



Global Drug Facility (GDF)

Rationale for standardising TB drugs

Introduction

Standardisation of drug regimens is an excellent way to contribute to DOTS expansion. In the context of TB drug supply standardisation means simplifying the drug management components: selection, needs estimation, procurement, distribution and rational use. The GDF standardisation programme contributes to the simplification goal in several ways.

TB drug selection

With DOTS as the focus, national TB programmes must select the most appropriate drug regimens and products based on available information, not excluding the guidelines published by WHO and IUATLD. Studies show that even when countries have established regimens, practitioners do not always adhere to those standards. For example, in the Philippines a recent market study (Philcat 2002) showed that of 24 practitioners surveyed there were 25 different TB treatment regimens used in their practices. The practitioners were from a mixture of both public and private health systems

The GDF has found that one of the best ways to simplify drug selection is by promoting fixed-dose combination (FDC) drugs. New formulations have been developed that allow first line TB treatment to include only two products, the 4-drug FDC for the intensive phase and the 2-drug FDC for the continuation phase. According to WHO treatment guidelines, this regimen can be used for patients diagnosed as either Category I or III. For the Category II patient, the regimen with three products may be used: the 4-drug FDC and Streptomycin for the intensive phase and the 3-drug FDC for the continuation phase. Using FDCs reduces the number of tablets the average TB patient will take on a daily basis from 16 tablets to 3-6 tablets whether for the intensive or continuation phase.

Overall the advantages of FDCs are the following:

- Reduces number of tablets a patient must swallow each day
- Simplifies dose calculations for practitioners since all drugs are included in a single tablet
- Prevents use of drug regimens other than those proposed by the TB programme
- Reduces risk of drug resistance since mono-therapy is avoided
- Follows WHO guidelines for TB control

The GDF is currently promoting further simplification of TB drug treatment by developing patient kits, where all drugs needed for a full course of treatment are included in a single package. The kits, called Stop TB Patient Kit, will use FDC drugs exclusively, and as a result all the drug selection advantages cited above will come into play.

Drug needs estimation

The TB treatment regimens of many national programmes require the supply of 6 individual drugs. This means that personnel calculating the quantities to order must make many calculations for each of the 6 drugs. For example:

$$\text{total quantities needed} = \frac{\text{ethambutol 400 mg x number patients x average number tablets x duration of treatment}}{\text{number of tablets in one container}}$$



Obviously, there are multiple chances of errors. GDF simplifies needs estimation by promoting the FDC products mentioned above where the number of different drugs is drastically reduced. For example, 14 (9+5) single-drug calculations must be done, but for FDCs only 5 (3 +2) calculations are required. Table 1 shows the impact of FDCs.

Table 1

Category of patient	Number of <i>single</i> products		Number of <i>FDC</i> products	
	Intensive phase	Continuation phase	Intensive phase	Continuation phase
I and III	4 (RHZE) *	2 (RH)	1(RHZE)	1 (RH)
II	5 (SRHZE)**	3 (RHE)	2 (SRHZE)	1(RHE)
Total	9	5	3	2

* rifampicin, isoniazid, ethambutol and pyrazinamide

** streptomycin, rifampicin, isoniazid, ethambutol, pyrazinamide

In developing the Stop TB Patient Kit, the GDF is simplifying needs estimation even more. For example, with the patient kit, the national TB programme need only know the number of expected patients in Categories I, II, and III. No calculations are needed since the number of products to order actually equals the number of patients in each treatment category.

Procurement

The objective of TB drug procurement is to purchase quality drugs from reliable suppliers at the best possible prices while insuring timely delivery. Procurement can be a complicated process even for experienced personnel. To be successful there must be appropriate drug needs estimation, a management information system, knowledge of competitive procurement practices, selection of quality suppliers, availability of an appropriate quality control system, and a functioning supplier monitoring system.

In terms of simplifying procurement GDF is making its products available in 2 ways, as free grants, or as direct procurement for those TB programmes that have their own funding but inadequate procurement systems. Advantages of procuring through the GDF are: competitive prices, pre-qualified manufacturers, independent batch laboratory analysis, pre-shipment inspections, user-friendly high-quality packaging and on-going technical support, in sum a quality procurement service.

TB drug distribution

Drug distribution involves many activities such as, clearing drugs through customs, transporting them from warehouse to health centres, and maintaining stock records, adequate stock levels, and appropriate conditions of storage no matter where drugs are stored until used. To have an optimum distribution system, there must be good documentation of all quantities entering and leaving storage areas, and of quantities dispensed to patients. One way to simplify this is by reducing the number of products moving within the distribution system.

GDF simplifies distribution by reducing the number of products being handled by a TB programme. With the FDC products and the Stop TB Patient Kit the number of product items are reduced significantly when compared with single drug products. Referring to Table 1 it is evident that the

number of different drug products needing distribution are reduced from 14 to 5 (4 FDC, 3 FDC, 2 FDC and streptomycin). A greater reduction is true if patient kits are being used to 2 different products (1 kit for Categories I and III, and 1 kit for Category II). This means there are fewer items to count and to document for proper inventory control.

Rational drug use

To promote rational drug use, health providers must prescribe the appropriate TB drugs in the right doses, drugs must be available in treatment centres, and patients must adhere to the drug regimens prescribed. If drug treatment regimens have not been standardized, procured in the appropriate quantities, and distributed in a timely manner, TB drugs will not be appropriate for nor available when patients and providers need them.

GDF simplifies rational use of TB drugs through its catalogue of user-friendly, quality products, including the FDCs and Stop TB Patient Kits. The many advantages of using these types of products include the following:

- Insures that prescribers use the exact drugs selected by the TB programme
- Facilitates stock management which promotes availability of adequate drug supplies
- Facilitates drug prescribing since dosage calculation is minimized
- Demonstrates to the patient that a full course of treatment is available when needed
- Prevents mono-therapy and development of multidrug-resistant TB
- Facilitates monitoring of prescribing habits to determine if DOTS is being followed

Guidelines for understanding the use of FDCs and Stop TB patient kits

TB programmes that want to switch to FDCs will be pleased to know that a comprehensive guide has been published by WHO. The resource called, “The Operational Guide for National Tuberculosis Control Programmes on the Introduction and Use of Fixed-Dose Combination Drugs” (WHO/CDS/TB/2002.308-WHO/EDM/PAR/2002.6), contains discussion and practical tools for using FDCs. A foldout tool called, “Scenario for a change over to 4-drug FDC/2-drug regimen,” contains specific activities for each step in the change over process. While the guidelines were prepared for introducing FDCs in a national programme, its principles can also be used for introducing the Stop TB Patient Kit, since the kit exclusively contains FDCs.

Contribution to DOTS

The purpose of innovative products and packaging is to promote DOTS and DOTS expansion to help countries meet the global TB control targets of a 70% case detection rate and an 85% cure rate of detected cases. FDC products and Stop TB Patient Kits were designed specifically for that purpose.

A word of caution that these products are not intended to replace the directly observed component of the DOTS scheme. WHO and its partners have collected ample evidence that patients must be observed taking their TB drugs for the full treatment period to reach the global TB targets.

Any inquiries about the GDF’s FDC drug products or the Stop TB Patient Kit should be directed to the email address: gdf@stoptb.org . Product information is available online at the website: www.stoptb.org/gdf/.