MedDRA was developed under the auspices of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). The activities of the MedDRA Maintenance and Support Services Organization (MSSO) are overseen by an ICH MedDRA Management Committee, which is composed of the ICH parties, the Medicines and Healthcare products Regulatory Agency (MHRA) of the UK, Health Canada, and the WHO (as Observer).
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Course Overview

- MedDRA background
- MedDRA's structure, scope, and characteristics
- MedDRA maintenance
- Coding conventions
- Synonym lists
- Quality assurance (QA) of coding
- MedDRA Term Selection: Points to Consider document
- Hands-on coding exercises
What is MedDRA?

Med = Medical
D = Dictionary for
R = Regulatory
A = Activities
**MedDRA Definition**

MedDRA is a clinically-validated international medical terminology used by regulatory authorities and the regulated biopharmaceutical industry. The terminology is used through the entire regulatory process, from pre-marketing to post-marketing, and for data entry, retrieval, evaluation, and presentation.

**MedDRA’s Purpose**

- Facilitate the exchange of clinical information through standardization
- Important tool for product evaluation, monitoring, communication, electronic records exchange, and oversight
- Supports coding (data entry) and retrieval and analysis of clinical information about human medical products including pharmaceuticals, biologics, vaccines, and drug-device combination products
MedDRA and the MSSO

- International support and development of terminology
- Foster use of MedDRA through communications and educational offerings
- "Custodians", not owners, of the terminology
- JMO (partner organization for Japanese-language MedDRA)
- Governed by a Management Committee (industry, regulators, multi-national, other interested parties)

Where MedDRA is Used

- Preclinical Testing
- Clinical Phase I
- Clinical Phase II
- Clinical Phase III
- Marketed Product Phase IV

Regulatory Authority and Industry Databases
- Individual Case Safety Reports and Safety Summaries
- Clinical Study Reports
- Investigators' Brochures
- Core Company Safety Information
- Marketing Applications
- Publications
- Prescribing Information
- Advertising
MedDRA Users Profile

- As of January 2019
  - 5,700 Subscribing organizations (MSSO+JMO)
  - 122 Countries
- Graph shows types of subscribing organizations

MedDRA Users by Region

<table>
<thead>
<tr>
<th>Country</th>
<th>Count</th>
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<tbody>
<tr>
<td>United States</td>
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<tr>
<td>Japan</td>
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<td>UK</td>
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<td>Denmark</td>
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<tr>
<td>Austria</td>
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</tr>
<tr>
<td>Russian Federation</td>
<td>37</td>
</tr>
<tr>
<td>Czechia</td>
<td>36</td>
</tr>
</tbody>
</table>
MedDRA Data Sharing

• Subscription grants access to MedDRA for one year
• Subscriber cannot grant any sublicense, publish or otherwise distribute MedDRA to a third party
• Data may be freely exchanged between current MedDRA subscribers
  – Sponsor-sponsor, sponsor-CRO, vendor-user, etc.
  – Use Self-Service Application to check organization’s subscription status
• Sharing MedDRA with a non-subscribing organization is a violation of the MedDRA license

MedDRA Data Sharing (cont)

• For details, see the Statement on MedDRA Data Sharing
MedDRA Overview

Scope of MedDRA

IN

Medical conditions
Indications
Investigations (tests, results)
Medical and surgical procedures
Medical, social, family history
Medication errors
Product quality issues
Device-related issues
Product use issues
Pharmacogenetic terms
Toxicologic issues
Standardized queries

OUT

Not a drug dictionary
Patient demographic terms
Clinical trial study design terms

Frequency qualifiers
Numerical values for results
Severity descriptors
Not an equipment, device, diagnostic product dictionary
MedDRA Structure

System Organ Class (SOC) (27)
- High Level Group Term (HLGT) (337)
- High Level Term (HLT) (1,737)
- Preferred Term (PT) (23,708)
- Lowest Level Term (LLT) (80,262)

MedDRA Version 22.0

System Organ Classes

- Blood and lymphatic system disorders
- Cardiac disorders
- Congenital, familial and genetic disorders
- Ear and labyrinth disorders
- Endocrine disorders
- Eye disorders
- Gastrointestinal disorders
- General disorders and administration site conditions
- Hepatobiliary disorders
- Immune system disorders
- Infections and infestations
- Injury, poisoning and procedural complications
- Investigations
- Metabolism and nutrition disorders
- Musculoskeletal and connective tissue disorders
- Neoplasms benign, malignant and unspecified (incl cysts and polyps)
- Nervous system disorders
- Pregnancy, puerperium and perinatal conditions
- Product issues
- Psychiatric disorders
- Renal and urinary disorders
- Reproductive system and breast disorders
- Respiratory, thoracic and mediastinal disorders
- Skin and subcutaneous tissue disorders
- Social circumstances
- Surgical and medical procedures
- Vascular disorders
High Level Group Terms

Subordinate only to SOCs and superordinate grouping for one or more HLTs

- SOC
  - Cardiac disorders
  - HLGT
    - Coronary artery disorders
  - HLGT
    - Cardiac arrhythmias
  - HLGT
    - Cardiac valve disorders

Not all HLGTs shown

High Level Terms

Subordinate to HLGTs and superordinate grouping for the PTs linked to it

- SOC
  - Cardiac disorders
  - HLGT
    - Cardiac arrhythmias
  - HLT
    - Cardiac conduction disorders
  - HLT
    - Rate and rhythm disorders NEC
  - HLT
    - Supraventricular arrhythmias

Not all HLTs shown
**Preferred Terms**

Represents a single medical concept

**SOC** Cardiac disorders

**HLGT** Cardiac arrhythmias

**HLT** Rate and rhythm disorders NEC

**PT** Arrhythmia

**PT** Bradycardia

**PT** Tachyarrhythmia

Not all PTs shown

---

**Lowest Level Term**

Synonyms, lexical variants, sub-elements

**SOC** = Cardiac disorders

**HLGT** = Cardiac arrhythmias

**HLT** = Rate and rhythm disorders NEC

**PT** = Arrhythmia

**LLT** Arrhythmia

**LLT** Arrhythmia NOS

**LLT** (Non-current) Other specified cardiac dysrhythmias

Not all LLTs shown
Non-Current Terms

- Flagged at the LLT level in MedDRA
- Not recommended for continued use
- Retained to preserve historical data for retrieval and analysis
- Terms that are vague, ambiguous, outdated, truncated, or misspelled
- Terms derived from other terminologies that do not fit MedDRA rules

MedDRA Codes

- Each MedDRA term assigned an 8-digit numeric code starting with “1”
- The code is non-expressive
- Codes can fulfill a data field in various electronic submission types (e.g., E2B)
- New terms are assigned sequentially
A Multi-Axial Terminology

• Multi-axial = the representation of a medical concept in multiple SOCs
  – Allows grouping by different classifications
  – Allows retrieval and presentation via different data sets
• All PTs assigned a primary SOC
  – Determines which SOC will represent a PT during cumulative data outputs
  – Prevents “double counting”
  – Supports standardized data presentation
  – Pre-defined allocations should not be changed by users
A Multi-Axial Terminology (cont)

SOC = Respiratory, thoracic and mediastinal disorders (Secondary SOC)

HLGT = Respiratory tract infections

HLT = Viral upper respiratory tract infections

PT = Influenza

SOC = Infections and infestations (Primary SOC)

HLGT = Viral infectious disorders

HLT = Influenza viral infections

Rules for Primary SOC Allocation

• PTs represented in only one SOC are automatically assigned that SOC as primary
• PTs for diseases, signs and symptoms are assigned to prime manifestation site SOC
• Congenital and hereditary anomalies terms have SOC Congenital, familial and genetic disorders as Primary SOC
• Neoplasms terms have SOC Neoplasms benign, malignant and unspecified (incl cysts and polyps) as Primary SOC
  – Exception: Cysts and polyps have prime manifestation site SOC as Primary SOC
• Infections and infestations terms have SOC Infections and infestations as Primary SOC
Primary SOC Priority

If a PT links to more than one of the exceptions, the following priority will be used to determine primary SOC:

1st: Congenital, familial and genetic disorders
2nd: Neoplasms benign, malignant and unspecified (incl cysts and polyps)
3rd: Infections and infestations

A Multi-Axial Terminology (cont)

PTs in the following SOCs only appear in that particular SOC and not in others, i.e., they are not multi-axial

- Investigations
- Surgical and medical procedures
- Social circumstances
### Can You Select the Primary SOC for This PT?

<table>
<thead>
<tr>
<th>PT</th>
<th>HLT</th>
<th>HLGT</th>
<th>SOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital HIV infection</td>
<td>Viral infections congenital</td>
<td>Infections and infestations congenital</td>
<td>Congenital, familial and genetic disorders</td>
</tr>
<tr>
<td>Congenital neonatal infections</td>
<td>Neonatal and perinatal conditions</td>
<td></td>
<td>Pregnancy, puerperium and perinatal conditions</td>
</tr>
<tr>
<td>Retroviral infections</td>
<td>Viral infectious disorders</td>
<td>Infections and infestations</td>
<td></td>
</tr>
<tr>
<td>Acquired immunodeficiency syndromes</td>
<td>Immunodeficiency syndromes</td>
<td></td>
<td>Immune system disorders</td>
</tr>
</tbody>
</table>
MedDRA Maintenance

• Users can send change requests (CRs) to MSSO for consideration
  – Organizations allowed 100 CRs/month
  – For simple changes (PT and LLT levels), response within 7-10 working days
  – Complex changes (above PT level) posted for comments mid-year

• Two MedDRA updates/year
  – 1 March X.0 (Complex release)
  – 1 September X.1 (Simple release)

WebCR

• Web-based tool for Change Requests (CR)
  – URL: https://mssotools.com/webcr/
  – Via the Change Request Information page

• Ability to submit CRs online
  – Requests must be in English

• Immediate confirmation

• Review unsubmitted CRs online

• Ability to query CR history back to v5.1
Submitting Changes

- Online change request submission tool
- Guides the user to enter all needed information

Submitting Changes (cont)

- Sample entry for a new PT in WebCR
- Justification and supporting documentation is important to help MSSO understand the need
Proactive MedDRA Maintenance

- What is the proactive approach?
  - Corrections/improvements made internally by the MSSO
  - General changes suggested by users

- Submitting ideas
  - Send to MSSO Help Desk. Justification is helpful.
  - Example: Review placement of bruise and contusion terms to facilitate coding and analysis

- Evaluation of proposals
  - Final disposition is not time limited; MSSO may take time to review
  - Proactive approach does not replace usual CR process

MedDRA Version Analysis Tool (MVAT)

- Web-based (https://tools.meddra.org/mvat)
- Free to all users

- Features
  - Version Report Generator (produces exportable report comparing any two versions)
  - Data Impact Report (identifies changes to a specific set of MedDRA terms or codes uploaded to MVAT)
  - Search Term Change (identifies changes to a single MedDRA term or code)

- User interface and report output available in all MedDRA languages
MSSO’s MedDRA Browsers

• MedDRA Desktop Browser (MDB)
  – Download MDB and release files from MedDRA website

• MedDRA Web-Based Browser (WBB)
  – [https://tools.meddra.org/wbb/](https://tools.meddra.org/wbb/)

• Features
  – Both require MedDRA ID and password
  – View/search MedDRA and SMQs
  – Support for all MedDRA languages
  – Language specific interface
  – Ability to export search results and Research Bin to local file system

MedDRA Desktop Browser (MDB) and Web-Based Browser (WBB) Update

• New functionality for users
  – Preview upcoming (supplemental) changes in next release*
  – View primary **and** secondary link information
  – Upload terms to run against SMQs
  – Advanced search options (e.g., NOT, OR)

*Supplemental view not available on MDB
WBB Supplemental View

• Where will Change Requests I submitted appear in next release of MedDRA?
• What are the changes in an area of MedDRA in the next release?

WBB Supplemental View (cont)

• Display changes color to pink
• Supplemental terms highlighted by broken green line
• Changes for the next release are displayed immediately after they are approved by the MSSO
MedDRA Browser Demonstration and Instruction

Coding Exercises
Assessing the Reported Information

- Consider what is being reported. Is it a:
  - Clinical condition - Diagnosis, sign or symptom?
  - Indication?
  - Test result?
  - Injury?
  - Procedure?
  - Medication error?
  - Product use issue?
  - Product quality issue?
  - Social circumstance?
  - Device issue?
  - Procedural complication?

  - **Is it a combination of these?**

The type of report will influence the way you search for a suitable LLT. It may indicate in which SOC you expect to find the closest match.

MedDRA Browsing Tips

- First, try using actual words from reporter
- Use “top-down” and “bottom-up” approaches
- Look at the “neighbors” and check the hierarchy
- Consider synonyms, e.g., “Liver” and “Hepatic”
- Use word stems, e.g., “Pancrea”
MedDRA Browsing Tips (cont)

• Use available resources for difficult verbatim terms (web search, medical dictionaries, colleagues)
• Use advanced Boolean search terms features (i.e., “begins with”, “exact match”, “ends with”, “not contains”, “and”, “or”) when needed
• Become familiar with MedDRA Concept Descriptions

Concept Descriptions

• Descriptions of how a concept is interpreted, used, and classified in MedDRA
• Not a definition
• Intended to aid accurate and consistent use of MedDRA in coding and retrieval
• Overcome differences in medical practice worldwide
  – Descriptions aim to be broadly consistent with definitions across different regulatory regions
• See Appendix B of MedDRA Introductory Guide
• Accessible in MSSO’s Browsers
Exercise 1

The patient states she has been experiencing headaches, dizziness and vertigo.

LLT → PT
LLT → PT
LLT → PT
Exercise 2

Lab results indicate an increase in erythrocytes.

________________ LLT → _______________ PT

Exercise 3

Drug was contaminated with Staphylococcus.

________________ LLT → _______________ PT
Exercise 4

A six year old boy was admitted for toxicity after accidentally ingesting the remaining antihypertensive tablets in the bottle.

_______________ LLT → ________________ PT
_______________ LLT → ________________ PT

Exercise 5

The patient’s urinary catheter was blocked.

_______________ LLT → ________________ PT
Coding with MedDRA

What are Coding Conventions?

- Written guidelines for coding with MedDRA in your organization
- Support accuracy and consistency
- Common topics
  - Misspellings, abbreviations and acronyms
  - Combination terms and “due to” concepts
  - “Always query” terms, e.g., “Chest pain”
- Should be consistent with the MedDRA Term Selection: Points to Consider document
Why Do We Need Coding Conventions?

• Differences in medical aptitude of coders
• Consistency concerns (many more “choices” to manually code terms in MedDRA compared to older terminologies)
• Even with an autoencoder, may still need manual coding

Can I Make Coding Conventions Specific to My Company/Product?

• MedDRA may reduce the need to do this because:
  – Increased size/granularity results in more accurate representation of data
  – Secondary SOC allocations allow for different “views” of the data
• This type of approach should be done cautiously
Synonym Lists

- Recurring verbatims – one-time assignment to an LLT
- Promotes consistency
- Increases likelihood of autoencoding “hit”
- Maintenance required

<table>
<thead>
<tr>
<th>Verbatim</th>
<th>LLT</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Throbbing above temple</td>
<td>Headache</td>
<td></td>
</tr>
<tr>
<td>Aching all over head</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulsing pain in head</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulsing pain in head</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscular pain in legs</td>
<td>Myalgia of lower extremities</td>
<td>LLT <em>Myalgia of lower extremities</em> is a better choice than LLT <em>Muscular pain</em> since it captures both the event and body site</td>
</tr>
</tbody>
</table>

Quality Assurance (QA) Reports

- Allows reviewers to check for consistency (both auto-encoded and human-coded terms)
- Check for adherence to/deviation from coding conventions
- Check for emerging drifts/biases
- Multiple data views (verbatim to coded terms; coded term to verbatim; by SOC, etc.)
MSSO developed and maintains list of unqualified test name terms
- These terms (e.g., PT *Blood glucose*) should never be reported as AEs
- Intended for use in E2B test name field only

List can be used to check data quality
- Identifies inappropriate terms in data fields other than test name data element
- Intended as recommendation only
Unqualified Test Name Term List (cont)

- Link on Support Documentation page on MedDRA website
- Spreadsheet of LLT/PT names and codes from SOC *Investigations*
  - >3,800 terms in v22.0
- Explanatory document
  - Purpose, uses, development of list
- Also available in Japanese on JMO website

ICH M1 Points to Consider Working Group (PtC WG)

- Regulators and industry from EU, US, and Japan
- Health Canada, Canada
- MFDS, Republic of Korea
- ANVISA, Brazil
- NMPA, China
- MSSO
- JMO
- WHO (Observer)

November 2017, Geneva, Switzerland
# PtC Documents

<table>
<thead>
<tr>
<th>PtC Category</th>
<th>PtC Document</th>
<th>Purpose</th>
<th>Languages</th>
<th>Release Cycle</th>
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<tbody>
<tr>
<td>Term Selection</td>
<td>MedDRA Term Selection: Points to Consider</td>
<td>Promote accurate and consistent coding with MedDRA</td>
<td>English and Japanese</td>
<td>Updated with each MedDRA release</td>
</tr>
<tr>
<td></td>
<td>MedDRA Term Selection: Points to Consider Condensed Version</td>
<td>Shorter version focusing on general coding principles to promote accurate and consistent use of MedDRA worldwide</td>
<td>All MedDRA languages (except English and Japanese)</td>
<td>Update as needed</td>
</tr>
<tr>
<td>Data Retrieval and Presentation</td>
<td>MedDRA Data Retrieval and Presentation: Points to Consider</td>
<td>Demonstrate how data retrieval options impact the accuracy and consistency of data output</td>
<td>English and Japanese</td>
<td>Updated with each MedDRA release</td>
</tr>
<tr>
<td></td>
<td>MedDRA Data Retrieval and Presentation: Points to Consider Condensed Version</td>
<td>Shorter version focusing on general retrieval and analysis principles to promote accurate and consistent use of MedDRA worldwide</td>
<td>All MedDRA languages (except English and Japanese)</td>
<td>Update as needed</td>
</tr>
<tr>
<td>General</td>
<td>MedDRA Points to Consider Companion Document</td>
<td>More detailed information, examples, and guidance on specific topics of regulatory importance. Intended as a &quot;living&quot; document with frequent updates based on users' needs. First edition covers data quality and medication errors.</td>
<td>English and Japanese</td>
<td>Updated as needed</td>
</tr>
</tbody>
</table>

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# MedDRA Term Selection: Points to Consider (MTS:PTC)

- Provides term selection advice for industry and regulatory purposes
- Objective is to promote accurate and consistent term selection to facilitate a common understanding of shared data
- Recommended to be used as basis for individual organization's own coding conventions
MedDRA Term Selection: PTC (cont)

- Developed by a working group of the ICH Management Committee
- Updated twice yearly with each MedDRA release
- Available on MedDRA and JMO websites
  - English and Japanese
  - Word ("clean" and "redlined"), PDF, HTML formats
  - "Redlined" document identifies changes made from previous to current release of document

MTS:PTC Points of Note

- In some cases with more than one option for selecting terms, a “preferred option” is identified but this does not limit MedDRA users to applying that option. Organizations should be consistent in their choice of option.
- Section 4.1 – Versioning (Appendix)
  - 4.1.1 Versioning methodologies
  - 4.1.2 Timing of version implementation
General Term Selection Principles

- Quality of Source Data
- Quality Assurance
- Do Not Alter MedDRA
- Always Select a Lowest Level Term
- Select Only Current Lowest Level Terms
- When to Request a Term
- Use of Medical Judgment in Term Selection
- Selecting More than One Term
- Check the Hierarchy
- Select Terms for All Reported Information, Do Not Add Information

Quality of Source Data Quality Assurance

- Quality of original information impacts quality of output
- Obtain clarification of data
- Can be optimized by careful design of data collection forms and proper training of staff
- Organizations’ coding guidelines should be consistent with MTS:PTC
- Review of term selection by qualified individuals
- Human oversight of automated coding results
Do Not Alter MedDRA

- MedDRA is a standardized terminology with a pre-defined term hierarchy
- Users must not make *ad hoc* structural alterations, including changing the primary SOC allocation
- If terms are incorrectly placed, submit a change request to the MSSO

Always Select a Lowest Level Term
Select Only Current LLTs

- Lowest Level Term that most accurately reflects the reported verbatim information should be selected
- Degree of specificity may be challenging
  - Example: “Abscess on face” → select “Facial abscess,” not simply “Abscess”
- Select current LLTs only
  - Non-current terms for legacy conversion/historical purposes
When to Request a Term
Use of Medical Judgment

- Avoid company-specific “work-arounds” for MedDRA deficiencies. If concept not adequately represented in MedDRA, submit Change Request to MSSO.
- If no exact match in MedDRA, use medical judgment to match to an existing term that adequately represents the concept.

Selecting More than One Term
Check the Hierarchy

- Can select more than one LLT to represent reported information. Document procedures.
  - Selecting one term may lead to loss of specificity
  - Selecting more than one term may lead to redundant counts
- Check the hierarchy above a selected LLT (PT, HLT, HLGT, SOC) to ensure placement accurately reflects meaning of reported term
Select Terms for All Reported Information

- Select terms for every AR/AE reported, regardless of causal association
- Select terms for device-related events, product quality issues, medication errors, medical and social history, investigations and indications as appropriate

Do Not Add Information

- Do not make diagnosis if only signs/symptoms reported

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain, increased serum amylase, and increased serum lipase</td>
<td>Abdominal pain</td>
<td>It is inappropriate to assign an LLT for diagnosis of “pancreatitis”</td>
</tr>
<tr>
<td></td>
<td>Serum amylase increased</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lipase increased</td>
<td></td>
</tr>
</tbody>
</table>
Autoencoder Pitfalls

- Inappropriate terms may be selected by autoencoder
- Review all autoencoding carefully
  - “Allergic to CAT scan” autoencoded as:
    LLT *Allergic to cats*
  - “Myocardial infarction in the fall of 2000” autoencoded as:
    LLT *Myocardial infarction*
    LLT *Fall*

Important Coding Errors

- Missed Concepts
  - All medical concepts described after the product is taken should be coded
  - Example: “The patient took drug X and developed alopecia, increased LFTs and pancreatitis”. Manufacturer only codes alopecia and increased LFTs (missed concept of pancreatitis)
  - Example: “The patient took drug X and developed interstitial nephritis which later deteriorated into renal failure”. Manufacturer only codes interstitial nephritis (missed renal failure concept)
**Important Coding Errors (cont)**

- "Soft Coding"
  - Selecting a term which is both less specific and less severe than another MedDRA term is "soft coding"
  - Example: "Liver failure" coded as hepatotoxicity or increased LFTs
  - Example: "Aplastic anemia" coded as unspecified anemia
  - Example: "Rash subsequently diagnosed as Stevens Johnson syndrome" coded as rash

**Term Selection Points**

- Diagnoses and Provisional Diagnoses with or without Signs and Symptoms
- Death and Other Patient Outcomes
- Suicide and Self-Harm
- Conflicting/Ambiguous/Vague Information
- Combination Terms
- Age vs. Event Specificity
- Body Site vs. Event Specificity
- Location-Specific vs. Microorganism-Specific Information
- Modification of Pre-existing Conditions
- Exposures During Pregnancy and Breast Feeding
- Congenital Terms
- Neoplasms
- Medical and Surgical Procedures
- Investigations
Term Selection Points (cont)

- Medication Errors, Accidental Exposures and Occupational Exposures
- Misuse, Abuse and Addiction
- Transmission of Infectious Agent via Product
- Overdose, Toxicity and Poisoning
- Device-related Terms
- Drug Interactions
- No Adverse Effect and “Normal” Terms
- Unexpected Therapeutic Effect
- Modification of Effect
- Social Circumstances
- Medical and Social History
- Indication for Product Use
- Off Label Use
- Product Quality Issues

Diagnoses and Provisional Diagnoses

<table>
<thead>
<tr>
<th>SINGLE DIAGNOSIS</th>
<th>DEFINITIVE DIAGNOSIS</th>
<th>PROVISIONAL DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single diagnosis without signs and symptoms</td>
<td>Single provisional diagnosis without signs and symptoms</td>
<td>Provisional diagnosis (only possible option)</td>
</tr>
<tr>
<td>•Diagnosis (only possible option)</td>
<td>•Provisional diagnosis (only possible option)</td>
<td></td>
</tr>
<tr>
<td>Example: “Myocardial infarction”</td>
<td>Example: “Possible myocardial infarction”</td>
<td>select “Myocardial infarction” select term as if definitive diagnosis</td>
</tr>
</tbody>
</table>

Similar principles apply for multiple diagnoses
### Diagnoses and Provisional Diagnoses (cont)

#### SINGLE DIAGNOSIS

<table>
<thead>
<tr>
<th>DEFINITIVE DIAGNOSIS</th>
<th>PROVISIONAL DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single diagnosis with signs/symptoms</td>
<td>Single provisional diagnosis with signs/symptoms</td>
</tr>
<tr>
<td>• Preferred: Diagnosis only</td>
<td>• Preferred: Provisional diagnosis and signs/symptoms</td>
</tr>
</tbody>
</table>

**Example:** "Anaphylactic reaction with rash, dyspnoea, hypotension, and laryngospasm" → select "Anaphylactic reaction"

**Example:** "Possible myocardial infarction with chest pain, dyspnoea, diaphoresis" → select "Myocardial infarction" "Chest pain", "Dyspnoea", and "Diaphoresis"

---

**Similar principles apply for multiple diagnoses**
Diagnoses and Provisional Diagnoses (cont)

- Always include signs/symptoms not associated with diagnosis

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction, chest pain, dyspnoea, diaphoresis, ECG changes and jaundice</td>
<td>Myocardial infarction Jaundice (note that jaundice is not typically associated with myocardial infarction)</td>
</tr>
</tbody>
</table>

What Terms to Select?

- Sepsis leading to shock from possible spontaneous bacterial peritonitis or bowel perforation

  Sepsis
  Shock
  Septic shock
  Spontaneous bacterial peritonitis
  Bowel perforation
### Conflicting/Ambiguous Information

- **First, try to obtain more specific information**

<table>
<thead>
<tr>
<th>Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperkalaemia with a serum potassium of 1.6 mEq/L</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LLT Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum potassium abnormal</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>LLT Serum potassium abnormal covers both of the reported concepts (note: serum potassium of 1.6 mEq/L is a low result, not high)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>GU pain</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LLT Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>“GU” could be either “genito-urinary” or “gastric ulcer”. If additional information is not available, then select a term to reflect the information that is known, i.e., LLT Pain</td>
</tr>
</tbody>
</table>

### Vague Information

- **First, try to obtain more specific information**

<table>
<thead>
<tr>
<th>Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turned green</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LLT Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unevaluable event</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Turned green” reported alone is vague; this could refer to a patient condition or even to a product (e.g., pills)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient had a medical problem of unclear type</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LLT Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ill-defined disorder</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Since it is known that there is some form of a medical disorder, LLT Ill-defined disorder can be selected</td>
</tr>
</tbody>
</table>
What Terms to Select?

- **Clinical complication of IUD**
  - IUD complication (PT Complication associated with device)
  - Intra-uterine death (PT Foetal death)
  - Unevaluable event

- **Hypoglycemia (blood glucose = 200 mg/dL)**
  - Blood glucose abnormal
  - Blood glucose increased
  - Hypoglycemia

Combination Terms

- **One condition is more specific than the other**

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrhythmia due to atrial fibrillation</td>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td>Hepatic function disorder (acute hepatitis)</td>
<td>Hepatitis acute</td>
</tr>
</tbody>
</table>

- **A MedDRA combination term is available**

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinopathy due to diabetes</td>
<td>Diabetic retinopathy</td>
</tr>
<tr>
<td>Rash with itching</td>
<td>Itchy rash</td>
</tr>
</tbody>
</table>
Combination Terms (cont)

• If splitting provides more clinical information, select more than one term
• In all cases of combination terms, apply medical judgment

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhoea and vomiting</td>
<td>Diarrhoea</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
</tr>
<tr>
<td>Wrist fracture due to fall</td>
<td>Wrist fracture</td>
</tr>
<tr>
<td></td>
<td>Fall</td>
</tr>
</tbody>
</table>

What Terms to Select?

• Retinal disease from HIV with near total blindness (R and L)
  Retinal damage
  Retinal disorder
  HIV disease
  Blindness
  HIV retinopathy
  Blindness, both eyes
Investigations

- Medical condition vs. investigation result

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycaemia</td>
<td>Hypoglycaemia</td>
<td>LLT Hypoglycaemia links to SOC Metabolism and nutrition disorders</td>
</tr>
<tr>
<td>Decreased glucose</td>
<td>Glucose decreased</td>
<td>LLT Glucose decreased links to SOC Investigations</td>
</tr>
</tbody>
</table>

Investigations (cont)

- Unambiguous investigation result

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose 40 mg/dL</td>
<td>Glucose low</td>
<td>Glucose is clearly below the reference range</td>
</tr>
</tbody>
</table>

- Ambiguous investigation result

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>His glucose was 40</td>
<td>Glucose abnormal</td>
<td>No units have been reported. Select LLT Glucose abnormal if clarification cannot be obtained.</td>
</tr>
</tbody>
</table>
Investigations (cont)

- Investigation results consistent with diagnosis

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated potassium, K 7.0 mmol/L, and hyperkalaemia</td>
<td>Hyperkalaemia</td>
<td>It is not necessary to select LLT Potassium increased</td>
</tr>
</tbody>
</table>

- Grouped investigation result terms

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased alkaline phosphatase, increased SGPT, increased SGOT and elevated LDH</td>
<td>Alkaline phosphatase increased SGPT increased SGOT increased LDH increased</td>
<td>Select four individual terms. A single term such as LLT Liver function tests abnormal should not be selected.</td>
</tr>
</tbody>
</table>

What Terms to Select?

- Testing showed increased serum creatinine and BUN, with increased BUN/creatinine ratio
  - Increased serum creatinine
  - BUN increased
  - Blood urea nitrogen/creatinine ratio increased
  - Renal function tests NOS abnormal

- Patient had features of aldosterone excess
  - Aldosterone increased
  - Aldosteronism
  - Blood aldosterone abnormal
Medication Errors

- See Appendix B of MedDRA Introductory Guide or MedDRA Browser (both WBB and MDB) for Concept Descriptions
- See Section 3 of MedDRA Points to Consider Companion Document for detailed examples, guidance and “Questions and Answers”
- “Top-down” navigation in HLGT Medication errors and other product use errors and issues is best approach for term selection

Medication Errors (cont)

- Medication error with clinical consequences

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient was administered wrong drug and experienced hypotension</td>
<td>Wrong drug administered Hypotension</td>
<td></td>
</tr>
<tr>
<td>Insulin was given using the wrong syringe resulting in the administration of an overdose. The patient developed hypoglycaemia.</td>
<td>Drug administered in wrong device Accidental overdose Hypoglycaemia</td>
<td>If an overdose is reported in the context of a medication error, the more specific term LLT Accidental overdose can be selected</td>
</tr>
</tbody>
</table>
Medication Errors (cont)

- Medication error **without** clinical consequences

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Preferred Option</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication was given intravenously instead of intramuscularly without any adverse effect</td>
<td>Intramuscular formulation administered by other route</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Intramuscular formulation administered by other route</td>
<td>No adverse effect</td>
</tr>
</tbody>
</table>

Medication Errors (cont)

- Important to record potential occurrence of medication error
- Unlikely to be reported as an adverse event but may need to be recorded in periodic safety reports

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacist notices that the names of two drugs are similar and is concerned that this may result in a medication error</td>
<td>Drug name confusion</td>
<td>Note: this example is a potential medication error and LLT <strong>Drug name confusion</strong> provides additional information about the nature of the potential medication error</td>
</tr>
<tr>
<td></td>
<td>Circumstance or information capable of leading to medication error</td>
<td></td>
</tr>
</tbody>
</table>

Note: this example is a potential medication error and LLT **Drug name confusion** provides additional information about the nature of the potential medication error.
Overdose, Toxicity and Poisoning

If overdose, poisoning or toxicity is explicitly reported, select the appropriate term

- **Overdose with clinical consequences**

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach upset from study drug overdose</td>
<td>Stomach upset</td>
</tr>
<tr>
<td></td>
<td>Overdose</td>
</tr>
</tbody>
</table>

- **Overdose without clinical consequences**

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Preferred Option</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient received an overdose of medicine</td>
<td>Overdose</td>
<td>✓</td>
</tr>
<tr>
<td>without any adverse consequences</td>
<td>Overdose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No adverse effect</td>
<td></td>
</tr>
</tbody>
</table>

What Term to Select?

- The patient’s renal function was measured every six months instead of on the monthly schedule recommended in the label for the drug
  - Medication monitoring error
  - Renal function test abnormal
  - Drug monitoring procedure incorrectly performed

- Unintentionally took more than maximum recommended dose due to dispensing error
  - Accidental overdose
  - Incorrect dose administered
  - Drug dispensing error
**Definitions of misuse may not always include the concept of therapeutic use; misuse may be similar to the concept of abuse in some regions.**

<table>
<thead>
<tr>
<th>Concept</th>
<th>Intentional?</th>
<th>By Whom?</th>
<th>Therapeutic Use?</th>
<th>Additional Sections in this Document</th>
</tr>
</thead>
<tbody>
<tr>
<td>Misuse</td>
<td>Yes</td>
<td>Patient/consumer</td>
<td>Yes*</td>
<td>3.16.1</td>
</tr>
<tr>
<td>Abuse</td>
<td>Yes</td>
<td>Patient/consumer</td>
<td>No</td>
<td>3.16.2</td>
</tr>
<tr>
<td>Addiction</td>
<td>Yes</td>
<td>Patient/consumer</td>
<td>No</td>
<td>3.16.3</td>
</tr>
<tr>
<td>Medication error</td>
<td>No</td>
<td>Patient/consumer or healthcare provider</td>
<td>Yes</td>
<td>3.15</td>
</tr>
<tr>
<td>Off label use</td>
<td>Yes</td>
<td>Healthcare provider</td>
<td>Yes</td>
<td>3.27</td>
</tr>
</tbody>
</table>

**Coding Exercises**

- **Narratives and short verbatims**
- **Assess the reported terms**
  - Identify what concepts are reported (diagnosis, death, investigations, etc.)
- **Refer to the appropriate sections of the MTS:PTC for guidance on term selection**
  - For example, Section 3.2 for death terms
- **Use MTS:PTC preferred options (forget your organization’s conventions)**
- **Use browser to search for and select LLTs (also record PT and primary SOC)**
Specific Tips for Narrative Exercises

• Overall, coding principles are the same as for short verbatim exercises
• Code all of the following:
  – Events (including procedures and investigations as needed)
  – Indications
  – Medical history
  – Social history

Sample Narrative

A 75-year-old male receiving Drug X for rheumatoid arthritis developed an area of darkened skin on his chest. The patient’s medical history is significant for peripheral vascular disease and cigarette smoking. The skin lesion was excised; it was revealed to be a seborrhoeic wart.
Course Summary

• In this course, we covered:
  – A review of MedDRA’s scope and structure, including primary SOC allocation rules
  – Coding conventions, synonym lists, and coding QA
  – Introduction to the MedDRA Term Selection: Points to Consider document
  – Coding exercises

MSSO Contacts

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