# Introduction of Bedaquiline in the Philippines

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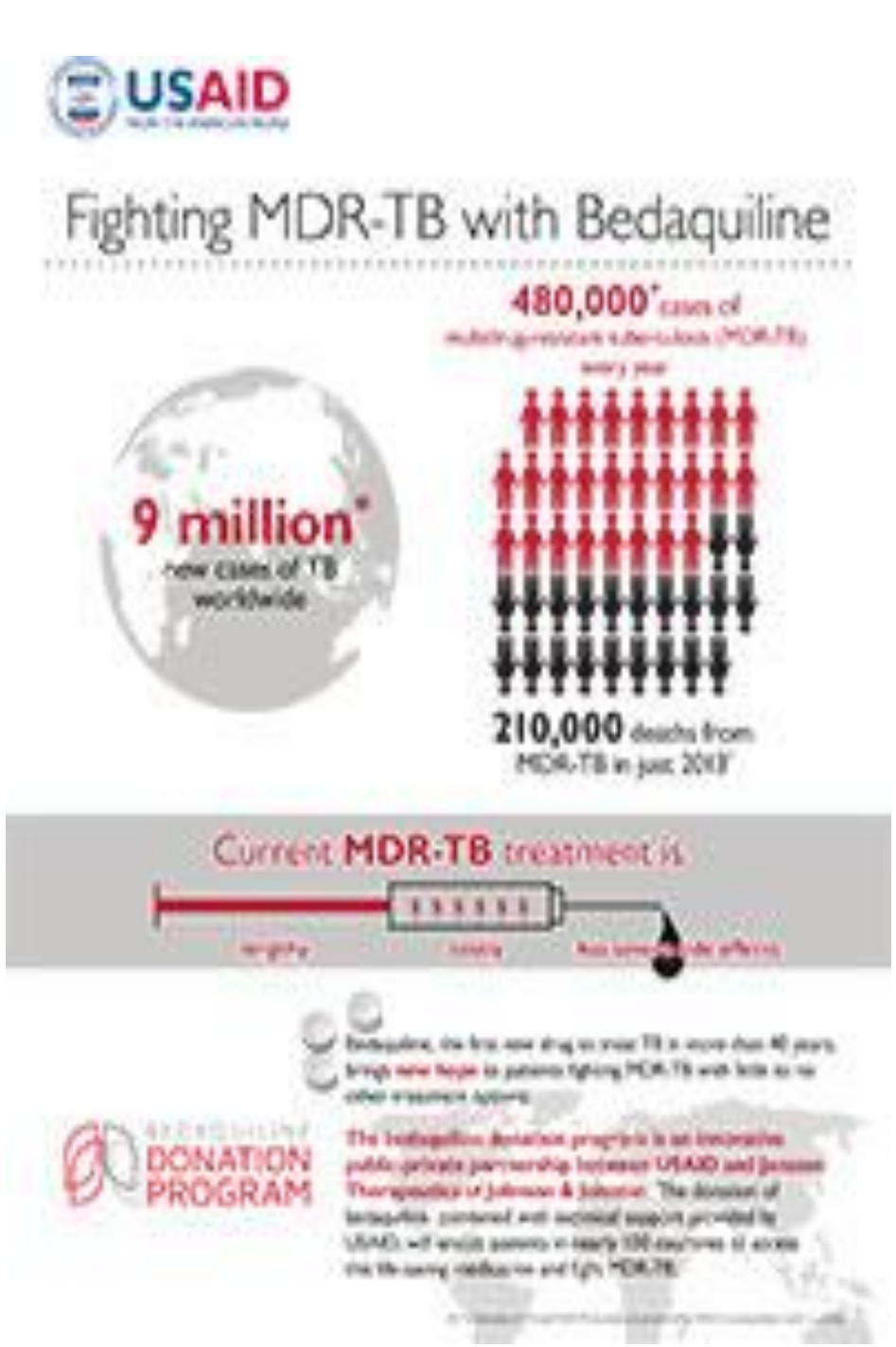
Vivian S. Lofranco, MD., PHSAE

National Clinical Coordinator, BDQ




- MDR-TB is highly contagious and notoriously difficult to treat.
- Bedaquiline , a novel drug  antibiotic developed after more than 40 yrs  Janssen Pharmaceuticals (parent company ,Johnson and Johnson)

The use of this drug in combination with existing second-line drugs provides new hope for MDR-TB patients with limited treatment options.

To maximize the use of bedaquiline to treat MDR-TB, the U.S. Agency for International Development (USAID) is serving as the implementing partner, providing technical assistance to strengthen recipient countries' health systems.

# Chronological Events prior to the implementation of BDQ …

February 2014 - Assessment of the NTP Program –DOH Philippines done by Dr Christian Lienhart and Dr Jennifer Furin.

March – December 2014 - development of the operational protocol, national implementation plan; submission of protocol to selected institutional ERB for approval;

October 2014 - BDQ was approved and registered by Philippine FDA , compassionate care and with restricted access via NTP.

March 2015


- Press release of USAID in partnership with Janssen donating drugs good for 30,000 courses ( Dr J. Garin, SOH and Ms Gloria Steele)

# Chronological Events prior to the implementation of BDQ …

| | |
|---|---|
| December 2015 | - capacity building of selected staff from 10 study sites on proper BDQ implementation |
| May 2016 | - launching of BDQ operational research in the Philippines |
| June 2016 | - start implemention of the BDQ OR in 10 study sites. |

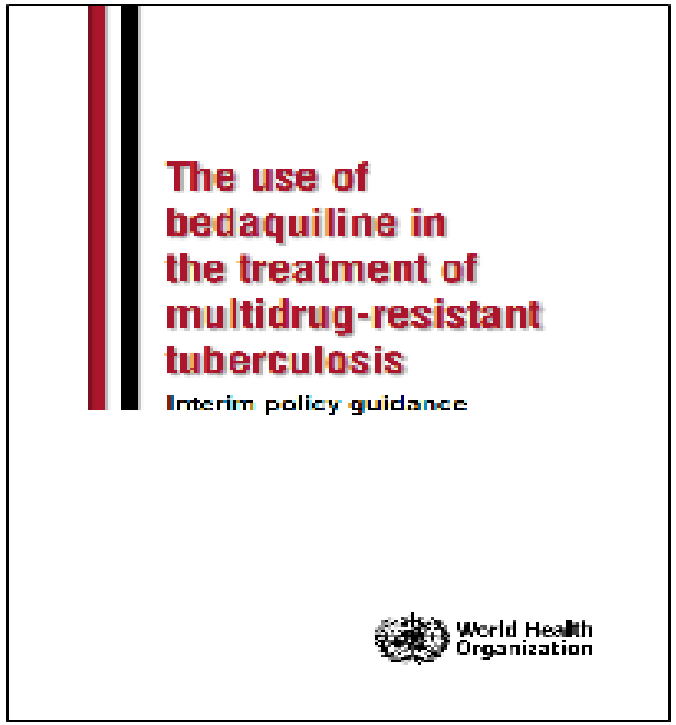
## Countries Participating in the Bedaquiline Donation Program.


Countries highlighted on the map represent countries that have reached out to the Global Drug Facility to access bedaquiline

- Armenia
- Bangladesh
- Belarus
- Bolivia
- Burma
- Cameroon
- Congo, Democratic Republic of
- Cote d'Ivoire
- Djibouti
- Dominican Republic
- Ethiopia
- France
- Georgia
- Haiti
- India
- Indonesia
- Liberia
- Kazakhstan
- Kenya
- Korea, Republic of
- Kyrgyzstan
- Lesotho
- Moldova, Republic of
- Namibia
- Netherlands
- Niger
- Nigeria
- Pakistan
- Papua New Guinea
- Peru
- Philippines
- Swaziland
- Tanzania, United Republic of
- Thailand
- Uganda
- Turkmenistan
- Uzbekistan
- Vietnam

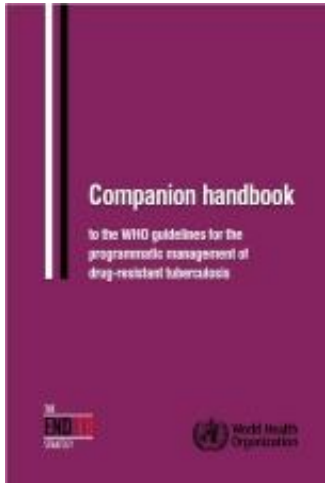
# Bedaquiline

- WHO published interim policy guidance for the use of Bedaquiline in the treatment of Multidrug-Resistant Tuberculosis last June 2013



# Bedaquiline

**Group 5**. Anti-TB drugs with limited data on efficacy and/or long term safety in the treatment of drug-resistant TB (This group includes new anti-TB agents)




| | |
|---|---|
| Bedaquiline | Bdq |
| Delamanid | Dlm |
| Linezolid | Lzd |
| Clofazimine | Cfz |
| Amoxicillin/ clavulanate | Amx/Clv |
| Imipenem/cilastatin[f] | Ipm/Cln |
| Meropenem[f] | Mpm |
| High-dose isoniazid | High dose H |
| Thioacetazone[g] | T |
| Clarithromycin[g] | Clr |

PROTOCOL

**Assessment of the Programmatic Approach in the Introduction of Bedaquiline for Drug - Resistant Tuberculosis Treatment in the Philippines: An Operational Study**

SPONSOR: Global Fund, USAID, NTP – DOH


# Bedaquiline Operational Research

General Objective: To determine the fidelity, feasibility, acceptability, effectiveness and safety of the programmatic approach in introducing Bedaquiline in the Philippines

Start of implementation: June 1, 2016

Study sites: same as in the 9-MTR

Inclusion criteria:

- Pre-XDR to Fluoroquinolones
- Pre-XDR to Second line injectable agent
- XDR-TB
- Intolerance to second-line drugs (ototoxicity, nephrotoxicity, etc.)

**Status of enrolment = 112**

# Rationale for introduction of Bedaquiline : an operational study

- Emergence of drug resistant TB is a major threat to global TB care and control.
- Reported cases of extensively drug resistant TB cases , INH and rifampicin resistant, fluoroquinolone and any SLI. An average of 9% of MDRTB have XDRTB. Currently , limited treatment resulting to low cure rates.

# Rationale for introduction of Bedaquiline : an operational study

- Bedaquiline is a novel regimen after 45 years, primary analysis under phase II , at week 24 showed statistically significant difference in culture conversion. BDQ has culture conversion of 83 days, compared to 125 days in the placebo group.

# Rationale for introduction of Bedaquiline : an operational study

- BDQ –approved by US FDA and European Medicines Association for DRTB
- Last October 2014, BDQ was approved and registered by Philippine FDA , compassionate care and with restricted access via NTP.

# Bedaquiline

WHO recommendation for the inclusion in the adult treatment regimen of MDR-TB is subject to five (5) conditions being met:

1. **Treatment is administered under closely monitored conditions**
    - sound treatment and management protocols
        - eligibility criteria
        - informed consent
        - roles and responsibilities
        - data capture
        - CEM
    - submitted to and approved by national ethics authority
    - oversight provided by independent group of experts

# Bedaquiline

- WHO recommendation for the inclusion in the adult treatment regimen of MDR-TB is subject to five (5) conditions being met:

**2. Proper patient  inclusion**

- 18 y/o and above
- pulmonary MDR-TB
- special caution: elderly, PLHIV
- not advisable: pregnant women, children
- may be considered in EP-MDR-TB

**3. Patient informed consent obtained**

# Bedaquiline

- WHO recommendation for the inclusion in the adult treatment regimen of MDR-TB is subject to five (5) conditions being met:

**4. Adherence to principles of designing a WHO-recommended MDR-TB regimen**

- Z+FQ+SLI+Pto/Eto+Cs(PAS)

  known ADRs, intolerance, contraindication to any component

  unavailability or lack of a guaranteed supply of a drug

- Pre-XDR-TB
- XDR-TB
- should not be added alone to a failing regimen
- dose strictly followed as recommended

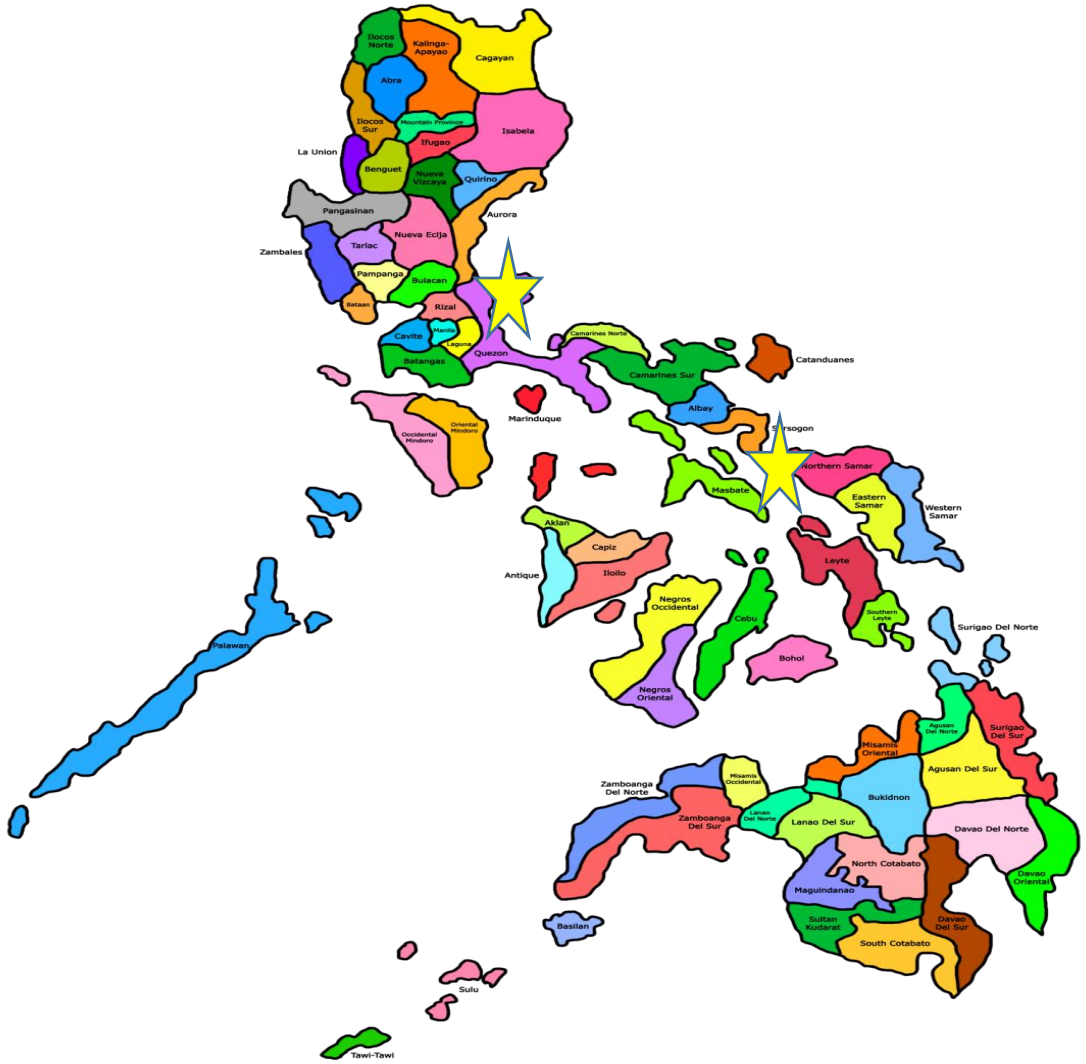
# Bedaquiline

- WHO recommendation for the inclusion in the adult treatment regimen of MDR-TB is subject to five (5) conditions being met:

**5. Pharmacovigilance and proper management of ADRs and prevention of drug-drug interactions**

- CEM
- Cfz and Mfx
- CYP3A4 inducer and inhibitor
- pre-existing health conditions

# Bedaquiline in the Philippines




| REgion | No. /% | Study sites |
|---|---|---|
| NCR | 53(47%) | LCP, JJRMH( tala), Batasan PTSI tayuman/QI,Santolan, Tumana, Tunasan,EAMC, |
| Region 1 | 2 (2%) | ITRMC in La Union |
| Region 3 | 4 (3.5%) | JBL Medical Center in Pampanga |
| Region 4-A | 3(3%) | BatMC ,Cainta Sta Rosa Quezon Medical center |
| Region 5 | 22(20%) | SMMGHC in sorsogon City |
| Region 6 | 3(3%) | WVMC in Iloilo City |
| Region 7 | 8(7%) | Eversley Medical center |
| Region 8 | 3(3%) | CalbayogCHO |
| Region 9 | 5(4.5%) | ZCMC Medical center |
| Region 10 | 9(8%) | XU-German Doctors Community DOTS clinic |
| TOTAL | 112 | |

As of July 31, 2017 = 112 patients enrolled

# SAFETY MONITORING

- Timely, accurate and complete and analysis of safety information from this study is crucial for the protection of patient.
- An active safety surveillance particularly cohort event monitoring is required for bedaquiline.

1. Adverse Events (AEs)
   - monthly reported to LCP, every 10th of the month;
   - quarterly reported by LCP to FDA/NTP

2. Serious Adverse Events(SAEs)
   - study sites to report SAEs to LCP within 12 hours, LCP will submit report to GDF and FDA within 24 hrs, cc NTP and J and J.
   - need to be reported within 24 hours upon awareness of the event by LCP to GDF and FDA within 24 hrs,cc NTP and J and J.

# Challenges

- Availability of BDQ and other second line drugs
- Short shelf life of BDQ tablets – (1-2 years only)
- Delay turn around time of LPA results :
  - important to know the FQ resistant ,
  - only 1 out 3 functional LPA equipment located at NTRL.
- Patient - centered care, long duration of treatment

Thank you very much