



health

Department:
Health
REPUBLIC OF SOUTH AFRICA



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NOTICE: FLUCYTOSINE 500MG TABLET STOCK SUPPLY AND IMPLICATIONS FOR THE TREATMENT OF CRYPTOCOCCAL MENINGITIS

The 2024 Adult Hospital Level and 2023 Paediatric Hospital Level editions of the Standard Treatment Guidelines (STGs) and Essential Medicines List (EML) currently recommend oral flucytosine as a critical part of the induction phase treatment regimen for cryptococcal meningitis (CCM) used in combination with intravenous amphotericin B and oral fluconazole. Recently, the supply of oral flucytosine has been inconsistent.

Availability of flucytosine

Flucytosine 500 mg (100 tablets) was not awarded on the HP02-2025AI tender, which commenced on 01 October 2025, and is therefore currently being procured through quotation.

A shipment of 4000 units of flucytosine 500 mg (100's) is expected in January 2026. This will also be procured on quotation. Once received, this stock will be sufficient to meet the projected demand for 2026. Provinces and facilities are reminded to ensure equitable and timely access to flucytosine and to facilitate availability across all levels of care.

Availability of amphotericin B deoxycholate

It should be noted that amphotericin B deoxycholate was not awarded on the HP02-2025AI tender and should be procured on quotation, where required.

Preferred regimens as per the STGs and EML

Given the improved safety profile and the potential for a shorter hospital stay¹, it should be noted that the **Adult Hospital Level STGs recommends the following preferred induction-phase regimen for CCM**, which includes liposomal amphotericin B:

Medicine	Treatment course
Liposomal Amphotericin B injection	10mg/kg stat dose
Flucytosine tablets	25mg/kg 6 hourly for 14 days
Fluconazole tablets	1200 mg daily for 14 days

The **recommended and preferred regimen for the induction phase treatment of CCM in the Paediatric Hospital Level STGs** is as follows:

Medicine	Treatment course
Amphotericin B deoxycholate injection	1 mg/kg/day for the first week
Flucytosine tablets	100 mg/kg/day in 4 divided doses for the first week
Fluconazole tablets	IV/oral, 12 mg/kg/day for the second week

Recommendations if flucytosine is unavailable

¹ NDoH Medicine Review, Liposomal Amphotericin B for Cryptococcal meningitis. 2024. Available from: <https://www.health.gov.za/nhi-edp-stgs-eml/>

Adult Hospital Level STGs and EML

Where flucytosine is completely unavailable, refer to the table below for the alternative induction phase regimens using IV amphotericin B deoxycholate:

Indication: Adult Hospital Level	Current STG	Alternative regimen if flucytosine is not available
Chapter 10: HIV and AIDS 10.2.4.2 Cryptococ- cal Meningi- tis	<p><u>Induction phase</u></p> <ul style="list-style-type: none"> • Liposomal amphotericin B, slow IV infusion over 2 hours, 10 mg/kg in dextrose 5%, single dose. <p>AND</p> <ul style="list-style-type: none"> • Flucytosine, oral 25 mg/kg 6 hourly for 14 days (see flucytosine weight-based dosing table below). <ul style="list-style-type: none"> ◦ Flucytosine requires dose adjustment in renal failure (see Appendix II for preventing monitoring and management of toxicity). <p>AND</p> <ul style="list-style-type: none"> • Fluconazole, oral 1200 mg daily for 14 days. <ul style="list-style-type: none"> ◦ Fluconazole requires dose adjustment in renal failure. <p><u>Consolidation phase</u> Follow with:</p> <ul style="list-style-type: none"> • Fluconazole, oral, 800 mg daily for 8 weeks. <p><u>Maintenance phase</u></p> <ul style="list-style-type: none"> • Fluconazole, oral, 200 mg daily. 	<p><u>Induction phase</u></p> <ul style="list-style-type: none"> • Amphotericin B deoxycholate, slow IV infusion, 1 mg/kg daily in dextrose 5% over 4 hours for 14 days. <ul style="list-style-type: none"> ◦ Ensure adequate hydration to minimise nephrotoxicity (see Appendix II for preventing monitoring and management of toxicity). <p>AND</p> <ul style="list-style-type: none"> • Fluconazole, oral 1200 mg daily for 14 days. <ul style="list-style-type: none"> ◦ Fluconazole requires dose adjustment in renal failure. <p><u>Consolidation phase</u> Follow with:</p> <ul style="list-style-type: none"> • Fluconazole, oral, 800 mg daily for 8 weeks. <p><u>Maintenance phase</u></p> <ul style="list-style-type: none"> • Fluconazole, oral, 200 mg daily.

Paediatric Hospital Level STGs and EML

The 2023 edition of the Paediatric Hospital Level STGs and EML currently recommends an alternative regimen for cryptococcal meningitis which does not contain oral flucytosine, but includes fluconazole as part of initial treatment, as indicated in the table below:

Indication: Paediatric Hospital Level	Current STG	Alternative regimen
Chapter 8: Infective/Infectious Diseases 8.12 Meningitis, Crypto- coccal	<p><u>Preferred initial treatment (2 weeks):</u></p> <p><u>First week:</u></p> <ul style="list-style-type: none"> • Amphotericin B deoxycholate, IV, 1 mg/kg/day as a daily infusion in 5% dextrose water over 4 hours. <ul style="list-style-type: none"> ○ Adjust dosing interval in patients with renal impairment. ○ Check serum potassium and magnesium at least 3 times a week. ○ Do not use a bacterial filter with amphotericin B deoxycholate. <p>Prehydration before administering amphotericin B deoxycholate to prevent renal impairment:</p> <ul style="list-style-type: none"> • Sodium chloride 0.9%, IV, 15 mL/kg plus potassium chloride 20 mmol/L infused over 2–4 hours. <p>PLUS</p> <ul style="list-style-type: none"> • 5-Flucytosine 100 mg/kg/day in 4 divided doses. <p><u>Second week:</u></p> <ul style="list-style-type: none"> • Fluconazole, IV/oral, 12 mg/kg/day. <p>○ Maximum dose: 800 mg.</p> <p>THEN</p> <p><u>Consolidation treatment (8 weeks):</u></p> <ul style="list-style-type: none"> • Fluconazole, oral, 12 mg/kg/day for 8 weeks. <p>○ Maximum dose: 800 mg.</p> <p><u>Secondary prophylaxis (maintenance treatment):</u></p> <ul style="list-style-type: none"> • Fluconazole, oral, 6 mg/kg/day. <p>○ Maximum dose: 400 mg.</p>	<p><u>Alternative initial treatment (2 weeks):</u></p> <ul style="list-style-type: none"> • Amphotericin B deoxycholate, IV, 1 mg/kg/day as a daily infusion in 5% dextrose water over 4 hours. <p>PLUS</p> <ul style="list-style-type: none"> • Fluconazole, IV/oral, 12 mg/kg/day. <p>○ Maximum dose: 800 mg.</p> <p>THEN</p> <p><u>Consolidation treatment (8 weeks):</u></p> <ul style="list-style-type: none"> • Fluconazole, oral, 12 mg/kg/day for 8 weeks. <p>○ Maximum dose: 800 mg.</p> <p><u>Secondary prophylaxis (maintenance treatment):</u></p> <ul style="list-style-type: none"> • Fluconazole, oral, 6 mg/kg/day. <p>○ Maximum dose: 400 mg.</p>

Consolidation and maintenance phases

It is important to complete the treatment of cryptococcal meningitis with the consolidation and maintenance phases as recommended in the STGs and EML.



Webinar outlining the STG and EML recommendation for CCM

The links to the webinar held on 8 April 2025, which provides guidance on the rational use of liposomal amphotericin B and amphotericin B deoxycholate injection for cryptococcal meningitis can be accessed as follows below:

- <https://knowledgehub.health.gov.za/webinar/rational-medicine-use-rmu>
- https://knowledgehub.health.gov.za/system/files/2025-04/Amphotericin%20B%20Deoxycholate%20and%20Liposomal%20Usage_Dr%20Gayle%20Tatz.pdf

Procurement information

NSN	Product	Supplier	Contract
180188046	Liposomal amphotericin B for injection containing 50 mg amphotericin B, 1 vial; 1 Injection	Key Oncologics (Pty) Ltd	HP02-2025AI
180188046	Amphotericin B 50mg Injection 10 ml	Non award – quotation available	

Circular dissemination

Provinces and healthcare facilities are requested to distribute and communicate this information in consultation with the Pharmaceutical and Therapeutics Committees and all other relevant stakeholders.

Kind regards

MS K JAMALOODIEN
CHIEF DIRECTOR: SECTOR-WIDE PROCUREMENT
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