Terminologies for coding of adverse reactions and drug information

Uppsala PV training course

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Aims & Goals

• To get enough knowledge about terminologies so that you can use them when coding in VigiFlow (or any other system) and searching in VigiLyze.

• What to do when you can’t find a term you are looking for.
Outline

• Understand the need for terminologies
• What main terminologies are used in UMC tools
• WHO Drug Dictionaries
• Medical terminologies (WHO-ART, MedDRA)
Definition of Pharmacovigilance

The science and activities relating to the...

• detection
• assessment
• understanding
• prevention

...of adverse effects or any other drug-related problem
Why do we need terminologies?

- To be able to retrieve data in a consistent way from a database
- To be able to store data in a consistent way in a database
## Freedom versus structure

<table>
<thead>
<tr>
<th>Free text</th>
<th>Coded data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete representation of complex data</td>
<td>Computerised retrieval and analysis easy and efficient</td>
</tr>
<tr>
<td>Flexible, expressive, familiar</td>
<td>Language independence</td>
</tr>
<tr>
<td>Computerised retrieval and analysis difficult</td>
<td>Data entry requires transformation of the information</td>
</tr>
<tr>
<td>Language dependent</td>
<td>risk of loss/distortion</td>
</tr>
</tbody>
</table>
Terminologies in the WHO ICSR database

- WHO-ART
- MedDRA
- ICD
- WHO DD
- ATC

+ lexicon tables

ICSR info
- Reaction
- Death cause
- Diagnosis
- Medicinal background
- Drug
WHO Drug Dictionaries

Malin Jakobsson, MSc Pharm
Product Manager
Outline

- What is coding?
- WHO Drug Dictionaries
- Drug analysis
- WHO Drug Dictionary users
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Substance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arinate</td>
<td>Artesunate</td>
</tr>
<tr>
<td>Arinate</td>
<td>Efra S.A</td>
</tr>
<tr>
<td>Arinate</td>
<td>Tanzania, United Republic of</td>
</tr>
<tr>
<td>Arinate</td>
<td>TABLETS, Unspecified</td>
</tr>
<tr>
<td>Arinate</td>
<td>Not specified</td>
</tr>
<tr>
<td>Arinate</td>
<td>Tanzania, United Republic of</td>
</tr>
<tr>
<td>Arinate</td>
<td>no form or strength information available</td>
</tr>
<tr>
<td>Arsitacam</td>
<td>Artesunate</td>
</tr>
<tr>
<td>Arsumax</td>
<td>Artesunate</td>
</tr>
<tr>
<td>Artemax</td>
<td>Artesunate</td>
</tr>
<tr>
<td>Artenex</td>
<td>Artesunate</td>
</tr>
<tr>
<td>Artesunate</td>
<td>Artesunate</td>
</tr>
<tr>
<td>Askasunate</td>
<td>Artesunate</td>
</tr>
<tr>
<td>Falcigo</td>
<td>Artesunate</td>
</tr>
<tr>
<td>Gsinate</td>
<td>Artesunate</td>
</tr>
<tr>
<td>Plasmotrim</td>
<td>Artesunate</td>
</tr>
</tbody>
</table>
What is coding?

Staderm given

Ibuprofen

Staderm tablets

Ibuprofen from Glaxo

Nurofen to treat migraine

A bunch of medicines

Ibuprofen

Nurfenpro

A blue pill

Pain killer

Ibbuprofen

Staderm tablets

Ibuprofen

Nurofen migraine

Nurofen to treat migraine

Nurfenpro

a lot of Nurfenpro

Migraine

Ibuprofen piconol

Brufen 40

Staderm.

A blue pill

The Uppsala Monitoring Centre

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What is drug coding?

- Staderm
- Ibuprofeno
- Nurfenpro
- Ibuprofen piconol
- Nurofen migraine
- Brufen 40
- Ibuprofen
- Staderm tablets

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The added value of WHO Drug Dictionaries
The WHO Drug Dictionaries
### The WHO Drug Dictionaries

**Holds standardized medicinal information on:**

- Trade name
- Active ingredient(s)
- MAHolder
- Strength
- Country of sales

### Released

- Quarterly (text files)
- Weekly (VigiFlow, CEM Flow)
- Monthly (VigiSearch/VigiLyze)
The WHO Drug Dictionaries

- CRT
- Japan
- SDGs
- WHO DD DRL
- WHO DDE
- WHO DDE+
- HD
- DDC
Product types in the WHO Drug Dictionaries

- Conventional drugs (Arinate, Cetamol)
- Biologicals (vaccines, biosimilars, heparins etc)
- Umbrella entries (antibiotics,
- Blood products
- Radiopharmaceutical diagnostics
- Herbal products
- Generic products
- Substance and substance synonyms
ATC classification
What is ATC?

- Anatomical Therapeutic Chemical (ATC)
- Originally created for drug utilization statistics
- Maintained by WHO Collaborating Centre for Drug Statistics Methodology
- Each product in the WHO Drug Dictionaries is assigned at least one ATC code
- More information: www.who.cc
## 5 ATC levels

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td><strong>Alimentary tract and metabolism</strong>&lt;br&gt;(1st level, anatomical main group)</td>
</tr>
<tr>
<td>A10</td>
<td><strong>Drugs used in diabetes</strong>&lt;br&gt;(2nd level, therapeutic subgroup)</td>
</tr>
<tr>
<td>A10B</td>
<td><strong>Oral blood glucose lowering drugs</strong>&lt;br&gt;(3rd level, pharmacological subgroup)</td>
</tr>
<tr>
<td>A10B A</td>
<td><strong>Biguanides</strong>&lt;br&gt;(4th level, chemical subgroup)</td>
</tr>
<tr>
<td>A10B A02</td>
<td><strong>Metformin</strong>&lt;br&gt;(5th level, chemical substance)</td>
</tr>
</tbody>
</table>
SDG classification
Standardised Drug Groupings (SDG)

Definition

“An SDG is any grouping of medicines having one or several properties in common. The individual grouping can be based on indication, chemical properties, pharmacodynamic properties and/or pharmacokinetic properties as well as any other property of interest.”
SDG Hierarchy

CYP3A4

- **Inducers**
  - Narrow
  - Broad

- **Inhibitors**
  - Narrow
  - Broad

- **Substrates**
  - Narrow
  - Broad

**Example**

- Phenobarbital
- Glucocorticoids
- Erythromycin
- Imatinib
- Paracetamol
- Codeine
The importance of using a standardised dictionary

- Facilitates data analysis
- All data in the dictionary handled the same way → standardised analysis
- No logic gaps in data extraction
- Facilitates communication and data exchange among different organisations
- Quality assured data
- Consistent workflow
Creation of a drug standard
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WHO DDs production team
WHO DDs: to be used in analysis

- Dosage forms
- Trade name
- Substance(s)
- Manufacturer
- Pharmaceutical form
- Drug information
- Reported drug
- Coded drug
- ATC
- SDG
- Drug(s) of interest

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Suspected/ interacting/ concomitant

• Trend: moving towards analyzing all medications on a report, not just the reactions.

• It is not always the medications stated as being suspected or interacting that truly was the cause of the reaction.

• Concomitant medications give information about underlying diseases, they might be interacting with the suspected drug and they contribute to give the whole picture of the patient.
Choice of specificity of drug information matters!

• What kind of analysis do you want to be able to do?
• How much information do you need for suspected vs concomitant medication?
• Instruct reporters how to report
Choice of specificity of drug information matters!

Example: generics products

Omeprazole (Sweden)

- Sandoz, Stada, Teva, Arrow, Evolan, Ranbaxy, Qdoxx, Altavis, Apofri, Alternova, Bluefish, BMM pharma, Evolan, Mylan, Pensa, Ratiopharm
Choice of specificity of drug information matters!

Ibuprofen suppositories

- One of the generic drugs melts too fast → no effect for patients

- What would happen if Ibuprofen + lack of effect was reported compared to Ibuprofen + manufacturer + lack of effect?
Users of the WHO Drug Dictionaries

Doctors & Patients

National Centre

VigiLyze*

VigiBase™

WHO DDE

WHO DDE

WHO DDE

WHO DDE

UMC Report import process

...and validation
WHO Drug Dictionary User Group

• Yearly meetings
  – USA
  – Europe
  – Japan
  – India

• User group portal
  – News, information, documentation

• Working groups
  – SDG, best practices, new developments
Summary

• You are all users of WHO Drug Dictionaries
• The WHO Drug Dictionaries are de facto standard for drug coding within the industry and within many national authorities
• Plan, decide and inform about the desired level of specificity of the drug information in order to be able to do the analysis in the best way
The need for a medical terminology

dyspnoea

fever

mood swings

heart disorder

SOB

? tinnitus

feeling high

local reaction

unconsciousness

unconsciousness

unconsciousness

headache

ALTE

rash

somnolence
Terminologies in the WHO ICSR database

- **WHO-ART**
- **MedDRA**
- **ICD**
- **WHO DD**

**ICSR info**
- Reaction
- Death cause
- Diagnosis
- Medicinal background
- Drug

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Why two terminologies for the same purpose

**MedDRA** can also be used to describe e.g. death causes, medicinal background, diagnosis

**MedDRA** is the standard in ICH* countries

**WHO-ART** is especially designed as a reaction vocabulary for spontaneous reporting

**WHO-ART** is less complex and contains fewer terms - less training is needed to use it
WHO-ART and MedDRA are medical dictionaries and it takes some training and medical knowledge to use them.
WHO-ART hierarchy

System Organ Class (SOC)
- Groups of preferred terms involving the same body organ

High level term (HLT)
- Groups of similar preferred terms

Preferred Term (PT)
- Principal terms for coding and presentation

Included Term (IT)
- Terms similar to preferred terms to aid coding
WHO-ART compared to MedDRA hierarchy

WHO-ART 13-1

System Organ Class
32

High level term
187

Preferred Term
2 178

Included Term
5 813

MedDRA 16.0

System Organ Class
26

High level group term
334

High level term
1 717

Preferred Term
20 057

Included Term
71 326
Scope of MedDRA

All aspects of drug safety:

- signs & symptoms
- diseases & indications for use
- investigations
- surgical and medical procedures
- medical / social / family history

Not all SOCs e.g. Investigations, intended for adverse event reporting

Some difficulties e.g. Hypertension vs. Blood pressure increased
# WHO-ART System Organ Classes

<table>
<thead>
<tr>
<th>Category</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin and appendages disorders</td>
<td>0100</td>
</tr>
<tr>
<td>Musculo-skeletal system disorders</td>
<td>0200</td>
</tr>
<tr>
<td>Collagen disorders</td>
<td>0300</td>
</tr>
<tr>
<td><strong>Central &amp; peripheral nervous system disorders</strong></td>
<td>0410</td>
</tr>
<tr>
<td><strong>Autonomic nervous system disorders</strong></td>
<td>0420</td>
</tr>
<tr>
<td><strong>Vision disorders</strong></td>
<td>0430</td>
</tr>
<tr>
<td><strong>Hearing and vestibular disorders</strong></td>
<td>0431</td>
</tr>
<tr>
<td><strong>Special senses other, disorders</strong></td>
<td>0432</td>
</tr>
<tr>
<td><strong>Psychiatric disorders</strong></td>
<td>0500</td>
</tr>
<tr>
<td><strong>Gastro-intestinal system disorders</strong></td>
<td>0600</td>
</tr>
<tr>
<td><strong>Liver and biliary system disorders</strong></td>
<td>0700</td>
</tr>
<tr>
<td><strong>Metabolic and nutritional disorders</strong></td>
<td>0800</td>
</tr>
<tr>
<td><strong>Endocrine disorders</strong></td>
<td>0900</td>
</tr>
<tr>
<td><strong>Cardiovascular disorders, general</strong></td>
<td>1010</td>
</tr>
<tr>
<td><strong>Myo-, endo-, pericardial &amp; valve disorders</strong></td>
<td>1020</td>
</tr>
<tr>
<td><strong>Heart rate and rhythm disorders</strong></td>
<td>1030</td>
</tr>
<tr>
<td><strong>Vascular (extracardiac) disorders</strong></td>
<td>1040</td>
</tr>
<tr>
<td><strong>Respiratory system disorders</strong></td>
<td>1100</td>
</tr>
<tr>
<td><strong>Red blood cell disorders</strong></td>
<td>1210</td>
</tr>
<tr>
<td><em><em>White cell and RES</em> disorders</em>*</td>
<td>1220</td>
</tr>
<tr>
<td><strong>Platelet, bleeding &amp; clotting disorders</strong></td>
<td>1230</td>
</tr>
<tr>
<td><strong>Urinary system disorders</strong></td>
<td>1300</td>
</tr>
<tr>
<td><strong>Reproductive disorders, male</strong></td>
<td>1410</td>
</tr>
<tr>
<td><strong>Reproductive disorders, female</strong></td>
<td>1420</td>
</tr>
<tr>
<td><strong>Foetal disorders</strong></td>
<td>1500</td>
</tr>
<tr>
<td><strong>Neonatal and infancy disorders</strong></td>
<td>1600</td>
</tr>
<tr>
<td><strong>Neoplasms</strong></td>
<td>1700</td>
</tr>
<tr>
<td><strong>Body as a whole - general disorders</strong></td>
<td>1810</td>
</tr>
<tr>
<td><strong>Application site disorders</strong></td>
<td>1820</td>
</tr>
<tr>
<td><strong>Resistance mechanism disorders</strong></td>
<td>1830</td>
</tr>
<tr>
<td><strong>Secondary terms - events</strong></td>
<td>2000</td>
</tr>
<tr>
<td><strong>Poison specific terms</strong></td>
<td>2100</td>
</tr>
</tbody>
</table>

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WHO-ART hierarchy
- an example

Grouping terms for analysis

Reportable terms

SOC
- Musculo-skeletal system disorders

HLT
- Arthropathy

PT
- Arthritis

IT
- Joint inflammation

IT
- Osteoarthritis

PT
- Arthropathy

IT
- Polyarthropathy

IT
- Joint dysfunction

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WHO-ART

Different languages linked through the Record Number System

Only record numbers are stored with case reports in the database

Record Number
0027

Rash
English

Erupcion cutanea
Spanish

Eruption
French

Erupcao Cutanea
Portuguese

皮疹
Chinese
WHO-ART - Critical terms

A subset of adverse reaction terms referring to, or possibly being indicative of, serious disease states, which have been regarded as particularly important to monitor

e.g. Death, anaphylactic shock, convulsions, erythema multiforme
How to enter information
An authentic ADR reporting form

A mix between structured fields and free text boxes
An 86-year-old female with bipolar disorder was admitted with anxiety, insomnia, fatigue, and acute renal failure. Although lithium levels were normal, lithium had been discontinued and replaced with carbamazepine 100 mg daily 2 days prior to admission.

She was also taking hydralazine 100 mg three times daily for hypertension for 2 years with no dosage change in 8 months. On hospital day 8, she developed fever and conjunctivitis followed by oral erosions and painful lesions on her nose, ears, back, and fingers.
## Extracted case information

<table>
<thead>
<tr>
<th>Original information</th>
<th>Closest WHO-ART terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>...anxiety...</td>
<td>Anxiety</td>
</tr>
<tr>
<td>...insomnia...</td>
<td>Insomnia</td>
</tr>
<tr>
<td>...fatigue...</td>
<td>Fatigue</td>
</tr>
<tr>
<td>...acute renal failure...</td>
<td>Renal failure acute</td>
</tr>
<tr>
<td>...fever...</td>
<td>Fever</td>
</tr>
<tr>
<td>...conjunctivitis...</td>
<td>Conjunctivitis</td>
</tr>
<tr>
<td>...oral erosions...</td>
<td>Erosion gingival</td>
</tr>
<tr>
<td>...painful lesions on her nose, ears, back, and fingers...</td>
<td>Skin ulceration</td>
</tr>
</tbody>
</table>
Reactions → Entering

Reaction coding interface (VF)

Reactions

- Entering

Default values

Hierarchy level

Search type

Enter search text (contains)

Submit search

reaction term

IT

contains

search

gastric ulcer
Reactions → Coding

Find term as exact as possible. Search on IT level. Don’t make assumptions.
Entering data - example WHO-ART

Be clear about what information you are entering.

What is a **local reaction**?
12 different terms in WHO-ART

If possible - go back to reporter and ask

- Urticaria localized
- Inflammation localized
- Anaesthesia local
- Osteoarthritis localised
- Convulsions local
- Numbness localized
- Coldness local
- Paralysis muscle local skeletal
- Localised oedema
- Infection localised
- Skin exfoliation localised
- Skin reaction localised
Fever vs Febrile

HAY FEVER
FEVER
DRUG FEVER
Q FEVER
FEVER NEONATAL
FEVER
CONVULSIONS
METAL FUME FEVER

FEBRILE NEUTROPENIA
FEBRILE REACTION
FEBRILE SEIZURE
ACUTE FEBRILE NEUTROPHILIC DERMATOSIS
Reactions ➔ Searching
Reactions → Searching (VigiBase) → Quick find

Choose level

Add search text

NOTE WHEN SEARCHING!
Avoid IT level
Use SOC, HLT or PT.

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Reactions → Searching

When looking for cases with ‘Gastric Ulcer’;

- **Wide search**
  System Organ Class level – ‘G-I system disorders’ – all cases with GI related disorders

- **’Middle level’ search**
  High level term – ‘Peptic ulcer’

- **Narrow search**
  Included term ‘Gastric Ulcer’ – only cases with the exact term are retrieved.
Variations of spelling Stevens Johnson syndrome

The problem of not using a controlled vocabulary
- all have been reported to UMC!
- enter only ‘Steven’
- search with ‘IT contains’
New terms for WHO-ART or drugs for WHO DD

Suggestion for new terms or drugs can be done if needed:

- first check your spelling
- search for all possible variants using broad search - SOC
Thank you!

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