

Patient Kits Promote Good Tuberculosis Pharmaceutical Management

February 2006
(reviewed 2010)



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This report was made possible through support provided by the U.S. Agency for International Development, under the terms of cooperative agreement number HRN-A-00-00-00016-00. The opinions expressed herein are those of the authors and do not necessarily reflect the views of the U.S. Agency for International Development.

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Acknowledgments

This document was prepared with contributions from Edgar Barillas, Thomas Moore, Chinwe Owunna, Pedro Guillermo Suarez, Hugo Vrakking, and Andrey Zagorski. Management Sciences for Health/RPM Plus acknowledges the valuable comments and suggestions of Jeremiah Chakaya Manager of Kenya National Leprosy and TB Control Programme and Samuel Gitau, Provincial TB and Leprosy Coordinator, Eastern province, Kenya.

Recommended Citation

Rational Pharmaceutical Management Plus. 2006. *Patient Kits Promote Good Tuberculosis Pharmaceutical Management*. Submitted to the U.S. Agency for International Development by the Rational Pharmaceutical Management Plus Program. Arlington, VA: Management Sciences for Health.

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ACRONYMS

DOT	Directly Observed Treatment
DOTS	World Health Organization internationally recommended strategy tuberculosis control
FDC	fixed-dose combination
GDF	Global Drug Facility
GMP	Good Manufacturing Practices
kg	kilogram
mg	milligram
MoH	Ministry of Health
NTP	National Tuberculosis Program
RPM Plus	Rational Pharmaceutical Management Plus Program
TB	Tuberculosis
TB PK	Tuberculosis Patient Kits
WHO	World Health Organization

INTRODUCTION

Even though the importance of completing the whole course of a tuberculosis (TB) treatment is not new, the practice of keeping the complete treatment for each patient in a container (to prevent the interruption of treatment) is rarely used today. The utilization of pre-packed TB patient kits (TB PKs) is a relatively new experience, dating from 2000-2001 when the national tuberculosis programs (NTPs) of South Africa and India and the Global TB Drug Facility (GDF) began promoting their use. These pioneer experiences have been recently nourished by other country experiences in Kenya, Philippines, Indonesia, Ecuador, Peru and Dominican Republic which have demonstrated that TB PK are a workable solution to the logistical and compliance problems faced by most NTPs.

This document presents the technical basis for the use of TB medicines in patient kits, a country experience, and guidelines for managing a TB PK system.

TECHNICAL BASIS FOR THE USE OF TB PATIENT KITS

A TB PK contains the full course of treatment for a single patient. There are two variations of the kits depending on where they are constituted—

1. Packs constituted in health facilities
2. Pre-packed TB patient kits (by manufacturers or suppliers)

The same basic principles are behind the constitution of a TB PK system: a complete course of treatment should be assured for each patient, and furthermore, treatment should not be started if there is no assurance that it will be completed.

From the provider point of view, the TB PK allows health workers to use a container that has all required medicines with appropriate strengths and quantities which limits confusion and wastage, making it easier to monitor the regularity of treatment, and preventing supply breakdowns for individual patients.

The TB PK also increases patient adherence. Since medicine stock-outs cause patients to lose confidence in the health system, the TB PK assures the TB patient that his or her medicines will be available from start to finish of the treatment. In addition, the patient may feel ownership of the patient kit and with the likelihood of completing the full course of treatment since he/she can see the quantity of medicines needed to be taken to achieve a cure during visits to the health center or dispensary.

What the TB PK does not do is eliminate the need for directly observed treatment (DOT) as proscribed by the World Health Organization (WHO) DOTS scheme. The five main components of the DOTS scheme require strict DOT at least during the intensive phase of TB treatment.

CONSTITUTION OF TB PATIENT PACKS IN HEALTH FACILITIES

Some countries (i.e., Peru, Ecuador, Dominican Republic) buy loose medicines to constitute packs¹ for each patient at the health-facility level, using any kind of container. This method is a good operative option if the country cannot purchase pre-constituted kits, or if policy prevents international purchasing and TB PK are not available on the local market.

In most countries where health facility TB PK reconstitution is followed, medicines are purchased and delivered to health services as loose items either in bulk (containers of a 1,000 tablets, for instance) or blister packs. Health service personnel assemble and organize the treatment for a particular patient in a single container, taking into account the regimens included in national guidelines for various body weight bands.

All medicines for a six-month (category I) or eight-month (category II) treatment are included in the container. Depending on political decisions or the resources of the NPT, the container may vary from plastic or paper bags² (figures 1 and 2), or disposable boxes (figure 3), to plastic containers specifically used for this purpose (figure 4).

All packs are labeled with the name of the patient, treatment category, and the date the treatment was initiated. The security stock is usually kept as loose medicines.



Figure 1. Ecuador—Treatment packed in plastic bags



Figure 2. Kenya—Treatment packed in paper bags supplied by the pharmaceutical company

¹ We use packs to distinguish them from pre-constituted TB patient kits.

² The TB patient packs provided in Kenya by Sanofi Aventis[®] are, in fact, a combination of loose drugs and blisters organized as a “pack” in a paper bag labeled with the name of the patient and date (see picture).



Figure 3. Ecuador—Treatment packed in disposable boxes



Figure 4. Dominican Republic—Treatment packed in plastic container specifically used for this purpose

The constitution of TB patient packs in health facilities shares some of the most significant features with pre-constituted patient kits (see section 4).

- Assurance that the treatment is being followed since the health worker does not have to select which drug to use
- Less preparation time by the health worker at the time of dose administration to the patient
- Improves patient's adherence
- Easier to monitor the treatment when comparing the treatment card with the number of doses remaining in the container

Some limitations of this method are—

- If the program is not procuring blister-packed medicines, there will be manipulation of exposed tablets in the process, contributing to the potential product mix-ups
- If the container is not appropriate (i.e., black plastic bags), medicines may be stored in suboptimal conditions (exposed to increased sunlight, heat, or humidity).
- If security stock is kept as loose medicines (instead of individual patient packs), health facilities may end up with a deficit or surplus of certain medicines

In the Dominican Republic, the security stock in health facilities was usually held as loose items. A rapid assessment conducted by RPM Plus³ illustrated a progressive depletion of the security stocks in some health facilities and, at the same time, overstocks of some medicines in others (see figure 5). RPM Plus recommended the organization of the security stock in patient packs for medium weight patients and enough to treat the expected number of patients to be detected during the subsequent three months.⁴

³ Barillas, E. 2004. Evaluación Final de la Prueba Piloto para la Implementación del Sistema de Suministro de Medicamentos e Insumos del Programa Nacional de Control de la Tuberculosis de Republica Dominicana. Presentado a USAID por RPM Plus.

⁴ In Dominican Republic, the medicines are distributed quarterly.

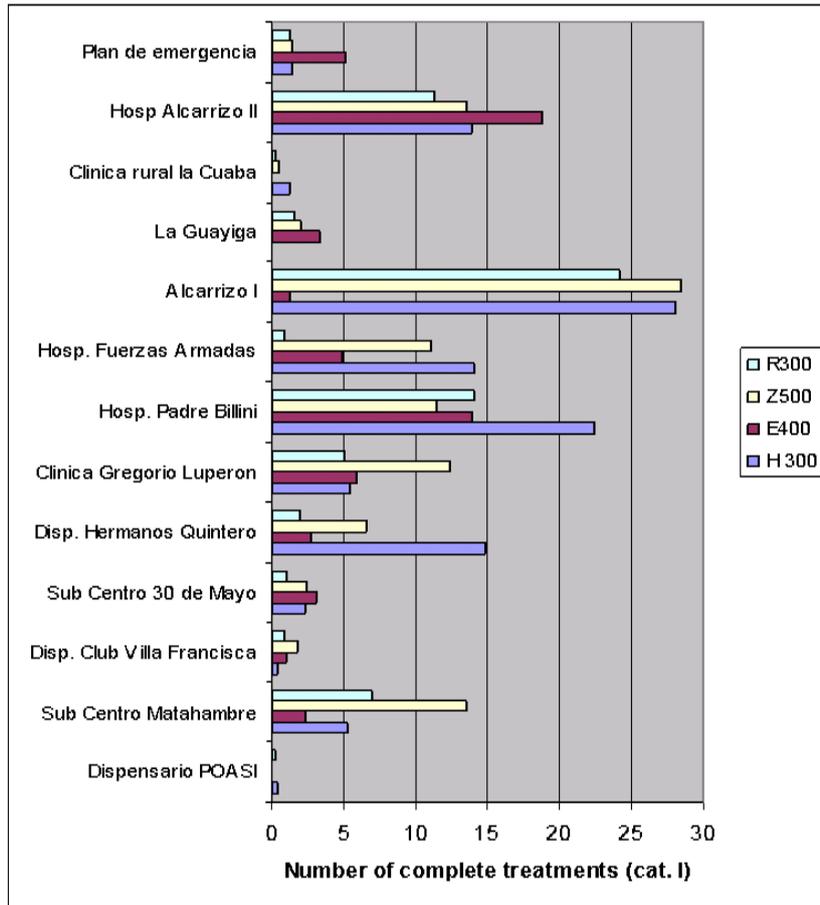


Figure 5. Number of complete treatments for each of the medicines used for category I patients (13 health facilities)

PRE-CONSTITUTED TB PATIENT KIT

A pre-constituted TB PK is delivered from the manufacturer containing a full course of treatment for TB. The kits include all medicines needed for treatment completion, be it six months for category I treatment, or eight months for category II. TB PK includes medicines for both the intensive and continuation phases (see figure 6).

Intensive phase medicines are segregated from continuation phase medicines within the TB PK. Commercial TB PK usually include blister packed fixed-dose combination (FDC) products where the drugs are formulated into one tablet; there are 2, 3, and 4-drug FDCs available for constituting a TB PK. In addition to the benefits already mentioned for the packs constituted in health facilities, pre-constituted TB PKs bring additional advantages since they are ordered as a finished product from the manufacturer.

- There is no manipulation of exposed tablets by personnel. The health worker does not have to gather and count different medicines since this is done by the manufacturer/supplier.
- Treatment is standardized since health workers simply select a single container with predetermined drugs, strengths, and quantities for administering to the patient versus multiple containers and dosages in various packaging configurations.
- Quantification for procurement or ordering is simplified whereby one patient *equals* one TB PK, as opposed to current methods which require quantifying multiple drugs in multiple doses.
- Distribution of TB drugs is improved in that one item is being transported versus multiple products in a variety of containers.



Figure 6. Pre-Constituted TB pack from GDF

- Stock management and inventory control are improved since one product is being handled versus multiple products.
- Community volunteers have a clear understanding of medicines and doses to be given to the patient.
- The TB PK has a single expiry date instead of multiple ones when loose drugs are used.

There are some disadvantages or issues that should be considered when switching to pre-constituted TB PK.

- TB-PKs may not be immediately available in local markets. The NTP may have to buy through international agencies such as the GDF.
- County may have to switch from monotherapy to FDC, which are usually the medicines included in the kits.
- Personnel must be trained on the following—use of FDC (if never used before in the country) and the adjustment of the TB PK according to the weight of the patient and reconstitution of the packs from remaining loose medicines (see *Distribution*).
- Organization for reconstituting the TB PK includes use of *supply boxes* for storing left-over blisters from TB PK. Loose medicines must be collected, new packing materials must be available, an area must be organized for the reconstitution process within the warehouse, and procedures such as Good Storage Practices should be in place and followed (see *Distribution*). During the actual reconstitution process, Good Manufacturing Practices (GMP) as they relate to packaging must also be followed.
- Larger storage space may be needed in all storerooms and warehouses.

Since the use of pre-packed TB PKs offer additional advantages to the packs that are constituted in health facilities, this paper presents a country experience and guidelines derived from the lessons learned.

KENYA'S EXPERIENCE IN USE OF TB PATIENT KITS⁵

Around 2000, Kenya was presenting an exponential increase in TB cases and pharmaceutical management was inadequate to face the new demand. National guidelines were not fully followed especially in the major hospitals, and there was incomplete ordering from districts and health units, which resulted in stock-outs and the need for replacements. The existing system was unreliable in terms of quantifying pharmaceutical needs and distribution.

TB control stakeholders agreed in 2002 that the introduction of TB PK (called “packs” in Kenya) was a feasible strategy to improve TB pharmaceutical management problems and encourage adherence to national TB guidelines.



Figure 7. TB PK used in Kenya

In 2003, NTP authorities and technicians took a number of steps—

- Visited India to learn about that country’s experience in the introduction of TB PK
- Conducted a nationwide stock-taking exercise to establish the stock levels of the loose medicines and the right moment to start new patients on the TB PK to avoid wastage
- Completed procurement of TB PKs in 2003 with the awarding of the contract to a local manufacturer. The TB PKs arrived in June 2004.

The implementation phase included the training of the provincial and district TB managers, medical assistants in charge of TB activities in districts or control zones, primary health technicians (PHTs), pharmacists, and nursing officers. The training included information and practical exercises on patient eligibility criteria (i.e., Categories I and III), adjustment of the number of doses according to the body weight, and inventory control.

The implementation was first piloted in August 2004 in 25 high burden districts. In November 2004, the strategy was extended to all 74 districts in Kenya.

The NTP, with technical assistance of RPM Plus, initiated a study in May 2005 to monitor the implementation of the TB PK. The study was based on a structured questionnaire. The sample size included 240 health facilities.

⁵ Based on: Gitau, S. 2005. *Patient Packs: the Kenya Experience*. Presented at the SEAM Conference in Accra, Ghana, June 2005.

Preliminary results from the evaluation visits showed that personnel were pleased with the introduction of the TB PK; they indicated that with the introduction of patient packs, it is easier to order medicines (95.6 percent of respondents); easier to dispense them (97.8 percent); brings a sense of ownership to the patients (77.8 percent), and guarantees uninterrupted supply of pharmaceuticals for registered patients.

But the data also showed that only 65 percent of respondents had a good knowledge of how to manage the TB PK, although 95.6 percent of respondents had been trained. Eighty-nine percent used stock cards as they should be doing, but only 62.2 percent of the cards were up to date. There were problems in inventory control and discrepancies with all data entries. About two thirds of the drug orders by treatment facilities were not placed in time, and one third were incorrect.

During the evaluation visits, the NTP realized that blister packs of 10 tablets (instead of 7 or multiples of 7) were unsuitable for weekly drug collection and the patient in the continuation phase. In addition, the tools to register quantities dispensed to patients and stock control were time consuming and not user friendly.

An RPM Plus mission to Kenya in May 2005⁶ documented other problems in the pharmaceutical management of TB PK.

- Because treatments are usually interrupted late in the intensive phase or during the continuation phase, some facilities were stocking an excess of EH (used in the continuation phase) because of patients who default, transfer, or die. A few other facilities, particularly those with a high proportion of patients in transit, had shortages of the same medicine. Reasons for this were later expanded to include overstocking since the TB PK were constituted for a heavy weight patient and the average Kenyan TB patient weighs 50 kilograms (kg).
- The mission identified that there was an unclear procedure for the collection of the *supply boxes*⁷ and the reconstitution of the Patient Packs. Whether the packs will be reconstituted in the district or provincial level remained ambiguous to the provincial coordinators at that point.
- In a few service points, the inventory control of the TB PK was still based on the loose medicines, imposing an unnecessary workload for the program coordinators.
- There was no single criterion regarding the number of treatment days per month; while the central unit was recommending 28 days, the health facilities were using 30.

As demonstrated in Kenya, the successful implementation of the TB PK requires extensive planning and close monitoring during the early implementation phase. The NTP has made the necessary adjustments according to these findings. The lessons learned in Kenya were used as a valuable input for the following sections. An additional resource for NTPs considering changeover to FDCs and patient kits is WHO's "Operational Guide for NTPs."⁸

⁶ Barillas, E. 2005. *Global Drug Facility Monitoring Mission to Kenya and Technical Assistance for the Implementation of the Tuberculosis Patient Pack: Trip Report, April 25th – May 6th*. Submitted to USAID by RPM Plus.

⁷ These are the boxes where the health providers deposit the blisters extracted from the TB patient pack after their adjustment according to the body weight.

⁸ World Health Organization. 2002. *Operational Guide for National Tuberculosis Control Programmes on the Introduction and Use of Fixed-Dose Combination Drug.*, WHO/CDS/TB/2002.308 – WHO/EDM/PAR/2002.6, Geneva.

GUIDELINES FOR PHARMACEUTICAL MANAGEMENT OF TB PATIENT KITS

The information presented in previous sections suggests that the TB PK is a reliable method to simplify the quantification of TB pharmaceutical needs, inventory control and distribution at all service levels. The following guidelines will assist the NTP in preparing a plan for the smoothest transition to TB PK possible.

Selection

The selection of TB medicines should be based on WHO/DOTS recommendations. Keep in mind that most commercial TB-PK are constituted with 2, 3, and 4 FDC products. Medicines should be in blisters to protect them during the adjustment of the kits (to the body weight of the patient) and the reconstitution in provincial stores. Blisters protect from undue mix-ups and from poor sanitary conditions during manipulation. The expiry date and the batch number must be registered on all blister sheets to maintain this vital information through the transfer of the medicines to the supply boxes and the kit reconstitution.

The TB PK if possible should be selected according to—

- The therapeutic regimens that the program is using (daily treatment during continuation phase versus three times a week, for instance)
- The number of days per month that the NTP uses as standard (26, 28, or 30)
- The average weight of TB patients in the health system so that most TB PKs will not need adjustment

It is necessary to standardize the technical specifications of the TB PK to assure the compliance of all providers. The NTP should specify the exact dimensions of the containers, quantities of tablets on a blister, which FDCs are to be used, color of the tablets, and inscriptions on all labeling and kit inserts, for example. Ideally, the design and labeling of the containers should allow their re-use. Useful recommendations that may be considered when drafting the specifications of the box and labels are—

- Label on end where patient name, TB register number, and registration date are to be written
- Label on inside lid of pack where the following are written: weight of patient, number of tablets to be taken in one dose, and spaces to tick when each dose is taken by the patient (Note: labeling not intended to replace the TB register)
- Labels of shipping container and inside containers identifying products as being for the NTP, whether Category I, II, or III TB PK and other required information to be identified
- Instruction booklet to guide the health care worker how to use the TB PK must be included

- Plastic bag inside shipping container to protect from humidity and contamination during shipping and storage

Keep in mind that most countries require the registration of all products included in a TB PK, before procurement. In many countries, the TB PK does not constitute a new product requiring registration.

Procurement

If there are enough suppliers, a restricted tender, limited to pre-qualified suppliers, is recommended for the procurement of TB PK. The competition among suppliers usually brings prices down.

Another option is a direct procurement through nonprofit international agencies to assure competitive pricing if enough suppliers do not exist. It is notable that the Global TB Drug Facility (GDF) offers high quality products and generally at the lowest prices found on the market today. In annex 2 you will find a list of the TB PK currently offered by the GDF. An updated list of the prices may be found at www.stoptb.org/gdf

Regardless of the provider, the NTP should assure the quality of the products. The following documentation should be requested from the provider.

- Registration of TB medicines in manufacturers' country
- GMPs' certification from the national drug regulatory authority in country of manufacture
- WHO-type batch analysis certificate for each batch delivered: a qualified pharmacist must check if all test data are within specifications as per relevant pharmacopeia
- Evidence that bioavailability studies conducted on the FDC products containing rifampicin showed effectiveness

The quality of the medicines should be determined through additional laboratory testing in national or independent labs. The GDF hires an independent laboratory to carry out this function for its products. For example, a random sample of sufficient size (i.e., one full Patient Pack out of every five batches) could be taken. Comparative dissolution tests are recommended for all components, and evidence that the supplier conducted bioavailability testing for FDCs containing rifampicin showing effectiveness of their products. Often a country does not have local technology for bioavailability testing so evidence from the supplier may be sufficient.

Distribution

There are advantages and challenges when using TB PK, primarily in terms of transportation, storage, and inventory control. Where TB PKs are used, the inventory control and requisition mechanism utilizes the "kit" as the accounting unit. This simplifies the estimation of needs, the requisition process, and the inventory control. Yet on the other hand, the program has to

create an inventory control system for loose blisters coming from the adjustment of TB PK (according to the weight of the patient), or from patients who die, transfer, or default. Loose blisters are stored in a supply box, as described in the following section. Annex 1 includes a sample form to manage the stock of the supply box.

All stores in the distribution chain should plan for additional space or shelves to hold an increase in working and security stocks (see figures 6 and 7). Provincial or district warehouses should also reserve some space for the reconstitution of the kits (see the following section).

Both the *push*⁹ or *pull*¹⁰ system and the *collection*¹¹ or *delivery*¹² system also apply to patient kits. If a good information system is in place, the combination of a *pull* and *delivery* system may work better because it relies on the demand of health facilities, and allows the supervision of health facilities and gathering of any surplus of loose medicines from the supply box.

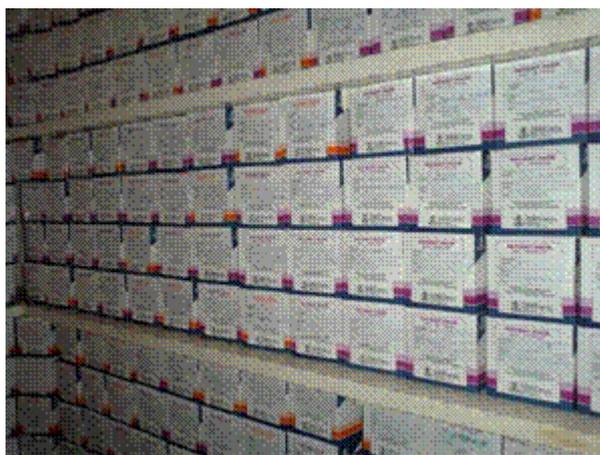


Figure 8. Kenya—Storage of TB-PK in health facility

Reconstitution of Packs

The excess medicines coming from patients who are of lighter weight or who transfer, default, and die should be stored in separate containers—supply boxes—for each type of drug. The provincial store seems to be the best level to reconstitute the TB PK, since the stocks-outs and surpluses can be better balanced at that level. The health facility should keep the equivalent of three months of consumption of TB PK as security stock,¹³ and loose medicines for patients to be transferred and to adjust the packs of heavy weight patients. The excess drugs must be collected by provincial stores on a quarterly basis for repacking. These movements of medicines should be recorded on appropriate forms (see example in annex 1).

⁹ Push means the national program decides quantities to distribute to each treatment facility or storeroom

¹⁰ Pull means each facility storing TB drugs orders the quantities they need

¹¹ Collection means the facility goes to the warehouse or storeroom to pick up its orders

¹² Delivery means the warehouse delivers quantities needed to the facility

¹³ This is usually the recommendation in countries where medicines and commodities are distributed 4 times during the year. See RPM Plus (2005), *Managing Pharmaceuticals and Commodities for Tuberculosis*, for details.



Figure 9. Kenya—Storage of TB PK in a health facility

For proper stock management, health facilities should register quantities of all medicines collected by the provincial store using appropriate inventory forms. Provincial stores should—

- Register quantities of all drugs collected from the health facilities in their inventory records
- Register all quantities of medicines used for reconstitution of the TB PK from their inventory records
- Register the reconstituted packs as a “single” unit in the inventory

The provincial store should be prepared with containers and packing materials for the reconstitution of packs and prepare a suitable area where reconstitution of TB PK can take place without mix-ups (e.g., packing tables free from other items). The NTP may procure additional boxes and labels from the same supplier of the TB PK. The delivery of these items may be included in the same contract. Another option is to re-use the empty boxes and attach new blank labels every time they are reused.

The personnel responsible for the reconstitution of the TB Packs should be trained to follow strict procedures for repacking such as GMP guidelines for packaging. Some of the aspects to be considered are—

- The medicines to include in the pack should have at least six months of shelf life
- The physical conditions should be adequate (no change of color in the tablets, torn blisters, or crushed tablets)
- The box should be labeled with a standard, pre-printed label
- The NTP may consider including a control number indicating that the TB PK has been reconstituted; the control number will correspond with repacking records stored at the provincial stores and should contain the following information

TB PK Control Number:				
Medicine	Manufacturer	Batch	Expiry Date	Quantity

- The preprinted labels should include patient personal data.
- It may be necessary to procure and keep in provincial stores a stock of certain loose medicines for the reconstitution of the Patient Packs. For instance, there may be an excess of ethambutol and isoniazid (EH) from the continuation phase (when patients sometimes default or die). This stock should be balanced with a corresponding amount of rifampicin, isoniazid, pyrazinamide, and ethambutol (RHZE) for the reconstitution of TB PK.

Annex 1 includes the guidelines recommended by RPM Plus for the reconstitution of TB Patient Packs in Kenya.¹⁴

Use

The TB PK prevents supply breakdowns for individual patients and makes it easier to monitor the regularity of treatment. TB PKs, however, are prepared for a specific weight band (i.e., 40-54 kg), which most patients fall within. Patient kits are easily adjustable by health workers at the start of treatment by removing or adding blister sheets. Blisters should be designed so that complete sheets are removed or added to the box for adjustments. The instructions for TB PK adjustment must be included in a booklet in each kit. Annex 3 demonstrates the instructions that were prepared by the Kenya NTP, with technical assistance from GDF and RPM Plus.

It is notable that the TB PK may not be the best option for—

- Patients who have already initiated treatment with loose medicines
- Patients who are likely to be transferred to other health facility just after starting therapy (e.g., where patients are hospitalized during intensive phase)
- Hospitals or other facilities with a large proportion of transfers

The health facility may consider transferring the “box” to the facility responsible for the conclusion of the treatment for patients who need to be transferred during intensive or continuation phases.

Since there will be patients with adverse drug reactions (WHO suggests about 2-5 percent of the total), health facilities (or provincial stores) should keep a limited stock of non-FDC, loose medicines.

¹⁴ Moore, T. and H. Vrakking. 2004. *Technical visit to Kenya for Tuberculosis Packs: Trip Report. April 25-May 1, 2004*. Submitted to USAID by RPM Plus.

Management Support

The introduction of TB PK must be carefully planned. Written procedures, activities, and budget estimations need to be discussed and approved by the NTP technicians and authorities.

Preparatory activities must be implemented before the arrival of the TB-PK.

- The training of personnel considering all the elements presented in previous sections of this document.
- The adaptation of the stores with additional shelves, space for storing, and reconstitution of TB PK keeping security of storage areas in mind.
- A nationwide stock taking exercise to establish the stock levels of the loose medicines. The progressive scale up of the introduction of TB PK may be considered to avoid wastage of loose medicines.
- The introduction of TB PK implies that the NTP needs to update the national TB guidelines, procedures, and forms.

Once the TB PKs have been distributed to health facilities, the NTP needs to implement a strict monitoring system to correct any unexpected problems that may arise.

ANNEX 1. REPACKING PROCEDURES FOR TB PATIENT PACKS (RECOMMENDED FOR KENYA BY RPM PLUS)

Every month—the district supervisor will pick up all Patient Packs from health centers that are no longer being used for a patient. For example, when a TB patient transfers to another health center for treatment, stops coming to the health center, or dies, Patient Packs are no longer used. Since drugs are costly and the Ministry of Health (MoH) provides TB treatment free of charge, it is in the best interest of everyone to repack unused drugs into new Patient Packs.

Every quarter—the district supervisor will take all partially-used patient packs from their districts to the Kenya Medical Supplies Agency provincial stores where repacking will take place.

Note: Partially used Patient Packs should be picked up as quickly as possible since the RHZE product inside the Patient Pack has only a two-year expiry date.

Set up line for unpacking and repacking

- Set up a packing line using tables or other suitable furniture
- Have the quality inspector verify that no materials from previous unpacking or repacking operations have been removed before starting a new repacking operation

Unpacking the partially used Patient Packs

- Gather all Patient Packs and group into Category I and Category III at the head of the packing line
- Obtain two empty boxes, one for each of the drugs to be *unpacked* so as not to mix the drugs in the same container
- Open each partially used Patient Pack received from the districts, remove the contents which consist of inner boxes and blisters, and place in one of the empty boxes—only place one product per box so as not to mix products
- Continue this procedure until all partially used Patient Packs have been unpacked

Packing the new Patient Packs for Category I (repack Category I Patient Packs first before proceeding to repack Category III packs.)

- Make sure the repacking line is clear of all materials except those for repacking Category I Patient Packs
- Obtain a copy of the form *Record of Repacking Patient Packs for Category I* to control the repacking operation

- Take a Patient Pack *empty* container for Category I (RHZE and EH) and stick on two labels as follows—
 - A new preprinted label over the original label containing information about the patient’s name, weight, and registration number
 - A new preprinted label over the other end of the Patient Pack with the following information—
 - Repacked by GOK-MoH-NTLP on _____(date)
 - Patient Pack number _____
- For the Patient Pack container, you just label two prepared inner containers as follows—
 - Take an unpacked inner empty container labeled for RHZE and place inside 24 blisters of 10 tablets of RHZE
 - Examine all 24 blisters and choose the shortest expiration data (earliest expiration date)
 - Using a permanent ink marker, change the expiration date on the RHZE container to the shortest expiration date
 - Take an unpacked inner empty container labeled for EH and place inside 36 blisters of 10 EH tablets
 - Examine all 36 blisters and choose the shortest expiration data (earliest expiration date)
 - Using a permanent ink marker, change the expiration date on the EH container to the shortest expiration date
- Place the two inner containers of RHZE and EH into the newly labeled Patient Pack outer container for Category I patients
- For each new pack that is repackaged, write the following information on the form *Record of Repacking Patient Packs for Category I*—
 - Heading information
 - Each drug name and strength placed into the new pack (for example: EH 400/150 milligrams [mg])
 - Name of manufacturer of each drug
 - Expiration dates for each drug
 - For each drug name, the manufacturer’s batch or lot number
 - Quantity placed inside the new Patient Pack for each drug

Note: the NTLP will decide if Patient Pack inner and outer containers will be reused for repacking purposes, otherwise new containers of the same dimensions may be provided in which case you may not need to place the labels as indicated above

Packing the new Patient Packs for Category III

- Make sure the repacking line is clear of all materials except those for repacking Category III Patient Packs
- Obtain a copy of the form *Record of Repacking Patient Packs for Category III* to control the repacking operation
- Take all Patient Pack empty outer containers and stick on two labels as follows—

- A new preprinted label over the original label containing information about the patient's name, weight, and reference number
- A new preprinted label over the other end of the Patient Pack with the following information:
 - Repacked by GOK-MoH-NTLP on _____(date)
 - Patient Pack Number _____
- For the Patient Pack outer-container you just label two inner-containers as follows:
 - Use an unpacked inner empty container labeled to contain RHZ and place inside 24 blisters of 10 tablets of RHZ
 - Examine all 24 blisters and choose the shortest expiration data (earliest expiration date)
 - Using a permanent ink marker, change the expiration date on the RHZ container to the shortest expiration date
 - Use an unpacked inner empty container labeled to contain EH and place inside 36 blisters of 10 tablets of EH
 - Examine all 36 blisters and choose the shortest expiration data (earliest expiration date)
 - Using a permanent ink marker, change the expiration date on the EH container to the shortest expiration date
- Place the two inner containers of RHZ and EH into the newly labeled Patient Pack outer container
- For each new pack that is repackaged, write the following information on the form *Record of Repacking Patient Packs for Category III*—
 - Each drug name and strength placed into the new Patient Pack (for example: EH 400/150 mg)
 - Name of manufacturer of each drug
 - For each drug name, the expiry date
 - For each drug name, the manufacturer's batch or lot number
 - For each drug name, the quantity placed inside the new Patient Pack

Note: the NTLP will decide if Patient Pack inner and outer containers will be reused for repacking purposes, otherwise new containers of the same dimensions may be provided in which case you may not need to place the labels as indicated above.

Quality control

- There should be a minimum of two people carrying out the repacking operation
- The second person could serve as the quality inspector since a second person must verify the following information recorded on the form *Record of Reacking Patient Packs for Category III*—
 - Drugs and strengths are correct
 - Quantities are correct
 - Expiry dates are correct
 - Names of manufacturers are correct
 - Manufacturer's batch or lot numbers are correct

Finishing the repacking operation

- When there are no longer enough drug blisters to fully pack another Patient Pack stop the repacking operation
- Take the few drugs left over and dispose of them according to the procedures established by the MoH
- Take any unused inner or outer Patient Pack containers and store for future repacking operations (unless the NTLP decides to only use new containers)

Clearing the repacking line

- Before any repacking operation begins, the quality inspector must observe that the repacking line has been completely cleared of materials from the previous repacking operation
- Quality control inspector will then sign that the line has been cleared at the top of the forms *Record of Repacking Patient Packs* and is ready to be used for repacking

Retaining the forms *Record of Repacking Patient Packs*

- Retain all the forms *Record of Repacking Patient Packs for Category I* and *Record of Repacking Patient Packs for Category III* in a safe place.
- Establish an electronic spreadsheet to enter the information from the forms. This allows for sorting and location of specific repacked goods according to batch number of expiry date. Each form entered should have a special code for resorting that consists of the date, form number, and repacking center. For example, 405041A would mean 4 May 2004, form 1, of repacking center A.
- You may need to refer to these forms in the future to discount any discrepancy found in one of the repacked Patient Packs or if there is another quality complaint from the districts.

List of Excess Drugs Removed from Health Units

District: _____

Date: ____/____/____

Health Unit: _____

Supervisor: _____

Note: please list all batch numbers and expiration dates of the same drug

Name of drug	Strength of drug	Expiry dates	Quantities
RHZE	150/75/400/275 mg		
RHZ	120/50/300 mg		
EH	400/150 mg		
RH	150/100 mg		
E	400 mg		
S	1 gm		
S	750 mg		

Record of Repacking Patient Packs for Category I

Date repacking operation is carried out: _____

Persons working on repacking line: _____

Persons conducting quality control inspections: _____ Line cleared of all previous materials _____

Patient Pack number	Names and strengths of drugs added to new Patient Pack	Expiry date of each drug added	Name of manufacturer of each drug added	Manufacturer's batch or lot number of each drug added	Quantity of each drug added	Initials of person repacking	Initials of quality inspector
1	RHZE (150/75/400/275 mg)						
	EH (400/150 mg)						
2	RHZE (150/75/400/275 mg)						
	EH (400/150 mg)						
3	RHZE (150/75/400/275 mg)						
	EH (400/150 mg)						
4	RHZE (150/75/400/275 mg)						
	EH (400/150 mg)						

Record of Repacking Patient Packs for Category III

Date repacking operation is carried out: _____

Persons working on repacking line: _____

Persons conducting quality control inspections: _____ Line cleared of all previous materials _____

Patient Pack number	Names and strengths of drugs added to new Patient Pack	Expiry date of each drug added	Name of manufacturer of each drug added	Manufacturer's batch or lot number of each drug added	Quantity of each drug added	Initials of person repacking	Initials of quality inspector
1	RHZ (120/50/300 mg)						
	EH (400/150 mg)						
2	RHZ (120/50/300 mg)						
	EH (400/150 mg)						
3	RHZ (120/50/300 mg)						
	EH (400/150 mg)						
4	RHZ (120/50/300 mg)						
	EH (400/150 mg)						

ANNEX 2. TB PATIENT KITS OFFERED BY THE GDF

Stop TB Patient Kit FOR

CATEGORIES I AND III PATIENTS

Contains all drugs needed to treat 1 patient of the middle weight band (40–54 kg)

Treatment consists of **Intensive Phase** of 56 daily doses (2 months) and **Continuation Phase** of 112 daily doses (4 months)

STOP TB KIT CONTAINS IN 2 SEPARATE BOXES

- for the **Intensive Phase**:
4-drug fixed-dose combination tablets (FDC-4)
(RHZE 150/75/400/275 mg)
- for the **Continuation Phase**:
2-drug fixed-dose combination tablets (FDC-2)
(RH 150/75 mg)

Tablets are packed in blister sheets of 7 rows of 4 tablets

CATEGORY II PATIENTS

Contains all drugs needed to treat 1 patient of the middle weight band (40–54 kg)

Treatment consists of **Intensive Phase** of 84 daily doses (3 months) and **Continuation Phase** of 140 daily doses (5 months)

STOP TB KIT CONTAINS IN 3 SEPARATE BOXES

- for the **Intensive Phase**:
 - a) 4-drug fixed-dose combination tablets (FDC-4)
(RHZE 150/75/400/275 mg)
 - b) Streptomycin, water, syringes and needles (S 1 g)
- for the **Continuation Phase**:
3-drug fixed-dose combination tablets (FDC-3)
(RHE 150/75/275 mg)

R: rifampicin; H: isoniazid; Z: pyrazinamide; E: ethambutol

ANNEX 3. INSTRUCTION BOOKLET FOR THE UTILIZATION OF TB PATIENT KITS

**TB patient pack for individual patient use treatment of category I
This TB patient pack contains the following—**

- **Instruction booklet**
- **Control card**, printed on the inside of the lid of the box
- **Tablets for the two-month Intensive phase of treatment—RHZE (150/75/400/275 mg)**
- **Tablets for the six-month Continuation phase of treatment—EH (400/150 mg)**

Contents

Treatment for Category I TB patients

Part I: How to prepare the TB Patient Pack for one patient

Part II: Intensive phase of treatment with RHZE (150/75/400/275 mg)—How to administer the correct number of tablets to one patient

Part III: Continuation phase of treatment with EH (400/150 mg)—How to administer the correct number of tablets to one patient

Part IV: Patient Health Education

Part V: Community TB treatment

Introduction

This TB Patient Pack contains enough anti-TB drugs for a full DOTS treatment course for one patient of category I, for both Intensive and Continuation phases.

- For the intensive phase (RHZE: 150/75/400/275 mg), tablets are given in 60 doses for 2 months (i.e., 30 doses per month). RHZE tablets contain the drugs rifampicin, isoniazid, pyrazinamide, and ethambutol.
- For the continuation phase (EH: 400/150 mg), tablets are given in 180 doses for 6 months (i.e., 30 doses per month). EH tablets contain the drugs ethambutol and isoniazid.

During the Intensive phase patients should only receive treatment directly observed by a trained health professional.

The TB Patient Pack contains 24 blister sheets of 10 tablets (= 240 tablets) RHZE for the Intensive phase and 36 blister sheets of 10 tablets (= 360 tablets) EH for the Continuation phase of treatment.

The number of drugs in the TB Patient Pack is for one person of average weight (55–70 kg). If the patient weighs less than the average weight, you will need to adjust the number of blister sheets in the TB Patient Pack according to the following instructions.

Before deciding to use a TB Patient Pack for a specific person, ask if the patient is going to remain until the end of his treatment at your health center. If the patient is not going to remain, use separate blisters/tablets, since it will be difficult to transfer the pack with the patient.

Part I. How to Prepare the TB Patient Pack for One Patient

1. For each new patient, take one TB Patient Pack
2. Write the following information on the label on the side of the kit:
 - a. Patient's TB register number: _____
 - b. Patient's name: _____
 - c. Date: _____
3. Record the name and weight on the control card on the inside of the lid of the TB patient pack.
4. Check the number of tablets to be administered in each dose, according to the patient's weight, using Table 1, and record the number of tablets to give to the patient for each dose on the control card printed on the inside of the lid of the TB patient pack.

Table 1. Category I treatment (2 months Intensive/6 months Continuation phase)

Patient weighs	Intensive phase Number of tablets	Continuation phase Number of tablets
less than 30 kg	consult NLTP manual	consult NLTP manual
30-39 kg	2	2
40-54 kg	3	2
55-70 kg	4	2
greater than 70 kg	consult NLTP manual	consult NLTP manual

- Depending on the weight of the patient, take out blister sheets as indicated in table 2.

Table 2. Patient Kit for Category I treatment (2 months Intensive/6 months Continuation Phases)

Patient weighs	RHZE blisters (oblong tablets)	EH blisters (round tablets)
less than 30 kg	consult the NLTP manual	
30-39 kg	remove 12 blister sheets	stays the same
40-54 kg	remove 6 blister sheets	stays the same
55-70 kg	stays the same	stays the same
greater than 70 kg	consult the NLTP manual	

5. To store extra blisters you removed from an individual patient pack, do the following—
 - a. Take any suitable empty box, like an empty medicines box
 - b. On the outside of the box write **Supply Box RHZE**

- c. Any extra blisters you removed when adjusting the patient boxes can be placed in the Supply Box
 - d. Any additional blisters you might need for treating “in-transit” patients or to extend the intensive phase with an extra month, you can take from the Supply Box
 - e. When a Supply Box is full, prepare a new Supply Box as described above—full supply boxes will be collected by your NLTP supervisor
6. In unusual cases, the treatment of a patient may need to be extended in the Intensive phase by an additional 1 month for a total of 3 months rather than the normal 2 months.
- a. For these patients, do the following—
 - i. For a patient in the weight band 30-39 kg, take out 6 blister sheets of RHZE from the *Supply Box*
 - ii. For a patient in the weight band 40-54 kg, take out 9 blister sheets of RHZE from the *Supply Box*
 - iii. For a patient in the weight band 55-70 kg, take out 12 blister sheets of RHZE from the *Supply Box*
 - b. Place the extra blister sheets of RHZE inside the individual patient pack for that patient; check the name on the side of the pack to make sure it is the correct patient
 - c. Continue to administer the same number of tablets for the additional month as you did for the first 2 months before starting treatment for the Continuation phase.
 - d. Double-tick the control card with a red pen in the boxes 1 through 30 for the Intensive phase.
7. If a patient defaults, dies, or transfers from your health center and the patient pack does not go with the patient, store the pack until your supervisor collects the pack on the next supervisory visit.

Part II. Intensive Phase with RHZE (150/75/400/275 mg)—How to Administer the Correct Number of Tablets to Each Patient

1. Take the TB patient pack you have prepared from the storage shelf.
2. Verify that the patient name on the side of the pack is the same as the patient you are getting ready to treat.
3. Open the TB patient pack, take the inner box containing RHZE (orange color), and remove the first blister sheet containing RHZE tablets (oblong tablets)
4. If you have already started treating this patient take out the blister sheet already in use from the pack
5. Observe the patient's weight and number of tablets you previously recorded on the control card on the inside of the lid of the TB patient pack, to know how many RHZE tablets to give the patient.
6. Remove the correct number of tablets from the blister sheet; double check that the number of tablets you are giving corresponds with the patient's weight (see following table)

Patient weighs	Number of RHZE tablets to give patient
less than 30 kg	consult the NLTP manual
30-39 kg	2
40-54 kg	3
55-70 kg	4
greater than 70 kg	consult the NLTP manual

7. Observe the patient taking the number of tablets you have prepared
8. Return the blister sheet to the patient pack. Return the blister sheet even if the last tablet has been removed; this serves as a double check of doses taken by the patient
 - a. Immediately tick the next dose number on the control card on the inside of the lid of the TB patient pack, to show that the drug was taken by the patient.
 - b. Be sure to tick the correct number of the dose given; doses are numbered 1 through 60 for the Intensive phase

Note: The control card never replaces the TB Treatment Card and the TB Register, which have to be filled in as usual.

Part III. Continuation Phase with EH (400/150 mg)—How to Administer the Correct Number of Tablets to Each Patient

1. Take the TB Patient Pack you have prepared from the storage shelf
2. Verify that the patient name on the side of the Pack is the same as the patient you are getting ready to treat.
3. Open the TB patient pack, take the inner box containing EH (blue box) and remove the first blister sheet containing the EH (round) tablets.
4. If you have already started treating this patient remove the drug blister sheet already in use from the Pack
5. All patients weighing between 30 and 70 kg receive 2 tablets per dose. If a patient weighs less than 30 kg or more than 70 kg, consult the NLTP manual
6. Remove the correct number of tablets from the blister; double check that the number of tablets you are giving corresponds with the patient's weight.
7. Observe the patient taking the number of tablets you have prepared
8. Return the blister sheet to the patient pack. Return the blister sheet even if the last tablet has been removed; this serves as a double check of doses taken by the patient
9. Immediately write on the control card that the drug was taken by the patient. You will do this by ticking the dose number printed on the inside of the lid of the TB patient pack
10. Be sure to record the correct number of the dose given; doses are numbered 1 through 180 doses for the continuation phase
11. When the patient's entire treatment is finished (intensive and continuation phases) keep the empty patient pack separate to show to your supervisor on his/her next visit.

Note: In some patients an adverse reaction to one or more TB drugs may occur. Adverse reactions, such as skin rashes are not very common, but when they do happen, immediately contact your supervisor to determine if the TB drugs for that patient should be changed or stopped altogether

Part IV. Patient Health Education—How to Inform the Patient After Diagnosis About His or Her Disease, Treatment, and Cure

The information a patient receives from the health worker at the start of his or her TB treatment is a crucial factor in patient compliance and eventual cure. The TB patient pack can contribute greatly to improve patient compliance and the chances to be fully cured, as long as the right messages are given.

The health worker should ensure that sufficient time is set aside to advise a patient (and his DOTS supervisor if applicable) when the TB treatment starts.

The health worker will do this by—

1. Giving some explanation on the disease of tuberculosis, its cause, development, and outcome if it is not treated
2. The health worker will then take one new TB patient pack, show it to the patient explaining this will be his personal treatment pack and demonstrating this by recording his name and TB register number on the outside label and the rest of the data on the control card on the inside of the lid.
3. The health worker will then explain how TB can be treated and cured: the intensive and continuation phases, and the duration of treatment, by showing the patient that the TB patient pack contains **all** the medicines needed to be cured, and by demonstrating the duration of the treatment by showing the 2 inner boxes and their contents.
4. The health worker then explains that the number of tablets to be taken is determined by the weight of the patient. The patient is then weighed, the number of tablets per dose is determined. This is demonstrated by removing the blisters RHZE as required, showing the number of tablets per dose in the blister sheet, and removing the first dose from the blister sheet.
5. The patient is then asked to take the first dose of RHZE tablets under the direct observation of the health worker.
6. Next the health worker explains how TB infects others and what can be done to prevent this. The patient will be encouraged to bring relatives and other acquaintances who have similar symptoms to the clinic for screening.
7. Finally the health worker will explain how multidrug-resistant (MDR) tuberculosis develops and how dangerous and costly this type of TB is to treat in the patient and in those persons he or she will eventually infect.
8. Stress once more that TB can be cured, but only by taking ALL the tablets in the TB Patient Pack, in the prescribed quantities, and without interruption.

Part V. How to Control Treatment when Patients Receive TB Drugs at Home

For TB treatment to be effective, every dose a patient takes must be directly observed by another person. Ask your supervisor if your national TB program has established a community volunteer system, whereby observed treatment is done by someone near the patient's home. If so, you can control TB drug treatment as follows—

1. Prepare the Patient Pack exactly as previously described
 - a. Label the pack with the patient's TB treatment register, name, and today's date.
 - b. Write the patient's name, weight, the number of tablets to take in one dose and the starting date of the treatment on the inside of the lid of the TB patient pack.
 - c. Adjust the number of RHZE blister sheets in the pack according to patient's weight.
2. Explain how to administer the drugs to both the patient and the community volunteer making sure to include the following information—
 - a. There are 2 phases of treatment: Intensive phase for 2 months and Continuation phase for 6 months
 - b. 4-drug combination tablets (RHZE) are given during the Intensive phase
 - c. 2-drug combination tablets (EH) should be given during the Continuation phase
 - d. How many tablets should be taken for 1 dose, for the RHZE tablets depends on the patient's weight. (see part I) The number of EH tablets per dose is 2 tablets for most patients. (see part III)
 - e. Write the number of tablets for 1 dose on the control card printed on the inside of the lid of the pack.
3. Explain how many doses must be given for each phase
 - a. Give a total of 60 doses for Intensive phase
 - b. Give a total of 180 doses for the continuous phase
4. Explain to the observer how to record each dose that is taken on the control card .
5. Tell patient and volunteer that empty blisters must be returned to the health center every time new drugs are collected and finally when treatment is finished.

Note: Tell patient to return to the clinic if signs of adverse reactions appear, such as unusual skin rashes.