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## **“FIRST-EVER TREATMENT GUIDELINES RELEASED FOR MAJOR CAUSE OF DEATH OF PEOPLE LIVING WITH HIV”**

A closer look at availability of recommended cryptococcal meningitis drugs: the case of South Africa

Annually over 7,000 cases of cryptococcal meningitis are reported in South Africa; this number is likely an underestimation of the actual burden. While increased access to ARV therapy can lead to reduced incidence of cryptococcal meningitis, mortality related to HIV-related cryptococcal meningitis remains unacceptably high across sub-Saharan Africa: in one setting in rural KwaZulu-Natal, South Africa, 41% of CM patients died in hospital within 30 days of admission.

Currently South African national guidelines for treatment of cryptococcal meningitis foresees an induction phase of Amphotericin B treatment for two weeks; followed by a consolidation phase of Fluconazole treatment for eight weeks which should be followed by a prophylaxis with Fluconazole treatment until CD4 > 200 for more than six months. While both Amphotericin B and Fluconazole are available in South Africa's private and public sectors, Amphotericin B is not commonly available in public hospitals. Only 35% of patients have been reported to be in rural KwaZulu-Natal received any Amphotericin B, with only 8% receiving what is considered an optimal 2-week course. Many patients only receive only Fluconazole.

As of mid-2011, Amphotericin B was available in the public sector for R32.42 (4 USD/vial) per 50 mg injection. Bristol Myers Squibb is the only registered supplier of Amphotericin B under the trade-name Fungizone, experienced a worldwide-shortage of Fungizone in August 2011 which severely impacted South Africa, with stock outs reported across the country. The South African government was forced to import Amphotericin B through another company at R51.30 (6.42 USD/vial) per 50 mg vial. The final price of Amphotericin B for supply in the public sector is under negotiation.

Liposomal Amphotericin B, manufactured by Gilead and sold under the brand name Ambisome is registered in South Africa but not available in the public sector. It is primarily used in the private sector at the cost of R1,946 (243.7 USD/vial) per 50 mg vial.

Without a significant reduction in price, Ambisome is not expected to be widely used to treat cryptococcal meningitis in the public sector, despite the reduced side effects and limited renal toxicity associated with its use in comparison to non-liposomal Amphotericin B.

While Flucytosine was previously included in South African cryptococcal meningitis treatment guidelines, this is not currently the case. Flucytosine is not registered in South Africa and is only available through Section 21 of the Medicines Act, which allows for an unregistered medicine to be used on a named-patient basis in exceptional situations in which a physician specifically requests Flucytosine.

Overall availability and access problem to CM drugs recommended by WHO in the countries in Africa where MSF operates. Fluconazole is registered in several African countries, often available from several suppliers and is the medicine of choice in the countries that provide treatment for cryptococcal meningitis.

Although access problem may exist also for fluconazole, the situation seems definitively very problematic for all other medicines recommended in the WHO GLs on cryptococcal meningitis. Amphotericin B 50 mg vial is registered in very few countries in Africa and even when registered suppliers often do not market this medicine. In South Africa is a component of the treatment of cryptococcal meningitis, but many patients do not have access to it in the public sector hospitals.

In Guinea Conakry as an example it is available only for the patients treated within the MSF programs. In Cameroun, although registered it is currently in stock out. In the countries where it is available, the price at supplier level range from 4 USD to 10 USD per vial, which means approximately 70 to 170 USD per 2 weeks treatment per patient. Commercial availability however does not mean that patients can have access to it.

Flucytosine, which is one of the three medicines jointly with fluconazole and Amphotericin B recommended by WHO in its regimens for cryptococcal meningitis, seem not to be registered in any country in sub-Saharan Africa, even not in South Africa where it was once part of the national treatment guidelines for this opportunistic infection.

Liposomal Amphotericin B, Ambisome, produced by Gilead, presents advantages in relation to Amphotericin B in terms of side effect, however it lags even much behind. Its cost, when registered and available in the private sector is prohibitive. In South Africa it can be accessed in the private sector at not less than 243.7 USD/vial.

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