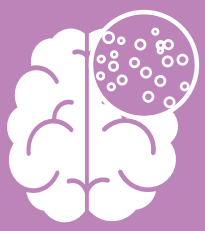
Cryptococcal meningitis

Bridging treatment gaps for a deadly HIV co-infection



FACTS

180,000

people die every year from HIV-related cryptococcal meningitis

70%

of people who get cryptococcal meningitis die from the disease

75%

of deaths from cryptococcal meningitis occur in sub-Saharan Africa

Cryptococcal meningitis is caused by the fungus cryptococcus neoformans, often found in soil and bird droppings. Most people are likely to breathe in this microscopic fungus at some point in their lives but never get sick from it. However, people with advanced HIV are particularly susceptible to it because they have weakened immune systems, resulting in illness that quickly leads to death unless treated. Despite advancements in access to antiretroviral treatment, hundreds of thousands of people with advanced HIV die each year from opportunistic infections – including cryptococcal meningitis – because affordable and accessible medicines to treat these infections are lacking.

The push for progress

In collaboration with key partners in 2021, DNDi developed plans to address access barriers to the key WHO-recommended medicines immediate-release (IR) flucytosine (5FC) and liposomal amphotericin B (LAmB) in low- and middle-income countries (LMICs), including by building strategic alignment among policymakers, donors, ministries of health, national implementing partners, civil society, and patient advocates.

While IR 5FC is a critical component of first- and second-line treatments for cryptococcal meningitis, current formulations of the drug – delivered in four divided doses per day – are poorly adapted for use in resource-constrained settings.

Following preparations with partners in 2021, we initiated a Phase I trial of a new sustained-release formulation of 5FC in early 2022 with the aim of delivering an affordable alternative formulation that is simpler for patients, nurses, and doctors.

Our goal is now to scale up access and R&D work to ensure more patients have access to life-saving medication to treat cryptococcal meningitis, particularly in LMICs across Africa. This includes advocating for the registration of 5FC in LMICs, identifying alternative quality-assured manufacturers of LAmB, and continuing development of a sustained-release formulation of 5FC.

DNDi
Drugs for Neglected Diseases *initiative*

Karin Schermbrucker-DNDi

Dr Kyla Comins examines cryptococcal meningitis survivor Cynthia Metuso at Tygerberg Hospital in Cape Town, South Africa. When Cynthia contracted cryptococcal meningitis, she was convinced she was going to die. The pain was so severe. With the help of life-saving treatment, she made a full recovery.

> “Cryptococcal meningitis is a devastating illness, and we have life-saving treatments, but these are not available to everyone. We must make sure that the people who need this treatment have access to it. Having flucytosine easily available to patients who need it would significantly improve their outcomes.

Addressing the supply and demand barriers that limit access to treatment

In collaboration with key partners, DND*i* plans to address the barriers to access for both IR 5FC and LAmB by working to unblock the market failures that limit the availability of to the two medicines in LMICs across the African continent. Key priorities include identifying alternative quality-assured manufacturers of LAmB and implementing activities to bring at least one generic product to the LMIC market.

In addition, DND*i* and partners are undertaking demand creation activities for LAmB across key indications and for IR 5FC for cryptococcal meningitis, while implementing mechanisms to track progress towards public health targets for advanced HIV disease.

Advancing the development of sustained-release flucytosine to simplify treatment of cryptococcal infections

DND*i*’s sustained-release 5FC project aims to deliver a simpler, sustained-release formulation of flucytosine that is both affordable and accessible. The project also aims to strengthen local capacities to conduct clinical trials.

Renowned scientists and institutions from Africa and Europe are working on this project led by DND*i* and funded by the European & Developing Countries Clinical Trials Partnership (EDCTP2) programme supported by the European Union, with additional funding from the Swiss Agency for Development and Cooperation (SDC), Médecins Sans Frontières International, and other private foundations and individuals.

Preparations for the Phase I trial began in 2021, with the trial kicking off at partner research facility, FARMOVS, in South Africa in early 2022. Phase II studies in Tanzania and Malawi will begin in 2023.