



Linezolid Fact Sheet

Background: DR-TB in South Africa

Tuberculosis is the leading cause of death in South Africa, and the country has a growing epidemic of drug-resistant tuberculosis (DR-TB). Every year, approximately 15,000 people are diagnosed with multi-drug resistant TB (MDR-TB), with a substantial proportion of these found to have more extensively drug resistant TB (XDR-TB).

MDR-TB is resistant to isoniazid and rifampicin—the two most commonly used anti-TB drugs—while XDR-TB is also resistant to at least half of the second-line medicines used to treat MDR-TB.

Less than half of the patients diagnosed with DR-TB in South Africa are started on treatment. Of those who do start on treatment, only about half of those patients with MDR-TB, and less than 20% of patients with XDR-TB are cured.

What are the treatment options for DR-TB patients?

Treatment consists of up to 20 pills a day, for at least two years, with painful injections for the first six months of treatment and many patients suffering terrible side effects. Treatment must consist of multiple drugs as part of a regimen, but options of drugs to include in regimens for XDR-TB patients are extremely limited.

Where does linezolid fit into DR-TB treatment?

Linezolid is a good treatment option which could be used effectively within a multi-drug regimen for DR-TB patients in whom standard second-line TB treatment is unlikely to provide an adequate chance of a cure. While not originally developed to treat TB, a number of clinical studies have found the antibiotic to be effective against DR-TB (see [here](#) and [here](#)).

In its 2011 guidelines, the World Health Organisation (WHO) recommends linezolid as a Group 5 drug for selected DR-TB cases, meaning the drug is of unproven efficacy.

The drug is also recognised in the South African National Department of Health's policy [guidelines](#) for the "Management of DR-TB," which says that linezolid should be considered as a third-line drug in the treatment of DR-TB if cost permits.

In Khayelitsha, Doctors Without Borders (MSF) has found linezolid-containing regimens to be effective in treating DR-TB in both HIV-positive and HIV-negative individuals. Seven patients have completed the two-year treatment on a linezolid-containing regimen, and been pronounced cured, with 25 others still on treatment.

How available is brand name linezolid in South Africa?

While MSF is one of a select few healthcare providers to offer linezolid to DR-TB patients, in line with national guidelines and protocols, linezolid is usually not provided as a treatment option for patients with extensive drug resistance, due to the prohibitively high cost of the brand-name drug in this country, and the cost constraints on provincial budgets.

How much does linezolid cost?

In the private sector market, the brand-name version of linezolid currently costs more than R700 (~US\$65) for a daily pill. For a patient taking one pill daily for up to two years, this amounts to over R520,000 (~US\$49,000) for the single drug, which is only one part of an already expensive multi-drug regimen.

Previously, the National Department of Health has purchased brand-name linezolid for the public sector through the antibiotics tender for R288 (~US\$27) per pill —but this tender has expired. The Department of Health has requested bids to supply linezolid through the TB drugs tender, but the brand-name manufacturer, Pfizer has chosen not to bid.

Generic versions of linezolid are manufactured in India at significantly lower prices than the brand name product. In 2013, the UK regulatory authority granted quality approval for a generic product. MSF purchases this generic from the manufacturer, Hetero, at a cost of US\$8 (~R85) per pill, for use in other DR-TB projects worldwide. To date, however, no quality assured generic product is registered in South Africa, so this product cannot be used in the country without special permission. With the South African Medicines Control Council's decision of June 26, 2014, MSF now has permission to import this generic version of the drug.

Why is linezolid so expensive?

Linezolid is under patent in South Africa until August 2014. As long as a pharmaceutical company like Pfizer holds a patent on a medicine, they can charge high prices, and generic companies are prevented from entering the market at a lower price. Countries have the right under international trade agreements to override legitimate patents in the interest of public health when lifesaving medicines are priced out of reach, and more affordable generics could be produced. However, South African laws that would allow this to happen are impractical to implement, and have never been tested to access a more affordable version of a brand-name medicine.

What would be the impact of having more affordable linezolid be available in South Africa?

Today, only a handful of patients in need are accessing linezolid in South Africa, whilst it is estimated that hundreds more would have a high chance of surviving if they were accessing the drug.

Timeline: Here's how MSF has been fighting for wider access to generic linezolid:

August 2011: MSF starts using linezolid as part of a multi-drug regimen to treat patients with XDR-TB or pre-XDR TB in Khayelitsha.

September 2012: MSF writes a letter to the manufacturer of brand name linezolid, requesting a price reduction. The letter goes unanswered, and the price remains at around R700 per tablet through the private sector.

May 2013: A generic linezolid product is [approved](#) by an Expert Review Panel for procurement by Global Fund-eligible countries. This product is subsequently registered in the UK by the Medicines and Healthcare Products Regulatory Agency.

September 2013: MSF becomes the first organisation worldwide procuring the UK-registered generic product from the manufacturer at the price of US\$8 (~R85) per pill, for use in its DR-TB projects around the world. The generic product costs 88% less than the brand name price paid by MSF in South Africa. However, since the product is not yet registered in South Africa, MSF cannot import or use it in South Africa without the permission of the Medicines Control Council (MCC).

December 2013: MSF applies to South Africa's MCC for special permission under section 21 of the *Medicines and Related Substances Control Act 101 of 1965*, in order to provide a cheaper, generic version of linezolid for patients in South Africa, based on the unaffordability of the brand name drug. The MCC is allowed to give this kind of approval for unregistered medicines to allow limited use for a renewable six-month timeframe.

December 2013: The MCC turns down the MSF application for linezolid, on the grounds that affordability is not a consideration. MSF rejects this reasoning, based on both previous section 21 applications being granted on affordability grounds—most notably to MSF to allow the use of generic antiretrovirals for treating HIV/AIDS in 2001—as well as given the constitutional obligation upon the state to take measures that progressively realise the right of everyone in South Africa to have access to health care services.

March 2014: MSF files an appeal of the MCC decision, which goes unanswered for over a month.

June 2014: MSF turns to litigation in order to appeal the MCC's decision, and files affidavits and a notice of motion in the South Gauteng High Court.

26 June 2014: Out-of-court negotiations resulted in a successful outcome for MSF. Following the provision of additional information to the MCC— to confirm the quality of the linezolid product to be used and MSF treatment protocol—the MCC grants approval for MSF importation of generic linezolid via a section 21 authorisation.

What happens next?

MSF will start providing generic linezolid as part of a multi-drug regimen to patients in Khayelitsha. However, generic linezolid will only be more widely available in South Africa if other healthcare service providers file similar section 21 applications, or if the MCC registers a generic linezolid product. Currently, the MCC is reviewing generic linezolid for full registration, including the linezolid product MSF will be using in Khayelitsha.

How do we prevent the story of linezolid from repeating for other drugs?

Pharmaceutical patents have an impact on medicine prices—when a company holds a patent on a drug in a country, it blocks price-lowering generic competition. This MCC decision on linezolid comes at the same time as South Africa's Department of Trade and Industry (DTI) has been leading a six-year process to amend the country's intellectual property (IP) laws. IP reforms designed in the interest of public health would help control medicine costs by preventing abusive patent monopolies (read more [here](#)). The DTI released a [draft](#) national policy for public comment in September 2013 (read the MSF/TAC/SECTION27 submission [here](#)), but has yet to incorporate comments into a final policy.

In January 2014, the “Pharmagate” scandal broke in the South African press, revealing that Big Pharma companies were trying to delay policy reform as a way to preserve their patent monopolies. The Minister of Health expressed [outrage](#) over this secret plot, and South Africa’s leading political parties have [promised](#) that finalising the IP policy is a priority, now that elections are over. If a pro-public health IP policy is finalised and implemented, lengthy battles like the one for generic linezolid would not need to repeat for other lifesaving drugs.