

# RANDOMISATION

## SINGLE DOSE ARM

**Liposomal Amphotericin B Ambisome**  
10mg/kg (Day 1 only)  
+  
**Fluconazole** 1200mg/day for 14 days (Day 1-14)  
+  
**Flucytosine** 100mg/kg/day for 14days (Day 1-14)

## CONTROL ARM

**Amphotericin B deoxycholate**  
1mg/kg/day for 7 days (Day 1-7)  
+  
**Flucytosine** 100mg/kg/day for 7 days (Day 1-7)  
**THEN**  
**Fluconazole** 1200mg/day for 7 days (Day 8-14)



**AMBITION-cm**

AMBIsome Therapy Induction Optimization



## SAFE ADMINISTRATION of STUDY DRUGS

Please also refer to the related WPD

### 1. PREHYDRATATION

Aim : avoid hypokalaemia and renal toxicity associated with L-AmB or d-AmB administration

**1L saline with KCl (20 mmol) over 2 hours before AmB infusion**

Do not supplement K if patient has pre-existing renal impairment or hyperkalaemia (>5.0 mmol/L)

### 2. ADMINISTRATION

**A single high dose of AMBISOME**  
10 mg/kg on day 1  
•Administer over 2 hours

OR

**A single daily dose of Amphotericin B**  
1 mg/kg/day on day 1 – 7  
•Administer over 4 hours

Inject AmB dose into 1000 ml bag of 5% Dextrose or 10% Dextrose  
•**Never** N.Saline as drug will precipitate

### 3. MONITORING

Monitor daily for symptoms and signs of **thrombophlebitis**

Monitor **renal function**  
(baseline and on D3, 5, 7, 10, 12, 14, 28)

Monitor **blood count and ALT**  
(baseline and D7, 14, 28)

If Ampho B or Ambisome therapy-induced **rigors** occur, the infusion lengths can be increased, and/or **paracetamol** or **hydrocortisone** may be administered under guidance of a doctor

#### Ambisome 10 mg/kg D1



Patient's weight	Number of vials	Total dose of Ambisome	Volume of reconstituted Ambisome (ml) at 4mg/ml	Additional dextrose (ml) to create a 1litre total infusion
40 kg	8	400 mg	100 ml	900 ml
41-45 kg	9	450 mg	112.5 ml	887.5 ml
46-50 kg	10	500 mg	125 ml	875 ml
51-55 kg	11	550 mg	137.5 ml	862.5 ml
56-60 kg	12	600 mg	150 ml	850 ml
61-65 kg	13	650 mg	162.5 ml	837.5 ml
66-70 kg	14	700 mg	175 ml	825 ml
71-75 kg	15	750 mg	187.5 ml	812.5 ml
76-80 kg	16	800 mg	200 ml	800 ml
81-85 kg	17	850 mg	212.5 ml	787.5 ml
86-90 kg	18	900 mg	225 ml	775 ml

#### Amphotericin B 1 mg/kg/day D1-7



Patient's weight	AmB dose	Amount drawn up from vial(s)	Number of vials
36-40 kg	40 mg	8 ml	1
41-45 kg	45 mg	9 ml	1
46-50 kg	50 mg	10 ml	1
51-55 kg	55 mg	11 ml	2
56-60 kg	60 mg	12 ml	2
61-65 kg	65 mg	13 ml	2
66-70 kg	70 mg	14 ml	2
71-75 kg	75 mg	15 ml	2
76-80 kg	80 mg	16 ml	2
81-85 kg	85 mg	17 ml	2
86-90 kg	90 mg	18 ml	2

If creatinine rises up to 2.5 mg/dl (220 µmol/l):

- Miss one dose. Check adequate hydration.
- Check creatinine next morning:
- If stable or improving and creatinine < 220 µmol/l:
  - restart daily dosing (1 mg/kg) paying close attention to adequate hydration
- If stable or improving, but still above 220 µmol/l:
  - institute alternate day dosing (1 mg/kg q 48 hours)
- If creatinine is increasing do not give amphotericin B and check again after 24 hours:
  - if stable or improving institute daily or alternate day dosing as above
  - If still increasing: STOP amphotericin B and SWITCH to fluconazole

AVOID other nephrotoxic agents such as aminoglycosides, NSAIDs if possible.

If doses of AmphoB are held due to toxicity the missed doses are not to be given after Day 7.

#### Flucytosine 100 mg/kg/day

Weight (kg)	Daily dose (mg) 100 mg/kg	Number of tablets per day	Suggested schedule of dosing*			
35-39	3500	7	2	2	2	1
40-44	4000	8	2	2	2	2
45-49	4500	9	3	2	2	2
50-54	5000	10	3	2	3	2
55-59	5500	11	3	3	3	2
60-64	6000	12	3	3	3	3
65-69	6500	13	4	3	3	3
70-74	7000	14	4	3	4	3
75-79	7500	15	4	4	4	3
80-84	8000	16	4	4	4	4

\*Each site can determine the specific timing of each six hourly dose providing the full quantity is prescribed over 24 hrs

Tablets can be crushed and given down an NG tube, if required  
If doses are held due to toxicity they are not given at a later date

## DRUGS INDUCED TOXICITY

#### Neutropenia

Grade III	Neutrophils < 600 x 10 <sup>6</sup> /L	Monitor FBC daily. If grade III is confirmed next day, halve dose of flucytosine (50%)
Grade IV	Neutrophils < 400 x 10 <sup>6</sup> /L	Stop flucytosine, until grade III level at which point resume at 50% dose

#### Thrombocytopenia

Grade III	25,000 - <50,000 cells/mm <sup>3</sup>	Monitor FBC daily. If grade III is confirmed next day, halve dose of flucytosine (50%)
Grade IV	< 25,000 cells/mm <sup>3</sup>	Stop flucytosine, until grade III level at which point resume at 50% dose

#### Fluconazole 1200 mg/day

Once daily dosing  
Capsules can be given down an NG tube, if required

If creatinine clearance reduces to <50ml/min:  
○ Give same initial dose  
○ Reduce subsequent doses by 50%  
If high-doses of FLU are held due to toxicity, the missed doses are not to be given after Day 14.  
Reduce to 800mg daily from D15.  
Reduce to 200mg daily from W10.