2015

NEW DRUGS FOR TREATING TB

AN OVERVIEW

A Resource for Journalists

Why is everyone suddenly talking about new drugs for treating TB?

Tuberculosis (TB) is a global health issue with an estimated 9.6 million cases detected in 2014, according to the World Health Organisation (WH0 [1] . Drug-resistance is now an established threat to global efforts to tackle TB, with an estimated 300,000 multi-drug resistant cases (MDR-TB) reported in 2014.

Despite the scale of the TB epidemic, there has been very little investment in research on new TB drugs. TB is generally perceived as a problem of developing countries and the pharmaceutical industry has been relatively reluctant to invest in TB drug development. It has been over 50 years since the last TB-specific drug, Rifampicin, entered the market.

What are these new drugs?

Recently, two new drugs for TB have been introduced – Bedaquiline and Delamanid. Both drugs are still in the final phase of clinical trials and cannot be universally used as yet. In 2012, Bedaquiline received 'accelerated approval' from the US-based Food and Drug Administration (US FDA) and in 2014, Delamanid was approved by the European Medicines Agency (EMA). The WHO has issued interim guidance for the use of both Bedaquiline[2](in 2013) and Delamanid[3] (in 2014).

Are many new drugs being studied?

There are over 15 drugs in various stages of clinical trials. Some of these are new drugs and some are old drugs that are being examined for other purposes. The majority of these are in the pre-clinical phase (i.e. about to enter trials among humans). Drugs in the second stage (Phase II) include Sutezolid (PNU-100480), Rifapentine (for Drug Sensitive TB cases), Linezolid and SQ-109.

Another new drug, PA-824, also called Pretomanid, is being evaluated in Phase III trials in combination with two existing drugs, Moxifloxacin and Pyrazinamide. This combination, called PaMZ regimen, is a novel approach in TB treatment and is being stated as a potential treatment for both drug sensitive and drug resistant TB. Bedaquiline and Delamanid though conditionally approved are also undergoing Phase III trials now.

Who manufactures these drugs?

Bedaquiline (Sirturo™) is manufactured by Janssen Pharmaceutica (affiliated to the American corporation, Johnson & Johnson). Delamanid (Deltyba™) is developed by Otsuka Pharmaceutical Co., Ltd. The development of the PaMZ regimen is supported by Global TB Alliance[4].

Whom are these drugs meant for? Will all TB patients receive the new drugs?

These new drugs are not meant for all TB patients as yet. According to the WHO guidance, both Bedaquiline and Delamanid are only intended for use in those with MDR-TB and only "when options to treat this condition using existing drugs have been exhausted".

How should the drugs be given?

WHO has prescribed five conditions governing the use of these two drugs. These include:

- Proper patient inclusion, which means that both drugs must be used with caution and not universally. They are

[1] http://www.who.int/tb/publications/global_report/gtbr15_annex02.pdf?ua=1

[2] http://www.who.int/tb/challenges/mdr/bedaquiline/en/

[3] http://www.who.int/tb/features_archive/delamanid/en/

[4] http://www.tballiance.org/portfolio/regimen/pamz

not recommended for use in pregnant women and children, and must be used with special caution in the elderly and adults with HIV.

- WHO-recommended treatment regimes for treating drug-resistance must be followed when these two new drugs are introduced. These drugs should never be used alone but as a part of a combination of approved second-line drugs. Bedaquiline and Delamanid should not be given together as a combination.
- Given that clinical trials are still ongoing, WHO recommends that treatment be observed carefully. All patients receiving these new drugs must be closely monitored.
- Active monitoring is especially important in the early detection and management of side effects of these new drugs.
- Informed consent is crucial, which means that patients must understand both the potential benefits and harms of using these new drugs in their treatment regimen.

How can patients in India access these drugs?

Currently, Delamanid is only available in Europe and not in India. In January 2015, the Drugs Controller General of India granted 'Conditional access' for Bedaquiline. This means that 500 patients with MDR-TB, will be chosen by the Central TB Division of the government and given access to this drug. Initially, this will be restricted to patients who access the public health system and not private hospitals.

The PaMZ regimen is of particular importance to India, because the Global TB Alliance has granted license to the Open Source Drug Discovery (OSDD) project of the Council of Scientific and Industrial Research (CSIR) of the Government of India to study the regimen. A Phase II clinical trial is now being conducted in New Delhi among MDR-TB patients. If the regimen proves successful, then India can influence the manufacture and pricing of Pretomanid, unlike in the case of Bedaquiline and Delamanid which are prohibitively expensive.

Does this mean that patients in the private sector cannot access these drugs, even if they need them?

Prior to conditional approval from the Government of India, a private hospital in Mumbai managed to procure Bedaquiline directly from the manufacturers on 'compassionate grounds' for 15 patients with MDR-TB. However, this is a long process that requires case-to-case approval and not all private sector doctors have direct access.

In September 2015, there were reports that the Government of India plans to make Bedaquiline available in the private market in select cities in India. It is likely that this will be highly regulated, at least at first, since irregular and improper use can further worsen drug-resistance in the country.

What is the international TB community doing to increase access to these new drugs?

In April 2015, the U.S. Agency for International Development (USAID) announced The Bedaquiline Donation Program. Under this agreement, Janssen, the manufacturer of Bedaquiline, will donate 30,000 treatment courses of the drug over a four-year period (worth approx. 30 million dollars). Countries who wish to apply for the drug can do so through the Stop TB Partnership's Global Drug Facility, provided they are

committed to following the WHO guidance on usage of the drug. India is on the list of eligible countries and can request donations of Bedaquiline.

Why do we need new TB drugs?

TB is our biggest public health problem. In recent times, the advent of the HIV epidemic and the emergence of drug resistance have aggravated the scale of the disease and its global impact. The existing TB treatment (six months, at minimum) is much too long and this leads to patients discontinuing treatment prematurely, increasing the risk to themselves and to others. We need new drugs that can lead to a shorter, safer, more effective treatment for both drug sensitive and drug resistant TB as well as drugs that are capable of being co-administered with HIV treatment regimens. Sustained research and investment in developing new drugs for TB treatment is therefore a global imperative.

This resource was developed by REACH as part of its efforts to improve the quality and frequency of media reporting on TB. The development of this resource is supported by a United Way Worldwide grant made possible by the Lily Foundation on behalf of the Lily MDR-TB Partnership.

If you have any questions, please write to us at media4tb@gmail.com.
For more information, please visit www.media4tb.org

Where's my story?

How many MDR-TB cases are there in your city/district/state? What are the existing treatment options, especially in the private sector?

What are the challenges faced by the limited access to Bedaquiline? Can something be done to overcome them? Should conditional or limited access to Bedaquiline be given to the private sector as well?

If/when these drugs are made available in the private market, follow-up on improved access (if any) is important. What do private practitioners think, will they prescribe these new drugs? Who will monitor the usage of these new drugs and ensure that there is no improper use?

Are there any instances of patients who have accessed these new drugs? What was their treatment outcome? What do they feel about access to these drugs?

Are healthcare practitioners trained to adequately handle the usage of these new drugs? Have they been trained on side-effect management, for instance?