

Use of MedDRA: Focus on the New Scope of Adverse Event Reporting

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Overview



- Existing terms in MedDRA for off label use, overdose, misuse, abuse, medication errors, and occupational exposure
- Current coding recommendations in MedDRA
Term Selection: Points to Consider document (MTS:PTC) for MedDRA
 - Significant revision to PTC document to support these types of terms

MedDRA® TERM SELECTION: POINTS TO CONSIDER

ICH-Endorsed Guide for MedDRA Users

Release 4.5
Based on MedDRA Version 16.0

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- There are two PTC documents
 - Term Selection
 - Data Retrieval and Presentation
- Using MedDRA is a big step forward
- Using MedDRA the same way is a leap toward harmonization

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Off Label Use – Terms in MedDRA (1)

- Currently in MedDRA

PT	Off label use
LLT	Adult product administered to child
LLT	Child product given to infant
LLT	Drug use for unapproved indication
LLT	Drug use in unapproved population
LLT	Drug use via unapproved administration route
LLT	Intentional use for unlabeled indication
LLT	Intentional use for unlabelled indication
LLT	Off label use

- MedDRA Introductory Guide, Appendix B (Concept Descriptions) includes the following:

Off Label Use

Off label use is defined as a practice of prescribing pharmaceuticals outside the scope of the drug's approved label, most often concerning the drug's indication.

- Off label use
This relates to situations where the medicinal product is intentionally used for a medical purpose not in accordance with the authorised product information

EMA. Guideline on good pharmacovigilance practices (GVP)
Module VI – Management and reporting of adverse reactions to medicinal products

3.26.1 Off label use when reported as an indication

"Off label use" refers to use of a product for an indication for which it is not labeled.

If a medical condition is reported as an indication **along with "off label use"**, the **preferred option** is to select terms for the medical condition and LLT *Off label use* or other appropriate LLTs linked to PT *Off label use* for the "indications" field. Alternatively, select a term for the medical condition/indication alone. Select LLT *Off label use* alone **only** if it is the only information available.

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Example

Reported	LLT Selected	Preferred Option
Hypertension; this is off label use	Hypertension	
	Hypertension Off label use	✓

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Example

Reported	LLT Selected	Comment
Off label use	Off label use	
Off label use in paediatric patients	Drug use in unapproved population	Refers to a population of patients
Drug X given to a 10 year old boy; the drug is not indicated for use below 18 years	Adult product administered to child	LLT <i>Adult product administered to child</i> is linked to PT <i>Off label use</i>

3.26.2 Off label use when reported with an AR/AE

If an AR/AE occurs as a result of off label use, the **preferred option** is to select LLT *Off label use*, or other appropriate LLTs linked to PT *Off label use*, and a term for the medical condition for the "indications" field in addition to a term for the AR/AE. Alternatively, select a term for the medical condition for the "indications" field and a term for the AR/AE in the "AR/AE" field.

Example

Reported	LLT Selected	Preferred Option	Comment
Patient was administered a drug off label for pulmonary hypertension and suffered a stroke	Stroke Pulmonary hypertension		Record LLT <i>Stroke</i> in an AR/AE field. Record LLT <i>Pulmonary hypertension</i> in an indications field.
	Stroke Off label use Pulmonary hypertension	✓	Record LLT <i>Stroke</i> in an AR/AE field. Record LLT <i>Off label use</i> and LLT <i>Pulmonary hypertension</i> in an indications field.

- Add revised definition of “off label use” to MTS:PTC and MedDRA Introductory Guide
- Remove all references to using specific “indications” and “AR/AE” data fields

“Overdose” LLTs (MedDRA v15.0) [TOTAL = 27]		
Accidental overdose	Drug toxicity due to accidental overdosage	Overdose
Accidental overdose (nontherapeutic agent or chemical)	Drug toxicity due to intentional overdose	Overdose accidental
Accidental overdose (therapeutic agent)	Intentional overdose	Overdose deliberate self-inflicted
Acute overdose	Medically prescribed overdose	Overdose effect
Chronic overdose	Multiple drug overdose	Overdose intentional
Deliberate overdose	Multiple drug overdose accidental	Overdose NOS
Drug overdose	Multiple drug overdose intentional	Prescribed overdose
Drug overdose accidental	Multiple drug overdose prescribed	Radiation overdose
Drug overdose deliberate self-inflicted	Non-accidental overdose	Suicide attempt other than overdose

- MedDRA Introductory Guide (v15.1), Appendix B (Concept Descriptions)

Overdose

More than medically recommended dose (in quantity and/or concentration) is administered.
An excessive dose.

- Overdose

This refers to the administration of a quantity of a medicinal product given per administration or cumulatively, which is above the maximum recommended dose according to the authorised product information. Clinical judgement should always be applied.

EMA. Guideline on good pharmacovigilance practices (GVP)
Module VI – Management and reporting of adverse reactions to medicinal products.

3.17.1 Overdose reported with clinical consequences

Select terms for overdose and for clinical consequences reported in association with an overdose.

Example

Reported	LLT Selected
Stomach upset from study drug overdose	Stomach upset Overdose

3.17.2 Overdose reported without clinical consequences

If an overdose report specifically states that there were no clinical consequences, select LLT *Overdose* and the additional LLT *No adverse effect* can be selected (See Section 3.20).

Example

Reported	LLT Selected	Comment
Patient received an overdose of medicine without any adverse consequences	Overdose No adverse effect	LLT <i>No adverse effect</i> can also be selected

- Provide additional examples of term selection

“Misuse” Terms [TOTAL = 7] (MedDRA v15.0)

Device misuse
Intentional device misuse
Intentional drug misuse
Intentional misuse
Intentional misuse by dose change
Intentional misuse in dosing frequency
Unintentional device misuse

- Concept has been challenging to define
 - Is all misuse “intentional”?
- No wording in current MTS:PTC addressing “misuse”

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- Misuse
This refers to situations where the medicinal product is intentionally and inappropriately used not in accordance with the authorised product information.

EMA. Guideline on good pharmacovigilance practices (GVP)
Module VI – Management and reporting of adverse reactions to medicinal products.

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- Add a new sub-section to MTS:PTC – Misuse, abuse and addiction
- Add definitions of these concepts to MTS:PTC and MedDRA Introductory Guide
- Provide examples of term selection

Abuse – Terms in MedDRA (1)

“Abuse” and “Abusive” Terms (MedDRA v15.0) [TOTAL = 95]			
Abusive behavior	Analgesic abuse	Cannabis abuse, episodic use	Diuretic abuse
Abusive behaviour	Antabuse effect	Cannabis abuse, in remission	Drug abuse
Alcohol abuse	Antabuse implant	Cannabis abuse, unspecified use	Drug abuse in remission
Alcohol abuse chronic	Antidepressant type abuse	Chemical abuser	Drug abuse NOS
Alcohol abuse, continuous drinking behavior	Antidepressant type abuse, continuous use	Child abuse	Drug abuser
Alcohol abuse, continuous drinking behaviour	Antidepressant type abuse, episodic use	Child abuser	Drug abuser NOS
Alcohol abuse, episodic drinking behavior	Antidepressant type abuse, in remission	Child sexual abuse	Elder abuse
Alcohol abuse, episodic drinking behaviour	Antidepressant type abuse, unspecified use	Cocaine abuse	Elder abuser
Alcohol abuse, in remission	Barbiturate abuse	Cocaine abuse, continuous use	Enema abuse
Alcohol abuse, unspecified drinking behavior	Caffeine abuse	Cocaine abuse, episodic use	Ex-drug abuser
Alcohol abuse, unspecified drinking behaviour	Cannabis abuse	Cocaine abuse, in remission	Hallucinogen abuse
Amphetamine abuse	Cannabis abuse, continuous use	Cocaine abuse, unspecified use	Hallucinogen abuse, continuous use

“Abuse” and “Abusive” Terms (MedDRA v15.0) [TOTAL = 95] (cont)			
Hallucinogen abuse, episodic use	Nondependent abuse of drugs	Opioid abuse, unspecified use	Tobacco abuse
Hallucinogen abuse, in remission	Nondependent abuse of drugs of amphetamine type	Physical abuse	Tranquillizer abuse
Hallucinogen abuse, unspecified use	Nondependent abuse of drugs of cocaine type	Polydrug abuse	Verbal abuse
Infection in patient who abuses drugs	Nondependent abuse of drugs of morphine type	Polysubstance abuse	Verbal abuser
Intravenous drug abuser	Nondependent abuse of drugs, antidepressants	Psychological abuse	Verbally abused
Laxative abuse	Nondependent abuse of hallucinogens	Sexual abuse	Victim of abuse
Narcotic abuse	Nondependent abuse of tobacco	Sexual abuser	Victim of child abuse
Neonatal complications of substance abuse	Non-dependent tobacco abuse	Spousal abuse	Victim of elder abuse
Neonatal complications of substance abuse NOS	Opioid abuse	Spousal abuser	Victim of sexual abuse
Nicotine abuse	Opioid abuse, continuous use	Steroid abuse	Victim of spousal abuse
Nondependent abuse of alcohol	Opioid abuse, episodic use	Substance abuse	
Nondependent abuse of cannabis	Opioid abuse, in remission	Substance abuser	Volatile solvent abuser

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- No wording in current MTS:PTC specifically addressing “abuse”
- MedDRA Introductory Guide (v15.1)

SOC *Psychiatric disorders*, “Basis for Classification”

Conditions associated with substance abuse (e.g., LLT *Enema abuse*, LLT *Laxative abuse* under PT *Drug abuse*, and PT *Alcoholism*) are included in SOC *Psychiatric disorders* in HLT *Substance-related disorders*.

According to DSM-IV, the official psychiatric term for addiction is “substance dependence.” Therefore, the word “addiction,” in general, only appears at the LLT level in MedDRA.

For new “abuse” terms in MedDRA, the text string is devised to distinguish terms in SOC *Social circumstances* from those in SOC *Psychiatric disorders*. “Abuse” terms are linked to SOC *Psychiatric disorders* and kept independent of “dependence” counterparts PTs. Terms that refer to a person, such as PT *Drug abuser*, are in SOC *Social circumstances*.

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- Abuse

This corresponds to the persistent or sporadic, intentional excessive use of a medicinal product, which is accompanied by harmful physical or psychological effects

EMA. Guideline on good pharmacovigilance practices (GVP)
Module VI – Management and reporting of adverse reactions to medicinal products.

- Add a new sub-section to MTS:PTC – Misuse, abuse and addiction
- Add definitions of these concepts to MTS:PTC and MedDRA Introductory Guide
- Provide examples of term selection

- Prior to MedDRA Version 8.0, only one term existed - *PT Medication error*
- Medication error section expanded in v8.0
 - Added HLT *Medication errors in SOC Injury, poisoning and procedural complications*
 - HLT *Maladministrations*
 - HLT *Medication errors due to accidental exposures*
 - HLT *Medication monitoring errors*
 - HLT *Overdoses*
 - HLT *Medication errors NEC*

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- MedDRA Introductory Guide (v15.1), Appendix B (Concept Descriptions)

Medication errors are defined as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in control of the health care professional, patient or consumer. Such events may be related to professional practice, health care products, procedures and systems, including prescribing, order communication, product labeling, packaging and nomenclature, compounding, dispensing, distribution, administration, education, monitoring and use.

- A preventable event
 - Intentional action is NOT an “error”
- Includes intercepted and not intercepted errors, because
 - Patient harm is NOT required
 - Inappropriate use of the medication is NOT required
- Applies to all stages of medication handling and process

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- Appendix B in MedDRA Introductory Guide
- To assist in understanding and appropriate use of medication error and product quality issue terms in regulatory reporting
- Medication error descriptions developed by FDA and MSSO

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3.15 – Medication/Administration Errors and Accidental Exposures

Reports of medication errors may or may not include information about clinical consequences.

Appendix B of the MedDRA Introductory Guide contains descriptions of the interpretation and use of certain medication error terms (e.g., “Dispensing error”).

3.15.1 Medication error reported with clinical consequences

3.15.2 Medication error reported without clinical consequences

3.15.3 Accidental exposures

3.15.4 Medication errors in the context of labeled interactions

3.15.5 Do not infer a medication error

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- There can be overlap between product quality issues and medication errors
- An example of both a product quality issue and a medication error is provided

Reported	LLT Selected	Comment
The mother administered insufficient amount of prescribed antibiotic because the lines on the dropper were hard to read	Product dropper calibration unreadable Insufficient dosage	Product quality issue and medication error

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- Add definition of medication error to MTS:PTC

**“Occupational Exposure”
Terms [TOTAL = 11]
(MedDRA v15.0)**

Occupational exposure to air contaminants
Occupational exposure to air contaminants NOS
Occupational exposure to drug
Occupational exposure to dust
Occupational exposure to extreme temperature
Occupational exposure to noise
Occupational exposure to radiation
Occupational exposure to toxic agent
Occupational exposure to toxic agents NOS
Occupational exposure to toxic agricultural agents
Occupational exposure to vibration

- Occupational exposure
This refers to the exposure to a medicinal product as a result of one's professional or non-professional occupation

EMA. Guideline on good pharmacovigilance practices (GVP)
Module VI – Management and reporting of adverse reactions to medicinal products.

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- Not specifically referenced, but covered under “accidental exposures”

3.15.3 Accidental exposures

The same principles apply to accidental exposures.

Example

Reported	LLT Selected
Nurse splashed injectable drug in her own eye resulting in excessive tearing	Inadvertent exposure to drug Excess tears
Child accidentally took grandmother's pills and experienced projectile vomiting	Accidental drug intake by child Vomiting projectile
Father applying topical steroid to his arms accidentally exposed his child to the drug by carrying her	Exposure via skin contact

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- Add a new sub-section to MTS:PTC – Accidental exposures and occupational exposures
- Add definition of “occupational exposure” to MTS:PTC and MedDRA Introductory Guide
- Provide examples of term selection

Summary

- There is regulatory interest in “special situations”
 - Off label use
 - Overdose
 - Misuse
 - Abuse
 - Medication errors
 - Occupational exposure
- MedDRA covers most such concepts and can expand as needed through Change Requests
- MTS:PTC also addresses some of these; more may come in the future

Thank You

