

Chapter 36

Drug Policy and Medication Availability

Overview

The majority of people needing palliative care in Africa do not have the opportunity to receive it. Lack of access to the necessary drugs is a principal limitation even though medicines required for symptom control are relatively cheap.

In 2003, approximately 6,000 people died of AIDS each day in sub-Saharan Africa (SSA). In that year approximately six million people in developing countries would have benefitted from antiretroviral therapy (ART), 4.1 million of whom lived in SSA. ART was only available to 440,000 of the people who would benefit from ART (MSF, 2003).

Access to ART is increasing rapidly following global and national efforts to decrease the cost and to increase funding. Rapidly increasing availability means policy makers must plan carefully to ensure correct use, reliable supplies and co-ordination of NGO and national programmes. Health care workers (HCWs) have a very important role in helping ensure correct and appropriate use and in advising policy makers. That said, it must not be forgotten that access to ART is still very limited in Africa, requiring that policies ensure that ART dissemination be integrated with palliative care and HIV prevention policies.

HCWs need to understand the international and national laws and policies relating to palliative care drugs. To use the drugs, HCWs must be familiar with laws covering their handling. Access to comprehensive palliative care and ART requires clear integrated policies. HCWs can play a pivotal role in advising and shaping the formation and on-going evolution of national policies.

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Overcoming Barriers To Drug Availability

Why Drugs are Not Available

The drugs required for palliative care are not available (IAA, 2002; Adams, 2000) for the following reasons:

Financial Issues:

- Poverty
- High cost of drugs
- Cost of transport
- Low or no wages for staff

Health System Issues:

- Shortage of trained staff, especially in rural areas (doctors, assistants, nurses, pharmacists, drug regulatory, patent officers, therapists)
- Erratic drug supplies
- Limited distribution
- Lack of regulation during distribution
- Confusing procedures
- Inaccessibility (many patients are too ill or poor to travel to health services)
- Uneven distribution of services (patients are often reluctant or afraid to travel, experience language barriers, or fear the unknown)
- Limited access to voluntary HIV counselling and testing (VCT)

Social Problems:

- Stigma and discrimination
- Lack of knowledge
- Denial of diagnosis
- Misinformation
- Inadequate integration of traditional healers into comprehensive care

Educational Issues:

- HCWs lack knowledge of
 - Palliation and symptom control
 - Use, scope, and side effects of ART
 - Treatment of opportunistic infections (OIs)
- Patients and carers fear that using opioids for analgesia will cause addiction and/or abuse
- Patients and carers lack knowledge of
 - Symptom control
 - HIV transmission and symptoms
 - Scope of ART

How to Make Drugs Available

HCWs must have access to all the necessary core drugs in order to be able to provide comprehensive palliative care. Overcoming barriers to availability requires:

- Reliable supplies
- Minimal cost of drugs and tests
- Patient access to health services
- Social acceptability of drugs
- Accountability for drug supply
- Education

The Value of a National Drug Policy

Developing a national policy on palliative care and one on AIDS and ART use confirms government policy and commitment. National policies:

- Allow identification and setting of priorities
- Help identify resources
- Enhance co-operation between public services, stakeholders, and donors
- Establish standards
- Maximise quality and prices of drugs, diagnostics, and equipment
- Allow adequate planning of resources and funding
- Provide a basis for resource mobilisation

It is essential to integrate policies and guidelines related to:

- Prevention
- Diagnosis
- ART
- Anticipating and mitigating side effects
- Minimising drug resistance
- Treatment of OIs
- Palliative care
- Education

When developing a national policy wider issues need to be accounted for and addressed:

- Food shortages
- Clean water
- Other diseases
- Unemployment

National policies should complement a country's essential medicines list (EML) and national treatment guidelines.

Essential Medicines Lists (EML)

Why an EML is important

The WHO model essential medicines list (EML) aims to detail the most efficacious, safe and cost-effective drugs required to meet the health needs of the majority of the population. Cost limitations were removed from the WHO criteria for essential drugs in 2001 – so essential but expensive drugs such as ART are now included. Cost-benefit analysis is used in compiling EMLs to ensure that efficacy and minimising side effects are considered alongside cost. Most countries adapt the WHO EML to produce their own EML based on local epidemiology, drug pricing, and resistance patterns.

The advantages of having a national EML include:

- Improved availability: Fewer drugs must be obtained and managing stock is easier.
- Lower cost: Whilst safety and efficacy are not compromised, generic drugs or the cheaper of two pharmacologically similar drugs are used. Bulk purchasing is practiced.
- Increased safety:
 - With fewer drugs, HCWs become more familiar with indications, dosages, interactions, side effects, and contraindications.
 - Decreased drug-related incidences
 - Drugs included are mainly generic or have been used clinically for a long time so potential problems are well known
- Focused training of HCWs
- Decreased resistance to antibiotics, antifungals, and antivirals
- Opportunity to critically examine all available evidence on safety and efficacy:
 - Individual HCWs have more difficulty obtaining information on a specific drug – centrally more resources are available to critically examine evidence.
 - The global market makes an enormous number of drugs available, and some traders are motivated by profit rather than safety, efficacy, and appropriateness in a particular market.
 - Some traders are not adequately trained.

Selecting Drugs for an EML

When recommending a drug for an EML, consider whether it is:

- Effective
- Essential for locally common diseases and symptoms
- The drug with fewest side effects
- Safe in the target population e.g. children, pregnancy
- Easily obtainable
- Inexpensive, cost-effective

In selecting drugs it is important to be realistic about their cost-benefit ratio. Resistance both in individual patients and the local population as a whole is a serious risk if patients can only afford part of a prescribed course of antivirals, antibiotics, or antifungals. There are increasing reports of primary resistance to ARVs (Waters, 2004). Paying for drugs can have a significant impact on the whole family, leaving no money for food, seed, or school fees. Therefore, cost-benefit analysis should be considered in the widest sense in each case.

How HCWs Can Influence the Selection of Drugs on Their National EML

Treatment and EML guidelines should be reviewed and updated regularly as new drugs become available and with changes in price, local resistance patterns, and disease burden. HCWs are in an ideal position to help develop an appropriate country EML and national treatment guidelines. See Appendix 2 for a suggested EML for palliative care services.

To assist in developing your national EML, provide to your National Drug Authority and Ministry of Health (the pharmaceutical officer and relevant department heads, such as HIV/AIDS) details of drugs you think should be included. Give as much detail as possible (if you do not have all the information, submit as much as you can), including:

- Indication(s)
 - Incidence of condition(s) drug used for in your country
- Current standard treatment or state that there is no comparison available
- Treatment details
 - Dose, frequency, duration
 - Need for specialist diagnostic or treatment facilities or skills
 - Regulatory status in country of origin
- Use in special populations (children, pregnancy)
- Effectiveness compared to standard treatment or other drugs used
 - Search strategy for clinical evidence
 - Summary of available data
 - Details of clinical trials
 - inclusion & exclusion criteria
 - number of patients recruited and number used
 - incidence of side effects seen
 - significance level of results
- Side effects and comparison of these to other drugs used for each indication
- Total cost (e.g., include monitoring facilities required) per treatment course or month
 - Cost of treatments already available
 - Cost of drugs in same pharmacologic group

Tips:

A drug is more likely to be included on your national EML if it is on the WHO EML.

Always examine critically information from drug companies and be aware that sometimes drugs readily available in Africa have been banned in Europe and the U.S.

The WHO model list is reviewed every 2 years (next review March 2007) and applications can be made for inclusions, changes, or deletions through the WHO web site (<http://www.who.int>).

National EMLs can also be influenced through good practice (you may end up treating family members of influential people).

Monitoring for Adverse Drug Reactions and Resistance

Assuring Safety and Effectiveness of Drugs

Adverse drug reactions are a serious problem throughout the world (WHO, 2002). Continual monitoring of the effectiveness and side effects of drugs allows increased safety, effectiveness, and earlier detection of problems, especially in specific patient groups.

Although safety and effectiveness is tested prior to licensing, pre-marketing safety data has limitations:

Children, patients with co-morbidities, pregnant and breastfeeding women, and elderly are usually excluded.

To detect an adverse drug reaction (ADR) which has an incidence of 1 in 10,000 people, >30,000 patients need to be treated. Most drugs have been studied in <5,000 humans before marketing, so when they are licensed only the most common ADRs are known.

The time scale with pre-marketing studies is limited and therefore information regarding chronic toxicity is limited. A number of serious ADRs to ART occur with long-term multiple drug therapy, and thus have not have been seen in the standard follow up time for clinical trials (Bisson, 2003).

Monitoring ADRs is especially important in providing palliative and HIV/AIDS care in Africa:

- Many drugs used in palliative care are used outside their licensed indication or licensed route.
- HIV and co-morbidities can alter how the drug is handled by the patient.

- Research is often carried out on Western populations, the occurrence of ADRs is different by country (and even by regions within countries). This may be due to differences in:
 - Diseases
 - Genetics
 - Diet
 - Drug manufacturing processes and storage conditions
 - Prescribing practices (indications, dose, and availability)
 - Use of traditional and complementary drugs that may alter handling of other drugs
- Monitoring allows identification of substandard and counterfeit products.

Tips:

Post-marketing surveillance is essential.

Effectiveness of monitoring depends on the active participation of HCWs and caregivers.

Numerous cases of drug withdrawals, restrictions, or relabelling following post-marketing reports come from astute HCWs and caregivers.

Data derived from monitoring within SSA is likely to be more relevant and of educational value. This data can then be used to help national regulatory decision making.

Monitoring for Toxicities and Resistance

Better safety data may also give insight into the mechanism of toxicity, identify patients at high risk of toxicity, help develop protocols for toxicity monitoring and management, and eventually assist in drug development. It is also important to monitor and report possible resistance.

Information on suspected toxicities should be disseminated as widely as possible so that other HCWs can be vigilant and help clarify links (e.g., whether toxicity is more likely when the drug is given with another drug, or when the patient has renal impairment).

Enhanced understanding of toxicities associated with ART and symptom control will improve care.

If Warned of Possible Toxicities Patients Will Have (Attawell, 2003):

- More accurate expectations
- Less disappointment and frustration when chronic, low-grade toxicities occur
- Increased trust in HCWs
- More openness and increased adherence

HCWs Will be Able to Tailor Advice to Individual Patients About:

- Timing of initial therapy
- Choice of regimen
- Drug substitutions or discontinuations

What to Do If You Suspect an ADR or Drug Resistance

Assessment

ADRs are often difficult to identify in patients with HIV/AIDS owing to the large number of treatments being prescribed and the numerous ways in which the disease and OIs can present.

If suspicious of an ADR, drug interaction, or resistance check and consider:

- What drug(s) the patient has *actually been taking* (not what has been prescribed) including doses and frequency
- Time between starting the suspected drug and adverse event
- Whether another drug has been started recently (including herbal & traditional medicines) that might interact
- Possible alternative causes
- Effect on adverse reaction if drug has been stopped

Reporting

An ADR should be reported unless it is a well known minor reaction. Report all ADRs to drugs licensed within the last five years even if they are minor and included in the product literature, as it is important to evaluate their frequency. Especially important is reporting ADRs in special population groups such as AIDS patients, children, pregnant women, and the terminally ill, where handling of drugs is often different.

Also report if there is a lack of efficacy, possible resistance, or pharmaceutical defect.

How to Report ADRs

Local case report forms should be available from your National Drug Authority. Some countries have these forms included in their national formularies (e.g., South Africa, Zimbabwe). If your country does not have official forms it is still of value to report any suspected ADRs and interactions. All possible relevant information should be included (the points listed above plus the patient's main disease and co-morbidities, the suspected reaction(s) and your contact details in case further information is required).

It is also very useful to write up case reports in local journals and communications to highlight possible problems to other HCWs.

WHO is developing the Global HIV Drug Resistance Surveillance Network to assist countries in monitoring, review resistance prevalence, improve understanding of factors that lead to resistance, and identify strategies to minimise the emergence and spread of drug resistance (<http://www.who.int/drugresistance>).

Developing National Drug Policies

Advocating for a National Drug Policy

Local Government

Education and support of local government officials aids planning and informed decision-making about drug requirements, the allocation of the drug budget for other health problems, and the balance between prevention, treatment of OIs, ART, and palliative care.

Policy Makers

Educating policy makers is critical to improving drug access, especially access to morphine. By educating policy makers Hospice Uganda facilitated palliative care being included as one of the essential clinical components in Uganda's five-year strategic plan, ensuring resources allocation and highlighting its importance. Policy makers should be educated in the clinical uses of drugs and in any legislation or policies that limit or prevent access.

Research

Policy should also encourage research, both in clinical practice and in methods of delivering service. Some of the research conducted in developed countries is not readily transferable (e.g., treatment and diagnostic tools in the West are developed for B subtype HIV, which is rarely found in SSA).

National Policy for Palliative Care

A survey on end-of-life care in HIV/AIDS in SSA highlighted the urgent need for palliative care (Harding, 2003). A national policy on palliative care should include ensuring access to oral morphine (addressing fears, who can prescribe it, ensuring a cheap and reliable supply). The absence of national policies and government officials' lack of understanding about the importance of palliative care were contributing issues in a number of countries.

Inclusion of palliative care in Uganda's five-year health plan has increased access to palliative care and the drugs required (Stjernsward, 2004; Ramsay, 2003). Advocacy on the part of HCWs played an important role in making this happen, demonstrating the essential advocacy role palliative care health workers can play. Teaching other HCWs and having discussions with Ministry officials is important. In addition, using palliative care principles in individual cases demonstrates the value of palliative care to other HCWs by example.

See other chapters in Part 6 (The Public Health Approach to Palliative Care) for more on national palliative care policies and on the components of care that support medication availability, such as sufficient human resources and adequate education of health providers, patients and carers, and community members.

Linking ART and Palliative Care National Policies

National policies on ART need to link in with a national palliative care policy as well as a policy on prevention of HIV infection (see Box 36.1 and Box 36.2).

Some projects have found a lower-than-anticipated uptake of ART. It is important to recognise that without also strengthening health services, infrastructure, human resources, referral systems, and education, establishing an ART programme can strain services and personnel, resulting in negative outcomes. Successful introduction of ART has been achieved in Chile following the formation of an advisory committee to manage treatment guidelines, coordination, logistics, and drug procurement (Attawell, 2003).

UNAIDS recommends including HIV/AIDS plans in poverty reduction strategic papers and heavily indebted poor countries documents, since addressing the epidemic is central to poverty reduction.

Box 36.1:

Benefits of ART in Resource-Limited Countries

Benefits of Using ART:

- ART can be used safely and effectively in resource-poor settings and by poor people.
- Reduction in OIs often makes managing HIV/AIDS patients on ARVs at primary care level easier than managing patients not on ARVs.
- Availability of treatment boosts staff morale because of the shift from care of the dying to helping patients return to good health.
- Synergy between prevention and treatment: the availability of treatment is an incentive to seek voluntary counselling and testing (VCT) to ascertain HIV status.
- Access to ART encourages patients to stay in the medical system.

Box 36.2:

Why Palliative Care Is Needed Even with ART

According to 2003 estimates:

- Zambia plans to provide ART for 10,000 adults; however, there are >500,000 people living with HIV/AIDS in Zambia.
- Malawi is planning to scale up access to reach approximately 25,000 patients, but there are 1 million people with HIV/AIDS, a third of whom might benefit from ART.
- In Mozambique, triple therapy cost was reduced (~ \$80 per month following generic supply from an Indian manufacturer) but this was still twice the average monthly wage.

Thus provision of comprehensive palliative care remains vital throughout Africa not only for those receiving ART but for those who will never have access.

Source: Attawell, 2003.

Structure of National Policies

The elements of a national policy are similar for both HIV/AIDS and palliative care policies.

Experience in Malawi and Kenya confirm that clear goals are necessary to identify priorities for scaling up access and integration into national strategic planning and existing health services (Attawell, 2003)

National policies need to be flexible and reviewed regularly so they can reflect changes in the wider environment, such as ARV price changes.

National Policy Should Include:

1. Goals and priorities
2. Guidance on integration with other policies and guidelines
3. Development of national guidelines
4. Generic drug quality assessment
5. Resources to allow accurate and continual quantification of requirements
6. Measures to assure uninterrupted drug supply (predicting demand)
7. Effective integration of communities, private health sector, donors, and traditional practitioners, including traditional birth attendants
8. Continual evaluation and adaptation of guidelines as appropriate
9. Monitoring the rational use of ARVs and other drugs
10. Ensuring proposed projects are viable
11. Education of:
 - Health personnel
 - Caregivers
 - Patients
 - Community
12. Strengthening existing health facilities:
 - Access and referral process
 - Guidance and resources for storage requirements
 - Maintenance and servicing of laboratory equipment

Including Children in National Drug Policies

National policies should specifically *include* children. WHO has expressed concern that many ART programmes exclude children (MSF, 2004).

2.5 million children worldwide live with HIV/AIDS

700,000 children <15 years old are newly infected each year

88.6% of these children live in SSA

The success of preventing mother to child transmission in developed countries has meant that there is little profit in paediatric formulations. Consequently, despite the increasing need in SSA, there are few paediatric formulations. There are no paediatric fixed-dose combinations, resulting in more expensive forms, unpleasant liquids, use of large volumes, and crushed tablets, increasing the likelihood of poor adherence and thus treatment failure and resistance.

Many serological diagnostic methods for HIV are not reliable for children <18 months of age and most laboratory tests for CD4 cell counts are not designed for use in young children.

Tip:

HCWs should help identify formulations, diagnostic and monitoring equipment required for children and campaign for their development.

Licensed and Unlicensed Drugs

The indications for which a drug can be used varies between countries, and in some cases varies according to the form of a drug. Many drugs are used outside their licence in palliative care (and paediatrics), either being given for a different indication or by a different route. Whilst in most situations this constitutes recognised clinical practice, use outside a licence becomes the HCW's responsibility.

Treatment Guidelines

National guidelines are essential. Guidelines aid in:

- Rational drug use
 - Only necessary drugs
 - The correct drug for the condition
 - The correct dose
 - The correct length of time
- Drug procurement: Care plans can be used to negotiate reduced prices with pharmaceutical companies.
- Lower and more predictable drug resistance
- Training of HCWs (standard clinical management protocols and limited number of drugs)
- Patient education
- Monitoring and evaluation

National guidelines should be evidence-based where possible. International guidelines should be carefully assessed and adapted. Data is often from clinical trials in developed countries.

Drug Supply

International Laws and Treaties Regulating Drug Supply

A number of international laws and treaties relate to drug handling. Of relevance to palliative care are the international treaties covering opioids and some antipsychotic drugs. Opioids are regulated under the 1961 UN Single Convention on Narcotic Drugs (amended by 1972 and 1988 protocols). The purpose of regulation is to guarantee the availability of opioids and other specified drugs for medical use, whilst preventing abuse. Drugs and raw materials are classified into different schedules to allow more stringent measures for some drugs than others. The convention:

- Stipulates rules regarding production, manufacture, and distribution
- Requires registration of anyone handling these drugs
- Monitors their use within each country
- Requires each country to estimate the annual amount of each specified drug it requires for medical use

The International Narcotics Control Board (INCB)

The INCB monitors implementation of the convention. The INCB requires each country to submit:

1. An annual estimate of the quantity of each specified drug it will require for medical use
2. Quarterly forms detailing the use of the specified drugs within the country

Before a country is allowed to import or grow any opioids the INCB must confirm that the annual estimate is reasonable. Once confirmed, the amount imported or produced should not exceed the national estimate. If medical demand increases beyond the submitted estimate an amendment can be submitted to the INCB. The INCB must confirm amendments as soon as possible, typically in a week. It is the governments' responsibility to:

Quantify national requirements

Specify the calculation method

Justify any large change(s) in the quantities required (e.g., expansion of palliative care services which increase access to morphine for pain relief)

If estimates are not submitted, the INCB bases that country's requirement on the previous year's estimate. This 'estimate system' applies to all countries world-wide, whether or not they are officially signed to the conventions.

Estimation of National Drug Usage

HCWs should advise governments on how increases in palliative care services might alter the national medical requirements for morphine, codeine, and other stipulated drugs. To estimate increases consider:

- The number of new patients accessing palliative care services (dependent on distribution, cost, prescribing habits, number of patients who access conventional medicine)
- The percentage of these patients likely to require morphine
- The average dose of morphine any patient requiring morphine is likely to need (often different for patients with cancer or AIDS)

Information for estimates can often be obtained from existing palliative care providers either within your country or from other African countries. Hospice Uganda and Mildmay, Uganda have good records of the percentage of their patients requiring morphine and the average dose.

Accountability

Factors limiting access to opioids include:

- Fear from government officials and some HCWs that opioid abuse will occur (either by HCWs, patients, or following diversion)
- Reluctance by HCWs to handle opioids because they are afraid of being accused of opioid abuse.

However, increasing availability of opioids for medical use does not lead to an increase in illicit use (Porter, 1980).

To allay fears and to comply with the INCB requirement to submit quarterly returns detailing use, accurate records of the movement of opioids and other drugs which might be diverted should be kept. Records should include details of:

- Quantities aquired
- Supplier
- Amounts dispensed or supplied
- Whom they were supplied to

To ensure accountability records need to be kept throughout the whole supply chain:

importation → manufacture → wholesale → transportation → movement within health centres → supply or destruction of expired drugs

Examples of suitable registers for keeping records for all stages can be found in the Guidelines for Handling Class A Drugs, produced by the Ugandan Ministry of Health, 2001 (available from Hospice Uganda).

Although not required by law, similar records are useful for tracking ARVs, to minimise 'leakage' and aid in stock control and uninterrupted supplies.

National Drug Laws

National Drug Regulatory Authorities

Drug laws vary between different countries. National Drug Regulatory Authorities (NDRAs) regulate their implementation. NDRA are responsible for drug evaluation and approval, and for guaranteeing the quality, safety, and efficacy of drugs registered within the country. Policies should ensure the NDRA has adequate capacity.

Drug Classes

Nationally approved drugs are usually classified into different 'classes'. Different restrictions as to who can prescribe, dispense, manufacture, etc., apply to the different classes. Morphine is usually under the tightest restrictions (often referred to as a 'controlled drug' or Class A drug) in respect to who can handle it. In some countries the class depends on the strength of the morphine preparation (i.e., fewer restrictions on lower-strength preparations).

Drug laws need to be relevant and practical to clinical practice. HCWs should:

- Highlight laws that are impracticable.
- Advise of new developments and drugs that may not be covered by the existing laws.
- Suggest ways of improving policy and laws.

Examples

In rural Uganda there is 1 doctor to 50,000 people. The law previously required that only doctors can prescribe morphine. Therefore, as many people requiring morphine for pain relief will not have access to a doctor, they will also not be able to access morphine. A suggestion may be to amend the law to allow palliative care specialist nurses to be able to prescribe morphine (and other drugs required for palliative care from a defined list).

In Malawi there are 60 pharmacists and an estimated 1 million persons living with HIV/AIDS, so it would not be practicable for only pharmacists to be allowed to dispense morphine, other palliative care drugs, or ARVs.

Preventing Diversion Whilst Assuring Availability

National policy should ensure that disciplinary standards are in line with medical policy and that all people involved in policing illicit drug use are aware of the circumstances in which drugs such as morphine can be legally prescribed, stored, and possessed.

Both the WHO and INCB have expressed concern at the restriction of access to opioids for medical purposes. They have outlined principles within drug laws that should *allow access for medical purposes*, whilst preventing diversion.

Drug Procurement

Ensuring reliable, timely, quality, and cost-competitive drug supplies and laboratory reagents is critical to maintaining symptom-free patients and preventing drug resistance and withdrawal reactions (see Chapter 4: Pain Management). For example, initial erratic ART supply in Gabon and Cote d'Ivoire caused high levels of drug resistance (Reynolds, 2003).

Planning and Assessment

Drug selection and procurement issues are central in initial planning and on-going assessment. The steps are (Gupta, 2004) to:

1. Assess demand and how it might change.
Consider epidemiology, ARV consumption, health service capacity, and access.
Anticipate how to cope if funding is withdrawn.
2. Define and assure quality standards.
3. Examine manufacturing capabilities.
4. Examine receipt, storage, and distribution.
Require secure supply chain: diversion of ARVs, risks, inappropriate use, and resistance development.
Wastage can occur if large quantities are imported which cannot then be stored correctly or distributed before the end of their shelf life.
5. Monitor prescribing, dispensing, and stock levels.
Monitoring needs to be timely and user-friendly with minimum burden for HCWs, and to allow for patient mobility, regimen changes, and drug substitution
6. Agree upon payment.
7. Ensure sufficient capacity in drug regulatory authority.
8. Identify areas for improvement.

Coordination and Quality Control

Coordination of procurement and quality control reduces the number of stakeholders and improves negotiation with industry (e.g., fixed negotiation rounds, yearly schedule for procurement). To assist in procurement in developing countries WHO provides up-to-date information on sources and prices of selected medicines and diagnostics for people living with HIV/AIDS (see <http://www.who.int/medicines>).

For drugs not assessed by WHO, MSF has assessments using standard procurement procedures at this Web site: <http://www.msf.org>.

Importation

Drugs must be registered with the NDRA before they can be imported; time needs to be allowed for registration. Questions to ask in planning:

Who is allowed to import Class A or 'restricted' drugs?

Who is allowed to supply drugs and restricted drugs?

What requirements need fulfilling?

In deciding which form(s) of a drug to import, consider differences in initial costs, manufacturing capacity and costs, shelf lives, and storage conditions.

Manufacture

Small-scale manufacture describes the production of drugs from raw materials in a health facility rather than in a factory. To enable manufacture of non-sterile drugs your health facility will require:

- Reliable source of raw materials
- Good water supply
- Accurate weighing scales and measures
- Funnels, bowls, pestle, and mortars
- Labels
- Verified formula
- Trained staff
- For some preparations, a method of heating to a known temperature

Questions to Ask In Planning:

- Who is allowed to manufacture morphine, other medicines?
- Would the health facility require a special license to manufacture morphine solution?

Other Logistic Considerations

Transportation

Questions to ask in planning:

- Are there any regulations covering the transportation to the hospitals, clinics, or health centres?
- Who can collect drugs from the wholesaler or manufacturer?
- Do further restrictions apply for Class A drugs?

Storage of drugs

Questions to ask in planning:

- Are special storage conditions required (e.g., a fixed lockable cupboard, refrigeration)?
- Do outlying clinics and rural health centres have suitable locked cupboards, refrigeration?

Prescribing

Questions to ask in planning:

- Are the laws regarding prescribing practical? (e.g., who can prescribe, and what quantity of opioids or ARVs can be prescribed at one time?)

Dispensing

Questions to ask in planning:

- Are dispensing laws practical?
- Are there enough staff allowed to dispense to all those requiring palliative care?
- What are the dispensing requirements? (e.g., labelling, packaging, special requirements for restricted drugs?)
- What should you do with any morphine returned when a patient no longer requires it?
- What should you do if you have some expired morphine?

Drug Costs

Achieving Affordability

Improved affordability can be achieved through:

- Increasing competition and price transparency
- Coordinating procurement
- Use of voluntary and compulsory licensing provisions
- Research and development to develop more affordable regimens
- International commitment
- Sustainable financing at national level
- Discouragement of nonsustainable donations and pilot initiatives
- Pressure on pharmaceutical companies (e.g., following pressure, GlaxoSmithKline cut the price of ZDV/3TC by almost half in all countries in SSA)

In ART programmes, affordability needs to account for treatment of OIs and laboratory tests as well as the cost of ARVs. In all cases it is important to consider:

- What are the feasibility and effectiveness of models for resource mobilisation (risk pooling, insurance, community resource mobilisation)?
- What is the range of costs and cost-effectiveness for different treatment options?
- What are the implications of the costs of treatment for families?

Patents and Intellectual Property Rights

Patents allow the company who developed a drug, testing method, or medical equipment some intellectual property protection and thus to set prices. This enables recouping of research and development costs. Unfortunately, this has resulted in many drugs being unaffordable in SSA.

The Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS), established in 1994, requires World Trade Organisation (WTO) members to grant and enforce patents in accordance with some minimum international rules. The agreement, however, does recognise the need to maintain access to essential medicines in lower income countries.

Least developed countries are not required to enforce or provide patents on pharmaceutical products until at least 2016.

The Doha agreement (2001) endorsed this principle:

'We agree that the TRIPS agreement does not and should not prevent members from taking measures to protect public health. Accordingly while reiterating our commitment to the TRIPS agreement, we affirm that the agreement can and should be interpreted and implemented in a manner supportive of WTO members' right to protect public health and, in particular, promote access to medicines for all.'

'In connection with this we affirm the right of WTO members to use, to the full, the provisions of the TRIPS agreement which provide flexibility for this purpose.'

TRIPS allows countries to grant compulsory licences for emergency situations:

‘Each member has the right to determine what constitutes a national emergency or other circumstances of extreme urgency, it being understood that public health crises, including those relating to HIV/AIDS, tuberculosis, malaria and other epidemics, can represent a national emergency or other circumstances of extreme urgency’.

However, drug patents that need not be granted are being granted in SSA. Patents can be challenged (Doha agreement) and campaigning can be successful:

In 1998, the South African Pharmaceutical Manufacturers Association and 40 pharmaceutical manufacturers brought suit against the South African government for violation of TRIPS (legislation allowing generics substitution of off-patent medicines, transparent pricing, and parallel importation). Campaigning ensued in support of the South African government, and the pharmaceutical companies dropped the case.

Campaigning in Kenya led to the addition of ‘Bolar provisions’ in their legislation – allowing local manufacturers to conduct appropriate trials, submit registration, and prepare for production prior to patent expiry.

To ensure access to required medicines HCWs should ensure their country operates its patent system to its best national interest. Some points are listed below:

- Keep number of patents to a minimum
- Least developed countries are exempt until at least 2016
- TRIPS allows parallel imports
- Ensure checks are in place to revoke invalid patents
 - If your country did not allow patenting of pharmaceuticals before a certain date, it is likely that patents with an earlier priority date will not be valid. Your patent office or the World Intellectual Property Organisation (WIPO) should have information on the date from which patents have been available on your country.
- Most experts agree TRIPS does not require patents for new uses of known substances.
- Governments can improve access through compulsory licensing of patented drugs or through making government use of a patent, but these are politically sensitive. Compulsory licensing allows parallel importation and the production or importation of generic medicines without the patent holder’s consent.
- To register a drug the first applicant has to provide evidence from clinical trials to show the Drug Regulatory Authority that the drug is effective, safe, and of quality. Usually subsequent generic versions have only to prove that they are equivalent. The TRIPS Agreement requires some protection for the original undisclosed test data. The U.S. and some European countries provide such protection by granting data exclusivity for 5 to 10 years. However, TRIPS does not require giving such exclusive rights. If this is done, affordable generic versions of medicines will be prevented from being registered for this time period, even if there is no patent. If a drug is not registered, it cannot legally be used in a country.
- TRIPS allows registration of generic medicines that third parties have a patent on, or related to, the product. Questions about the validity of patents are totally separate from questions about drug regulatory approval, (i.e., whether a medicine is safe, effective, and of quality).

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