FACTS

Unknown
burden hinders global response

Often leads to amputation

Occurs most often in the so-called 'mycetoma belt'
between latitudes 15° S and 30° N

MYCETOMA

Developing safe, affordable treatments to prevent devastating disability

One of the world's most neglected diseases, mycetoma is a devastating, slow-growing infection that destroys skin, muscle, and bone. Most likely transmitted after a thorn prick or cut allows fungi or bacteria from soil to enter the body, it mainly affects the feet and legs. Mycetoma occurs in multiple countries across the 'mycetoma belt', which stretches across five continents between the latitudes of 15° S and 30° N. The fungal version of mycetoma, known as eumycetoma, can cause severe deformities, disability, and mental health issues due to the stigma associated with the chronic, unrelenting course of the disease and lack of effective treatment, which often leads to amputation.

The push for progress

Following advocacy from DNDi and our partners, the World Health Organization (WHO) added mycetoma to its list of neglected tropical diseases (NTDs) in 2016 – an important step in raising awareness of the disease and encouraging investment in research for diagnostics and treatments. In 2017, DNDi partnered with the Mycetoma Research Center (MRC), a WHO collaborating centre in Khartoum, Sudan, and Japanese pharmaceutical company Eisai Co., Ltd., to begin enrolling patients in the first-ever randomized controlled clinical trial for eumycetoma treatment. Completed in 2021, the trial showed that the drugs fosravuconazole and itraconazole are both effective – but much more is needed.

Our goal is now to develop new treatments for mycetoma that can prevent devastating amputation and disability – and ensure access to available treatments for all people in need.

Moving forward with a simpler, more affordable treatment

Initiated by DNDi and partners in 2017, the **first-ever double-blind, randomized clinical trial for fungal mycetoma** tested the efficacy of a weekly dose of fosravuconazole compared with daily itraconazole – the current standard of care – in treating moderate-sized lesions in patients requiring surgery. Results presented at the 13th European Congress on Tropical Medicine and International Health in November 2023 suggested that fosravuconazole 200 mg and itraconazole 400 mg combined with surgery had similar efficacy under clinical trial conditions.
The itraconazole regimen is administered twice daily with food; the fosravuconazole regimen is administered weekly with no food requirement and with limited drug-drug interactions. Long-term follow-up completed in 2023 showed recurrence rates remained low for both regimens. This project was recognized as DNDi's 2023 Project of the Year in clinical research.

DNDi
Best Science for the Most Neglected

> **“I am slowly losing hope for the future that I was looking forward to. What spouse will want a partner who cannot support his family?**

Meles, from the Amhara Region of Ethiopia, was first diagnosed with mycetoma when he was seven years old and has lived with the disease for over 20 years. Having undergone eight rounds of surgery on his affected foot over the years, he had to sell his car when he became unable to drive – losing his only source of income.

Photo credit: Kumera Gemechu - DNDi

Expanding access to treatment

DNDi continued moving forward with efforts to support the registration of fosravuconazole in Sudan in 2023 despite ongoing conflict in the country, while also working to expand registration and access to both itraconazole and fosravuconazole in Africa and South Asia. In July 2023, DNDi met with Senegalese health authorities and a multi-disciplinary team working on mycetoma at Cheikh Anta Diop University and Gaston Berger University, as well as with patients and communities in the Louga region of the country. The visit was critical to establishing a common agenda for mycetoma patients in Senegal, including agreeing on the need to incorporate the disease into national NTD control programmes, understand its burden, rapidly increase access to current treatments, and pave the way for new treatments as they become available.

Convening research experts

In June 2023, DNDi organized a meeting of mycetoma clinical experts in Nairobi, including representatives from seven African countries, Europe, India, Japan, and Mexico, to set out a framework for much-needed epidemiological studies to fill knowledge gaps on the burden of mycetoma across multiple continents. The meeting also addressed important aspects of clinical trial design and drug development for new treatments that are not only simpler and more effective, but also suitable for children and women of childbearing potential.

Two meetings with experts in pre-clinical research were held in Geneva in July and Utrecht in November with participants from Belgium, Brazil, Mexico, the Netherlands, Sudan, and Sweden. Participants concluded that mycetoma drug discovery requires the development and validation of new pre-clinical models for eumycetoma.

Identifying new drug candidates: MycetOS

The Mycetoma Open Source project (MycetOS) uses an ‘open source pharma’ approach to discover new treatments targeting *Madurella mycetomatis,* the most common cause of fungal mycetoma. Participating researchers engage through community-driven, in-kind scientific contributions, with all ideas and results published immediately in real time to an open-access database free of intellectual property constraints.

Drug discovery efforts continued throughout 2023 with support from Erasmus MC, University College London, University of Sydney, and the University of Bayreuth. New participants joining the MycetOS community allowed for modelling activities to be incorporated into the collaboration. The project remained focused on finding novel treatments for eumycetoma through compound screening, *in vitro* testing, and translational modelling.