Active tuberculosis drug-safety monitoring and management (aDSM)

Framework for implementation

THE END TB STRATEGY

World Health Organization

Active tuberculosis drug-safety monitoring and management (aDSM)

Framework for implementation

World Health Organization

Editing and design by Inis Communication – www.iniscommunication.com

Printed by the WHO Document Production Services, Geneva, Switzerland WHO/HTM/TB/2015.28

Contents

Abbreviations

ADR	adverse drug reaction
aDSM	active tuberculosis drug-safety monitoring and management
AE	adverse event
ALT	alanine aminotransferase
AST	aspartate aminotransferase
GDF	Global Drug Facility
GTB	Global TB Programme
EMP	WHO Essential Medicines and Health Products Department
KNCV	KNCV Tuberculosis Foundation, Netherlands
MDR-TB	multidrug-resistant TB
MSF	Médecins Sans Frontières
NPV	national pharmacovigilance system
NTP	national TB programme
PMDT	programmatic management of drug-resistant TB
SAE	serious adverse event
SGOT	serum glutamic-oxaloacetic transaminase
SGPT	serum glutamic pyruvic transaminase
TB	tuberculosis
TDR	Special Programme for Research and Training in Tropical Diseases
TSH	thyroid stimulating hormone
ULN	upper limit of normal
USAID	United States Agency for International Development
XDR-TB	extensively drug-resistant TB
γGT	gamma glutamyl transferase

Background

Health programmes that systematically monitor patient safety are at an advantage to prevent and manage adverse drug reactions (ADRs), as well as improve health-related quality of life and treatment outcomes. National tuberculosis programmes (NTPs) that actively pursue drug-safety monitoring and management are also better prepared to introduce new tuberculosis (TB) drugs and novel regimens.

The prospect of new anti-TB drugs and use of novel regimens led WHO to release its first implementation manual for pharmacovigilance of anti-TB drugs in 2012 *(1)*. Later in 2012, WHO provided interim advice that the use of shorter regimens for multidrug-resistant TB (MDR-TB) be accompanied by the collection of drug-safety data within a framework of observational research *(2)*. In 2013 and 2014, the WHO interim policies on bedaquiline and delamanid recommended active pharmacovigilance as one of the five conditions to be met when using these drugs to treat MDR-TB patients *(3,4)*.

NTPs and other stakeholders are now starting to introduce new anti-TB drugs and novel MDR-TB regimens according to WHO recommendations. A number of programmes managing MDR-TB patients have also introduced active pharmacovigilance to monitor drug-safety and take early action to avert treatment interruption and other unfavourable patient outcomes *(5–7)*.

The application of pharmacovigilance methods (such as cohort event monitoring) described in the 2012 implementation manual for pharmacovigilance of anti-TB drugs in 2012 *(1)*, was largely based on experience with the use of drugs for malaria, human immunodeficiency virus (HIV) and noncommunicable diseases. This however led to practical questions related to the implementation of drug-safety monitoring alongside other components of programmatic management of drug-resistant TB (PMDT).

The lack of familiarity of many TB practitioners with the principles of drug-safety monitoring and the limited capacity of national drug-safety authorities in some countries to provide the necessary support, generated a demand for more explicit guidance. A recent survey conducted by Médecins Sans Frontières (MSF) and the Stop TB Partnership Global Drug Facility (GDF) in the 27 high MDR-TB burden countries, showed concerns about ADRs being one of the main barriers to the introduction of bedaquiline and delamanid (MSF/GDF, unpublished information).

Several stakeholders expressed concern that the introduction of new anti-TB drugs may be slowed down or even prevented due to a lack of capacity for countries to mount active pharmacovigilance. In response, the WHO Global TB Programme (WHO/GTB) convened key technical and funding agencies to a meeting in Geneva, Switzerland on 28–29 July 2015

to discuss essential requirements for the implementation of active pharmacovigilance and proper management of ADRs when introducing new anti-TB medicines or novel MDR-TB regimens. This document reflects the consensus achieved during this meeting and in subsequent discussions involving NTP managers of selected countries and the WHO Essential Medicines and Health Products Department (see list of contributors in Annex 1).

Other WHO documents – particularly the *Companion handbook to the WHO guidelines for the programmatic management of drug-resistant TB* (henceforth termed "PMDT Handbook" in this document) *(8)*, *Policy implementation package for new TB drug introduction (9),* and the current WHO/GTB website on TB drug safety as well as the associated frequently asked questions *(10)* – will be updated accordingly.