treatment regimen).

12. Directly observed therapy (DOT), whereby a health care worker visits the person and observes them swallowing every dose of their TB medicines, is used by ARPHS for around half of people with drug susceptible TB, but is

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[1] Institute of Environmental Science and Research Limited (ESR). (2015) *Tuberculosis in New Zealand: Annual Report 2014* (Report Ref: FW15062). Retrieved from ESR's Public Health Surveillance Website: https://surv.esr.cri.nz/surveillance/AnnualTBReports.php

considered mandatory for all people with MDR-TB. DOT is given daily for people with drug susceptible TB, but for most people with MDR-TB, the doses need to be split for tolerability reasons i.e. DOT is given twice daily. DOT can be face to face, or in more recent years, via TeleDOT (via a secure video link). To date, several people with MDR-TB in the Auckland region have had one of their twice daily DOT doses observed via TeleDOT (with the other dose being observed by face to face DOT). The supply of TB medicines for each person receiving DOT is kept at ARPHS (unless the person is on TeleDOT).

13. The standard process for dispensing TB medicines is that the prescribing clinician will fax each person's TB prescription directly to ARPHS, rather than giving it to the person themselves. The main reason for this is that TB medicines are not usually stocked in community pharmacies, so ARPHS has set up a system whereby a few nominated community pharmacies in the Auckland region dispense all the TB medicines for ARPHS.

14. In the case of a person with MDR-TB, the TB medicines are usually dispensed by the Auckland Hospital Retail Pharmacy, because the second-line medicines that are required for MDR-TB treatment regimens are hospital-only medicines. Therefore the community pharmacies do not have ready access to these medicines.

15. In 2011 the Ministry of Health arranged for a small national stockpile (of some of the more difficult to source MDR-TB medicines) to be established, held and managed by the Auckland District Health Board Pharmacy. The purpose of the stockpile, sufficient for two months of treatment for two patients, was to improve the ability to initiate treatment of MDR-TB cases nationwide. The plan was for medicines from the stockpile to be accessed upon the recommendation of the TBCN (which was only set up in 2014).

SPECIFIC FEEDBACK ON PROPOSAL

Proposal to fund bedaquiline for treatment of XDR-TB

16. Bedaquiline is not only indicated for the treatment of XDR-TB. The World Health Organization (WHO) has published interim policy guidance regarding the use of bedaquiline in the treatment of MDR-TB, and The U.S. Food and Drug Administration has approved the use of bedaquiline in certain circumstances.

17. In summary, bedaquiline may be indicated for treatment of adults with pulmonary MDR-TB (that may not yet fit the definition of XDR-TB), where due to the pattern of resistance, an effective treatment regimen cannot otherwise be provided for the patient. This might include situations such as MDR-TB with additional resistance to fluoroquinolones, or MDR-TB where other standard second line drugs are deemed to be contraindicated, or unlikely to be effective, or where the patient has significant side effects/intolerance to other standard second line drugs.

18. Accordingly, we recommend the proposal be amended to include the option of using bedaquiline in the treatment regimen of multidrug-resistant tuberculosis (MDR-TB) in adults.

An MDR-TB treatment regimen should include the option of bedaquiline

19. As the proposal stands, approval from 'a multidisciplinary clinical team with expertise in the treatment of tuberculosis, with input from infectious disease and respiratory specialists', is required before bedaquiline can be administered to a patient who has XDR-TB.

20. Similar to this, and in line with our recommendation that bedaquiline be included as an option in an MDR-TB treatment regimen, we consider the TBCN should be the expert team that recommends the addition of bedaquiline to a regimen for MDR-TB.

Special Authority for Subsidy and Hospital Pharmacy Specialist Prescription

21. Bedaquiline should only be prescribed by respiratory physicians and infectious diseases physicians (e.g. as is currently the case for moxifloxacin). Bedaquiline should only be dispensed from a hospital pharmacy. We recommend that the proposal be amended accordingly.

Supervision of treatment for a patient taking bedaquiline

22. DOT is already the expected standard of care for all MDR-TB patients in New Zealand. Therefore there should be a requirement that every dose of bedaquiline must be given by DOT.

CONCLUSION

23. Thank you for the opportunity to provide input into Pharmac's proposal to list bedaquiline for the treatment of XDR-TB.

24. In addition to this written submission, we are happy to provide additional information and/or discuss these issues further with Pharmac.

Appendix 1 - Auckland Regional Public Health Service

Auckland Regional Public Health Service (ARPHS) provides public health services for the three district health boards (DHBs) in the Auckland region (Auckland, Counties Manukau and Waitemata District Health Boards).

ARPHS has a statutory obligation under the New Zealand Public Health and Disability Act 2000 to improve, promote and protect the health of people and communities in the Auckland region. The Medical Officer of Health has an enforcement and regulatory role under the Health Act 1956 and other legislative designations to protect the health of the community.

ARPHS' primary role is to improve population health. It actively seeks to influence any initiatives or proposals that may affect population health in the Auckland region to maximise their positive impact and minimise possible negative effects on population health.

The Auckland region faces a number of public health challenges through changing demographics, increasingly diverse communities, increasing incidence of lifestyle-related health conditions such as obesity and type 2 diabetes, infrastructure requirements, the balancing of transport needs, and the reconciliation of urban design and urban intensification issues.