

OPEN LETTER TO GILEAD & VIATRIS: WE NEED AFFORDABLE TREATMENTS FOR THE RISE OF SERIOUS INVASIVE FUNGAL DISEASES

23 June 2021

To:

Daniel O'Day, Chief Executive Officer, Gilead Sciences

Rajiv Malik, President, Viartis

We are writing with grave concern regarding the lack of adequate supply and affordable access to **liposomal amphotericin B (L-AmB)**ⁱ to treat mucormycosis. This life-threatening fungal infection has further compounded the crisis of Covid-19 in India and Nepal. The rapidly increasing need for L-AmB to treat mucormycosis as a devastating complication of Covid-19 comes against a larger backdrop of the persistent unaffordable pricing of this crucial antifungal drug, including in the private market; lack of access to the offered access price for cryptococcal meningitis;ⁱⁱ and difficulty accessing a predictable and affordable supply for the neglected tropical disease visceral leishmaniasisⁱⁱⁱ as well as several other systemic fungal infections such as talaromycosis^{iv}.

Mucormycosis is an often-fatal disease, which requires urgent surgery and treatment with antifungals. Without timely access to antifungal treatment, people with mucormycosis can develop bone necrosis, lose vital organs - such as their eyes -- or die.

There is simply not enough supply of L-AmB in India, and what is available is priced too high in the private market. Both factors result in the lack of treatment of mucormycosis in India, as well as inadequate dosing and therefore poor outcomes for those who do receive treatment. A large number of vials (150-300 vials) is needed to treat each person with mucormycosis.^v The one million vials Gilead has committed for India to treat mucormycosis is vastly insufficient as it could only cover an estimated 3,400 to 6,000 patients, whereas the need is at least four times as high, and rising. According to the government of India, the number of mucormycosis cases increased from 9000 in late May to 28,252 cases on 7 June 2021.^{vi}

Further, while India's public sector is eligible for lower prices for L-AmB through Gilead's 'access' programme for the treatment of cryptococcal meningitis, prices in the private sector, upon which millions of people in India rely, remain high (US\$69) and have risen significantly due to shortages. Although Gilead announced in late 2018 a lower price of US\$16.25 USD per vial for 116 countries,^{vii} including India, L-AmB was still priced higher in the private sector at US\$69 and the same price was asked of patients during the Covid-19 pandemic. In other countries eligible for the 'access' price, Médecins Sans Frontières (MSF) has reported prices as high as US\$200.^{viii}

In addition to price and supply for the treatment of mucormycosis in India, we are concerned that there is not enough stable supply of L-AmB to treat cryptococcal meningitis, visceral leishmaniasis (kala azar), and mucormycosis globally. For example, given the government of India's necessary step to reallocate supply of L-AmB from the kala azar programme to mucormycosis, we are very concerned that people vulnerable to leishmaniasis will not have adequate treatment if these vials are not replaced

in time. Therefore, we ask that Gilead re-prioritize the manufacturing of L-AmB and extend the access pricing to Covid-19 patients and governments. In 2019 Gilead committed to increase its L-AmB production with the manufacturing site in La Verne, but did not make good on this commitment as the manufacturing capacity was instead redirected in 2020 for remdesivir, Gilead's drug that has questionable effectiveness against Covid-19. Also, Gilead has long hidden the liposomal technology – a key component of manufacturing L-AmB – as a trade secret,^{ix} which combined with challenging regulatory pathways has undermined a stable global supply as generic competition has been significantly delayed. Finally, some alternative manufacturers are contributing to the supply chain and while they await evaluation, Gilead and its distributors must make the drug available in sufficient quantities, and at the access price of US\$16.25 USD per vial to ensure that the present crisis is addressed.

We ask that Gilead and Viartis take the following steps immediately:

1. Accelerate the realisation of the nearly three-year-old promise of a US\$16.25 per vial for 116 countries for cryptococcal meningitis, and prioritise registering L-AmB in these countries.
2. Extend the indications eligible for the US\$16.25 price per vial to mucormycosis. Ensure the private sector in India can secure the lower 'access' price of US\$16.25 per vial of L-AmB and take steps to rein in markups by local distributors that are resulting in higher prices.
3. Increase supply dedicated to India, Nepal and other low and middle-income countries facing a major increase in COVID-19 cases and associated opportunistic fungal infections. Provide information and the timeline of the delivery of the committed one million vials for the treatment of mucormycosis in India.
4. Increase manufacturing of L-AmB, including re-dedicating an additional manufacturing line. Provide information including timelines and volumes that Gilead will manufacture over the next 18 months and the price of these vials.
5. Share necessary know-how and the regulatory dossier with manufacturers and WHO to enable additional suppliers.

Gilead has failed to ensure a predictable and affordable supply of L-AmB for both kala azar and cryptococcal meningitis. Don't compound the unnecessary suffering and death by also failing people suffering from mucormycosis in the wake of Covid-19.

We look forward to hearing from you as soon as possible, preferably by June 25, 2021 in response to the requests above. We would also like to discuss these issues further with your respective offices on July 1, 2021 at 3pm CEST/9am EST.

Sincerely, on behalf of the organizations and individuals below,

Sharonann Lynch, Global Health Policy & Politics Initiative, O'Neill Institute for National and Global Health Law, Georgetown University
Leena Menghaney, Regional Head (South Asia), Access Campaign, Médecins Sans Frontières (MSF)
Reshma Ramachandran, MD MPP, Physician Fellow, National Clinician Scholars Program, Yale University School of Medicine

Organizations

Access to Rights and Knowledge (ARK) Foundation, Nagaland, India
Action Canada for Sexual Health and Rights, Canada
African Services Committee, United States
The AIDS and Rights Alliance for Southern Africa (ARASA), Namibia
AIDS-Free World, United States
All India Drug Action Network (AIDAN), India
APCASO, Thailand
Apvieniba HIV.LV, Latvia
Asia Pacific Network of People Living with HIV/AIDS (APN+)
Association of people living with HIV/AIDS, Laos
Coalition of Women Living with HIV and AIDS, Malawi
Eastern Africa National Networks of ADS and Health Service Organizations (EANNASO), Tanzania
Federation of Gender and Sexual Minorities (FSGMN), Nepal
Foundation for Integrative AIDS Research (FIAR), United States
The Global Coalition of TB Activists, International
Global Hindu Charity Foundation, Nigeria
Global Justice Now (UK), United Kingdom
The Global Network of People Living with HIV (GNP+), Global
Global Network of Sex Work Projects, Scotland, UK
Health GAP, International
HIV Legal Network, Canada
Hopers Foundation, India
I-MAK, United States
IFARMA Foundation, Colombia
Indonesia AIDS Coalition, Indonesia
Initiative for Medicines, Access, & Knowledge (I-MAK), United States
ITPC-LATCA, Guatemala
Khmer HIV/AIDS NGO Alliance (KHANA), Cambodia
MSF Access Campaign, Global
National Association of People living with HIV (NAPN+), Nepal
National Association of Women Living with HIV (NFWLHA), Nepal
National Network of People with HIV/AIDS (TANEPHA), Tanzania
National Network of PUD and Drug Service Organizations, Nepal
Nepalese Migrant Network, Nepal
Network Group Against AIDS-Nepal (NANGAN), Nepal
Network of Female Sex Workers (JMMS), Nepal
Oxfam America, United States
People's Vaccine, Global
Positive Malaysian Treatment Access & Advocacy Group (MTAAG+), Malaysia

Prison Foundation, Nepal
Recovering Nepal, Nepal
Sankalp Rehabilitation Trust, India
SECTION27, South Africa
Southern African Programme on Access to Medicines & Diagnostics (SAPAM), South Africa
TB Proof, South Africa
Third World Network, International
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Treatment Action Group, United States
Vietnam Network of People Living with HIV (VNP+), Vietnam
Yayasan Peduli Hati Bangsa, Indonesia
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Young Women Empowerment Network, Namibia
Youth Rise, Nepal
Zambia Sex Workers Alliance, Zambia

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Mona Mishra, India
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Rachael Crockett, CSO representative ACT-A Therapeutic Pillar, UK

ⁱ L-AmB is a powerful antifungal agent that is known for its ability to treat serious invasive fungal infections caused by various fungal species.

ⁱⁱ US CDC Foundation, GAFFI, St. George's University, Wits University, ITPC, University of Minnesota, DNDi, Botswana Harvard AIDS Institute Partnership, CHAI, Unitaid, University of New Mexico, LSHTM, MSF. Ending cryptococcal meningitis deaths by 2030: Strategic framework. [Online]. 2021 [Cited 2021 3 June]. Available from: <https://msfaccess.org/ending-cryptococcal-meningitis-deaths-2030-strategic-framework>

ⁱⁱⁱ Sundar, S., & Chakravarty, J. (2010). Liposomal amphotericin B and leishmaniasis: dose and response. *Journal of global infectious diseases*, 2(2), 159–166. <https://doi.org/10.4103/0974-777X.62886>

^{iv} L-AmB is indicated for treatment of Aspergillus species, Candida species, Cryptococcus species, Histoplasmosis and talaromycosis as well as empiric therapy for presumed fungal infection in febrile, neutropenic patients

^v A treatment course for mucormycosis is likely to require a minimum of 21 days before switching to oral treatment. High dosing required amounts to a high number of vials needed (e.g. 70 kg patient on AmBisome 5-10mg/kg/day would require 147 to 294 vials for 3 weeks treatment). The calculated minimum price for a treatment course would thus be USD 10,143 to 20,286 in the private sector.

^{vi} 28,252 cases of mucormycosis cases in the country; Maharashtra, Gujarat lead the tally: Health Minister. Times Now News. [Online]. 2021 June 7 [Cited 2021 12 June]. Available from: <https://www.timesnownews.com/india/article/28252-cases-of-mucormycosis-cases-in-the-country-maharashtra-gujarat-lead-the-tally-health-minister/767491>

^{vii} Gilead Sciences. Gilead Sciences announces steep discounts for Ambisome to treat cryptococcal meningitis in low- and middle-income countries. [Online]. 2018 Sep 7 [Cited 2021 18 May]. Available from: <https://www.gilead.com/news-and-press/company-statements/discount-for-ambisome>

^{viii} MSF. Untangling the Web: HIV medicine pricing and access issues, 2020. [Online]. 2020 [Cited 2021 18 May]. Available from: <https://msfaccess.org/untangling-web-hiv-medicine-pricing-access-issues-2020>

^{ix} Gilead. FORM 10-K: Annual Report Pursuant to Section 13 OR 15(d) of the Securities and Exchange Act of 1934 [Online]. 2003 [Cited 2021 12 June]. Available from: <https://investors.gilead.com/node/23696/html>