MedDRA and Reporting of Adverse Events

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MedDRA Overview

- What is MedDRA
- Where it is used
- Who uses it
- Features

Integration with other terminologies

World SIVA AE tool and MedDRA
What is MedDRA?

Med = Medical

D = Dictionary for

R = Regulatory

A = Activities
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.
Where MedDRA is Used

- Individual Case Safety Reports and Safety Summaries
- Clinical Study Reports
- Investigators’ Brochures
- Core Company Safety Information
- Marketing Applications
- Publications
- Prescribing Information
- Advertising
- Regulatory Authority and Industry Databases
Regulatory Use in ICH Regions

- **US FDA**
  - Not mandated but *de facto* standard in US
  - Used in several FDA databases
- **Japanese Ministry of Health, Labour and Welfare**
  - Mandatory use in electronic reporting
- **European Union**
  - Mandatory use in electronic reporting
  - EudraVigilance database
  - Good Pharmacovigilance Practices (GVP) specifically mention MedDRA
- **Biopharmaceutical industry**
Who Else Uses MedDRA?

- Countries beyond the ICH regions
- WHO’s international drug monitoring center (Uppsala Monitoring Centre)
- Academic researchers
- Toxicologists
- Others

More than 4,000 organizations worldwide in more than 90 countries
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
- Pharmacogenetic terms
- Toxicologic issues
- Standardized queries

OUT
- Frequency qualifiers
- Numerical values for results
- Severity descriptors
- Not an equipment, device, diagnostic product dictionary
- Patient demographic terms
- Clinical trial study design terms
- Not a drug dictionary
MedDRA Structure

- System Organ Class (SOC) (27)
  - High Level Group Term (HLGT) (335)
    - High Level Term (HLT) (1,732)
      - Preferred Term (PT) (21,920)
    - Lowest Level Term (LLT) (75,818)
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
MedDRA Structure (cont)

- **SOC** = Cardiac disorders
- **HLGT** = Cardiac arrhythmias
- **HLT** = Rate and rhythm disorders NEC
- **PT** = Arrhythmia
- **LLT** Arrhythmia
- **LLT** Arrhythmia NOS
- **LLT** Dysrhythmias
- **LLT (Non-current)** Other specified cardiac dysrhythmias

Not all LLTs shown.
Codes and Languages

Hoofdpijn
Dutch

Headache
English

Céphalée
French

Bolest hlavy
Czech

Cefaleia
Portuguese

Kopfschmerz
German

Fejfájás
Hungarian

Cefalea
Italian

頭痛
Chinese

Cefalea
Spanish

Electronic Submission

10019211
Integration with Other Terminologies

• Subsets of MedDRA terms used as basis for several other AE terminologies
  – NCI’s Common Terminology Criteria for Adverse Events (CTCAE v4.0)
  – National Institute of Child Health and Human Development’s Pediatric AE terminology
  – EVERREST project’s maternal and fetal AE terminology
• Integration of MedDRA terms and codes facilitates exchange of information
• MedDRA is an international standardized terminology
  – No need to create separate terms for the other terminology
• Other terminology can incorporate its own features
  – Definitions
  – Severity rating scales
CTCAE v4.0 Example

- CTCAE v4 is a subset of MedDRA LLTs, organized by SOC, allowing seamless data exchange
- CTCAE definitions and severity scale added

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult respiratory distress syndrome</td>
<td></td>
<td></td>
<td>Present with radiologic findings; intubation not indicated</td>
<td>Life-threatening respiratory or hemodynamic compromise; intubation or urgent intervention indicated</td>
<td>Death</td>
</tr>
<tr>
<td>Definition: A disorder characterized by progressive and life-threatening pulmonary distress in the absence of an underlying pulmonary condition, usually following major trauma or surgery.</td>
<td></td>
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<tr>
<td>Allergic rhinitis</td>
<td></td>
<td>Moderate symptoms; medical intervention indicated</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Definition: A disorder characterized by an inflammation of the nasal mucous membranes caused by an IgE-mediated response to external allergens. The inflammation may also involve the mucous membranes of the sinuses, eyes, middle ear, and pharynx. Symptoms include sneezing, nasal congestion, rhinorrhea and itching.</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Apnea</td>
<td></td>
<td>Present; medical intervention indicated</td>
<td>Life-threatening respiratory or hemodynamic compromise; intubation or urgent intervention indicated</td>
<td>Death</td>
<td></td>
</tr>
<tr>
<td>Definition: A disorder characterized by cessation of breathing.</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
World SIVA AE Tool and MedDRA

- Interest in collaboration to integrate MedDRA into tool
- Preliminary mapping performed

<table>
<thead>
<tr>
<th>Minor risk descriptors</th>
<th>World SIVA sedation AE term</th>
<th>LLT</th>
<th>PT</th>
<th>Primary SOC</th>
<th>MSSO comment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Oxygen desaturation (75-90%) for &lt;60s</td>
<td>Oxygen saturation decreased</td>
<td>Oxygen saturation decreased</td>
<td>Investigations</td>
<td>MedDRA does not include numerical values for investigation results</td>
</tr>
<tr>
<td></td>
<td>Apnoea, not prolonged</td>
<td>Apnoea</td>
<td>Apnoea</td>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>&quot;Prolonged&quot; concept for apnoea is not in MedDRA. Terms referring to duration are not generally included.</td>
</tr>
</tbody>
</table>

- Next steps?
Thank you

Questions?