



World Health Organization

DAP/97.9  
English only  
Distribution: Restricted

# **Standard treatments and essential drugs for HIV-related conditions**

## **Access to HIV-related drugs**



December 1997

**Action Programme on Essential Drugs**

© World Health Organization 1997

The contents of this restricted document may not be divulged to persons other than those to whom it has been originally addressed. It may not be further distributed nor reproduced in any manner and should not be referenced in bibliographical matter or cited.

## Acknowledgements

This document was prepared by Dr Robin Gray. Particular thanks are due to Dr Awa Coll-Seck, Director of the Department of Policy, Strategy and Research of UNAIDS for her comments and observations and to Dr J. Perriens also of the Department of Policy, Strategy and Research of UNAIDS for the draft UNAIDS list of drugs for opportunistic infections and palliative care and for information on morbidity. Dr Q.M. Islam of the Reproductive Health Technology unit in the Division of Family Planning and Population generously allowed use of the selected list of drugs for sexually-transmitted diseases in emergency situations. Dr Eric van Praag of the Office of HIV/AIDS and sexually-transmitted diseases was most helpful and supportive of the whole enterprise. Dr F. Luelmo of the Global Tuberculosis Programme made pertinent and useful observations. Ms Pascale Brudon and Dr Vincent Habiyambere of the Action Programme on Essential Drugs kindly read the draft and made useful contributions and suggestions and Dr Hans Hogerzeil suggested using national treatment guidelines. Ms Daphne Fresle advised on the categorization of the document. Particular thanks are due to Dr Jonathan Quick, Director, Action Programme on Essential Drugs, for his support and the substantial use of the introductory part of a text he presented on access to HIV-related drugs given on 17 November 1997 in Nairobi, Kenya. Most thanks go to Ms Michèle Clarke and Ms Monique Renevier for their secretarial work clarifying the lists, tables and text so making the work more user-friendly than it was.

### *Postscript*

The WHO Expert Committee on the Use of Essential Drugs met from 1 to 5 December 1997. A number of changes to the Model List of Essential Drugs were made, some pertinent to the treatment of HIV-related diseases and sexually transmitted diseases. The additional drugs and sections are indicated with an asterisk in the lists to be found in Annex 6 and Annex 8.

# Contents

<b>Acknowledgements .....</b>	<b>i</b>
<b>1. Introduction.....</b>	<b>1</b>
1.1 Background.....	1
1.2 Rational drug selection and use.....	1
1.3 Listing HIV-related diseases and morbidity data .....	2
1.4 Selection of first and second choice treatments.....	2
<b>2. Objectives .....</b>	<b>5</b>
<b>3. Comments on the tables and lists .....</b>	<b>7</b>
3.1 HIV-related diseases and STDs on the basis of ICD 10 .....	7
3.2 Leading HIV-related diseases and STDs and relative frequencies by risk group .....	7
3.3 Review of the most recommended treatments for each HIV-related health problem.....	8
3.4 HIV-related diseases and STDs standard treatments and essential drug lists .....	10
3.5. Estimation of drug needs.....	10
3.6 Conceptual model for disease priorities and treatment ranking .....	10
3.7 Conclusions.....	11
3.8 Possible further steps.....	11
<b>ANNEXES:</b>	
Annex 1. ICD 10 codes of HIV-related diseases and STDs .....	13
Annex 1a. Proposed WHO clinical staging system for HIV infection and disease (1990).....	15
Annex 2. HIV-related diseases in adults mentioned in 18 reports.....	17
Annex 3. HIV-related diseases crude global morbidity patterns .....	19
Annex 4. WHO and selected national treatment recommendations .....	23
Annex 5. WHO recommended dosage schedules/treatments for STDs.....	37
Annex 6. WHO recommended drugs: EDL drugs and non-EDL drugs for STDs.....	41
Annex 7. WHO recommended dosage schedules/treatments for HIV-related diseases and drugs for symptomatic treatment.....	43
Annex 8. Recommended current WHO EDL (1997) and non-EDL drugs for HIV-related diseases .....	47
Annex 9. Drugs for STDs in emergencies .....	51
<b>Bibliography .....</b>	<b>55</b>

# 1. Introduction

To ensure access to drugs three key objectives must be met:

1. rational selection and use (therapeutic access);
2. affordability (financial access);
3. availability (physical access).

This document is about selections, already made, for the treatment of HIV opportunistic infections, sexually-transmitted diseases (STDs) and for palliative care.

## 1.1 Background

Problems in assuring availability, affordability, quality, and rational use of drugs are universal and are greatest in low income countries. All countries are increasingly faced with difficult therapeutic and economic decisions about pharmaceuticals.

Access to HIV-related drugs presents a range of particularly challenging political, social, ethical, economic, and medical difficulties. Many priority drugs are still on patent, are extremely costly and not presently available from international low-cost suppliers. Health systems in many developing countries struggle simply to ensure reliable access to even the most basic essential drugs.

Drugs are only one element in the continuum of care for people living with HIV/AIDS. They are an essential element. Health systems must have the capacity to diagnose and monitor HIV infections and HIV-related conditions. Treatment regimes may be complex and side effects are common. Effective treatment also depends on people living with HIV/AIDS (PLWH) being actively involved with and well informed about their treatment and on a social support network.

Proper use of HIV-related drugs requires education of doctors, nurses, pharmacists and other health providers. Improper use results in ineffective treatment and for antiretrovirals resistance.

## 1.2 Rational drug selection and use

There is virtually no system in the world which offers unlimited access to all drugs. Careful selection of priority drugs is essential. Selection focuses therapeutic decisions, professional training, public information, financing, supply and quality assurance efforts on those drugs which will have the greatest impact in a given health care setting.

HIV-related drugs have four main therapeutic targets:

1. Sexually-transmitted infections (STIs) (for the prevention of spread).
2. Opportunistic infections and HIV-related cancers.
3. Supportive and palliative care.
4. Antiretroviral (ARV) therapy for prevention of antenatal transmission and treatment of HIV positive people.

Drug selection is a local decision for any organization involved in procuring, distributing, prescribing and dispensing drugs. This includes ministries of health, NGOs providing care, PLWH groups involved in treatment, and other health care organizations.

The process for rational drug selection and use follows four basic steps:

1. Listing of the HIV-related conditions and sexually-transmitted diseases which are being routinely diagnoses in the specific health care setting.
2. For each condition selection of first and, if needed, second choice drug or non drug treatments.
3. The resulting standard treatments and drug list form the basis for professional and public education on appropriate local treatment of HIV-related conditions.
4. The resulting list is the basis for financing, quantifying of needs and distribution.

### 1.3 Listing HIV-related diseases and morbidity data

A selection of papers on HIV-related disease morbidity have been taken in an attempt to find common global patterns of opportunistic infection rates. The results are confusing. Reported patterns of HIV-related morbidity vary among countries and patient groups. Health Services also vary in their capacity to diagnose and monitor HIV-related opportunistic infections and cancers. This step is particularly important because it is not only the basis of treatment selection and the listing of needed drugs but also is the basis of quantification when morbidity rates are known.

### 1.4 Selection of first and second choice treatments

Selection of the first and second choice treatments is based on the best available evidence on comparative efficacy, safety, quality, local appropriateness and cost. This study has taken the current recommendations of others. Published literature originating from WHO divisions, UNAIDS and four national treatment guidelines have been taken. The recommendations cover palliative treatment, sexually-transmitted diseases and opportunistic infections and the treatments have been collated. Lists have been made of the recommended drugs for these three therapeutic targets. These lists of recommended drugs have been

subdivided into those on WHO Model List of Drugs and those which are outside the list.

Based on identification of the local HIV-related and STD disease patterns the drug lists presented may be used as the starting basis to select standard treatments for HIV-related and STD disease. The lists may be used by a ministry of health, NGOs providing care and PLWH groups involved in treatment and other health care organizations.

## 2. Objectives

The objectives of the report were:

1. As preparation for a submission to the EDL Expert Committee meeting in December 1997, for inclusion of additional drugs needed for the treatment of HIV-related diseases.
2. As the basis of a future document useful to WHO country representatives;
3. As the basis of a UNAIDS/WHO joint statement on STD and HIV-related disease treatment guidelines.
4. As a possible basis for quantification and assessment of cost impacts of HIV-related disease.
5. As a relevant list of drugs for HIV-related diseases as a basis for drug selection for UN staff pharmacies.

The work concentrates on drugs for opportunistic infections, sexually-transmitted diseases and palliation but not malignancies or anti-retroviral drugs. It was divided into the following elements.

1. To list the HIV-related diseases and STDs on the basis of ICD 10.
2. To list the leading HIV-related diseases and STDs with their relative frequencies by risk group, stage of disease or other classification.
3. To review for each HIV-related health problem the most recommended WHO standard treatment or other standard treatments advocated by other organizations.
4. To comment on areas where discrepancies exist between WHO standard treatments.
5. To propose standard treatments for HIV-related diseases and STD.
6. To estimate drug needs based on the proposed standard treatments and epidemiological statistics on morbidity rates.

The above tasks were based on a review of the literature on HIV-related diseases and STDs, WHO manuals and recent articles in scientific journals.

## 3. Comments on the tables and lists

### 3.1 HIV-related diseases and STDs on the basis of ICD 10<sup>1</sup>

#### Annex 1. ICD 10 codes of HIV-related diseases and STDs

The code numbers given in brackets are for diseases when they occur in non HIV positive individuals. While there are specific codes for syphilis and gonorrhoea in pregnancy no such coding exists for HIV positive women who are pregnant. HIV positive children of HIV positive mothers have no special coding other than Z 21 (Asymptomatic HIV status).

An alternative system of schematizing HIV-related conditions is in **Annex 1a. WHO Staging System for HIV infections and disease (1990)**<sup>2</sup>. The CDC revised surveillance case definition has not been listed<sup>3</sup>.

Certain specific diseases of local importance such as penicilliosis, disseminated leishmaniasis, rapidly evolutive Chagas disease and non pulmonary pneumocystis carinii infection do not fall into any the above classifications.

### 3.2 Leading HIV-related diseases and STDs and relative frequencies by risk group

#### Annex 2. HIV-related disease in adults mentioned in 18 reports

Eighteen reports, documents and scientific articles covering HIV-related diseases were reviewed and each "mentioned disease" recorded. The histogram shows the wide variation in reported HIV-related disease in these articles. Tuberculosis is the only condition mentioned in all the documents while there are ten diseases mentioned in only one document. Reports vary from those providing highly accurate etiologic pathological diagnoses to others combining physical sign diagnoses (e.g. oral candidiasis or herpes zoster) and symptoms (e.g. headache). The second page of Annex 2 lists the sources.

#### Comment

Variation in reported HIV-related disease reflects the availability or absence of diagnostic services in a country, and variations in patterns of HIV-related diseases in different populations, subgroups, clusters, continents or countries.

<sup>1</sup> ICD 10, International Statistical Classification of Diseases and Related Health Problems, Tenth revision, vol. 1 & 3, World Health Organization, Geneva 1994.

<sup>2</sup> Acquired Immunodeficiency Syndrome (AIDS), Interim Proposal for WHO Staging System for HIV Infections and Disease, Weekly Epidemiological Record, 1990, 65, 221-228.

<sup>3</sup> Centers for Disease Control and Prevention. Revision of the CDC surveillance case definition for acquired immunodeficiency syndrome. MMWP 1987; 36(1S): 3S-15S.

### **Annex 3. HIV-related diseases crude morbidity patterns**

Fifteen articles containing percentages of HIV-related diseases were reviewed. Data came from Africa and Europe and from Côte d'Ivoire, Malawi, Mexico, Tanzania, Thailand, Uganda, USA, and Zaire. Seventeen HIV-related diseases which figured prominently were selected to make a crude analysis. For each condition the percentages reported were summated and an average calculated. An absence of reporting was not taken as an absence of the condition and were not used in the calculation. These percentages are listed in the column "Average %": maximum and minimum percentages are tabulated in the following columns. The source documents are listed in the second part of Annex 3. These statistics are crude.

#### **Comment**

There is great variation in reported percentages of HIV-related diseases (e.g. penicilliosis is only reported from Thailand). The origins of these variations will be multiple and include true differences in disease pattern, variations in diagnostic facilities, adherence to reporting protocols, access of populations to health care facilities and others. The literature is confusing and it is not always easy to determine whether percentages refer to frequency, distribution, incidence or prevalence.

#### **Conclusion**

The differences in reported HIV-related disease patterns indicate true variations in HIV-related disease morbidity but other variables will skew the figures. The data is difficult to interpret.

#### **Suggestion**

A re-analysis and further search for morbidity rates on the basis of continent or geographic areas and by symptomatology might yield more meaningful morbidity rates.

Sexually-transmitted disease frequencies have not be recorded yet but they also suffer from the same problems as HIV-related diseases: namely variable patterns of disease incidence in countries with different degrees of diagnostic capability and resultant variation in reporting. Some countries rely on the symptom categories of genital ulcer, urethral discharge and vaginal discharge when reporting STDs. Treatment guidelines are based on those categories in such countries.

### **3.3 Review of the most recommended treatments for each HIV-related health problem**

#### **Annex 4 - WHO and selected national treatment recommendations**

Four WHO sources, a draft UNAIDS document and the most recent national treatment guidelines of South Africa, Zimbabwe, Kenya and Malawi were taken as references. The recommended treatments are displayed in the annex with the source documents tabled on the first page. It is recognised that other source material, perhaps more up-to-date but less readily accessible, could have been

used as well. A search in national guidelines for treatment of all opportunist infections was not undertaken at this stage.

## Comment

WHO tends not to recommend standard treatments while national guidelines do. WHO publications present a choice with the implication that the first mentioned is the “best”. It is possible to identify a probable standard treatment but it is not usually stated as such. WHO programme documents, however do tend to give recommended treatments. For example in early syphilis benzathine benzylpenicillin (BBP) is mentioned as the “recommended” regime in a clinical management text with procaine benzylpenicillin (PBP) as an “alternative”. In another text on prescribing information it is one or the other, though benzathine benzylpenicillin is mentioned first.

For a condition such as gonorrhoea a standard treatment is not possible because antibiotic resistance rates in different countries varying widely. In emergency situations, however, where refugees and displaced persons are involved ciprofloxacin (ciproflaxin) is recommended where antibiotic sensitivities are not known (see Addendum).

## Standard treatments

A single dose of benzathine benzylpenicillin might be designated as the standard treatment for early syphilis with the alternative doxycycline for penicillin non pregnant allergic patients: tetracycline could be mentioned as an alternative. For pregnant penicillin allergic patients erythromycin appears to be the standard: a course of doxycycline should follow delivery because of doubts raised about the efficacy of erythromycin. Such a scheme of first choice treatments of primary syphilis might be schematized thus:

Standard treatment for primary syphilis	benzathine benzylpenicillin
Alternative treatment	procaine benzylpenicillin
Standard for non pregnant penicillin-allergic patients	doxycycline
Alternative treatment	tetracycline
Standard for pregnant penicillin allergic patients	erythromycin
Standard post delivery penicillin allergic patients	doxycycline
Standard for an infant born of a mother treated for syphilis	benzylpenicillin

Podophyllum resin for genital warts is nearly a standard, however, trichloroacetic acid is mentioned as an “or” and “en passant” in another text. The selection of a **best choice standard treatment** is possible and might well be even more difficult than the selection of drugs for the WHO Model List of Essential Drugs. If it is truly not possible to have a standard treatment then an explanation as to why should be given. Safety, efficacy, availability, cost, route and duration of administration, stability and many other factors need to be considered. If BBP and PBP for syphilis are equal on all the above counts other than duration of administration ( one dose/2 injections at one sitting versus 10 daily injections) then BBP should become the standard and recognized as such and PBP is an alternative.

## Conclusion

The WHO Model Prescribing Information series is superb but it is difficult to extract information rapidly from it because of its form of presentation. It would only be a short step to summarize treatments in tabular form and designate standard treatments where possible. As there is the WHO Model List of Essential Drugs so there could be a WHO Model List of Standard Treatment Guidelines. Suggestion. Further work and discussion is needed to identify if there is a need for standard treatments, standard alternatives and explanations for treatments which cannot be standardized.

### 3.4 HIV-related diseases and STDs standard treatments and essential drug lists

*Annex 5 - WHO recommended dosage schedules/treatments for STDs:* tabulates drugs and dosage schedules by ICD 10 categories of STDs with source documents at the end.

*Annex 6 - WHO recommended drugs: EDL drugs and non EDL drugs for STDs:* lists the WHO recommended drugs for STDs by WHO Model Essential Drugs List sections and sub-sections.

*Annex 7 - WHO recommended dosage schedules/treatments for HIV-related diseases and drugs for symptomatic treatment.*

*Annex 8 - Recommended current WHO EDL and non-EDL drugs for HIV-related diseases.*

### 3.5. Estimation of drug needs

Drug needs can only be estimated when standard treatments are defined and reasonably accurate disease morbidity statistics are available.

### 3.6 Conceptual model for disease priorities and treatment ranking

The Division of Family and Reproductive Health has produced a draft basic minimum requirement list of STD drugs needed in situations of conflict and displacement (Annex 9, Drugs for STDs in Emergencies). This concept has been expanded to include other STDs and other drugs both within and without the WHO Model List of Essential Drugs (Annex 9). The template presented for STDs, where diseases are prioritized and treatments ranked, may also be used when considering HIV-related diseases and their treatments.

### 3.7 Conclusions

- Morbidity data is confusing.
- WHO tends to give treatment options and less frequently recommendations or first choice treatments.
- Newer drugs and treatment regimes, such as recently marketed anti-retrovirals or triple therapy, are not included in current WHO publications or documents.

### 3.8 Possible further steps

- *Submissions to the Expert Committee on Essential Drugs.* There is a need to clearly define which drugs, needed for the treatment of HIV-related diseases, should be put forward for possible inclusion in the WHO Model list of Essential Drugs (1997). A detailed examination and assessment of those drugs currently recommended for HIV-related diseases but not on the current Model Essential Drugs List needs to be made prior to identifying and deciding which should be submitted to the expert committee.

Additionally, the list of Essential List Drugs used for HIV-related diseases requires review to identify inappropriate or unnecessary drugs when used in the setting of HIV-related disease.

- *Morbidity rates.* Find more morbidity statistics (if they exist) and re-analyse by different geographical areas and by symptomatology or syndromic diagnosis.
- *Standard treatments.* Determine if there is a perceived need for global standard treatments. Discuss the concept of standard treatments and standard alternatives with relevant persons. Initiate a process to identify standard treatments.
- *Quantification.* Before proceeding to quantification circulate a document of standard treatments for comments, observations and suggestions to UNAIDS relevant WHO divisions and individuals.

Antiretroviral drugs, drugs for HIV-related malignancy drugs and palliative care. Further documents might be developed on the above topics as a joint DMP/DAP/UNAIDS undertaking

- *Future.* There is no reason why standard treatments with standard alternatives and non standardized treatments with explanations could not be drawn up for many drug treatable conditions in the ICD 10.

## Annex 1. ICD 10 codes of HIV-related diseases and STDs

The additional category numbers in brackets are the ICD 10 codes for diseases when they occur in non HIV positive individuals.

### Sexually-transmitted diseases (STD) using ICD 10 (1992)

A 50-53	Syphilis	A 58	Granuloma inguinale
A 50	Congenital syphilis	A 60	Genital herpes
A 51	Early syphilis	A 63	Genital warts
A 52	Late syphilis	N 76	Vaginitis Candidosis (B37.3)
A 52.1	Neuro syphilis		Trichomonas (A59)
O 98.1	Syphilis in pregnancy		Bacterial vaginosis (A 64)
A 54	Gonorrhoea	N 73	Pelvic Inflammatory Disease
A 54.3	Ophthalmia neonatorum due to gonorrhoea	N 74.3	Gonococcal P.I.D.(A 54.2)
	Gonorrhoea in pregnancy (O 98.2)	N 74.4	Chlamydial P.I.D
A 55	Chlamydial infection		
	Lymphogranuloma venereum		
A 56	Other chlamydial infection		
	Neonatal conjunctivitis (P39.1)		
A57	Chancroid		

### B 20-24 HIV-related diseases using ICD 10 (1992)

#### B20 Human Immunodeficiency Virus (HIV) disease resulting in infectious and parasitic diseases

**B 20.0 Mycobacterial infection**  
 Pulmonary tuberculosis (A15-16)  
 Extrapulmonary tuberculosis (A17, 18,19)  
 Myco. avium-intracellulare complex (A31)

**B 20.1 Other bacterial infections**  
 Salmonella (enteritis A02.0)  
 Shigella (A 03)  
 Campylobacter (enteritis A.04. 5)  
 Clostridium difficile (A04.7)

**B 20.6 Pneumocystis carinii pneumonia** (B59)

#### B. 20.8 Other infectious and parasitic diseases

Entamoeba histolytica (A06)  
 Giardia intestinalis (A07.1)  
 Cryptosporidiosis spp (A07.2) chronic enteric

<p>Legionella species (A 48)  Salmonella (septicaemia A 92.1)  Haemophilus influenzae (B 96.3, J 14)  Strep. pneumoniae(J 13)  Helicobacter</p> <p><b>B 20.2 Cytomegalovirus disease (B 25)</b></p> <p><b>B 20.3 Other viral infections</b>  Herpes virus (B 009)  systemic  Herpes genitalis (A 60)  Herpes of the lip (B 00.1)  Herpes zoster (B02.9)  Influenza (J11)</p> <p><b>B 20 4 Candidiasis(B37.9)</b></p> <p>Oral candidiasis (B37.0)  Oesophageal candidiasis</p> <p><b>B 20.5 Other mycoses</b></p> <p>Coccidioidomycosis (B 38)  Histoplasmosis (B 39)  Aspergillosis (B 44)</p> <p><b>Z 21 Asymptomatic human immunodeficiency virus (HIV) status</b></p>	<p>Isospora belli (A07.3)  Coccidiosis (A07.3)  Nocardiasis (A 43.9)  Cryptococcosis (B 45)  Cryptococcal meningitis (B45.1)  Toxoplasma gondi (B58)  Microsporidia (B60.8)  Strongyloidiasis (B78)</p> <p><b>B 21 Human Immunodeficiency Virus HIV disease resulting in malignant neoplasms</b></p> <p>B21.0 Kaposi's Sarcoma</p> <p>B 21.2 Lymphoma</p> <p><b>B 22 Human Immunodeficiency virus HIV disease resulting in other specified conditions</b></p> <p>B 22.0 HIV encephalitis</p> <p><b>B 23 Human immunodeficiency Virus HIV disease resulting in other conditions</b></p> <p>B 23.1 Persistent generalized lymphadenopathy</p> <p><b>No specific code number allocated for pregnancy and HIV + status</b></p>
<p><b>HIV-related disease</b></p> <p><b>Chronic diarrhoea:</b></p> <p>Salmonella spp. (A 02)  Shigella flexneri (A 03)  Campylobacter spp (A 04)  Entamoeba histolytica (A 06)  Cryptosporidiosis spp (A 07.2)  Isospora belli (A 07.3)  Coccidial dysentery (A 07)  Giardia lamblia (A 07)  Cytomegalovirus disease(B 25)  Myco. avium-intracellulare complex (A 31)  Candida (B 37)  Strongyloides stercoralis (B78)</p>	<p><b>HIV-related disease</b></p> <p><b>Respiratory Conditions</b></p> <p>Myco. tuberculosis (A15-16)  Myco. avium-intracellulare complex (A 31)  Nocardiasis (A 43)  Cytomegalovirus disease(B 25)  Coccidioidomycosis (B 38)  Histoplasmosis (B 39)  Cryptococcosis (B 45)  Toxoplasma gondi (B 58)  Pneumocystis carinii (B 59)  Strep. pneumoniae (J 13)  Haemophilus influenzae (J 14 B 96.3)  Kaposi's Sarcoma</p>

## Annex 1a. Proposed WHO clinical staging system for HIV infection and disease (1990)

### Clinical stage 1:

1. Asymptomatic
2. Persistent generalized lymphadenopathy (PGL)

Performance scale 1: asymptomatic, normal activity

### Clinical stage 2:

3. Weight loss, <10% of body weight.
4. Minor mucocutaneous manifestations (seborrheic dermatitis, prurigo, fungal nail infections, recurrent oral ulcerations, angular cheilitis).
5. Herpes zoster within the last 5 years.
6. Recurrent upper respiratory tract infections.

And/or performance scale 2: symptomatic normal activity.

### Clinical stage 3:

7. Weight loss 10% of body weight.
8. Unexplained chronic diarrhea > 1 month.
9. Unexplained prolonged fever (intermittent or constant) >1 month.
10. Oral candidiasis.
11. Oral hairy leukoplakia.
12. Pulmonary tuberculosis, within the past year.
13. Severe bacterial infection (pneumonia, pyomyositis)

And/or performance scale 3: bed-ridden, <50% of the day during the last month

### Clinical stage 4:

14. HIV wasting syndrome
15. Pneumocystis carinii pneumonia
16. Toxoplasmosis of the brain
17. Cryptosporidiosis with diarrhea >1 month
18. Cryptococcosis, extrapulmonary
19. Cytomegalovirus (CMV) disease of an organ other than the liver, spleen or lymph nodes.
20. Herpes simplex virus infection, mucocutaneous >1 month, or visceral any duration.
21. Progressive multifocal leukoencephalopathy.
22. Any disseminated endemic mycosis (i.e. histoplasmosis, coccidiomycosis).
23. Candidiasis of the oesophagus, trachea, bronchi or lungs.
24. Atypical mycobacteriosis, disseminated.
25. Non-typhoid salmonella septicaemia.
26. Extrapulmonary tuberculosis.
27. Lymphoma.
28. Kaposi's sarcoma
29. HIV encephalopathy

And/or performance scale 4: bed-ridden, >50% of the day during the last month

## Annex 2. HIV-related diseases in adults mentioned in 18 reports

HIV-related disease	Mentions	5	10	15	18
Tuberculosis					
Kaposi Sarcoma					
CMV					
PCP					
Toxoplasma gondi					
Herpes virus					
Cryptococcal meningitis					
MAC					
Oesophageal candidiasis					
Herpes zoster					
Oral candidiasis					
Cryptosporidiosis spp					
PML or HIV encephalitis					
Isospora belli					
Histoplasmosis					
Lymphoma					
Salmonella (septicaemia)					
Salmonella (intestinal)					
Herpes virus systemic					
Coccidioidomycosis					
Nocardiasis					
Strongyloides					
Pneumococci pneumonia					
Haemophilus influenzae					
Legionella species					
Shigella					
Clostridium difficile					
Aspergillosis					
Microsporidia					
Giardia intestinalis					
Entamoeba histolyticum					
Penicilliosis					
Helicobacter					
Herpes genitalis					
Influenza					
<b>SYMPTOMS/SIGNS</b>					
Diarrhoea					
Skin conditions					
Fever					
Respiratory conditions					
STDs					
Headache					
Lymphadenopathy					
Anaemia					
Pain					
Cough					
Nausea					
Dyspnea					
Meningitis					

A number of states or conditions such as a slim disease, wasting syndrome, AIDS dementia complex and others have been omitted from the HIV-related diseases listed.

## Papers reviewed

1. **Treatment of HIV infection UNAIDS/Draft, January 1997.**
2. **HIV/AIDS Surveillance in Europe (WHO), No 49, p 25, March 1996.**
3. **AIDS in Africa, a manual for physicians, Peter Piot et al. WHO, Geneva, 1992**
4. **How HIV-related opportunistic infections vary round the world, The AIDS Report, Harvard AIDS Institute 1994, (Spring) pp 3-7**
5. **Consultation on opportunistic infections in developing countries WHO, p.7, 18- 21 September 1989.**
6. **HIV and Essential Drugs in Malawi, Lissner and Lunt, R, WHO, 26 November.- 9 December 1989.**
7. **Opportunistic diseases amongst HIV-infected persons, Chan et al. AIDS, Vol. 9, No 10, 1 1148-1149, 1995**
8. **The mortality and pathology of HIV infection in a West African city, Lucas S B, AIDS, 1993, Vol. 7 No 12, pp 1569-1578.**
9. **Aids-defining disease surveillance, Jones et al., AIDS, Vol. 8 No 10 p 1491.**
10. **Epidemiology and Prevention of Acquired Immunodeficiency Syndrome, Drotman D.P. and Curran, J.P., Public Health and Preventive Medicine, 13th Edition p.118, ?1993.**
11. **AIDS in Africa: what drugs do the carers want or need? Lamont A.C. et al Tropical doctor, 26, 72-76, 1996.**
12. **AIDS-drug Cost Estimator, WHO, GPA/DAP, 5 January 1990.**
13. **Guidelines for making rational choices on use of drugs and clinical management within AIDS prevention and control programmes: Laing R.O., WHO GPA, April 1990.**
14. **Proven causes of death in HIV-infected patients treated for tuberculosis in Abidjan, Côte d'Ivoire, Greenberg A.E. AIDS, Vol. 9, No 11, pp. 1251-1254, 1995.**
15. **Trends in Infectious Diseases and Cancers amongst persons dying of HIV infection in the United States from 1987 to 1992, Selik R.M. Annals of Internal Medicine vol. 123, No.12, pp 933-936.**
16. **AIDS in Africans living in London, O'Farrell N. Genitourin. Med., 71 358-362, 1995.**
17. **AIDS-defining illness and survival, Luo et al. AIDS, Vol. 9 No 1, p 61, 1995.**
18. **Guidelines for clinical management of HIV infections in Adults, WHO/GPA/HCS/91.6.**

## Annex 3. HIV-related diseases crude global morbidity patterns

Data taken from fifteen sources: papers reporting prevalence, incidence, frequency, distribution, estimates and guesses

EU = Europe, AF = Africa, CA = Central America, SA = South America, AS = Asia

Continent	EU	EU	AF	AF	AF	AF	AF	AF	CA	CA	SA	AS	USA	USA	Average %	Min %	Max %	
Country	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.			
Source of data	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O			
Diseases																		
Oral candidiasis			90		16							87	30	44		53.4%	16%	100%*
PCP	22	25	5	4				17	1	24	24	22	26	64	57	24.2%	1%	64%
Tuberculosis	20	12	40	54	15	11	11	13	41	28	25	32	20	2	2	21.7%	2%	54%
Oes. Candidiasis	17	23	40		24			27	31		5	24	4	11	6.7	20.9%	5%	40%
CMV	6	25	7	26				4	13	65	69	5	4	5	5	20.9%	4%	69%
Kaposi Sarcoma	8	21		13	4	14		4	16	40	30	5	2	21	10	14.6%	4%	40%
Toxoplasmosis G	9	18	18	21	2			5	11	19	17	14	2	2.5	4	11.4%	2%	21%
Cryptococcosis	3	30	7	5	5			5	19	7	11	5	2	7	6	9.3%	2%	30%
Cryptospor	3	9	28	4				6	1		7	8	2	3	6	7.7%	1%	28%
Herpes Z			10	3	10							14	2	5	3	7.5%	3%	14%
Herpes V	2	25	5	3		7		3		5	5	12	10	4	3	7.0%	2%	25%
MAC	3	8		4						5	6		2	4	3	4.4%	2%	8%
Salm sept.	0.5		10						10			3		0.2	0.5	4.0%	0.2%	10%
Histoplasmosis	0.1			3					1	5	10		8		1	4.0%	0.1%	10%
Aspergillosis				3						7	3			0.1	1	2.8%	0.1%	7%
Isospora belli	0.2	4	8					1		1	1	6	2	0.2	0.2	2.5%	0.2%	8%
Nocardiasis				5						1	1			0.1		1.8%	0.1%	5%
Penicilliosis													X			4%		25%

\* Source C quotes the incidence of oral candidiasis as being 80-100%

Sources of data used in crude morbidity rates table and brief description of statistics given in the source

<u>Countries/continents</u>	<u>Sources of morbidity data</u>	<u>Description of statistics provided by authors</u>	
1. Europe	HIV/AIDS Surveillance in Europe (WHO), No 49, March 1996 p 25 (ref. 2)	AIDS indicative diseases diagnosed between Jan. 1994 and 31 March 1996 (%)	(N = 45,507)
2. Africans in Europe	Sonnet, J. and Taelman, H., Clinical aspects of AIDS and AIDS-related complex, Oxford, Oxford University Press, 1986, pp. 78-89. Quoted in AIDS in Africa, Piot P. et al. A Manual for Physicians, 1992, WHO	Frequency of opportunistic infections in patients with AIDS. % of AIDS patients with opportunistic disease (%)	(N = 56)
3. "Africa)	Consultation on opportunistic infections in developing countries WHO, 18-21 September 1989, p.7 (ref. 5)	Incidence of HIV-related conditions in Africa..	Informed guess
4. Côte d'Ivoire	The mortality and pathology of HIV infection in a West African city, Lucas S B, AIDS, 1993, Vol. 7 No 12, p 1569-1578 (ref. 8)	Text says "Table 1 shows the frequency.....". (%) The prime causes of death and pathological prevalence in autopsy sample patients in HIV positive cadavers.....those having one or more CDC-listed AIDS defining pathologies (AIDS path N = 175) ( %)	(N = 175)
5. Malawi	HIV and Essential Drugs in Malawi, Lissner and Lunt, R 26 Nov. 9 Dec. 1989 (ref. 6)	"case presentation estimates" (%). Occurrence estimate ranges for presenting signs, symptoms and diseases used in the AIDS drug Cost Estimator	Informed guess
6. Tanzania	Neurological Disorders in AIDS and HIV disease in the Northern Zone of Tanzania Howlet W. et al. AIDS, 3, 289-296, (1989). Quoted in AIDS in Africa, Piot P. et al.	Frequency of opportunistic infections in patients with AIDS % of AIDS patients with opportunistic disease (%)	(N = 200 )
7. Uganda	Surveillance and AIDS in Uganda, Berkley, s. et al. AIDS, 3: 79-85 (1989) Quoted in AIDS in Africa, Piot P. et al.	Frequency of opportunistic infections in patients with AIDS % of AIDS patients with opportunistic disease (%)	No information
8. Zaire	La clinique du SIDA en Afrique, Colebunders, R. et al.. Médecine et maladies infectieuses, 15: 350-355 (1986) Quoted in AIDS in Africa, Piot P. et al.	Frequency of opportunistic infections in patients with AIDS % of AIDS patients with opportunistic disease (%)	(N = 196 )
9. Zaire	A clinical and pathological comparison of the WHO and CDC case definitions for AIDS in Kinshasa Zaire. Is passive surveillance valid? Nelson A.M. et al. AIDS, 1993, 7: 1241-1245. Quoted in Perriens J., Clinical Aspects of HIV-related Opportunistic Infections in Africa: Tuberculosis and Candidiasis Gent, 1994,	AIDS defining opportunistic diseases in HIV infected patients. Frequency of indicator disease meeting the Centers for Disease Control and Prevention (CDC) case definition (%)	(N = 63)
10. Mexico	Comparative demographic and autopsy findings in acquired immunodeficiency syndrome in two Mexican populations. Jessurun J. et al. J. AIDS 1992, 6: 467-473. Quoted in Perriens J., Clinical Aspects of HIV-related Opportunistic Infections	"The first 58 patients who died of AIDS and were autopsied in two hospitals". Comparison of the main autopsy findings (%)	(N = 58 )

<u>Countries/ continents</u>	<u>Sources of morbidity data</u>	<u>Description of statistics provided by authors</u>	
11. Mexico	K The Spectrum of Clinical and Pathological Manifestations of AIDS in a Consecutive series of Autopsied Patients, Alejandro Mohar, et al AIDS, 1992, 6(5): 467-673 Quoted in Perriens J., Clinical Aspects of HIV-related Opportunistic Infections	Distribution of opportunistic infections in 177 Mexican AIDS cases, based on clinical and autopsy diagnoses. (%)	(N = 177)
12. Brazil	L Characteristics of acquired immunodeficiency syndrome in Brazil, Moreira E.D. et al American Journal of Tropical Medicine and Hygiene, 1993, 48(5), pp. 687-692 Quoted in Perriens J., Clinical Aspects of HIV-related Opportunistic Infections	Infections diagnosed in 111 patients with acquired immunodeficiency syndrome (%)	(N = 111)
13. Thailand	M Clinical Aspects of HIV-related Opportunistic Infections in Africa: Tuberculosis and Candidiasis, Perriens J., Gent, 1994		
14. USA	N Opportunistic diseases reported in Aids patients frequencies associations and trends. Selik R. et al. AIDS 1987 1: 175-182	Opportunistic diseases reported in > 0.1% of AIDS patients in the United States. Denominator 30,632 AIDS patients reported between 1 June 1981 and 9 February 1987. (% of AIDS patients)	(N = 30,632)
15. USA	O Epidemiology and Prevention of Acquired Immunodeficiency Syndrome, Drotman D.P. and Curran, J. P., Public Health and Preventive Medicine, 13th Edition p.118 (1993) (ref. 10), quoting from Selik R.M. et al. Impact of the 1987 revision of the case definition of acquired immunodeficiency syndrome in the United States, J-Acquir-Immune-Defic-Synd. 1990; 3(1): 73-82	Percentages of AIDS cases reported with AIDS-indicative diseases amongst cases diagnosed from September 1987 through 1988 in the USA and US territories. (%)	(N =28,920)

## Annex 4. WHO and selected national treatment recommendations

### References: Columns 1-8

Column numbers	Source Documents
1) WHO MAN G.	WHO/GPA. Management of sexually-transmitted diseases WHO/GPA/TEMP/94.1
1) WHO MAN G.	WHO/GPA. Guidelines for the Clinical Management of HIV infection in Adults WHO/GPA/IDS/HCS/91.6
2) WHO/MPI.	WHO Model Prescribing Information. Drugs used in sexually-transmitted diseases and HIV Infection, Geneva, 1995
3) WHO/TB/HIV.	TB/HIV, A Clinical Manual, WHO/TB 96.200
4) UNAIDS.	DRAFT NOT CLEARED BY UNAIDS, Treatment of HIV Infection Jan 1997
5) STGL/Mal.	Malawi Standard Treatment Guidelines, 2nd Edition 1993
6) CGL/Ken	Clinical Guidelines for Diagnosis and Treatment of Common Conditions in Kenya, November 1994
7) EDL/Zim.	EDLIZ Essential Drugs List for Zimbabwe, including guidelines for treatment of medical conditions common in Zimbabwe 1994
8) EDP/S/A.	Essential Drugs Programme, South Africa, Standard Treatment Guidelines and Essential Drugs List, Primary Health Care, 1996 Ed.

### Abbreviations

Numbers 1,2,3, =	standard treatments
A.=	alternatives
+	drug to be used in conjunction with another drug
X =	included in list
GU =	genital ulcer
UD =	urethral discharge
VD =	vaginal discharge
NR =	not recommended
RxNA =	treatment not available
M =	condition mentioned but no treatment proposed
w =	weeks
Z =	mentioned as being prohibitively expensive

Disease	Drugs	WHO Guidelines					National Guidelines							
		WHO MAN G	WHO/ MPI	WHO TB/HIV	UN AIDS	STGL Mal	CGL Ken	EDL Zim	EDP S/A					
		1991/94	1995	1996	1997	1993	1994	1994	1996					
A 50-53 Syphilis														
A 50.0 Congenital	benzylpenicillin		X							X	X			
	procaine benzylpenicillin		X											
A 51 Early	benzathine benzylpenicillin 2.4 m IU	1	X	X						X	X	X		GU
	procaine benzylpenicillin 1.2 m IU	A	X	X										
	tetracycline 500mg	A	X	X										
	doxycycline 100mg	2	X	X						X	X	X		
	erythromycin 500mg	3	X	X						X	X	X		+ GU
A 52 Late	procaine benzylpenicillin 1.2 m IU	2	X	X								X		
	benzathine benzylpenicillin 2.4 m IU	1	X											
A 52.1 Neuro	benzylpenicillin 4 m IU	1	X							X				
	procaine benzylpenicillin 1.2 m IU + probenecid	A	X											
A 54 Gonorrhoea	ciprofloxacin 500 mg	1+	X	X										UD/VD
	ceftriaxone 250 mg	1+	X	X										
	cefixime 400 mgs	1+	X	X							X			
	spectinomycin 2g	1+	X	X							X			VD
	(TMP/SMX) trimethoprim (80 mg) /sulfamethoxazole (400 mg)	1	X	X								UD		
	thiamphenicol		X											
	gentamicin 240 mg		X	X						X				
	kanamycin 2g	1+	X								X	UD		
	nofloxacin											2ndline		
	amoxicillin										X			
	augmentin + probenecid										X			
Ophthalmia neonatorum	tetracycline ointment 1%		X							Proph				Proph
(Prophylaxis)	erythromycin ointment 1%		X							+Rx PO				+Rx
	silver nitrate solution 1%		X											
A 55 Chlamydial infection, LGV	tetracycline 500mg	+ A	X	X										
	doxycycline 100mg	+1 UD	X	X								X(1)UD		RxBubo+pen

Disease	Drugs	WHO Guidelines				National Guidelines			
		WHO MAN G	WHO/ MPI	WHO TB/HIV	UN AIDS	STGL Mal	CGL Ken	EDL Zim	EDP S/A
A 56 Other chlamydial infection	erythromycin 500mg	+ A	X	X		X		X(2)	
	sulfadiazine 1g		X	X					
	tetracycline 500mg		X				X		
	doxycycline 100mg		X			X			+UD/VD
A 57 Chancroid	erythromycin 500mg		X			X			
	erythromycin 500mg (1st choice)	1	X	X		X		X(2)	
	ciprofloxacin 500 mg	A	X	X		X		X(3)	
	ceftriaxone 250 mg	A	X	X		X			
	spectinomycin 2g	A	X	X					
	TMP/SMX 2 tablets	A	X	X				X(1)	
	When syphilis cannot be excluded ADD benzathine benzylpenicillin G 2.4 million IU		X				X		
A 58 Granuloma inguinale	TMP/SMX 2 tablets (first choice)	1	X	-			X	X(1)(+Pen)	X
	tetracycline 500mg	A	X	-			X		
	doxycycline		X					X(2)	
	chloramphenicol 500mg		X	-					
A 60 Genital herpes	gentamicin 1 mg/kg		X	-					
	erythromycin+ lincomycin (pregnancy)		X	-			X		
	streptomycin		NR				X		
	aciclovir 200mg tabs	1	X	X	X		X		
A 63 Genital warts	aciclovir 5mg/kg iv								
	calamine						X		
	podophyllum 20%	1	X	X		X			X
	trichloroacetic acid	1	X	X		X			

Disease	Drugs	WHO Guidelines				National Guidelines			
		WHO MAN G	WHO/ MPI	WHO TB/HIV	UN AIDS	STGL Mal	CGL Ken	EDL Zim	EDP S/A
N 76.0 Vaginitis Trichomonas (A59)	metronidazole 2g								
	metronidazole 400-500mg	1	X	X		X	X	VD UD2line	VD
	metronidazole 2g		X	X					
Bacterial vaginosis (A 64)	metronidazole 400-500mg								
	nystatin 100,000IU	1	X	X					
	micronazole 200mg	1	X	X					
Candidosis (B37.3)	clotrimazole 500mg	1	X	X					
N 73 Pelvic Inflammatory Disease Chlamydial Gonococcal (A 55.2)									
	ceftioxone 250 mg		X						
	doxycycline 100mg		X						
	tetracycline 500mg		X				X		
	metronidazole 400.-500mg		X				X		
	doxycycline 100mg		X				X		
	gentamicin 1.5mg/kg								
	amoxicillin 500mg (+ augmentin + probenecid)						X		
Hospitalised	ciprofloxacin 500mg		X						
	doxycycline 100mg		X						
	metronidazole 400.-500mg		X						
	doxycycline 100mg		X						
	gentamicin 1.5mg/kg		X						
Severely ill	clindamycin 900mg		X						
	doxycycline 100mg		X						
	tetracycline 500mg		X						
	metronidazole 400.-500mg								
	benzylpenicillin								
	chloramphenicol								X

Disease	Drugs	WHO Guidelines					National Guidelines						
		WHO MAN G	WHO/ MPI	WHO TB/HIV	UN AIDS	STGL Mal	CGL Ken	EDL Zim	EDP S/A				
Symptomatic diagnoses Genital ulcer (for syphilis)	benzathine benzylpenicillin 2.4 m IU OR	X				X	1X	1X					
	procaine benzylpenicillin 1.2 m IU OR	X					1X					1X	
	tetracycline 500mg OR	X					X						
	doxycycline 100mg OR	X											
	erythromycin 500mg PLUS	X									1AX		
	erythromycin 500mg (1st choice)	X											
	ciprofloxacin 500 mg OR	X					X	1X	2X			1X	
	ceftriaxone 250 mg OR	X						2X	3X				
	spectinomycin 2g OR	X						2X					
	TMP/SMX 2 tablets OR PLUS	X											
(for granuloma inguinale)	TMP/SMX 2 tablets (first choice)	X					1X	1X					
	tetracycline 500mg	X					X						
	doxycycline	X											
	chloramphenicol 500mg	X											
	gentamicin 1 mg/kg	X											
	erythromycin(in pregnancy)	X											
	TMP/SMX 2 tablets	X											
	streptomycin	X											
	Urethral discharge (for gonorrhoea)	amoxicillin + augmentin + probenecid											
		ciprofloxacin 500 mg OR	X					1X	2X				
ceftriaxone 250 mg OR		X					1X						
cefixime 400 mgs OR		X											
spectinomycin 2g OR		X											
kanamycin 2g OR		X											
(TMP/SMX) trimethoprim (80 mg) /sulfamethoxazole (400 mg)		X											

Disease	Drugs	WHO Guidelines				National Guidelines				
		WHO MAN G	WHO/ MPI	WHO TB/HIV	UN AIDS	STGL Mal	CGL Ken	EDL Zim	EDP S/A	
(for chlamydia)	gentamicin 240mg i.m					X				
	PLUS doxycycline 100mg OR	X				X	1X	1X		1X
	tetracycline 500mg OR	X					1X			
	erythromycin 500mg	X				X	2X	2X		
	metronidazole									
Vaginal discharge (for gonorrhoea)	norfloxacin									
	ciprofloxacin 500 mg OR	X						2X		
	ceftriaxone 250 mg OR	X						3AX		1X
	cefixime 400 mgs OR	X								
	spectinomycin 2g OR	X							3X	PX
	kanamycin 2g OR	X							1X	
	(TMP/SMX) trimethoprim (80 mg) / sulfamethoxazole (400 mg)	X							1AX	
	gentamicin 240mg i.m					X				
	PLUS doxycycline 100mg OR	X				X			1X	1X
	tetracycline 500mg OR	X								
(For vaginitis)	erythromycin 500mg PLUS	X				X				PX
	metronidazole 2g OR	X				X				1XPX
	metronidazole 400-500mg PLUS								2X	
	gentian violet									X
	nystatin 100,000IU OR	X								X
micronazole 200mg OR	X								X	
clotrimazole 500mg	X								X	
tinidazole									X	

Disease	Drugs	WHO Guidelines					National Guidelines					
		WHO MAN G	WHO/ MPI	WHO/ TB/HIV	UN AIDS	STGL Mal	CGL Ken	EDL Zim	EDP S/A			
B 20.0 Mycobacterial infection												
Mycobacterium avium-intracellulare complex (A31.0)		M Rx symptoms										
Treatment												
	clarithrombin 1000mg orally/day + ethambutol 15mg/kg orally/day + rifabutin 300mg orally per day											
	rifabutin 300mg orally per day + ethambutol 15mg orally per day + clofazimine 100mg orally per day + ciprofloxacin 1500mg orally per day	X (M) X (M) X (M)										
	clofazimine + rifampicin		X									
	cycloserine		X									
	ethionamide		X									
	amikacin	X (M)										
Prophylaxis												
	clarithromycin 1000mg orally daily OR azithromycin 1200mg orally daily OR rifabutin 300 mg orally per day											
M tuberculosis (A15-16)												
	isoniazid(H)											
	rifampicin (R)											
	pyrazinamide (Z)											
	streptomycin (S)											
	ethambutol (E)											
Prophylaxis												
Extrapulmonary tuberculosis												
B 20.1 other bacterial infections												
Pneumococci pn. (J 13)												
Haemophilus influenzae (B 96.3)												
	amoxicillin						X					
	TMP-SMX						X					

Disease	Drugs	WHO Guidelines				National Guidelines			
		WHO MAN G	WHO/ MPI	WHO TB/HIV	UN AIDS	STGL Mal	CGL Ken	EDL Zim	EDP S/A
Legionella spp (A 48)									
Helicobacter,									
Shigella (A 03)	TMP-SMX naladixic acid	X		X					
Campylobacter spp	erythromycin 2g daily for 5 days	X		X					
Salmonella (enteric A02.0)	TMP-SMX chloramphenicol	X		X					
S. septicaemia A92.1)	metronidazole	X		X					
Clostridium difficile (A04.7)									
B 20.2 (B 25) cytomegalovirus disease		Rx symptoms		Rx too costly		NM	NM	NM	MN
<u>Treatment</u>	ganciclovir i.v	X resp	X	(M)	X				
	foscarnet i.v				X				
	cidofovir				X				
<u>Prophylaxis</u>	ganciclovir i.v		X		X				
	foscarnet i.v				X				
	cidofovir				X				
B 20.3 other viral infections									
Herpes virus (B 009)	aciclovir	X	X	X	X	RxS			
Herpes genitalis (A 60)	aciclovir		X				X	RxS	
Herpes zoster (B02.9)	aciclovir	X	X	X	X	RxS	M	RxS	
	foscarnet				X				
influenza (I11)									
B 20.4 (B37.9) candidiasis							M		
<u>Prophylaxis</u>	nystatin								

Disease	Drugs	WHO Guidelines				National Guidelines			
		WHO MAN G	WHO/ MPI	WHO TB/HIV	UN AIDS	STGL Mal	CGL Ken	EDL Zim	EDP S/A
Candidiasis prophylaxis Oral candidiasis (B37.0) Treatment	fluconazole	X(1)		X	X	X		X(1)	
	gentian violet		X						
	polyvidone iodine		X						
	chlorhexidine		X						
	nystatin	X(1)	X	X				X(2)	
	amphotericin B	X(2)	X	X	X				
	ketoconazole	X(2)	X	X	X				
	fluconazole	X(2)	X						
	clotrimazole	X(2)		X					
	miconazole	X(2)	X	X	X			X(3)	
Dermal candidiasis	gentian violet								
	nystatin								
Oesophageal candidiasis	nystatin	X(2)	X			X		X(1)	
	ketoconazole	X(1)	X		X				
	fluconazole		X		X			X(2)	
	amphotericin B		X		X				
	itraconazole				X				
Vaginal candidiasis (see STD section)									
B 20.5 other mycoses coccidioidomycosis (B 38) Treatment	amphotericin B	X							
	amphotericin B								
Histoplasmosis (B39) Treatment	amphotericin B	M			NM	NM	NM	NM	NM
	amphotericin B	X	X						
Propylaxis ketoconazole	amphotericin B	X	X						
	itraconazole	X							
aspergillosis (B 44) B 20.6 pneumocystis carinii pneumonia (B59) First line Treatment	itraconazole	NM	NM	M	NM	NM	NM	NM	NM
	TMP-SMX oral or i.v.	X(1)	X	X	X			X	X

Disease	Drugs	WHO Guidelines				National Guidelines			
		WHOMAN G	WHO/ MPI	WHO TB/HIV	UN AIDS	STGL Mal	CGL Ken	EDL Zim	EDP S/A
Second line	pentamidine i.v	X(2)	X		X				
Third line	dapsone + TMP				X				
	primaquine + clindamycin				X				
	atovaquone				X				
Others	eflornithine		X						
	trimetrexate		X						
	prednisolone/methylprednisolone	X	X					X	
Prophylaxis	TMP-SMX	X	X	X	X				
	pyrimethamine-sulfadoxine	X	X						
	pentamidine	X	X		X				
	dapsone				X				
<b>B. 20.8 other infectious and parasitic diseases</b>									
Entamoeba h. (A06)	metronidazole	X							
Giardia I. (A07.1)	metronidazole	X							
cryptosporidiosis spp (A07.2)	paromomycin, azithromycin symptomatic treatment	Symp.Rx only	No Rx	Symp.Rx only	X		NM	NM	NM
chronic enteric.									
Isospora belli (A07.3)	TMP-SMX (160mg+800mg)	X	X	X	X		NM	NM	NM
Nocardiasis (A 43.9)		NM	NM		NM		NM	NM	NM
Prophylaxis	TMP-SMX								
	pyrimethamine-sulfadoxine			X					
Treatment	pyrimethamine-sulfadoxine + chloramphenicol			X					
	TMP-SMX			X					
Toxoplasma gondi (B58)									
Prophylaxis	pyrimethamine	X	X	X	-		NM	RX not on EDL	NM
	sulfadiazine	X	X		-				
	sulfadoxine			X					
	clindamycin	X	X		-				
First line treatment	pyrimethamine tablet 25mg PLUS sulfadiazine tablet 200mg OR sulfadoxine 500mg	X	X	X	X				
		X	X		X				

Disease	Drugs	WHO Guidelines					National Guidelines					
		WHO MAN G	WHO/ MPI	WHO TB/HIV	UN AIDS	STGL Mal	CGL Ken	EDL Zim	EDP S/A			
<b>Second line</b>	calcium folinate (leucovorin) PLUS		X			X						
	pyrimethamine	X										
	clindamycin	X										
	dapsone											
	atovaqone											
<b>cryptococcosis (B 45)</b>		X										
<b>Cryptococcal meningitis (B45.1)</b>												
<b>Prophylaxis</b>	amphotericin B i.v. .0.5-1.0mg/kg weekly	X	X									
	fluconazole 200mg orally daily	X	X	X								
	itraconazole		X									
	amphotericin B i.v.0.5-1.0mg/kg daily	X	X									
	+											
<b>Treatment</b>	flucytosine orally for 6 weeks		X									
	fluconazole (400mg) daily		X	X 10 w								
	metronidazole 400mg 3x daily for 7 days		-	X								
	albendazole (experimental)		-									
	thiabendazole, 25mg/kg 3x daily for 3 days	X										
<b>Stongyloidiasis (B.78)</b>	albendazole, 400mg daily for 3 days	X										
		X										

Disease	Drugs	WHO Guidelines				National Guidelines				
		WHO MAN G	WHO/ MPI	WHO TB/HIV	UN AIDS	STGL Mal	CGL Ken	EDL Zim	EDP S/A	
Symptomatic diagnoses Chronic diarrhoea		X								
	TMP-SMX	X								
	loperamide	X								
	diphenoxylate	X								
	codeine	X								
	mebendazole	X								
	thiabendazole	X								
	albendazole	X								
	metronidazole	X								
	diloxanide	X								
	erythromycin	X								
	rifabutin	X								
	clofazimine	X								
	ethambutol	X								
	amikacin	X								
			X							
	Respiratory conditions	phenoxymethylpenicillin	X							
ampicillin		X								
TMP-SMX		X								
isoniazid		X								
rifampicin		X								
pyrazinamide		X								
ethambutol		X								
prednisolone		X								
pentamidine		X								
amphotericin B		X								
ganciclovir		X								
			X							
Lymphadenopathy		benzathine benzylpenicillin	X							
		tetracycline	X							
		isoniazid	X							

Disease	Drugs	WHO Guidelines				National Guidelines			
		WHO MAN G	WHO/MPI	WHO TB/HIV	UN AIDS	STGL Mal	CGL Ken	EDL Zim	EDP S/A
Lymphadenopathy (continued)	rifampicin	X							
	pyrazinamide	X							
	ethambutol	X							
	ketoconazole	X							
	itraconazole	X							
	pyrimethamine	X							
	sulfadiazine	X							
	benzylpenicillin	X							
	chloramphenicol	X							
	amphotericin B	X							
Headache	fluconazole	X							
	clindamycin	X							
	ampicillin	X							
	chloramphenicol	X							
	isoniazid	X							
	rifampicin	X							
	pyrazinamide	X							
	ethambutol	X							
	amphotericin B	X							
	fluconazole	X							
Fever	phenoxymethylpenicillin	X							
	ampicillin	X							
	TMP-SMX	X							
	pentamidine	X							
	prednisolone	X							

**Abbreviations**

Numbers 1,2,3, = standard treatments were identified

A.= alternatives

+ sign indicates drug to be used in conjunction with another

X = included in list

GU = genital ulcer

UD = urethral discharge

VD = vaginal discharge

NR = not recommended

RxNA = treatment not available

M = mentioned but no treatment proposed

w = weeks

Z = mentioned as being prohibitively expensive

## Annex 5. WHO recommended dosage schedules/treatments for STDs

### Sexually-transmitted diseases

Disease	Drug	Dosage
A 50-53 Syphilis Congenital syphilis	benzylpenicillin OR procaine benzylpenicillin	
Syphilis (Primary)	benzathine penicillin G 2.4 million IU OR  procaine penicillin G 1.2 million IU	i.m. injection at a single session often split into two doses at separate sites) daily by i.m. injection for 10 consecutive days
	OR if allergic to penicillin tetracycline 500mg OR doxycycline 100mg OR if pregnant erythromycin 500mg	orally 4x for 15 days orally 2x daily for 15 days orally 4x for 15 days
Late	procaine penicillin G 1.2 million IU OR benzathine penicillin G 2.4 million IU	daily by i.m. injection for three weeks weekly i.m. injection at a single session (often split into two doses at separate sites) for three weeks
Neuro	benzathine penicillin G 4 million IU OR procaine penicillin G 1.2 IU PLUS probenecid 500mg	4 hourly i.v. for 2 weeks daily by i.m.injection for 2 weeks orally 4x daily for 2 weeks
A 54 Gonorrhoea	ceftriaxone 250 mg OR spectinomycin 2g OR ciprofloxacin 500 mg OR cefixime 400 mgs OR kanamycin 2g OR thiamphenical 2.5g OR (TMP/SMX) trimethoprim (80 mg) /sulfamethoxazole (400 mg) OR gentamicin 240 mg by i.m	single i.m injection single i.m injection single oral dose single oral dose i.m. injection as a single dose orally daily for 2 days 10 tablets daily for 3 days
Ophthalmia neonatorum: prophylaxis	tetracycline ointment 1% (1st choice ) OR erythromycin ointment 1% OR silver nitrate solution 1%	injection as a single dose (TB/HIV) apply once apply once apply once
A 55 Chlamydial infections Lymphogranuloma venereum(A55)	doxycycline 100mg OR tetracycline 500mg OR <u>In pregnancy</u> erythromycin 500mg OR sulfadiazine 1g	orally 2x daily for 14 days orally 4x daily for 14 days  orally 4x daily for 14 days orally x4 daily for 14 days
Other chlamydial infections(A56)	doxycycline 100mg OR tetracycline 500mg OR <u>In pregnancy</u> erythromycin 500mg OR sulfadiazine 1g	orally 2x daily for 7 days orally 4x daily for 7 days  orally 4x daily for 7 days orally x4 daily for 7 days

Disease	Drug	Dosage
A 57 Chancroid	erythromycin 500mg OR ciprofloxacin 500 mg OR ceftriaxone 250 mg OR spectinomycin 2g OR TMP/SMX 2 tablets  When syphilis cannot be excluded PLUS benzathine penicillin G 2.4 million IU	orally 3x for 7 days orally as a single dose i.m. injection as a single dose by i.m. injection as a single dose orally 2x daily for 7 days  i.m. injection at a single session (often split into two doses at separate sites)
A 58 Granuloma inguinale	TMP/SMX 2 tablets OR if unresponsive tetracycline 500mg OR chloramphenicol 500mg OR gentamicin 1 mg/kg <u>In pregnancy</u> erythromycin + lincomycin streptomycin not recommended	orally 2x daily for 14 days orally 4x for 14 days orally 4x daily for 21 days  i.m.injection 3x daily for 21 days
A 60 Genital Herpes	aciclovir 200mg tabs	orally 5x daily for 7 day or until healed
A 63 Genital warts	podophyllum resin 20% trichloroacetic acid	topical application 1-2 times per week until cleared
N 76.0 Vaginitis Trichomonas (A 59)	metronidazole 2g OR metronidazole 400-500mg	orally as a single dose orally 2x daily for 7 days
Bacterial vaginosis (A64)	metronidazole 2g OR metronidazole 400-500mg	orally as a single dose orally 2x daily for 7 days
Candidosis (B 37.3)	nystatin 100,000IU OR micronazole or clotrimazole 200mg OR clotrimazole 500mg	2 pessaries intravaginally daily for 14 days intravaginally once daily for 3 days intravaginally once as single dose
N 73 Pelvic inflammatory disease Ambulatory patients	ceftriaxone 250 mg PLUS doxycycline 100mg OR tetracycline 500mg PLUS metronidazole 400.500mg, FOLLOWED BY doxycycline 100mg	by i.m. injection 2x daily orally 2x daily orally 4x daily orally 2x daily for 4 days orally twice daily for 10 days
Hospitalized patients	ceftriaxone 250mg PLUS doxycycline 100mg OR ciprofloxacin 500mg PLUS doxycycline 100mg PLUS metronidazole 400.500mg FOLLOWED BY doxycycline 100mg	by i.m injection twice daily orally 2x daily orally 2x daily orally 2x daily orally 2x daily for 4 days  orally twice daily for 10 days
Severely ill patients	gentamicin 1.5mg/kg PLUS clindamycin 900mg FOLLOWED BY doxycycline 100mg OR tetracycline 500mg	i.v. injection 3x daily i.v. 3x daily for a minimum of 4 days orally 2x daily for 10 days orally 4x for 10 days

**Treatment of the newborn**

Disease	Drug	Dosage
<b>Syphilis</b>		
Infant born to a treated / seropositive mother	benzathine benzylpenicillin 50,000 IU/kg	single i.m. dose
A 50 Early congenital syphilis	benzylpenicillin 50,000 IU/kg	i.v. (or i.m. in two divided doses) for 10 days
Infant with abnormal CSF	OR procaine benzylpenicillin 50,000/kg	i.m. daily for 10 days
Infant with normal csf	benzathine benzylpenicillin 50,000 IU/kg	single i.m. dose
<b>A54.3, P39.1</b>		
Ophthalmia neonatorum	as above	
Prophylaxis due to gonorrhea (A54.3)	ceftriaxone 50mg/kg (max 125mg)	i.m. single dose
	OR	
	kanamycin 25mg/kg (max 75mg)	i.m. single dose
	OR	
	spectinomycin 25mg/kg (max 75mg)	i.m. single dose
due to chlamydia (P39.1)	if above treatment fails to result in improvement and pus continues to drain change to erythromycin syrup 50mg/kg	x 4 daily for 14 days
	OR	
	cotrimoxazole (trimethoprim 40mg/sulfamethoxazole 200mg) oral suspension	x 2 daily for 14 days x 2 daily for 14 days

WHO Model Prescribing Information, Drugs used for sexually-transmitted diseases and HIV Infections WHO 1995, TB/HIV, A Clinical Manual WHO/TB/96.200, Management of sexually-transmitted diseases WHO/GPA/TEMP 94.1, STD Case Management WHO/GPA/TCO/PMT/95.18D

## Annex 6. WHO recommended drugs: EDL drugs and non-EDL drugs for STDs

### WHO Model List of Essential Drugs for Sexually Transmitted Diseases

---

#### 6.2 ANTIBACTERIALS

##### 6.2.1 Beta lactam drugs

**benzylpenicillin** powder for  
injection, 600mg (=1million IU), 3g  
(=5million IU) (sodium or potassium  
salt) in vial

**benzathine benzylpenicillin**  
powder for injection 1.44g benzyl  
penicillin (=2.4 million IU units) in  
5-ml vial

**procaine benzylpenicillin** powder  
for injection 1g (= 1 million IU), 3g  
(= 3 million IU)

**ceftriaxone** powder for injection,  
250mg (as sodium salt) in vial

##### 6.2.2 Other antibacterials

**chloramphenicol** capsule 250mg

**ciprofloxacin** tablet 250mg (as  
hydrochloride)

**doxycycline** capsule or tablet 100mg  
(hydrochloride)

**erythromycin** capsule or tablet  
250mg (as stearate or ethyl  
succinate)

**gentamicin** injection , 10mg, 40mg  
(as sulfate)/ml in 2-ml vial

**metronidazole** tablet, 200-500mg

**spectinomycin** powder for injection,  
2g (as hydrochloride) in vial

**sulfadiazine** tablet 500 mg

**sulfamethoxazole** (400 mg) +  
**trimethoprim** (80 mg) (SMX/TMP)  
tablet 400mg + 80 mg

**clindamycin** tablets 150 mg,  
injection, 150mg (as phosphate)/ml

#### 6.3 ANTIFUNGAL DRUGS

**nystatin** tablet 100,00, 500,000 IU,  
pessary 100,000 IU,

#### 6.4 ANTIVIRALS

##### \*6.4.1 Antiherpes

\***aciclovir** tablet, 200mg, powder for  
injection 250 mg(as sodium salt)

#### 13.1 ANTIFUNGAL DRUGS

**miconazole** ointment or cream, 2%  
(nitrate)

#### 13.5 DRUGS AFFECTING SKIN DIFFERENTIATION AND PROLIFERATION

**podophyllum** resin solution, 10-25%

#### 21.1 OPHTHALMIC PREPARATIONS

**tetracycline** eye ointment 1%  
hydrochloride

**silver nitrate** solution (eye drops)  
1%

---

#### Drugs not on the WHO Model List of Essential Drugs

---

**clotrimazole** pessary 100mg

**cefixime** tablets

**kanamycin** injection

**trichloroacetic acid**

## Annex 7. WHO recommended dosage schedules/treatments for HIV-related diseases and drugs for symptomatic treatment

### Z 21 Asymptotic human immunodeficiency virus infection

#### Drug

zidovudine  
didanosine  
zalcitabine  
others

### B 20-24 HIV-related diseases

Disease	Drug	Dosage
<b>B 20</b>		<b>Please see page 46 for reference of tuberculosis treatment</b>
Mycobacterium tuberculosis	isoniazid tablet 100-300mg(H)	5mg/kg, 3 times weekly for 10 weeks
Pulmonary (A15-16)	rifampicin capsule or tablet 150mg, 300mg (R)	10mg/kg, 3 times weekly for 10 weeks
	pyrazinamide tablet 400mg (Z)	25mg/kg, 3 times weekly for 35 weeks
	streptomycin powder for injection 1g (as sulfate) in vial(S)	15mg/kg, 3 times weekly for 15 weeks
	ethambutol tablet 100-400mg (hydrochloride),(E)	15mg/kg, 3 times weekly for 30 weeks
	isoniazid tablet 100-300mg(H)	
<b>Prophylaxis</b>		
<b>Extrapulmonary tuberculosis (A 17, 18, 19)</b>		
<b>B 20.0</b>		
<b>Myco. avium-intracellulare complex (A31.0)</b>	clarithromycin PLUS ethambutol PLUS rifabutin OR rifabutin PLUS ethambutol PLUS clofazimine capsule, 50mg, 100mg PLUS ciprofloxacin tablet 250mg (as hydrochloride) clofazimine + rifampicin	1000mg orally / day 15mg/kg orally / day 300mg orally per day 300mg orally per day 15mg orally per day 100mg orally per day 1500mg orally per day
<b>Prophylaxis</b>	cycloserine ethionamide clarithromycin OR azithromycin OR rifabutin	1000mg orally daily 1200mg orally daily 300 mg orally per day
<b>B 20.1 Other bacterial infections</b>		
Salmonella (enteric A02.0)	TMP-SMX sulfamethoxazole + trimethoprim tablet, 100mg + 20mg, 400mg + 80mg OR chloramphenicol capsule 250 mg	2 tablets (400 + 80mg) daily for 5 days 500mg 4x daily for 7 days
Shigella (A 03)	TMP-SMX OR naladixic acid tablet 250mg, 500mg	2 tablets (400 + 80mg) daily for 5 days 1g 4x daily for 5 days

Clostridium difficile (A04.7)	<b>metronidazole</b> tablet 200-500mg	400mg 3x daily for 7 days
Legionella species (A 48)		
Salmonella (septicaemia A92.1)	<b>chloramphenicol</b> OR <b>ampicillin</b> powder for injection 500mg (sodium salt) in vial PLUS <b>gentamicin</b> injection 10mg, 40mg (as sulfate) in 2-ml vial	
Haemophilus influenzae (B 96.3)	<b>amoxicillin</b> capsule or tablet 250mg, 500mg (anhydrous) <b>TMP-SMX</b>	
Pneumococcal pneumonia (J 13)		
Helicobacter		
<b>B 20.2 cytomegalovirus disease(B 25)</b>		
Treatment	<i>ganciclovir</i> , powder for injection, 500 mg in vial	5mg/kg by slow i.v. infusion every 12 hours for 14-21 days then 5mg/kg daily indefinitely
Prophylaxis	<i>foscarnet i.v</i> <i>cidofovir</i> <i>ganciclovir i.v</i> <i>foscarnet i.v</i> <i>cidofovir</i>	
<b>B 20.3 other viral infections</b>		
<b>Herpes virus (B 009)(systemic)</b>	<i>aciclovir</i> powder for injection, 500mg in vial	10mg/kg i.v. 3x daily for 10 days
Herpes genitalis (A 60)	<i>aciclovir</i> . for less severe cases tablet, 200mg	5mg/kg iv 3x daily for 5 days OR 5x daily for 7 days
Prophylaxis	<i>aciclovir</i> tablet 200mg	2 tablets 2x daily
<b>Herpes zoster (B02.9) (systemic)</b>	<i>aciclovir</i>	10mg/kg i.v. 3x daily for 7 days
influenza (J11)		
<b>B 20 4 (B37.9) candidiasis</b>		
<b>Oral candidiasis (B37.0)</b>		
Treatment	<b>gentian violet</b> application <b>polyvidone iodine</b> mouth wash <b>chlorhexidine</b> mouth wash <b>nystatin</b> tablet, 500,00IU,  <i>miconazole</i> tablet 250mg <b>amphotericin B</b> lozenger <b>ketoconazole</b> tablet, 200mg	4x daily until symptom free for two days. 4x daily for 10 days 10mg 4x daily 200-400mg 1x daily until remission
<b>Oesophageal candidiasis</b>	<i>clotrimazole</i> <b>ketoconazole</b> tablet, 200mg  <b>amphotericin B</b> powder for injection, 50mg in vial. <b>fluconazole</b> solution for injection 2mg/ml in ampoule,  <b>fluconazole</b> tablet, 400mg	200-400mg 1x daily until remission 1mg/kg by i.v. infusion for 10-14 days 200mg i.v. as initial loading dose followed by 100mg daily for 21 days orally or i.v. as initial loading dose followed by 200mg daily for 4 weeks
Prophylaxis	<b>itraconazole</b> <i>clotrimazole</i> <i>miconazole</i> <b>nystatin</b> 500,00IU tablet <b>ketoconazole</b> 200mg tablet <b>fluconazole</b> (see STD section)	2x daily 1x daily
<b>Vaginal candidiasis</b>		
<b>coccidioidomycosis (B 38)</b>		
Treatment	<b>amphotericin B</b> powder for injection, 50mg in vial.	0.5-1.0mg/kg i.v daily for 6 weeks
Prophylaxis	<b>amphotericin B</b>	0.5mg/kg i.v weekly
<b>Histoplasmosis (B39)</b>		
Treatment	<b>amphotericin B</b>	0.5-1.0mg/kg i.v daily for 6 weeks
Prophylaxis	<b>amphotericin B</b> <b>ketoconazole</b>	0.5mg/kg i.v weekly
<b>aspergillosis (B 44)</b>		

Annex 7. WHO recommended dosage schedules/treatments for  
HIV-related diseases and drugs for symptomatic treatment

<b>B 20.6 pneumocystis carinii pneumonia (B59)</b>		
First line treatment	TMP-SMX tablet	100mg/kg sulfamethoxazole + trimethoprim 20mg/kg orally in two to four divided doses for at least three weeks
	TMP-SMX concentrate for i.v infusion, 80mg + 400mg in 5-ml ampoule	75mg/kg sulfamethoxazole + trimethoprim 15mg/kg in four divided doses administered in 5% glucose solution over 60 minutes. Dosage form should be substituted as soon as tablets can be ingested.
Second line	pentamidine isetionate 200mg powder for injection in vial	4mg/kg by i.v infusion over > 60 minutes daily for at least three weeks
	TMP-SMX and pentamidine Rx require steriod cover	
	prednisolone tablets 40mg methylprednisolone	40mg 2x daily for 5 days followed by 40 mg daily for 5 days then 20 mg daily for 10 days. if pO <sub>2</sub> <70mmHg
Third line	dapsone tablet, 50mg, 100mg PLUS TMP trimethoprim 400mg, 200mg OR primaquine PLUS clindamycin	tablet 7.5mg, 15mg (as diphosphate) injection 150mg (as phosphate)/ml
	atovaquone eflornithine,	injection 200mg (hydrochloride)/ml in 100ml bottles
Others		
Prophylaxis	TMP-SMX	sulfamethoxazole 25mg/kg + 5mg/kg in divided doses daily on three consecutive days each week for life
	pyrimethamine/sulfoxine	25mg pyrimethamine + 500mg sulfoxine 1 tablet 3x daily single dose of 300mg monthly
	pentamidine (aerosol) powder for inhalation, 300mg of pentamidine isetionate in vial	
	dapsone	
<b>B. 20.8 other infectious and parasitic diseases</b>		
Entamoeba histolytica (A06)	metronidazole tablet	500mg 3x daily for 7 days
Giardia intestinalis (A07.1)	metronidazole tablet	250mg 3x daily for 5 days
cryptosporidiosis spp (A07.2) chronic enteric	(Experimental treatment proposed by UNAIDS Paromomycin, azithromycin)	
Isospora belli (A07.3)	TMP-SMX tablet (160mg+800mg Treatment and Prophylaxis: TMP-SMX	4x daily for 10 days.
Nocardiasis (A 43.9) Treatment	sulfadoxine tablet 500mg PLUS pyrimethamine tablet 25mg	2 tablets 2x daily for 6 weeks 2 tablets 2x daily for 6 weeks
	sulfadoxine tablet 500mg PLUS pyrimethamine tablet 25mg	one tablet weekly one tablet weekly
<b>Cryptococcosis (B 45) cryptococcal meningitis</b>		
Treatment	amphotericin B	i.v. 0.5-1.0mg/kg daily for at least 6 weeks
	PLUS flucytosine OR fluconazole tablet 200mg	100-150mg/day orally for 6 weeks 400 mg/day orally (or iv) for 12 weeks
Prophylaxis	amphotericin B	i.v. .0.5-1.0mg/kg weekly
	fluconazole tablet 200mg	one tablet daily
	itraconazole	200-400mg/day orally

<b>Toxoplasma gondi (B58)</b>		
First line treatment	pyrimethamine tablet 25mg	total of 200mg in divided doses on the first day, followed by 75-100mg daily for 6 weeks.
	PLUS sulfadiazine tablet 500mg	total of 6-8g orally or i.v in four divided doses daily for 6 weeks
	OR sulfadoxine tablet 500mg PLUS calcium folinate	2 tablets 2x daily for 6 weeks
Second line	leucovorin (calcium folinate)	5-10mg/day orally
	pyrimethamine	25-100mg/day orally
	PLUS clindamycin	600-1200mg/day i.v. or orally
	OR dapsone	100mg/day orally
	<i>atovaqone</i>	25-100mg/day orally
Prophylaxis	pyrimethamine tablet 25mg	25-50mg daily orally
	sulfadiazine tablet 500mg	2-4g daily orally
	sulfadoxine tablet 500mg	
	clindamycin	
<b>Microsporidia (B60.8)</b>	metronidazole tablet 400mg	3x daily for 7 days
	albendazole (experimental)	

N.B. Recommended dosages for treatment of tuberculosis have been taken from document WHO/TB/97.220.

**HIV-Related Diseases, symptomatic treatment: UNAIDS recommended drugs**

<u>Analgesics</u>	acetyl salicylic acid	tablet, 400-600mg
	paracetamol	tablet, 500mg
	ibuprofen	tablet, 200mg
	indomethacin	tablet, 25mg
	codeine	tablet 30mg
	<i>pentazocine</i>	tablet 50mg, injection 30mg/ml ampoule
	pethidine	injection 50mg/ml ampoule
	morphine	tablet, 10mg (sulfate), injection 10mg (sulfate or hydrochloride) in 1ml ampoule, oral sol.,
<u>Anti-diarrhoeals</u>	<i>loperamide</i>	tablet 2mg
	<i>diphenoxylate</i>	tablet 5 mg
<u>Tranquilizers</u>	diazepam	tablet 5mg, injection 5ml/ampoule
<u>Anticonvulsants</u>	carbamazepine	tablet 200mg
	valproic acid	enteric coated tablet 200mg, 500mg (sodium salt)
<u>Antihistamines</u>	promethazine	1mg/ml syrup
	chlorpheniramine maleate	tablets 4mg
	diphenhydramine	tablet 50mg
<u>Major tranquilizers</u>	chlorpromazine	tablet 100mg, injection 25ml ampoule
	haloperidol	tablet 5mg, 5mg ampoule
<u>Antidepressants</u>	amitriptyline	tablet 25mg
<u>Anticholinergics</u>	atropine sulfate	injection 1mg/ml
<u>Corticosteroids</u>	dexamethazone	tablet 0.5mg, injection 4-5mg/ml
	prednisolone	tablet 5mg, injection 25mg ampoule
<u>Topicals</u>	calamine lotion	
<u>Diuretics</u>	furosemide	tablet 40mg, injection 20mg ampoule

All drugs in italics are not on the WHO Model List of Essential Drugs and the main reference used was the **WHO Model Prescribing Information, Drugs used in sexually-transmitted diseases and HIV Infections**, and a draft copy of a paper entitled **Treatment of HIV Infections** from UNAIDS.

## Annex 8. Recommended current WHO EDL (1997) and non-EDL drugs for HIV-related diseases

Drugs and sections marked with an asterisks were added to the WHO Model List of Essential Drugs at the meeting of the WHO Expert Committee on the Use of Essential Drugs held from 1 to 5 December 1997.

### WHO Model List of Essential Drugs for HIV-related diseases

#### 6.1.1 ANTHELMINTHICS

**albendazole** chewable tablet, 400mg  
**mebendazole** chewable tablet, 100mg, 500mg

#### 6.2 ANTIBACTERIALS

##### 6.2.1 Beta lactam drugs

**benzylpenicillin** powder for injection, 600 mg, 3 g (as sodium salt) in vial  
**amoxicillin** capsule or tablet 250mg, 500mg (anhydrous)  
**ampicillin** powder for injection, 500mg/ 1g (as sodium salt) in vial  
**ceftazidime** powder for injection 250mg ( as pentahydrate) in vial  
**ceftriaxone** powder for injection, 250mg (as sodium salt) in vial

##### 6.2.2 Other antibacterials

**chloramphenicol** capsule 250mg, oral suspension, 150 mg (as palmitate)/5ml, powder for injection 1g (as sodium succinate) in vial  
**ciprofloxacin** tablet 250mg (as hydrochloride)  
**gentamicin** injection 10mg, 40mg (as sulfate) in 2- ml vial  
**metronidazole** tablet, 200-500mg, injection 500mg in 100ml vial  
**naladixic acid**, tablet 250mg, 500mg

**spectinomycin** powder for injection, 2g (as hydrochloride) in vial  
**\*sulfadiazine** tablet, 500 mg, injection 250mg (sodium salt) in 4 ml ampoule  
**\*sulfamethoxazole+trimethoprim (SMX-TMP)** tablet 100mg+20mg, 400mg+80mg oral suspension, 200mg+40mg/5 ml  
**\*injection**, 96 mg/ml in 5 and 10 ml ampoule  
**trimethoprim** tablet 100mg, 200mg, injection 20 mg/ml in 5ml ampoule  
**\*clindamycin capsules\***, 150 mg, injection 150mg (as phosphate)/ml

##### 6.2.3 Antileprosy drugs

**clofazimine** capsule, 50mg, 100mg  
**dapsone** tablet, 50mg, 100mg

##### 6.2.4 Antituberculous drugs

**ethambutol(E)** tablet, 100-400mg  
**isoniazid(H)** tablet 100-300mg  
**isoniazid + ethambutol** tablet 150+400mg  
**pyrazinamide (Z)** tablet 400mg  
**rifampicin (R)**capsule or tablet 150mg, 300mg  
**rifampicin+ isoniazid** 150mg+75mg, 300mg+150mg, 150mg+150mg  
**rifampicin + isoniazid + pyrazinamide** tablet 150mg+75mg+400 mg, 150mg+150mg+500mg  
**streptomycin (S)** powder for injection 1g (as sulfate) in vial

### 6.3 ANTIFUNGAL DRUGS

**amphotericin B** powder for injection, 50mg in vial.

**ketoconazole** tablet 200 mg, oral suspension 100mg/5ml.

\*alternatives to ketoconazole:

\***fluconazole** solution for injection 2 mg/ml in ampoule,

\***fluconazole** tablet 200mg

\***itraconazole** 200-400 mg/day PO

**nystatin** tablet, 500, 000 IU

**flucytosine** capsule, 250mg, infusion 2.5 g in 250 ml

### 6.4 ANTIVIRALS

#### \*6.4.1 Antitherpes

\***aciclovir** tablet, 200mg, powder for injection 250 mg(as sodium salt)

#### \*6.4.2 Antiretrovirals\*

\***zidovudine**, only for prevention of mother to child transmission of HIV, tablet, 100mg, 250 mg, injection 10mg/ml in 20ml vial, oral solution 50mg/5ml

#### 6.5.2. Antileishmaniasis drugs

**pentamidine isetionate**, powder for injection , 200mg, 300mg in vial

#### 6.5.3 Antimalarial drugs

**primaquine** tablet 7.5mg, 15mg (as diphosphate)

**sulfadoxine/ pyrimethamine** tablet, 500mg+25mg

#### \*6.5.4 Antipneumocystosis and antitoxoplasmosis drugs

\***pyrimethamine** tablets, 25 mg

\***sulfamethoxazole+trimethoprim** injection, 20 mg/ml in 5 ml ampoule

\***pentamidine** tablet, 200mg, 300 mg

#### 6.5.5 Antitrypanosomal drugs

**eflornithine**, injection 200mg (hydrochloride)/ml in 100ml bottles

### 8.2 CYTOTOXICS

**calcium folinate** (leucovorin) tablet, 15mg

### 13.1 ANTIFUNGAL DRUGS

**miconazole** cream 2%

### 13.2 ANTI INFECTIVE DRUGS

**methylrosanilinium chloride** (gentian violet) aqueous solution 0.5%

### 13.3 ANTI INFLAMMATORY AND ANTIPRURITIC DRUGS

**calamine** lotion

### 15.1 ANTISEPTICS

**chlorhexidine** solution 5% (digluconate) concentrate for dilution

**polyvidone**, solution, 10%

### **Drugs not on the WHO Model List of Essential Drugs used for HIV-related diseases**

**amphotericin B** lozenges

**clarithromycin** 1000mg/day PO

**rifabutin** 300mg/day PO

**cycloserine**

**ethionamide**

**clotrimazole**

**paromomycin** 200mg/day PO

**azithromycin** 500-1250mg/day PO or 1200mg/week PO

**ganciclovir** powder for injection, 500mg in vial, 3000mg/day PO

**foscarnet** 90-120mg/kg/day IV

**cidofovir** 5mg/kg/week or 5mg/kg/2 weeks

**atovaquone** 25-100 mg/day PO

**trimetrexate**

**miconazole** oral gel

**pentamidine** (aerosol) powder for inhalation, 300mg of pentamidine isetionate in vial

**Drugs from the WHO Model List of Essential Drugs used for symptomatic treatment of HIV-related diseases**

2.1 NON-OPIOID ANALGESICS

**acetylsalicylic acid** tablet, 100-500mg

**ibuprofen** tablet, 200mg, 400mg

**paracetamol** tablet, 100-500mg

2.2 OPIOID ANALGESICS

**codeine** tablet 30mg

**morphine injection**, 10mg (sulfate or hydrochloride) in 1 ml ampoule; oral solution 10mg/5ml; tablet 10mg (sulfate)

**pethidine** 50mg/ml in 2ml ampoule, tablet 50mg-100mg

3 ANTIALLERGICS AND DRUGS USED IN ANAPHYLAXIS

**chlorphenamine** maleate tablets 4mg, injection 10mg in 1ml ampoule

**diphenhydramine** tablet 50mg

**dexamethasone** tablet 500µg, 4mg, injection, 4mg (as disodium phosphate ) in 1-ml ampoule

**promethazine** 1mg/ml syrup (to be found in the WHO EDL section 1.3 Preoperative medication and sedation of short term)

**prednisolone** tablet 1mg, 5mg

5.ANTICONVULSANTS

**carbamazepine** scored tablet 100-200mg

**diazepam** injection 5ml/ampoule

**valproic acid** enteric coated tablet 200, 500mg (sodium salt)

13.3 ANTI-INFLAMMATORY AND ANTIPRURITIC DRUGS

**calamine** lotion

16 DIURETICS

**furosemide** tablet 40mg, injection, 10mg/ml in 2ml ampoule

17.2 ANTIEMETICS

**promethazine** 1mg/ml syrup

17.5 ANTISPASMODICS

**atropine** tablet 1mg (sulfate)

injection 1mg (sulfate) in 1ml ampoule

24.1 DRUGS USED IN PSYCHOTIC CONDITIONS

**chlorpromazine** tablet 100mg (hydrochloride),

injection 25ml ampoule

(hydrochloride)/ml

in 2ml ampoule

**haloperidol** tablet 2mg 5mg, injection, 5mg in 1-ml ampoule

24.2 DRUGS USED IN MOOD DISORDERS

**amitriptyline** tablet 25mg (hydrochloride)

24.3 DRUGS USED IN GENERALIZED ANXIETY AND SLEEP DISORDERS

**diazepam** scored tablet 2mg, 5mg

---

**Drugs not on the WHO Model List of Essential Drugs used for the symptomatic treatment of HIV-related disease**

**pentazocine** tablet 50mg, injection, 30mg/ml ampoule

**loperamide** tablet 2mg

**diphenoxylate** tablet 5mg

---

## Annex 9. Drugs for STDs in emergencies

The Division of Family and Reproductive Health is in the process of finalizing "Guidelines for the management of reproductive health services during conflicts and emergencies". Within this document is the description of an Emergency Reproductive Health Kit which includes drugs needed for the treatment of STDs. They are displayed in the following grid (next page). Diseases are divided syndromically and no attempt is made to provide for all sexually-transmitted diseases. On the next page, is a model or template summarizing the treatment of STDs. In the left hand column are the STDs and syndromes which may be divided into priority 1 and priority 2 diseases. The second column contains the "standard treatments". While it is not possible to have a universal standard treatment for gonorrhea ciprofloxacin may be considered the standard treatment in situations of conflict and displacement where antibiotic sensitivities are not known. The third column contains alternative drugs which are on the WHO Model Essential Drugs List. To the right of the heavy black line are non-essential drugs lists.

Such a template where diseases are prioritized and treatments ranked may be used for considering treatments for HIV-related opportunist infections. One of the objectives of this initial report is to help start the process of identifying which drugs, needed for HIV-related diseases, now to the right of the "black line", should cross to the left.

**STD drug requirements and costs: 10.000 people for 3 months \*\*\***

	%	Numbers	Treatment protocol	Cost/Tx (in \$)	Total drug needs	Total cost (in \$)
Total population		10,000				
Population at risk. 15-44 yrs	50%	5,000				
Expected % STD	5%	250				
Expected % genital ulcers	20% of 250	50	benzathine benzylpenicillin 2.4 MU x 1 + erythromycin 500mg x 3 x 7	0.4+ 1.1	50	75
Expected % urethral discharge	50% of 250	125	ciprofloxacin 500mg x1 + doxycyline 100mg x 2x 7	2.5 + 0.3	125	350
Expected % cervicitis	5% of 250	13	ciprofloxacin 500mg x1 + doxycyline 100mg x 2x 7	2.5 + 0.3	13	35
Expected % vaginitis	25% of 250	63	metronidazole 250mg x 8 + nystatin tab x1x14	0.65 + .835	500	59
Total						519

\*\*\* From the WHO draft "Guidelines for the management of reproductive health services during conflict and displacement" derived from "the treatment of STDs according to WHO GPA management of STDs using a syndromic approach Costs are approximate, 1995 (1994)"

## Model for considering STD treatments

Symptom/Disease	Model Essential Drugs List		Other drugs
	Standard treatment drugs***	Alternative treatment drugs	
<b><u>Priority 1 diseases</u></b>  Syphilis (GU) Chancroid (GU) Gonorrhoea UD/VD) NSU/chlamydia UD/VD) Trichomonas (VD) Candida (VD)	benzathine benzylpenicillin erythromycin ciprofloxacin doxycycline metronidazole nystatin	procaine benzylpenicillin ceftriaxone spectinomycin chloramphenicol thiamphenicol gentamicin TMP-SMX clindamycin sulfadiazine ceftriaxone	cefixime miconazole clotrimazole kanamycin
<b><u>Priority 2 diseases</u></b>  Ophthalmia neonatorum  Granuloma inguinale  Genital warts  Herpes genitalis	tetracycline ointment 1%  TMP-SMX  podophyllum resin	AgNO3 drops 1%	erythromycin ointment 1%    aciclovir
<b>10 diseases</b>	<b>9 standard treatment drugs</b>	<b>21 total EDL drugs</b>	<b>6 Non EDL drugs</b>

\*\*\*

Terms other than standard which might be applied to this group of drugs

1st line  
 1st choice  
 recommended  
 recommended 1st choice  
 1st choice  
 core  
 best treatment  
 selected

selected essential  
 selected priority  
 indispensable  
 vital  
 basic  
 favored  
 priority  
 priority essential

## Bibliography

### WHO Major publications and documents

WHO Model Prescribing Information. Drugs used in Mycobacterial Disease, 1991.

WHO Model Prescribing Information Drugs used in sexually-transmitted diseases and HIV Infection, 1995.

WHO Model Prescribing Information Drugs used in Parasitic Diseases, 1995.

TB/HIV, a Clinical Manual WHO/TB/96.200.

WHO Technical Report Series 810 Management of patients with sexually-transmitted diseases, 1991.

Treatment of Tuberculosis, Guidelines for National Programmes, Second Edition 1997 WHO, Geneva, WHO/TB/97.220.

AIDS in Africa, a manual for physicians, Peter Piot et al. WHO Geneva, 1992.

### WHO papers and documents

Guidelines for the clinical management of HIV Infection in Adults WHO/GPA/HCS/91.6.

Guidelines for the clinical management of HIV Infection in Children WHO/GPA/HCS/93.3.

Management of sexually-transmitted diseases WHO/GPA/94.1

Assessment of STD drug needs selected case studies GPA/STD/92.2 (STD in The Gambia, Zimbabwe, Sri Lanka, Papua New Guinea, Jamaica and Honduras by Dr.Q.M. Islam).

Core list of Essential Drugs for the treatment of sexually-transmitted diseases, GPA/STD/92.3.

WHO's present activities to improve provision of drugs to developing countries GPA/CRD/IFP.2/92.1.

Assessment of the needs of drugs for TB, candidiasis and anti-retrovirals in developing countries GPA/CRD.2.92.2.

Overview of common HIV-related diseases in developing countries and drugs and vaccine requirements for appropriate treatment GPA/IFP/3.

Impact of the HIV Epidemic on Essential Drugs and Supplies, Republic of Zambia, DAP Nov., 1988.

Consultation on opportunistic infections in developing countries WHO, 18-21 September, 1989, p.7.

HIV and Essential Drugs in Malawi, Lissner and Lunt, R 26 Nov. 9 Dec. 1989.

Treatment of HIV infection, UNAIDS/draft, January 1997.

AIDS-drug Cost Estimator, WHO, GPA/DAP, January 1990.

Guidelines for making rational choices on use of drugs and clinical management within AIDS prevention and control programmes: Laing R.O. WHO GPA April, 1990.

HIV/AIDS Surveillance in Europe (WHO), No 49, March 1996 p 25.

### **Other sources**

AIDS in Africa: what drugs do carers want or need? Lamont A C et al *Tropical Doctor*, 1996 April, 72-76, pp. 72-76.

Bed Occupancy due to HIV/AIDS in an urban hospital medical ward in Uganda, Tembo G et al. *AIDS*, 1994, Vol. 8 No 8, pp. 1169-1171 (50% of medical admissions were HIV positive).

The mortality and pathology of HIV infection in a West African city, Lucas S B, *AIDS*, 1993, Vol. 7 No 12, p 1569-1578.

AIDS-defining disease surveillance, Jones et al. *AIDS*, 1994, vol. 8, No 10, p. 1491.

Opportunistic diseases amongst HIV-infected persons, Chan et al. *AIDS*, 1995, Vol. 9, No 10, pp. 1148-1149.

How HIV-related Opportunistic infections vary round the world, *The AIDS Report*, Harvard 1994, (Spring) pp 3-7.

Epidemiology and Prevention of Acquired Immunodeficiency Syndrome, Drotman D.P. and Curran, J.P., *Public Health and Preventive Medicine*, 13th Edition p.118 (?1993).

Trends in infectious diseases and cancers amongst persons dying of HIV infection in the United States from 1987 to 1992, Selik R.M. et al. *Annals of Internal Medicine* 15 Dec. 1995, Vol. 123, No. 12, pp 933-936.

Aids in Africans living in London, O'Farrel N, et al. *Genitourinary Medicine*, 1995; 71, 358-362.

Autopsy proven causes of death in HIV patients treated for tuberculosis in Abijan, Côte d'Ivoire, Greenberg, E.A. et al. *AIDS*, 1995, Nov. Vol. 9, No, 11, pp 1251-1254.

*Clinical Guidelines, Diagnostic and Treatment Manual*, MSF, 1993.

Opportunistic diseases amongst HIV-infected persons, Chan et al. *AIDS*, 1995, Vol. 9, No 10, pp. 1148-1149.

Aids-defining disease surveillance Jones et al. *AIDS* Vol. 8 No 10 p 1491.

Proven causes of death in HIV-infected patients treated for tuberculosis in Abijan, Côte d'Ivoire, Greenberg A.E. *AIDS*, 1995, Vol. 9, No 11, pp. 1251-1254.

Trends in Infectious Diseases and Cancers amongst persons dying of HIV infection in the United States from 1987 to 1992, Selik R.M. *Annals of Internal Medicine* vol. 123, No.12, pp 933-936.

AIDS-defining illness and survival, Luo et al. *AIDS*, 1995, Vol. 9 No 1 p 61.

\* \* \* \* \*