



*PEPFAR COPS, January 2021 – Raef Makar – MSF Access Campaign*

# Outline

- **AHD»** 20 Points to consider for HIV Programs
- **Opportunistic Infections»**
  - Cryptococcal Meningitis (main highlight)
  - Implementation Considerations
- **Diagnostic blindspots»**
  - CD4 at baseline
  - TB LAM
  - CrAg
- **Prevention of Advanced HIV**
- **Differentiated Service Delivery for AHD**



# 20 Points for HIV Programs

## TREATING & PREVENTING AIDS

### Diagnostic and medicine checklist for the management of HIV and advanced HIV



Diagnostics	Medicines	
HIV Rapid Diagnostic Test (RDT)	<u>PrEP</u> : TDF/3TC or TDF/FTC	TPT children
Early infant diagnosis (EID) nucleic acid amplification test (NAAT)	1 <sup>st</sup> Line ARVs Adults	Cotrimoxazole
Routine Viral Load (RVL)	1 <sup>st</sup> Line ARVs Paeds	Fluconazole
CD4 count	2 <sup>nd</sup> Line ARVs Adults	Flucytosine
Xpert MTB/RIF (Ultra) NAAT	2nd Line ARVs Paeds	Liposomal amphotericin B
TB LAM RDT	TB medicines	Regionally appropriate OI and cancer treatment (e.g. KS, CMV, penicilliosis)
CrAg RDT	TB prophylaxis therapy (TPT) adults	



# Cryptococcal Meningitis

- *Why should CM be important for PEPFAR?*
  - In 2018, 223,000 cases of Crypto, with 181,000 deaths among PLHIV
  - 2nd leading cause of death for PLHIV → 15% of HIV-related deaths.
  - Most countries only have fluconazole available to treat people with Crypto Meningitis → 54% mortality at 10 weeks.
  - **Just starting people on ARVs is not going to eliminate opportunistic infections and advanced HIV...**





# Cryptococcal Meningitis

## Main Highlights


*PEPFAR COP 2021 supports:*

- *Cryptococcal antigen (CRAG) testing*
- *Preemptive therapy with fluconazole*
- *Management of cryptococcal meningitis according to the WHO 2018 (or later, should they be revised).*



# Crypto Treatment

- Preferred Crypto treatment per WHO guidelines
- Preferred WHO 2018 Guideline Option:
  - **Amphotericin B + flucytosine x 1 week**
  - ⇒ **reduced mortality by 38% compared to previous 2 week regimen**
  - ⇒ **Safer – reduced anemia by 69%**
  - ⇒ **Preference is liposomal amphotericin B, which is better tolerated than the deoxycholate version**

 Liposomal amphotericin B is preferred over amphotericin B deoxycholate, since liposomal amphotericin B has demonstrated equivalent efficacy and better safety compared with the conventional form of amphotericin B deoxycholate (44,45). However, access to liposomal amphotericin B remains extremely limited in low- and middle-income countries because of its high cost.



# Crypto Treatment

- Liposomal Ampho B → \$16.25 USD per vial [from Gilead](#) for LMICs
- Flucytosine 500 mg tabs → \$110 USD per bottle of 100 tabs



Cryptococcal Meningitis Treatment - Pricing for 50 kg patient					
Price	Amphotericin B Deoxycholate (1mg/kg/day)	Liposomal Amphotericin B (3 mg/kg/day)	5FC (100mg/kg/day)	Fluconazole	Total
Induction options					
ampho B + 5FC x1 week then fluconazole (1200mg) x 1 week	49€*  *1 vial per day to have 50 mg dose	€ 277*  *approx. 3 vials per day	€67*  *10 tabs per day	€ 2.40	Conventional Ampho B based: <b>118€</b>  Liposomal Ampho B based: <b>346€</b>



# Implementation Considerations

- Access to essential antifungal drugs remains inadequate
- Drug toxicity and laboratory monitoring costs continue to be important barriers.
- Lack of competition between manufacturers, and lack of in-country registration and high costs are the main barriers.
- Although liposomal amphotericin B is included in the 2015 WHO EML and it has been off patent since 2016, the current price of liposomal amphotericin B per vial remains substantially higher than that of amphotericin B deoxycholate.



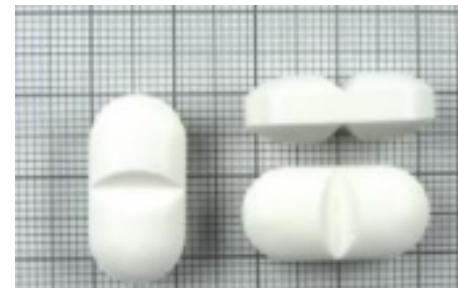
The originator manufacturer has reduced the cost of liposomal amphotericin B for managing visceral leishmaniasis in some countries; however, preferential pricing has not yet been consistently applied to cryptococcal meningitis





# Prevention of Advanced HIV

- *Nov 2019 COP:* "No PLHIV in PEPFAR programs should pay for cotrimoxazole".
- **Updated COP:** "No PLHIV in PEPFAR programs should pay for cotrimoxazole, TB preventive treatment, or fluconazole for secondary prophylaxis or pre-emptive treatment of cryptococcal meningitis."
- Cotrimox 800/160 mg – prevention of PCP and bacterial infections
- INH – prevention of TB
- Vit B6 – prevention of neuropathy from INH
- FDC – CTX/INH/B6, PQ approved - \$2 per pack



# #1 Diagnostic blindspot: CD4 at baseline

## CD4 baseline testing

- Problem: PEPFAR limits CD4 baseline testing to settings/risk groups with AHD prevalence >15% either overall or in specific risk groups
- What should happen: PEPFAR should support CD4 at baseline and re-entry into care regardless of rates of AHD
- Why it's important
  - EVERY PLWHA that is CD4<200 or has AHD needs extra workup and care.
  - CD4 is essential for diagnosing (especially asymptomatic) advanced HIV disease (AHD) as clinical staging/symptom screening alone misses **half of people with AHD** at entry and re-entry into care, including
    - TB-LAM, even in the absence of TB symptoms
    - CrAG testing for cryptococcal meningitis
    - Fluconazole for people CD4<100
- The tests (US\$4-80)
  - Rapid POC Omega Visitect AHD
  - Benchtop Abbott PIMA
  - Benchtop BD FACSPresto (more suitable for hospital and central labs)



# #2 Diagnostic blindspot: TB LAM

## TB-LAM

- Problem: The POC Alere TB-LAM test is available and affordable but **NOT IN FACILITIES** and **NOT USED**
  - **Also, many countries are not ‘in step’ with WHO recommendations**
- What should happen: TB-LAM should be in ALL outpatient and inpatient settings
- Why it's important
  - TB-LAM testing increases the diagnosis of TB, particularly at lower CD4 cell counts, and shortens the time to TB treatment with a subsequent reduction of deaths.
  - TB-LAM usage INCREASES overall yield of TB cases
  - A better test that works for ALL PLWHA will be available in early 2022 (estimated)
- The test: Abbott Determine POC TB LAM LFA: US\$3.50/test



# #3 Diagnostic blindspot: CrAg

## CrAg RDT for the diagnosis of cryptococcal meningitis (CM)

- Problem: The CrAg test is not widely available and not used
- What should happen: PEPFAR and countries should scale-up use for that ALL PLWHA with a symptoms (headache) receive a CD4 and all with  $CD4 < 200$  receive a CrAg test
- Why it's important
  - Cryptococcal meningitis (CM) is the second-leading killer of PLWHA, second only to TB
  - Early diagnosis and treatment is paramount to reducing CM-related mortality
- The test: POC CrAg LFA (IMMY=US\$2.00, Biosynex=US\$2.40)







# Components to consider when designing a differentiated service delivery model for advanced HIV disease

- Identifying advanced HIV disease
- Clinical package to screen, prevent and treat advanced HIV disease
  - Policy barriers to where tests placed and who can perform the test
- Rapid ART initiation and/or regimen switch
- Linkage to OPD/PHC ongoing care
- Post initiation/switch follow up

# What does the PEPFAR COP say?

maximizing access these interventions. Use of DSD models that distinguish between those who are clinically unwell and admitted to hospital, those who are unwell but able to be managed in the outpatient department and those who are clinically well but have advanced disease may be particularly helpful and provide guidance for up-referral and allow resources to be deployed where they are most needed. See <http://www.differentiatedcare.org/Resources/Resource-Library/DSD-for-advanced-HIV-disease-toolkit> for more detail. Patients with advanced HIV

# Resources

- <http://www.differentiatedservicedelivery.org/Resources/Resource-Library/DSD-for-advanced-HIV-disease-toolkit>
- <https://samumsf.org/en/news/advanced-hiv-disease-toolkit>
- WHO IATT Formulary – Pediatric ARVs:  
<https://www.who.int/hiv/pub/paediatic/optimal-paediatic-arv-formulary/en/>
- ARV Procurement Working Group (APWG):  
<https://www.arvprocurementworkinggroup.org/?l=en>
- Untangling the Web: HIV Medicine Pricing & Access Issues, 2020:  
<https://msfaccess.org/untangling-web-hiv-medicine-pricing-access-issues-2020>

# Thanks! Merci!

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