AMBITION-*cm*

AMBIsome Therapy Induction OptimizatioN

Work Practice Document: 21
Health Economics sub-study

Title of study	High Dose AMBISOME© on a Fluconazole Backbone for Cryptococcal Meningitis Induction Therapy in sub-Saharan Africa: A Phase III Randomized Controlled Non-Inferiority Trial
Acronym	Ambition-cm – AMBIsome Therapy Induction OptimizatioN
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Revision History:		
Version Number	**Effective Date**	**Reason for Change**
1.0		First version

Purpose
This document describes the processes to be followed for the health economics sub-study.

Scope
This WPD applies to the collection of data on D1 and W10 of the Ambition study

General

1. The aim of this sub-study is to collect data to formulate an argument for expanded access to Ambisome in Africa. Collecting data on the societal costs of cryptococcal meninigitis from both the provider and patient perspective is essential.

2. Data will be collected from all patients across all sites.

3. Data is collected on D1 and W10 of the study.

4. If a patient is confused then the data can be collected from the next of kin / relative

5. Data is entered onto the Electronic Data Capture system.

6. Please follow the below interview guide to help you when collecting data.

The following questions need to be completed on D1 eCRF: Medical Expenses

1. Patient ID

   This is auto-populated by the database but if using the paper CRF then you will need to enter it yourself.

2. Who is the main source of information?
   Patient □   Next of kin/Relative □

   If the information comes from a combination of both then select the patient. If patients are confused then the next of kin will be the main source of information.

3. Which currency do you use?
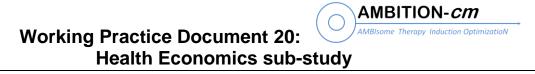
   Botswanan Pula □   Ugandan Shilling □
   Malawian Kwacha □   US Dollar □
   South African Rand □   Zimbabwean Dollar □

   We want patients to be consistent with the currency that they use. If they have used multiple currencies we want them to give us the amount in the currency they select below. They may need to convert from one currency to the other if this is the case.

4. Over that last 4 weeks, how much have you spent on activities relating to your health?

    This is to include travel, consultation fees, hospital admissions, medication, equipment etc. Subsequent questions will break this down into the constituent parts but this will get the patient thinking about how much of their own money they have spent on health. If the patient pays a regular contribution for medical insurance then do not include that here as we only need additional out-of-pocket expenses.

5. Over that last 4 weeks, how much has someone else spent on activities relating to your health?

    Some patients will have had help from their parents, partner, friends or family members. They may not know the answer to this but this can be an estimate.

6. How much in total has been spent on your healthcare in the last 4 weeks?

    This needs to be the combined total of Q4 and Q5.

7. How long have you been sick with your current condition?
    _____ (days)

    How long they have been suffering with this episode of cryptococcal meningitis. They may have only recently been diagnosed but we want to know how long they have been unwell which may be days or months.

8. What would you have been doing if you were not sick with your current condition?

    Working □   Maintaining the house □

    Studying □   Nothing □

    Caring for children □   Other, Specify: _____

    We want to know the main activity that the patient does but acknowledge that they may have multiple roles. If they have a job then select working first as this is the activity that brings in money.

9. How much time did you take off work?
    _____ (days)

    This should only be answered if the patient has a paid job.

10. How much time did a caring family member or primary caregiver take off work to accompany you to the hospital?
    _____ (days)

Some patients will be supported by someone else to attend appointments, look after them at home, visit them in hospital. If multiple people have taken time off then please record information for the person who has taken the most time off.

11. Did you lose earning as a result?
Yes □   No □

This question only applies to those in paid employment. Some patients will get sick pay and will not lose any earnings. Others will not get sick pay and we want to know how much they may have lost. This may be an estimate.

12. If YES, how much did you lose?

This may be the daily income of the patient multiplied by the number of days of work missed.

13. How much do you/your family spend on food in a week?

This question and the next two questions are used to gauge the economic status of the patient and their household as well as to understand the proportion of their money which has been diverted to paying for healthcare. They may be estimates or the patient may not know the answer but try to get a rough figure for each of these.

14. How much do you/your family spend on rent and utilities per month?

This is the household expenditure on rent/mortgage, electricity, gas, water, internet, telephone contracts etc.

15. How much have you spent on large items (e.g. furniture, electrical items, cars) in the last year?

Large, one-off purchases like those listed in the question give us an idea of the economic status of the household and which expensive items they can afford with their income.

16. Which form of transport did you take to get here today?

Bus □   Hired motorbike □
Train □   Own car □
Ambulance □   Own motorbike □
Private taxi □   Hired Bicycle
Own Bicycle □   Foot □
Other □

17. How much did you spend on the transport (in total)?

The cost to the patient of reaching the hospital on the day of their admission.

18. How long did it take you to reach there?

_____ (in hours and minutes)

19. Did you take out any loans to pay for your healthcare?
Yes □   No □

These questions relate to the current illness (cryptococcal meningitis).

20. Did you sell anything to pay for your healthcare?
Yes □   No □

21. Do you have private healthcare insurance?
Yes □   No □

22. If YES, did you use it to help pay for your healthcare?
Yes □   No □   Not applicable □

Although some patients may have health insurance they may not yet have used it and may therefore be using their own money to pay for care.

23. Do you receive any welfare or social service support?
Yes □   No □

To understand if the patient is in receipt of additional financial support from the government which may include employment allowance, disability allowance, housing allowance etc.

24. Have you received any treatment or care for your present condition, before coming to the hospital?
Yes □   No □

This set of questions will tell us how much the patient has spent on this episode of cryptococcal meningitis up to a maximum of three distinct visits to different healthcare providers. They will also enable us to understand the journey patients undertake before they reach the hospital.

Please enter the answers to these questions on D1 eCRF: Medical Expenses Part 2

25. If YES, where did you receive treatment or care for your present condition, before coming to the hospital?

Government healthcare □   Pharmacy □
Private healthcare □   Home □
NGO healthcare □   Other, Specify: _____

This is the most recent visit to a healthcare provider. Complete this set of questions up to a maximum of three times, starting with the most recent visit.

26. Which form of transport did you take to reach there?

Bus □   Hired motorbike □
Train □   Own car □

Ambulance ☐   Own motorbike ☐
Private taxi ☐   Bicycle ☐
Own Bicycle ☐   Foot ☐
Other ☐

27. How much did you spend on the transport (in total)?

    The cost of return transport for that visit.

28. How long did it take you to reach there?

    _____ (in hours and minutes)

29. Who provided treatment or care during this visit?

    Doctor ☐   Nurse ☐
    Traditional healer ☐   Family/Friend ☐
    Spiritual healer ☐   Pharmacist ☐
    Clinical Officer ☐   Other, Specify: _____

    Select the most senior person that was seen. A doctor holds a medical degree and in some
    countries is known as a medical officer. In other countries there are clinical officers who provide
    care but these individuals do not hold a medical degree. The terms medical officer and clinical
    officer are often used interchangeably so try to ascertain if the person who provided the care holds
    a medical degree.

30. Did you pay for the consultation you received during that visit?
    Yes ☐   No ☐

    The cost paid for seeing that individual. It may be that there was a single fee for the whole
    consultation which covered all of the consultation/tests/medication and if this is the case record
    that here. If only medication was bought and the advice given was free then record that in Q32. If
    the cost was covered by insurance then any additional costs should be recorded here but if it was
    all covered by insurance then do not enter anything here.

31. If YES, how much did you pay for the consultation?
    _____

32. Did you buy other medication for relief?
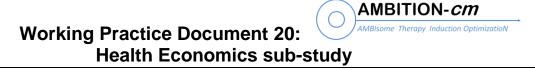   Yes ☐   No ☐

    This may be medication that was prescribed or recommended. It may also be medication that the
    patient opted to buy without any instruction to do so.

33. How much did you pay?

Ensure that Q30 and Q32 encompass the full cost of that episode. If there is a one-off cost for the entire episode that was submitted in Q30 then do not repeat the cost of medication here.

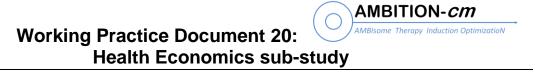34. Before this, did you go to another place for the treatment of the current condition?
    Yes □   No □

    └──────→ Complete questions 17 to 26 again from p.6 of this CRF.

    Repeat this series of questions for the second and third most recent visits to healthcare facilities for this episode of cryptococcal meningitis, if applicable. If a patient has sought care on more than three occasions then capture the most recent.

The following questions need to be completed on D1 eCRF: Education

35. What is your profession?

    The primary occupation of the individual. If they do not have a job then you can state their primary role in the household (student, carer, retired etc.)

36. How many years of education did you complete?

    The total number of years spent in education, including years that were repeated. This should be the total of years spent in primary, secondary and higher education. If someone took an extra two years to complete primary education then include that in the number of years spent in primary education. The answer to this question may be zero.

37. What is your highest education certificate?

    This question is free text so you can enter whichever applies. If someone did not attend school then you can state that they have no education certificate here.

38. Did you go to primary/elementary school?
    Yes □   No □

39. If Yes, for how many years?
    _____

40. Did you go to secondary school?
    Yes □   No □

41. If Yes, for how many years?
    _____

42. Did you go to Higher education?
    Yes □   No □

    This could be university, college, a vocational institution etc.
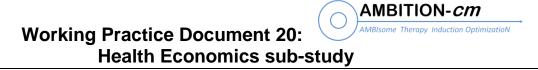
43. If Yes, for how many years?

    _____

44. Are you the person who earns the highest income in your household?
    Yes ☐   No ☐

    It is important to understand what the breadwinner of the household does for a living. This can be used to estimate the socio-economic status of the household. The patient themselves may identify as the head of the household but we want to know about the person who earns the most money through work.

If NO, please complete the questions below on behalf of the Person who earns the highest income

This will generate a new eCRF: Education (person who earns the highest income)

45. If no, what is their profession?

    If the patient does not know then it is OK for them to estimate these answers.

46. What is their highest education certificate?

    _____

47. How many years of education did they complete?

    _____

48. Did they go to primary/elementary school?
    Yes ☐   No ☐

49. If Yes, for how many years?
    _____

50. Did they go to secondary school?
    Yes ☐   No ☐

51. If Yes, for how many years?

    _____

52. Did they go to Higher education?
    Yes ☐   No ☐

53. If Yes, for how many years?

    _____

ADDITIONAL MEDICAL EXPENSES QUESTIONS
To be completed if the patient went to more than a single place for treatment before coming to the hospital

ADDITIONAL MEDICAL EXPENSES 2

Where did you receive treatment or care for your present condition, before coming to the hospital?

Government healthcare □   Pharmacy □
Private healthcare □   Home □
NGO healthcare □   Other, Specify: _____

Which form of transport did you take to reach there?

Bus □   Hired motorbike □
Train □   Own car □
Ambulance □   Own motorbike □
Private taxi □   Bicycle □
Foot □

How much did you spend on the transport (in total)?

_____

How long did it take you to reach there?

_____ (in hours and minutes)

Who provided treatment or care during this visit?

Doctor □   Nurse □
Traditional healer □   Family/Friend □
Spiritual healer □   Pharmacist □
Clinical Officer □   Other, Specify: _____

Did you pay for the consultation you received during that visit?
Yes □   No □

If YES, how much did you pay for the treatment of your current condition?
_____
Did you buy other medication for relief?
Yes □   No □

How much did you pay?
_____

Before this, did you go to another place for the treatment of the current condition?
Yes □   No □

ADDITIONAL MEDICAL EXPENSES 3

Where did you receive treatment or care for your present condition, before coming to the hospital?

Government healthcare □   Pharmacy □
Private healthcare □   Home □
NGO healthcare □   Other, Specify: _____

Which form of transport did you take to reach there?

Bus □	Hired motorbike □
Train □	Own car □
Ambulance □	Own motorbike □
Private taxi □	Bicycle □
Foot □	

How much did you spend on the transport (in total)?

_____

How long did it take you to reach there?

_____ (in hours and minutes)

Who provided treatment or care during this visit?

Doctor □	Nurse □
Traditional healer □	Family/Friend □
Spiritual healer □	Pharmacist □
Clinical Officer □	Other, Specify: _____

Did you pay for the consultation you received during that visit?
Yes □   No □

If YES, how much did you pay for the treatment of your current condition?
_____

Did you buy other medication for relief?
Yes □   No □

How much did you pay?
_____

Before this, did you go to another place for the treatment of the current condition?
Yes □   No □

On W10 the first form is generated again with some of the questions omitted. The aim of this second questionnaire is to understand the expenses incurred during the 10-week period of the Ambition study. The education eCRF will not be generated again.

Training

Each staff member receives or has direct access to applicable Working Practice Documents (WPDs).

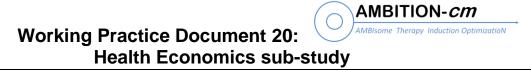Each staff member reviews the applicable WPDs once a year.

All WPD training is documented and tracked in the WPD training logbook located in the Project Coordinator's office.

New staff is trained on applicable WPDs within 30 days of employment and all WPDs within 90 days of employment.

Staff members whose duties fall within this WPD scope are retrained within 14 days of the approval of each WPD revision.

References
1. Declaration of Helsinki, 2013: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/ accessed 12th June 2017

2. International Conference on Harmonisation (ICH) Guideline For Good Clinical Practice E6(R1), 1996

3. Integrated Addendum To ICH E6(R1): Guideline For Good Clinical Practice E6(R2), 2016

4. Ambition Trial Protocol

Staff signatures: (signing below indicate that you have read this SOP and understand the material contained in it)

Date	Name (Please print)	Signature