Southern African HIV Clinicians Society

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Our Issues, Our Drugs, Our Patients

www.sahivsoc.org
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A Clinician's Perspective on Stock-outs

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HIV Clin Soc Conference

April 2016

Mail&Guardian
AFRICA'S BEST READ

Survey uncovers shortages in critical medication

10 JUN 2015 16:10 | MIA MALAN

ORIGINAL

A survey of stock levels of HIV drugs is in stark contrast to health department claims that "there is no shortage".

HIV Medicine Aluvia Stock-Out Dogs South Africa, Raising Patent Concerns

Intellectual Property Watch | International IP Policy News

28/10/2015 BY MUNYARADZI MAKONI FOR INTELLECTUAL PROPERTY WATCH — 1 COMMENT

CAPE TOWN, South Africa – While Médecins Sans Frontières have blamed stock-outs of 'Aluvia' on the refusal to licence a patent for a generic of the HIV medicine in South Africa by AbbVie pharmaceutical company leading to persistent supply problems, the company said it has taken measures to address the problem.

DAILY MAVERICK

SOUTH AFRICA

GroundUp: There's no excuse for medicine stockouts, Minister – here's the proof

GROUNDUP SOUTH AFRICA 01 JUL 2015 03:08 (SOUTH AFRICA)

The anonymously written cover letter said that it is true that some medicines are in short supply because of problems with supply by pharmaceutical companies. "But this is being used as a smokescreen to cover up the reason for the majority of stock-outs. The [KwaZulu-Natal medicine] depot is failing [clinics and hospitals] due to poor management and lack of knowledge of supply chain. Maintenance of stock levels at the depot, processing of orders, and distribution to its customers are the main reasons [for stockouts]."

GroundUp previously reported on stockouts in Ilembe District of

Yet, there's no shortage of the drug in Gauteng. Instead, activists say that dysfunction and tardiness at the province's drug depot is to blame.

items include medicines you can buy over-the-counter at pharmacies or even corner cafes, such as paracetamol.

The lists GroundUp received show that on 10 June:

- King Edward Hospital had 389 items out-of-stock
- Northdale Hospital had 246 items out-of-stock
- Edendale had 200 items out-of-stock
- Greys Hospital had 132 items out-of-stock
- Ladysmith Provincial Hospital had 191 items out-of-stock
- East Street Clinic had 96 items out-of-stock.

And as of 5 June Imbalenhle Clinic had 159 items out-of-stock.

SO… What does this mean for the CLINICIAN, but more importantly the PATIENT?

- **STOCKOUTS OF IMPORTANT DRUGS COULD LEAD TO…**

1. Suboptimal, ineffective treatment
2. Drug resistance
3. Prolonged, unnecessary hospitalisation
4. Increased side effect rates and high drug toxicity
5. Increased drug burden and poor-compliance
6. Increased drug-drug interactions
7. Risk of opportunistic infections
8. Poor immunological recovery/ virological failure
9. Unnecessary cost implications
10. Delay in initiation of treatment whilst alternatives are sourced
11. MORTALITY

Kranzer, Tropical Med & Int Health, 2011

Mr AD …

- 45yr Male
- HT on HCTZ 25mg/d + Enalapril 20mg bd
- HIV+ CD_4 252 on 3TC/TDF/EFV 2011
  - Baseline CD_4 43
- Referred to CHBAH in December 2013 for Virological failure
  - VL 250 000
- Genotype resistance studies
  - M184V
  - K65R
  - Multiple PI mutations
- Initiated on 3TC/AZT/Atazanavir/rit January 2014

- March 2014 – STOCKOUT Atazanavir
- Changed to 3TC/AZT/Lopinavir/rit March 2014
  - 'Holding' therapy
  - Patient develops **diarrhoea**
  - Dehydrated and hypokalaemic –hospitalisation required
  - Unacceptable symptoms and pill burden
    - Skips doses
  - PTB April 2014 (son is TB contact)
    - Refuses to take increased Lopinavir/rit dose (4 tabs bd)
    - HAART should be 10 tablets/d + TB Rx 4 tabs/d + HT 3 tabs/d =

    - **July 2014 : VL – 220 000, CD_4 200**

- End of July 2014 – Atazanavir back in STOCK!
- Mr AD restarts treatment

  - Worry is potential for Atazanavir resistance
  - Sub-optimal treatment with Lopinavir/rit
  - Lopinavir/rit under-dosing whilst on Rifampicin
  - Unacceptable side-effects for patient
  - Unacceptable pill burden
  - Potentially avoidable hospitalisation

Virological Failure and Drug Resistance in Patients on Antiretroviral Therapy After Treatment Interruption in Lilongwe, Malawi

Luebbert, Tweya, Chaweza, Mwafilaso, Hosseinipour, Ramroth, Schnitzler, Neuhann, CID 2012

- 133 patients 2008-2009
- At least 1 treatment interruption on First line HAART
  - Mean duration ART prior to interruption – 14.3months
  - Mean duration of interruption **– 61 days** (IQR 43-87)
- HIV VL at least 2m following Rx resumption
- Genotype resistance interpretation
- VL detectable in **39%**(n=52) pts (>1000 copies/ml in 30%(n=40))
- 36/40 had DRT
- 32/36 had NNRTI mutations **(24% of total)**
- 27/36 had NRTI mutations **(20% of total)**
- **24% required a regimen change and started a PI**

Impact of Stock-outs on Death and Retention to Care Among HIV Infected Patients On Combination ARV Therapy in Abidjan, Côte d'Ivoire

Pasquet, Yazdanpanah et al, Plos One 2010

- 1 February 2006 – 1 June 2007
- Cohort study of **1554 patients** initiating HAART
- Followed for a mean 13.2 months
- 72 pts discontinued HAART / 98 had modified regimens
  - **11% AFFECTED BY STOCK-OUTS**
- Stock-outs **doubled the risk of interruption in care or death**
- **Regimen modifications did not increase the risk of death and resulted in no interruption**
  - Regimen I easier to adjust – majority of modifications included NVP→EFV

Ms JM …

- 28yr Female
  - Newly diagnosed HIV positive, CD_4 79
  - Presents with headache, LOW, photophobia – 3w duration
  - Haemodynamically stable, no focal signs
  - LP Poly 2 **Lymph 130** Eryth 0
    Prot 0.8 Gluc 3.4
    India Ink positive **CLAT positive**
    Culture – Cryptococcus neoformans

- Patient is initiated on Amphotericin B 1mg/kg/d IVI
  + Fluconazole 400mg 12hrly po

Ms JM cont …

- Day 3 of Amphotericin B treatment – NO STOCK recorded on script
- Patient treated with Fluconazole 1200mg/d
- Repeated LP and supportive measures
- RIP day 10

WOULD THIS OUTCOME HAVE BEEN DIFFERENT IF AMPHO B HAD BEEN AVAILABLE???

TRIALS…

- Liposomal Ampho B + 5-Flucytosine
  - DEFINITELY better EFA and better outcomes

- Ampho B vs Fluconazole
  - OLD!
  - Small numbers
  - Low dose Ampho – 0.3mg/kg/d
  - Low dose Fluconazole – 200mg/d
  - HIV negative – Chemo, steroids, other immunosuppressive conditions

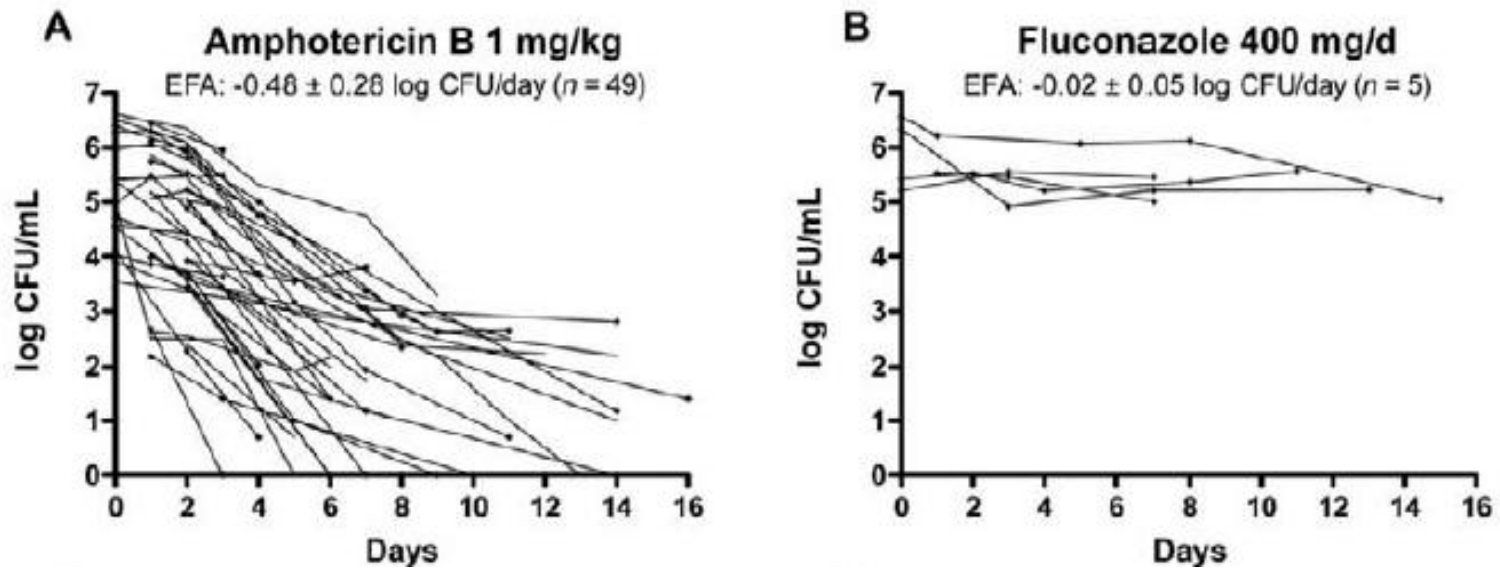
Fungal Burden, Early Fungicidal Activity, and Outcome in Cryptococcal Meningitis in Antiretroviral-Naïve or Experienced Patients Treated with Amphotericin B or Fluconazole

Bicanic, Meintjies, Wood, Hayes, Rebe, Bekker, Harrison, CID 2007

- Determine and compare the early fungicidal activity (EFA) and toxicity of Ampho B and Fluconazole

AMPHO B – 49 patients	FLUCONAZOLE – 5 patients
GCS >10	GCS <10
1mg/kg/d for 7days	400mg/d
Followed by po Flucon 400mg/d X 8w	10w
EFA -0.48±0.28 log CFU/ml CSF/d	**EFA -0.02±0.05 log CFU/ml CSF/d**
HIV VL 44 000 copies/ml	Higher HIV VL – 420 000 copies/ml
74 000 CFU	Higher baseline fungal burden – 340 000 CFU
4 renal impairment, 1 required discontinuation	No adverse events
Median survival 153 days	Median survival 61 days

- Overall – mortality 17% at w2, 37% at w10



Bicanic et al, CID, 2007

What Can We As Clinicians Do?

- Try to avoid treatment interruption as far as possible
  - UNDERSTAND THE IMPORTANCE AND POTENTIAL SEVERITY OF INTERRUPTING TREATMENT
  - Consider replacement drugs
    - Individual tablets instead of combination and vice versa
    - Replacement drugs with best possible efficacy
    - Short-term private buy-out if affordable
    - Referral to another centre
    - Paediatric syrup – avoid depletion of paediatric supplies!
  - Try to incorporate safety nets at your centre
    - Electronic systems for stock flow and management
    - Early/timely ordering
    - Use drugs with the soonest expiry date first
  - Go 'OVER and ABOVE'
    - Public-private partnerships
    - Compassionate use supplies from drug companies


Never Lose Hope
When the Sun goes down
The Stars come out
Roy Aylmer Image