FAQs regarding procurement of Bedaquiline (BDQ) through the Global Drug Facility (GDF)

1. How to procure BDQ through GDF?
   The manufacturer Janssen Pharmaceutica NV has signed a contract with the Stichting International Dispensary Association (IDA), a procurement agent for the Stop TB Partnership's Global Drug Facility (GDF), to facilitate access to BDQ.
   For more information regarding BDQ procurement conditions and prices please contact GDF at gdf@who.int

2. Is there special funding available to cover the cost of BDQ?
   Purchase of BDQ should be financed through the normal channels of financing of MDR-TB through the NTP; there is no special funding.

3. What requirements have to be fulfilled in order to procure BDQ through GDF?
   The revised MDR-TB Procurement Request Form and Technical Agreement (MPTA) will need to be completed, and is available at:
   http://www.stoptb.org/gdf/drugsupply/procurement_forms.asp.

   *An annex on bedaquiline needs to be completed to confirm that the conditions laid out in the WHO Interim Policy Guidance on Bedaquiline (*http://apps.who.int/iris/bitstream/10665/84879/1/9789241505482_eng.pdf*) are met.*
   The annex will be provided to NTPs by GDF and order will be processed upon receipt of signed copy.

   After the MPTA and annex has been submitted and processed by the GDF, countries will receive a price quotation from IDA (as GDF's procurement agent). Once approved and funds are deposited with IDA or with available grant funding, order delivery is initiated with the supplier, freight forwarder and quality control agent.

4. Can NGOs procure bedaquiline through the GDF?
   Yes, the GDF will provide exclusive access for all NGO's with treatment programmes endorsed by the National Tuberculosis Programme (NTP) in a given country. Check with the NTP in your country to find out which NGO's would be eligible.

5. Can private health care providers procure bedaquiline through the GDF?
   The GDF handles procurement for those private providers that have established an approved treatment programme that has been endorsed by the National Tuberculosis Programme (NTP) in a given country. Check with the NTP in your country to find out which private providers would be eligible.

6. How long is the lead time between placing an order for bedaquiline and its availability in a treatment facility?

For accelerated or urgent requests, this can be within a month. For standard requests, the lead time typically ranges from 4 to 6 months. Factors that influence the lead time include availability of stocks, availability of funds for drug purchase, completeness of application submitted to the procurement agent, regulatory requirements, and transportation/logistics issues.

7. When can an NTP place an order for bedaquiline or for bedaquiline in combination with other second-line drugs (SLDs)?
   Any time that drugs are needed. It is highly recommended that whenever feasible the procurement of bedaquiline is grouped with the procurement of other second-line drugs, since bedaquiline should always be used as part of comprehensive MDR-TB treatment regimen combination including at least 4 other quality-assured drugs to which a patient is likely to respond[1].

8. How does the availability of bedaquiline through GDF relate to the WHO Interim Policy Guidance?

   The WHO Interim Policy Guidance on Bedaquiline http://www.who.int/mediacentre/news/notes/2013/bedaquiline_mdr_tb_20130613/en/ *issued in 2013 specifies that bedaquiline may be used as part of an MDR-TB treatment regimen for specific subgroups of MDR-TB patients and provided five conditions are met.* Bedaquiline is recommended for patients who have MDR-TB and when options to treat this condition using existing drugs have been exhausted. The drug is to be given in addition to the multidrug treatment regimen recommended by WHO. Given the limited experience on its use, bedaquiline is recommended for use in adults affected with pulmonary MDR-TB. Special caution is needed when the drug is used in the elderly, in pregnant women, and in persons living with HIV who are taking antiretroviral medication. Bedaquiline should not be used to treat latent TB infection.

   Furthermore the WHO Interim Policy Guidance on Bedaquiline[2] *specifies that bedaquiline* may *be used as part of an MDR-TB treatment regimen provided the following five conditions are met.*

Condition	Description
Effective treatment and monitoring	Treatment must be closely monitored for effectiveness and safety, using sound treatment and management protocols approved by relevant national authorities
Proper patient inclusion	Special caution is required when Sirturo® is used in people aged 65 and over, and in adults living with HIV. Use in pregnant women and children is not advised
Informed consent	Patients must be fully aware of the potential benefits and harms of the new drug, and give documented informed consent before embarking on treatment

[1] http://apps.who.int/iris/bitstream/10665/84879/1/9789241505482_eng.pdf
[2] http://www.who.int/mediacentre/news/notes/2013/bedaquiline_mdr_tb_20130613/en/

Adherence to WHO recommendations	All principles on which WHO-recommended MDR-TB treatment regimens are based, must be followed, particularly the inclusion of four effective second-line drugs. In line with general principles of TB therapeutics, Sirturo® alone should not be introduced into a regimen in which the companion drugs are failing to show effectiveness
Active pharmacovigilance and management of AEs	Active pharmacovigilance measures must be in place to ensure early detection and proper management of adverse drug reactions and potential interactions with other drugs

9. What pharmacovigilance measures need to be implemented for bedaquiline?
   As per Question 9 above, active pharmacovigilance measures must be in place to ensure early detection and proper management of adverse drug reactions and potential interactions with other drugs. Further details on recommendations for pharmacovigilance for TB can be found at: http://www.who.int/medicines/publications/pharmacovigilance_tb/en/index.html

10. What is the quality assurance status of Bedaquiline?
    To date, bedaquiline was granted accelerated approval by the US FDA on 28 Dec 2012[3] *(*http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm333695.htm)

    Bedaquiline was registered by Pharmstandard in the Russian Federation in December 2013.

    The European Commission (EC) granted conditional approval of bedaquiline on 6 March, 2014.

    The Ministry of Food and Drug Safety (MFDS) in South Korea also granted approval to bedaquiline on 21 March, 2014.

    *Since the US is a Stringent Regulatory Authority (SRA), and bedaquiline has been included in a WHO Guideline (*http://apps.who.int/iris/bitstream/10665/84879/1/9789241505482_eng.pdf*), bedaquiline meets the requirement of being a quality-assured drug eligible for procurement through GDF.*
    WHO has not yet issued an expression of interest (EOI) for BDQ prequalification.

11. Is bedaquiline currently registered in my country?
    At the present time, bedaquiline is registered only in the United States, the Russian Federation and Korea. Regulatory approval is currently being sought by the manufacturer, Janssen, with regulatory authorities in China, Columbia, Kazakhstan, India, Philippines, South Africa, Thailand and Vietnam. Janssen is actively pursuing registration in high MDR-TB burden countries to facilitate access.

[3] http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm333695.htm

12. When will bedaquiline be registered in my country?
    Regulatory filings are a complex process. As part of the agreement between Janssen and IDA, the GDF procurement agent, Janssen will prioritize registration in high MDR-TB burden countries and based on where bedaquiline is being used.

13. *Can I procure bedaquiline through GDF even if the product is not yet registered in my country?*
    Yes. Many countries have a "waiver process" in place on a shipment-by-shipment basis to allow access to drugs that are procured via GDF. National Tuberculosis Programme will work together with IDA, the GDF procurement agent, to facilitate issuance of such a waiver as needed for each product shipment. In addition, under the IDA agreement, Janssen is committed to use reasonable commercial efforts to obtain registrations in high burden countries, where registration is mandatory

14. Can bedaquiline also be procured directly from the manufacturer (Janssen)
    With few exceptions, access to Bedaquiline for the majority of low and middle income countries is only available from the GDF.

15. I've heard that there is a Compassionate Use/Early Access Programme in place for bedaquiline. Is this programme still in operation?
    Compassionate use and Early Access Programmes are typically limited to patients with the most severe forms of disease for whom all other treatment options have been exhausted, and these programmes run on a "named patient" basis requiring intensive administrative measures.
    In general, these Programmes cease when a product has been approved by local regulatory authorities and/or the product is otherwise commercially available.

16. How is bedaquiline supplied and how should it be stored?
    The current information (as of December, 2013) is that bedaquiline is supplied as uncoated white to almost white round biconvex 100 mg tablets with debossing of "T" over "207" on one side and "100" on the other side. The tablets are packaged in white high density polyethylene (HDPE) bottles with child-resistant polypropylene (PP) closure with induction seal liner. Each bottle contains 188 tablets (enough to treat one patient for the 6 month period indicated).
    NDC 59676-701-01
    Keep out of reach of children.
    Dispense in original container. Tablets dispensed outside the original container should be stored in a tight light-resistant container with an expiration date not to exceed 3 months.
    Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F). [See USP Controlled Room Temperature]

17. What is the shelf life of bedaquiline?

As of December 2013, the product shelf life is 24 months. Janssen is anticipating that data supportive of 36 months shelf life will be provided to regulatory authorities by Q3 2014.

18. Can bedaquiline be used to treat drug-sensitive TB? Or latent TB?
    Currently bedaquiline is only licensed for use in MDR-TB, as part of a combination treatment regimen. While studies are underway (under the direction of the TB Alliance) to investigate the utility of bedaquiline for treating drug-sensitive TB, at the present time the drug must not be used for that indication.
    Bedaquiline is not indicated for the treatment of latent, extra-pulmonary or drug-sensitive tuberculosis or for the treatment of infections caused by non-tuberculous mycobacteria

19. Does bedaquiline have to be used in combination with other drugs?
    Yes. Per the WHO Interim Policy Guidance[4], bedaquiline should be used as part of a combination therapy of at least four drugs to which a patient's organism is likely to be susceptible. Bedaquiline should never be added alone to a failing regimen or be used without other companion drugs.

20. Should all TB patients now be treated with bedaquiline?
    No. Up to now, bedaquiline has only been approved for use in patients who have MDR-TB and when options to treat this condition using existing drugs have been exhausted. The drug is to be given in addition to the multidrug combination therapy recommended by WHO. Given the limited experience on its use, bedaquiline is recommended for use in adults affected with pulmonary (lung) MDR-TB. Special caution is needed when the drug is used in the elderly, in pregnant women, and in persons living with HIV who are taking antiretroviral medication
    Bedaquiline is not indicated for the treatment of latent, extra-pulmonary or drug-sensitive tuberculosis or for the treatment of infections caused by non-tuberculous mycobacteria

21. How long is the treatment with bedaquiline? What is the dose?
    Bedaquiline should be given for a maximum of six months on top of the WHO recommended combination treatment regimen. The manufacturer recommends 400 mg daily (4 tablets) for 2 weeks followed by 200 mg 3 times per week for the remaining 22 weeks.

22. Can bedaquiline be used to shorten treatment of MDR-TB?
    No, there is no evidence as yet that this drug can reduce treatment duration. Moreover there is no experience of the use of this drug in short MDR-TB treatment regimens. While bedaquiline is expected to improve the likelihood of a successful outcome for individual patients, its overall impact on public health and transmission of MDR-TB in countries cannot as yet be established.

[4] http://www.who.int/mediacentre/news/notes/2013/bedaquiline_mdr_tb_20130613/en/