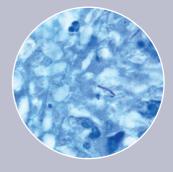
# A PRACTICAL HANDBOOK ON THE PHARMACOVIGILANCE OF MEDICINES USED IN THE TREATMENT OF TUBERCULOSIS

#### ENHANCING THE SAFETY OF THE TB PATIENT







World Health Organization

A practical handbook on the pharmacovigilance of medicines used in the treatment of tuberculosis

ENHANCING THE SAFETY OF THE TB PATIENT



WHO Library Cataloguing-in-Publication Data:

A practical handbook on the pharmacovigilance of medicines used in the treatment of tuberculosis: enhancing the safety of the TB patient

 Drug monitoring. 2.Drug utilization review – methods.
Antitubercular agents – adverse effects. 4.Adverse drug reaction reporting systems. 5.Handbooks. I.World Health Organization.

ISBN 978 92 4 150349 5

(NLM classification: QV 771)

#### © World Health Organization 2012

All rights reserved. Publications of the World Health Organization are available on the WHO web site (www.who.int) or can be purchased from WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel.: +41 22 791 3264; fax: +41 22 791 4857; e-mail: bookorders@who.int). Requests for permission to reproduce or translate WHO publications – whether for sale or for noncommercial distribution – should be addressed to WHO Press through the WHO web site (http://www.who.int/about/licensing/copyright\_form/en/index.html).

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use.

Designed by minimum graphics Printed in France

# **Contents**

Abbreviations and acronyms Acknowledgements Preface: Why pharmacovigilance for anti-TB medicines? Key messages				
A. Introduction 1				
1. 2. 3. 4.	Pharmacovigilance General aims Specific aims Pharmacovigilance centre (PvC)	1 2 2 3		
B. Which approach to pharmacovigilance? 5				
1. 2. 3.	Spontaneous reporting Targeted spontaneous reporting (TSR) Active surveillance	5 5 5		
C. Spo	ntaneous reporting	7		
1. 2. 3. 4. 5. 6. 7. 8. 9. 10.	Introduction Objectives and methodology Minimum reporting requirements How to report What to report When to report Who should report Follow-up Sharing the results Data entry	7 7 8 9 10 12 12 12 12 12 12 13		
D. Tar	geted spontaneous reporting (TSR)	14		
1. 2.	Introduction Objectives and methodology	14 14		

E. Coh	ort event monitoring (CEM)	16
1.	Introduction	16
2.	Objectives and methodology	16
3.	Implementation	19
4.	Establishing the cohort(s)	20
5.	Acquiring the data	22
6.	Database for CEM	32
7.	Maximizing the reporting rate	35
8.	Practical advice and information	37
9.	Clinical review	38
F. Data	a processing	43
G. Rel	ationship and causality assessment	45
1.	Background	45
2.	Relationship ("objective phase")	45
3.	Categories of relationship	47
4.	Processes for establishing the relationship	50
5.	Causality ("subjective phase")	52
H. Spe	cial types of event	53
1.	Serious events	53
2.	Pregnancy	53
3.	Lactation exposure	55
4.	Deaths	55
5.	Lack of efficacy	55
6.	Late onset reactions	56
7.	Co-morbid conditions	56
I. Sign	al identification	57
1.	Introduction	57
2.	Selection criteria for events to investigate	58
3.	Methods of signal identification	58

J. Evaluating a signal 62				
1.	Gene	ral approach	62	
2.	2. Other experience		62	
3.	3. Searching for non-random patterns		63	
4.	4. Comparison with control events		63	
5.	5. Pharmacology			
6.		rtaking epidemiological studies	64	
7.	Comr	nunication and feedback	64	
K. Ide	entifying	risk factors	65	
1.	Intro	duction	65	
2.	ldent	fication	65	
L. Dai	ta descr	iption and analysis	67	
M. Or	ganizati	on	70	
1.		lation	70	
2.	•	al issues	71	
3.	Struc		74	
4.	Comr	nunication	76	
Annexes 81				
An	nex 1.	Useful websites and other resources	83	
An	inex 2.	Form for spontaneous reports of suspected adverse drug reactions (ADRs) (Ghana)	90	
۸n	inex 3.	Relationship between sample size and probability of	90	
	IIICA 0.	observing an adverse event (AE)	91	
Annex 4.		Abbreviations for tuberculosis (TB) medicines and regimens	92	
Annex 5.		List of adverse drug reactions (ADRs) commonly associated with anti-tuberculosis (TB) medication	93	
An	nex 6.	Treatment initiation form	94	
An	nnex 7.	Treatment review form	99	
An	nex 8.	Tuberculosis identity card	104	
Annex 9.		Manual coding sheet	105	
Annex 10.		Major clinical categories in events dictionary	107	
An	inex 11.	Decision tree for cohort event monitoring	108	
Gloss	arv		109	

# **Abbreviations**

ADRs	adverse drug reactions (to medicines, vaccines, herbal and traditional medicines)
AIDS	acquired immunodeficiency syndrome
ARV	antiretroviral
АТС	Anatomic Therapeutic Chemical Classification (for medicines)
BMI	body mass index
CEM	cohort event monitoring
CemFlow	electronic tool for data entry and analysis in cohort event monitoring
DD	(WHO) Drug dictionary
DF	dosage form (for combination therapy)
DOB	date of birth
DOTS	internationally agreed strategy for TB control
Е	ethambutol
E2B	standardized data elements for transmission of ICSRs
FDC	fixed dose combination
GEATM	Global Fund to Fight AIDS TR and Malaria

### 预览已结束,完整报告链接和二维码如下:



https://www.yunbaogao.cn/report/index/report?reportId=5\_28506