



## Southern African HIV Clinicians Society (SAHCS)

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### ***Letter of support - enabling access to best-practice care for patients with cryptococcal meningitis***

Following the recent publication of two media articles highlighting challenges regarding treatment for patients with cryptococcal meningitis (CM), the Southern African HIV Clinicians Society (SAHCS) would like to take the opportunity to state their support for improved access to best-practice care for these patients, including the access to the life-saving medications 5-flucytosine (5FC) and liposomal amphotericin-B (L-AmB). (1, 2)

Cryptococcal disease is one of the most important opportunistic infections among people living with advanced HIV disease and is a major contributor to illness, disability and mortality, particularly in sub-Saharan Africa. Globally, CM is responsible for 15% of AIDS-related deaths, with annual global deaths estimated at over 180 000, of which 135 900 occur in sub-Saharan Africa. (3, 4) Just under 6 500 cases of CM were detected by the National Institute of Communicable Diseases (NICD) surveillance in 2019. (4) The same year SAHCS released an updated guideline for the management of CM, which recommended the inclusion of 5FC, and L-AmB in cases with poor kidney function. (5)

This SAHCS 2019 guideline was directly influenced by the Antifungal Combinations for Treatment of Cryptococcal Meningitis in Africa (ACTA) trial, which reported its findings in March 2018. The study convincingly demonstrated that the addition of 5FC to CM treatment regimens improved one year survival to more than 70% (6), considerable improvement over the then standard of care. Despite strong recommendations to shift the standard of care to regimens with the lowest mortality rate, access to lifesaving drugs remained very limited in South Africa.

More recently, the same group of investigators involved in ACTA published the findings of the AMBITION study that aimed to simplify the management of CM, while reducing toxicity and maintaining improved survival. This multicentre, multinational, randomised controlled trial added a single high dose of L-AmB to a full oral regimen of 5FC and fluconazole and showed equal efficacy to the current best standard of care. This new regimen was rapidly embraced by the WHO resulting in the release an updated 2022 guideline strongly recommending this new regimen as the preferred induction regimen. (7)

A barrier to implementation of this new regimen in resource limited settings is not only the prohibitive cost of L-AmB and 5FC but also the fact that there is no additional survival gain over the current standard. Thus, the question is "Why pay more if the outcome is no different?". One of the most important benefits of this new regimen is that it simplifies management enough to ensure that most patients will complete the intensive phase of treatment and benefit from rapid reduction of organism load expected of this phase. Apart from reduced toxicity, there is also a reduced need for extended intravenous access thereby eliminating complications associated with prolonged venous cannulation. Further benefits include reduced hands-on care by nurses and doctors, and the possibility of a shortened hospital stay relieving in-patient burden. All of these might be considered "soft benefits" but in the setting of an overburdened and under-staffed health system, these benefits are tangible and worthy of consideration.

SAHCS' journey to increase access to CM treatment dates back to the early 2000s. Alongside the development of CM management guidelines and online training, SAHCS has strongly advocated for the approval of best-practice medications at affordable prices. SAHCS has been working intimately

with a 5FC access programme initiated by MSF in 2018 and subsequently transferred to the Clinton Health Access Initiative (CHAI) Foundation in 2019. This programme made donation stocks of 5FC accessible and available to public sector hospitals with a high burden of CM across the country. This was with the full approval and close collaboration of provincial health structures. SAHCS designed online modules on the management of CM, with a particular focus on the safe and effective use of 5FC. This training remains accessible, on demand for convenience, and accessed through the SAHCS online learning platform. (8) So far, over 200 health care providers across all provinces have received training. The objective is for all front-line clinicians involved in the management of CM to be adequately skilled.

SAHCS is committed to the promotion of high-quality evidence-based HIV healthcare in Southern Africa and appeals for universal access to 5FC and L-AmB for treatment of CM. SAHCS fully supports NDoH, the South African Health Products Authority, and allied healthcare organisations to fast track the availability of flucytosine and liposomal amphotericin B as lifesaving medications.

## References

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