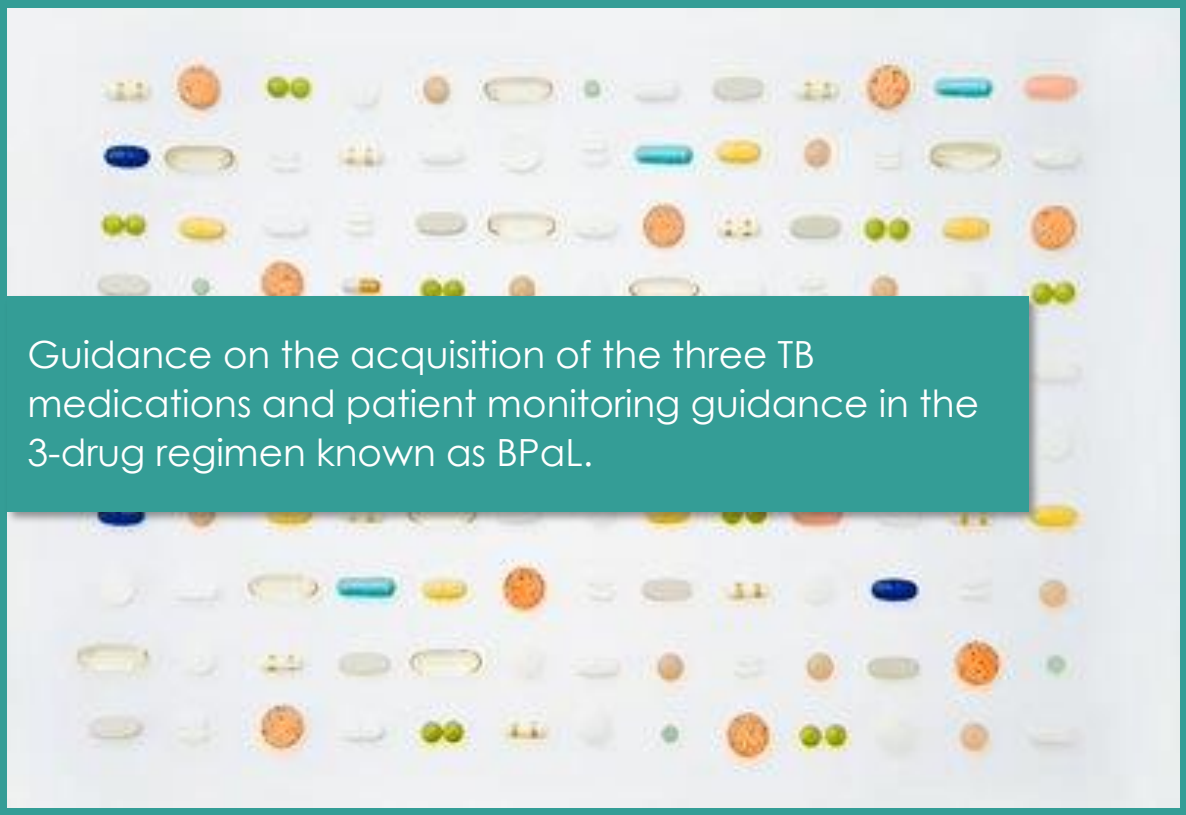
BPaL Guidance

2022



Guidance on the acquisition of the three TB medications and patient monitoring guidance in the 3-drug regimen known as BPaL.

Washington State Department of Health

March 2022

Publication # 343-203

After a trial in South Africa demonstrated 90% effectiveness 6 months post-treatment, on August 14, 2019, the US FDA approved a six-month regimen of **bedaquiline** (Sirturo), in combination with **pretomanid** tablets and **linezolid** (Zyvox) for the treatment of highly treatment-resistant tuberculosis (TB) of the lungs such as extensively drug-resistant (XDR) or multidrug-intolerant TB. "Nix-TB is a pivotal tuberculosis trial that tests the three-drug BPaL regimen, consisting of bedaquiline, pretomanid, and linezolid – collectively referred to as the BPaL regimen. The trial enrolled 109 people with XDR-TB as well as treatment-intolerant or non-responsive MDR-TB. Nix-TB data have demonstrated a successful outcome in 95 of the first 107 patients after six months of treatment with BPaL and six months of post-treatment follow-up...." (https://www.tballiance.org/portfolio/trial/5089)

On February 2, 2022 the CDC published guidance recommending the use of pretomanid 200mg daily for 26 weeks in the treatment of adults with pulmonary XDR, pre-extensively drug-resistant (pre-XDR) (i.e., resistant to isoniazid, rifampin, and at least one fluoroquinolone or injectable medications (i.e., amikacin, kanamycin, capreomycin) or treatment-intolerant (TI) /nonresponsive (NR) MDR TB when a safe and effective treatment regimen cannot otherwise be provided and when administered in combination with bedaquiline and linezolid as the BPaL regimen.

BPaL Medication Overview

RCW 70.30.045: Expenditures for tuberculosis control directed—Standards—Payment for treatment. (wa.gov)

"Tuberculosis (TB) is a communicable disease and TB prevention, treatment, control, and follow-up of known cases of tuberculosis are the basic steps in the control of this major health problem. In order to carry on such work effectively in accordance with the standards set by the secretary under RCW **70.28.025**, the legislative authority of each county shall budget a sum to be used for the control of TB, including case finding, prevention, treatment, and follow-up of known cases of TB. Under no circumstances should this section be construed to mean that the legislative authority of each county shall budget sums to provide tuberculosis treatment when the patient has the ability to pay for the treatment. Each patient's ability to pay for the treatment shall be assessed by the local health department." *(underline added by WA DOH TB Program)*
This means that TB Medication Coverage is offered on *discretionary* basis (per NTCA Access Guide).It is recommended that all three medications be started at the same time. If there is a delay in receiving any one of the medications, it will impact your patient's treatment start date. Bedaquiline will typically take the longest to get approved.

Keys:

- Read through this document and the NTCA guidance on the NTCA website to gather all the information that will be needed and to familiarize yourselves with the potential requirements and processes. Each of the 3 medications are acquired in different ways.
- Like any medication purchased through the King County pharmacy, once an LHJ opens a bottle it cannot be returned to the pharmacy to be redistributed to another LHJ.
- **If the medication did not originally come through the King County pharmacy**, it cannot be returned to them for distribution to other LHJs.
- Discuss with a DOH Nurse Consultant to join the ***Longitudinal Case Consultation Panel*** monthly meetings for expert MDR treatment guidance. Expert consultation is recommended for the management of any multi-drug resistance case.

Accessing Bedaquiline (Sirturo)

Metro Medical
Only way to access to bedaquline
(See weblink in below in Keys)
pharmacy direct number 866.716.5486;
client services 800.768.2002
email: CustomerSvc@metromedical.com
LHJ will need LHJ's Tax ID and Provider's NPI #

It is crucial that you read both this document and the NTCA Guidance document. This graphic is only an overview and is missing essential details.

Ensure Metro Medical prescription is correctly written
The prescription for all 6 months will be seperated into 3 items on a single Rx form
(See Example on Page 6 in this document)

Sirturo is on the HCA Medicaid forumulary as a preferred medication

Janssen's CarePath
for patients with insurance
Metro Medical will contact patient's insurance regarding coverage
Metro Medical will connect you/your patient to issue a CarePath co-pay assistance card

No income verfication needed

Call Janssen's CarePath if you haven't heard back **within 3 days**

Johnson & Johnson Patient Assistance Foundation (JJPAF)
(See link to Application Form below in Keys)
for patients with insurance who CarePath rejected or patients without insurance

Income verification by patient (Appl Form Q#2)
or JJPAF can do this verification if patient checks box under question #4
HCP will need to complete Sirturo prescription for the entire 6 month treatment on pg 3 of application (example in Appendix A)
FAX completed form to Johnson and Johnson at 1-888-526-5168.

JJPAF gives you Retail Card #, Group # and BIN # (all 3 are required). Give all three of these numbers to Metro Medical to process your medication order (ask, this may change)

Call Janssen's JJPAF if you haven't heard **within 3 days** 1-888-526-5168.

Bedaquiline (Sirturo)

400mg QD for 2 weeks (14 doses) followed by 200 mg 3 times a week (72 doses over 24 weeks) for a total of 26 weeks (total of 86 doses over 26 weeks) ***Note:** no dose modifications allowed.

The manufacturer of bedaquiline has a special contract in place with Metro Medical to be the sole distributor of the drug to the US market. In Washington depending upon insurance status there are different pathways to obtaining this medication. Metro Medical will contact the patient's insurance company (whether private or state insurance) to determine coverage and associated co-pays.

If bedaquiline is not fully covered by your patient's insurance, there is an assistance program available for coverage of co-pays up to $7500. The co-pay program is called Janssen's CarePath. Ask Metro Medical about CarePath, they are responsible for connecting the TB program or patient to access the Janssen CarePath co-pay assistance card.

Before contacting Metro Medical, gather **all** the information required so missing information doesn't slow down the process and ensure that the patient has completely filled-out any required information. (See page 10 of the NTCA Access Guide for list of required information).

Health Care Authority (HCA) is working with all their Managed Care Organizations to contract with Metro Medical for Medicaid patients. United Health Care is the first to have a contract in place.

Uninsured patients or coverage rejected by Janssen's CarePath can use Johnson & Johnson Patient Assistance Foundation (JJPAF).

Keys:

- The ordering prescriber must match the MD on the application.
- You must go through Metro Medical/Cardinal Health to access bedaquiline. Ingrid Glasper, Manager customer service, Ingrid ingrid.glasper@cardinalhealth.com
- Ensure that the Metro Medical prescription is written as shown in the examples below. This is different from how the prescription section of the JJPAF application is completed.
- Going through Metro Medical is the only way to access CarePath assistance to cover bedaquiline cost.
- Metro Medical, Janssen's CarePath, and JJPAF all seem to have a 3-day turn around on most aspects of this process. If you haven't heard back in 2-3 business days call them back.
- Once JJPAF has been approved, you contact Metro Medical to let them know your patient has been approved and you provide Retail Card #, Group # and BIN # (all 3 are required) --all three should have been given to you by JJPAF (ask, this may have changed and may not be needed).
- **Do not accept any rejection** of your JJPAF application – there is an established precedent for the JJPAF providing bedaquiline for free when a TB program risks depleting their funds in order to pay for bedaquiline. It is Janssen's position that TB programs should never have to use their funds to pay for this medication.

Packaging issue:

You will need 200 tablets of bedaquiline and if you purchase a full bottle it may be packaged with only 188 pills. Mention the exact quantity of pills your patient needs when speaking with Metro Medical. Bedaquiline was originally packaged for a 24-week regimen but BPaL requires 26 weeks to completion. An extra bottle of bedaquiline will need to be ordered. Typically, bedaquline has a two-year expiration date.

Writing Metro Medical Services Prescription:

1. 1-month supply on 1st line,
2. Months 2 through 6 on line #2,
3. Add the last 2 weeks on line #3.

Example of prescription:

Item #	Medication	Quantity	Directions for Use
	Sirturo 100mg tabs (NDC:59676-0701-01) 1	68 tabs	400mg by mouth daily for 2 weeks, then 200 mg three times a week for 2 weeks
	Sirturo 100mg tabs 2	24 tabs with 4 refills	200mg three times a week
3	Sirturo 100mg tabs	12 tabs	200 mg three times a week

Two examples of how to complete prescriptions of **Johnson & Johnson Patient Assistance Foundation (JJPAF) Application** (from Seattle King County Public Health March 2022):

Name of product: Sirturo
Strength: 100 mg Sig: 4QDx2wk>2TIW24wk
Quantity: 200 Days supply: 182
Number of Refills *(maximum 11)*: 0

ICD Code *(HCP-administered products only)*: A 15.9
Name of Product: Sirturo
Strength: 100mg tablet Sig: 4QD x 2wks -> 2TIW x 24 wks
Quantity: 200 Days' Supply: 182 Number of Refills *(maximum 11)*: 0

2022 ICD 10 Codes for TB and MDR TB

Accessing Pretomanid

Ensure prescription is correctly written:

200 mg once daily for 26 weeks
No dose modifications allowed

It is crucial that you read through both this document and the MPPAP Application directions as this page is only overview graphic and there are other details provided elsewhere.

Patients with prescription drug coverage

Access through your patient's local pharmacy or LHJ's drug wholesaler

Prior Authorization needed from insurance company

As of February 7, 2022 pre-authorization is no longer required in the HCA Medicaid Formulary

Currently a "drop ship" item at Cardinal Health

Uninsured or Insured without drug coverage*

Mylan Pretomanid Tablets Patient Assistance Program (MPPAP)

Customer Service 800-796-9526

Mylan Pretomanid Tablets Patient Assistance Program (MPPAP) Eligiblity

Patient must be a US citizen or legal resident living in US

Annual gross household income below 400% FPL (Verification required)
*Patient must meet <u>one</u> of the following (verification for either required):

- No prescription insurance coverage of any type **or**
- has **Commercial** prescription drug coverage **only** for **generic** products (No State or Federal insurance programs such as Medicaid, Medicare, or Tricare)

Patient & provider both certify that they will not submit a claim or resell, trade or barter for a credit for any free product received through MPPAP.

Approved applications: Drugs will be shipped to LHJ free of charge

Pretomanid

200 mg once daily for 26 weeks (200mg tablet) ***Note:** no dose modifications allowed

Pretomanid is a nitroimidazole, a class of novel anti-bacterial agents. Pretomanid has been developed by TB Alliance and is approved by the US FDA to treat XDR-TB or treatment-intolerant/non-responsive MDR-TB**, ONLY** in combination with bedaquiline and linezolid, as part of the BPaL regimen.

- Pretomanid is now a preferred medication in the HCA Medicaid formulary.
- **Prior Authorization needed from insurance company**
- Quick acquisition might be difficult if a patient has prescription coverage and does not qualify for the Mylan Pretomanid Tablets Patient Assistance Program (MPPAP) to get it directly from the manufacturer.
- Pretomanid is currently a "drop ship" item, the patient's pharmacy may be reluctant to order if they have to pre-pay for medication.
- The LHJ may be responsible for full amount or the co-pay (amount depends on insurance coverage).
- If patient does not have a regular pharmacy (easiest) then reach out to an FQHC or an independent community pharmacy (e.g. Health Mart, Health Atlas, Bob Johnson's in Seattle).
- The WA Pharmacy Association can assist in finding a pharmacy. See contact information below.

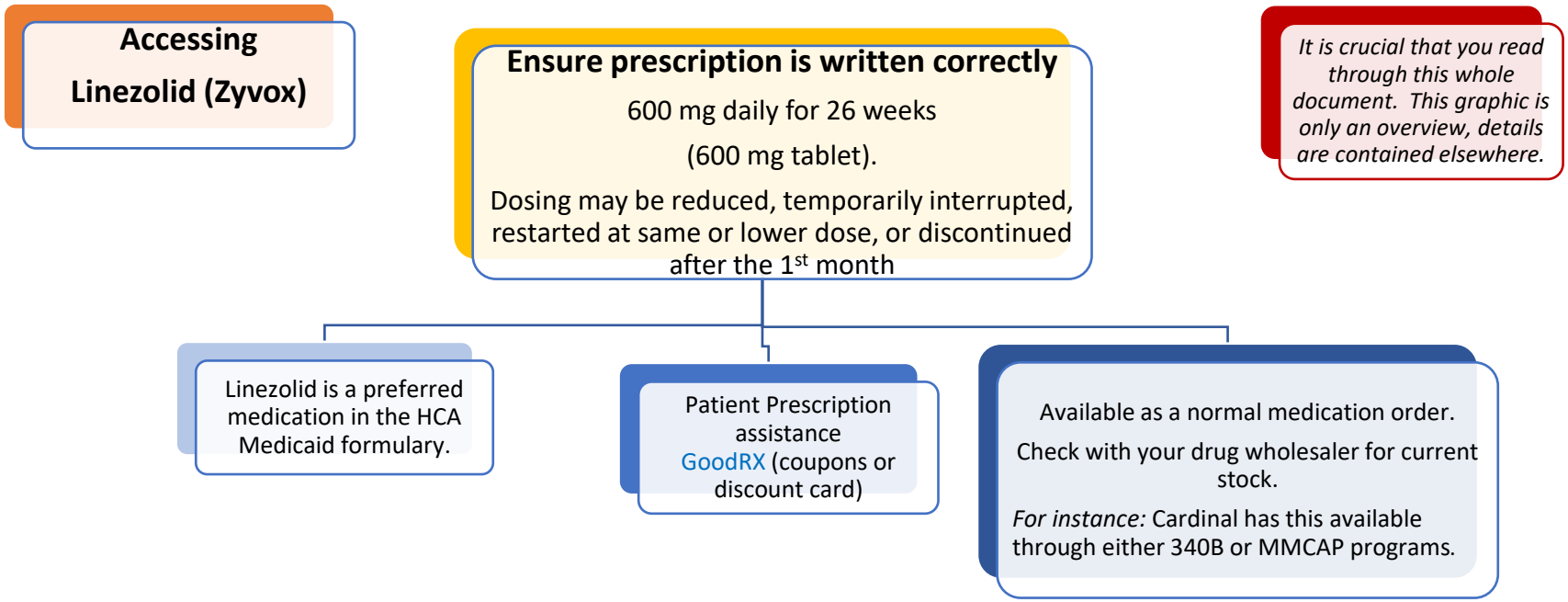
Manufacturer Assistant Program
To participate in the Mylan Pretomanid Tablets Patient Assistance Program (MPPAP): An eligible patient does **not have any** prescription drug coverage and **must be** a US citizen or legal resident.

MPPAP Customer Service Phone: 1.800.796.9526
Contact customer service to receive application form.
(Occasional reminder calls to Customer Service may help expedite)
FYI: Due to a merger, Mylan has changed their name to Viatris, so you may see either name.

Email/Mail or Fax application to:
781 Chestnut Ridge Road
Morgantown, WV 26505
Fax: 1.877.427.7290
Email: MylanPAP@mylan.com

Medication will be shipped in 24-48 hours directly to the ordering LHJ's TB clinic. MPPAP approval lasts one year. The patient is eligible to receive replenishment medication during that year. Replenishment Authorization (form submitted by physician) approval will be considered on an 'as needed' basis.

If a pharmacy is resistant to ordering a dropship medication you can receive assistance setting this up with the receiving pharmacy by contacting:
The **Washington State Pharmacy Association**
Phone: 425-228-7171
Fax: 425-277-3897
askwspa@wsparx.org



Linezolid (Zyvox)

600 mg daily for 26 weeks (600 mg tablet). Dosing may be reduced, temporarily interrupted, restarted at same or lower dose, or discontinued after the 1st month.

- Linezolid is a preferred medication in the HCA Medicaid formulary.
- Ask pharmacy to check with their drug wholesaler for current stock. For example, Cardinal Health has it listed available through either 340B or the MMCAP programs.
    - If your LHJ doesn't have accounts set up to access the medication, please reach out to us at: TBServices@doh.wa.gov

Note: 600 mg daily is less than the linezolid dose used in Nix (1200 mg daily). However, the higher dose resulted in linezolid adverse effects in all patients. Both growing clinical experience and the ZeNix trial (not yet published) have shown that a daily dose of 600 mg is effective in treating drug-resistant TB. The 600 mg daily dose may be further reduced based on results from therapeutic drug monitoring (*see* below).

Patient Monitoring and Dosing Information

Most of the information in this section is from the Curry Drug Resistant TB Survival Guide, 3rd Edition

- ADVISE PATIENTS TO AVOID BECOMING PREGNANT.
- In the NIX study, medication was administered orally, with food.
- In NIX, if a patient was still culture positive between 4 and 6 months of treatment, they were given an additional 3 months of treatment.
- Cultures should be done frequently to document when patient has converted to culture negative. Start every 1-2 weeks initially, then decrease frequency to monthly. (See table below: **Activities for monitoring treatment response for MDR-TB** Table 1: Curry Survival Guide, pg.204)
- Post-treatment monitoring for relapse at 1, 2, 3, 6, 9, 12, 15, 18, 21 and 24 months.

Baseline examinations

Laboratory exams: HIV test, CBC, TSH, pregnancy test for people of childbearing age, and a comprehensive metabolic panel (obtain 24-hour creatinine clearance for any elevation of creatinine or question of renal insufficiency). **Curry Guide Tool 4: *Laboratory Flow Sheet*** may be helpful in summarizing bloodwork results that will be assessed at baseline and throughout treatment.

Hearing, vision (acuity and color), **and vestibular function** should be assessed at baseline and results documented. The Curry Survival Guide **Tool 5: *Vision Screening Flow Sheet*** and **Tool 6: *Hearing and Vestibular Flow Sheet*** may be helpful for tracking these serial monitoring results.

Radiography should be obtained prior to treatment initiation. Posteroanterior (PA) views (and lateral in children) of the chest for pulmonary disease are recommended. Additional views and/or CT scan may be helpful in some instances.

Sputum for nucleic acid amplification test (NAAT), acid-fast bacilli (AFB) smear, culture, and drug-susceptibility testing (DST): At the start of treatment, obtain 3 sputa for AFB smear and culture.

Important note: In a patient started on a standard TB regimen (RIPE) for 4 weeks or more prior to starting an MDR-TB regimen and for whom the initial isolate was not known to be resistant to **all** first-line drugs at baseline, request a repeat DST from a subsequent positive TB culture obtained near the time of MDR-TB regimen initiation. This will help to ensure that no additional resistance developed during the initial period of therapy.

Curry Survival Guide Tool 3: *Bacteriology Flow Sheet* *(Chapter 8, page 237)* may be helpful for summarizing the important mycobacteriology, molecular tests, and DST results.

EKG: For patients who will be taking bedaquiline (BDQ), a baseline EKG is recommended.

Coordinate EKG monitoring either with outside providers, at the TB clinic, or utilize remote/mobile monitors after baseline. If with outside providers/clinics, make sure to address isolation issue if applicable. Not all clinics have isolation exam rooms.

Psychosocial assessment: Assess for existing mental health and social conditions that may impact treatment. ***See Curry Survival Guide*** *section:* ***Psychosocial Support*** *page 219*

Therapeutic Drug Monitoring (TDM)

The University of Florida is one lab providing TDM for BPaL cases in the US. Contact WA DOH for requests for TDM and related Minimum Inhibitory Concentration (MIC).

WA DOH TB Program: TBServices@DOH.WA.GOV; 206-418-5500

University of Florida uses an analytical chemistry method which allows for a patient's drug regimen to be tailored individually. The lab monitors drug concentrations in the patient's blood serum and then recommends adjustments to the size or frequency of the doses.

This approach allows the clinicians to analyze how a patient absorbs, metabolizes and clears a drug, which allows them to find the right dose early during treatment and optimize outcomes.

One of the BPaL drugs, linezolid, is effective but carries a risk of concentration-related adverse drug reactions. TDM allows clinicians to balance the competing goals of giving enough of a drug to kill the bacteria that cause TB, while not harming the patient. (There is not consensus on the use of TDM for bedaquiline or pretomanid.)

Florida has encouraged TDM to generate robust data on the use of BPaL and the potential relationship between drug levels and outcomes. Additional visits and phlebotomy may place a burden on patients. TDM for linezolid is useful to reduce potential drug toxicity, however TDM does not need to be part of routine care.

Activities for monitoring treatment response for MDR-TB (Table 1: Curry Survival Guide (page 204)

Monitoring evaluation	Recommended frequency
Evaluation by clinician	• **During the intensive phase:** Every day during the first weeks if hospitalized and at least every week if treated as outpatient, until the treatment is well tolerated. • Once stable, the patient is seen twice a month or once a month. • **During the continuation phase:** Monthly assessments unless there is a medical necessity to see the patient more often. The DOT provider sees the patient daily between consultations and signals any concerns to the case manager and clinician.
Treatment adherence and tolerance	• Daily at every DOT encounter by the DOT worker.
Sputum smears and culture	• Obtain 3 sputa at the start of treatment and every 2 weeks until smear conversion, followed by 2-3 sputa every month until culture conversion, and then at least 1 sputum monthly throughout treatment.
Weight	• At start of treatment, weekly until stable, and then monthly throughout treatment.
Height	• At start of treatment for all (to be able to assess lean body weight or BMI); monthly for children (to assess growth).
Drug-susceptibility testing (DST)	• At baseline for first- and second-line anti-TB drugs. Repeat DST for patients who remain culture-positive at month 3 or revert after month 4 (see Curry Survival Guide **Chapter 2, *Diagnosis*** pages 19-21 for more on testing for drug resistance).
Chest radiograph	• At baseline, every 3 to 6 months during treatment, and at the end of treatment.

Drug Specific information

Bedaquiline (BDQ)		**Weeks 1 – 2:** 400 mg (4 tablets of 100 mg) given orally, once daily **Weeks 3 – 26:** 200 mg (2 tablets of 100 mg) three times per week, for a total dose of 600 mg per week
	Therapeutic Drug Monitoring (TDM):	• Therapeutic drug monitoring at about 2 weeks after starting therapy, obtain levels at 5h and 24h after dose is given. (There is not consensus on the use of TDM for bedaquiline or pretomanid.) • Draw 2 ml of serum for each collection.
	Other Monitoring:	• EKG at baseline, 2, 12 and 24 weeks of treatment. Stop bedaquiline if QTc > 500 and monitor EKGs frequently until QTc returns to normal. • Baseline potassium, calcium and magnesium, repeat if QTc prolongation occurs. • Baseline and monthly ALT, AST, Alk phos and T. bilirubin.
Pretomanid		200 mg once daily for 26 weeks (200mg tablet) ***Note:** no dose modifications allowed (*adapted from NIX trial procedures and data*)
	TDM:	• Therapeutic drug monitoring at about 2 weeks after starting therapy, obtain levels at 5h and 24h after the dose is given. (There is not consensus on the use of TDM for bedaquiline or pretomanid.) • Draw 2 ml of serum for each collection.
	Other Monitoring:	• ECG at baseline and monthly during treatment. • Baseline electrolytes, repeat if QTc prolongation occurs. • Visual acuity at baseline and monthly. • Baseline and monthly CBC and liver profile. • Amylase and lipase if abdominal pain develops.
Linezolid (LZD)		600 mg daily for 26 weeks (600 mg tablet)
	TDM:	Therapeutic drug monitoring (TDM) through University of Florida is available and typically is ordered after two weeks of treatment. Dosing may be reduced, temporarily interrupted, restarted at same or lower dose, or discontinued after the 1st month. See Curry Survival Guide TDM for linezolid pages 128-129 • Obtain therapeutic drug monitoring blood levels after 2 weeks of therapy. Obtain the levels just before the next dose is given (trough level) as well as levels at 2 hours and 6 hours after the dose is given- for a total of 3 blood draws in one day. ▪ identify who will follow this process along at the hospital lab and being in close communication ▪ Plan to meet patient at the lab for in-person DOT after the trough sample is drawn and to ensure blood levels are drawn on time. • Draw 2 ml of serum for each collection.

		▪ WA State PH Lab (PHL) can do all the specimen processing if LHJ is unable to centrifuge the collection tubes if it gets to state PHL within an hour (although we have received collection tubes at two hours and still able to separate the serum). Once PHL has all three blood draws, they can plan for shipment to University of Florida after freezing the serum for shipment. ▪ For LHJs unable to use the PHL, see laboratory guidance provided in this document Sample Handling Instructions. • Use this form for submitting your specimens to University of Florida. Infectious disease pharmacokinetics lab requisition. Forms and Catalog » Infectious Disease Pharmacokinetics Laboratory » College of Pharmacy » University of Florida (ufl.edu) • University of Florida Pharmacokinetics Laboratory contact information • The results will come to the managing provider listed on the requisition. Please send a copy of results to TBServices@doh.wa.gov. • Once we obtain the organism's MIC for LZD, we can discuss whether it is appropriate to decrease the LZD to 600mg po TIW to minimize toxicity vs. maintaining the 600mg daily dose. Our goal is to get a level of linezolid that is 4-16x the MIC* and to maintain the trough level <2, a level that several studies have found is associated with low frequency of adverse effects. *NOTE: the NIX trial looked only at daily LZD 1200mg, but many patients had to stop linezolid due to neurologic or hematologic toxicity. Several studies have indicated that risk of these toxicities is low if the trough level is <2.
Linezolid (LZD)	**Other Monitoring:**	• Monitor for peripheral and central neuropathy as well as optic neuritis with each dose. Neuropathies can be unusual, including loss of taste, hearing, numbness, pain or tingling among other things. Ensure staff is alert to this, hold TB meds if symptoms develop and ask physician for evaluation. • Monitor CBC weekly during the initial period, then monthly and as needed based on symptoms. • Screen monthly for visual acuity and color discrimination.

Monitoring Timeline & Checklist

Timing of labs, EKG etc., Patient will likely be seen WEEKLY for first month

Baseline:

- ☐ CMP (including potassium and calcium)
- ☐ magnesium (order separately)
- ☐ CBC
- ☐ EKG
- ☐ HIV test
- ☐ TSH
- ☐ Hearing test
- ☐ Vestibular function/balance
- ☐ CXR (**And** every 3 to 6 months during treatment and at the end of treatment)
- ☐ Sputum every 1to 2 weeks
- ☐ Vital signs + weight
- ☐ Vision (Snellen and Ishihara color test)
- ☐ Pregnancy test for people of childbearing age

1 week:

- ☐ Monitor CBC (for LZD) weekly during the initial period, then monthly and as needed

2 weeks:

- ☐ CMP (for BDQ)
- ☐ CBC (for LZD)
- ☐ EKG (for BDQ)
- ☐ Therapeutic drug monitoring levels (for LZD, 24-hour trough, 2-hour post dose, 6-hour post dose)

3 weeks:

- ☐ Monitor CBC (for LZD) weekly during the initial period, then monthly and as needed

4 weeks (1 month):

- ☐ CMP
- ☐ CBC
- ☐ EKG
- ☐ Vision (Snellen and Ishihara color test)
- ☐ Vital signs + weight
- ☐ Monthly sputum

8 weeks (2 months):

- ☐ CMP
- ☐ CBC
- ☐ EKG
- ☐ Vision (Snellen and Ishihara color test)
- ☐ Vital signs + weight
- ☐ Monthly sputum

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Monitoring Timeline & Checklist

Timing of labs, EKG etc., Patient will likely be seen WEEKLY for first month

12 weeks (3 months):

- ☐ CMP
- ☐ CBC
- ☐ EKG
- ☐ Vision (Snellen and Ishihara color test)
- ☐ Vital signs + weight
- ☐ Monthly sputum

16 weeks (4 months):

- ☐ CMP
- ☐ CBC
- ☐ EKG
- ☐ Vision (Snellen and Ishihara color test)
- ☐ Vital signs + weight
- ☐ Monthly sputum

20 weeks (5 months):

- ☐ CMP
- ☐ CBC
- ☐ EKG
- ☐ Vision (Snellen and Ishihara color test)
- ☐ Vital signs + weight
- ☐ Monthly sputum

24 weeks (6 months):

- ☐ CMP
- ☐ CBC
- ☐ EKG
- ☐ Vision (Snellen and Ishihara color test)
- ☐ Vital signs + weight
- ☐ Monthly sputum

26 weeks/end of treatment:

- ☐ CMP
- ☐ CBC
- ☐ EKG
- ☐ Vision (Snellen and Ishihara color test)
- ☐ Vital signs + weight
- ☐ **CXR**

Post treatment:

☐ Perform post-treatment monitoring for relapse at 1, 2, 3, 6, 9, 12, 15, 18, 21 and 24 months. Ask at the ***Longitudinal Case Consultation Panel*** meetings recommended monitoring and timing.

Resources / Articles of interest

- **Provisional CDC Guidance for the Use of Pretomanid** as part of a Regimen [Bedaquiline, Pretomanid, and Linezolid (BPaL)] to Treat Drug-Resistant Tuberculosis Disease."2/2/2022

- **Drug-Resistant Tuberculosis: A Survival Guide for Clinicians**, 3rd Edition (Entire Guide as well as by chapter) 10/2019.
- **Treatment of Drug-Resistant Tuberculosis**
  An Official ATS/CDC/ETS/IDSA Clinical Practice Guideline 9/2019

- **NTCA Bedaquiline Access Guidance**
  WHO - catalogue of M.TB mutations and their association with drug resistance:
- **Companion Handbook to the WHO Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis**. Geneva: World Health Organization; 2014. 15, Management of contacts of MDR-TB patients.

- For **TDM frequency** see the Infectious disease pharmacokinetics lab requisition form

- **Novel 6-Month Treatment for Drug-Resistant Tuberculosis, United States**. *Emerging Infectious Diseases*, *27*(1), 332-334. Haley, C. A., Macias, P., Jasuja, S., Jones, B. A., Rowlinson, M., Jaimon, R....Goswami, N. D. (2021).
  Same article posted on CDC EID page

- **Reduced dosing of linezolid in three-drug TB regimen lessens side effects** Findings from the 6-month ZeNix trial indicated that a three-drug regimen for highly resistant tuberculosis was safer and just as effective when it included reduced doses or shorter durations of linezolid, researchers reported

- **David Horne, MD, September 20, 2021 presentation**: BPaL Time to use for all MDR TB Horne 09 20 2021 TB ECHO - YouTube

- Link to University of Florida Theraputic Drug Monitoring Forms: Forms and Catalog » Infectious Disease Pharmacokinetics Laboratory » College of Pharmacy » University of Florida (ufl.edu)

Bedaquiline Resources:

NTCA webpage has detailed information on accessing Bedaquiline.

- NTCA Bedaquiline Access Guide
  - **List of Contacts** for Bedaquiline procurement see page 1
  - Johnson & Johnson Patient Assistance Foundation (JJPAF) program and JJPAF Application
  - Step by step details on how to fill out application form start on page 29

Contacts for Assistance

- Washington State TB Program: 206-418-5500 or TBService@doh.wa.gov
- Public Health: Seattle & King County, TB Program: Tuberculosis (TB) Control Program - King County
- Washington TB Collaborative Network (WTCN):
    - Phone: 206-744-4579
    - Email: tb.wa@wtcnservices.com
    - Download the WTCN brochure to learn more.