MedDRA User Group - indication coding

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XEVMPD background

EMA awarded a contract to Kinapse in 2010 for Data Quality aspects of EudraVigilance

- ICSR quality aspects
- Submissions to XEVMPD/Article 57 database
- All information on entries for XEVMPD including MedDRA coding of information
  - MAHS submit XEVMPD data and attach a copy of SmPC in the relevant local language
  - Kinapse perform validation and quality review of entries and provide feedback to MAHs on all aspects including MedDRA coding
- Coding of indications is recognised to be a challenge!!
  - Aim is to be consistent in approach for migration to IDMP
MedDRA coding of indication

Concepts that may sometimes trigger differences between EMA product version and Company product version:

- The coding of indication needs to capture the information related to disease, symptom or procedure (see guidance, chapter 1.2.19.3 MedDRA code);

- The coding of indication *should not* capture information on underlying disease, comorbidities or population specifics
  - E.g.: a medicinal product treating “infection in patients with HIV” should code the infection but not HIV;
  - The rationale behind is to facilitate the data migration for ISO IDMP

- Coding of MRP products using the English common text (EMA is using the nationally authorised SmPC, as differences from country to country exist and need to be captured as such)
  - Companies sometimes will use the common text to create one set of codings and apply it across all countries where the product is authorised
MedDRA coding of indication

Concepts that trigger the majority of discordances between EMA version and Industry version:

- Efforts should be made to capture the most detailed level of information, as available in MedDRA

- Information not listed in SmPC should not be coded in the dictionary ("if is listed as indication, we need to capture it; if is not we should not")

  - Service provider informs us that the SmPC is incorrect, incomplete, poorly translated etc. (same for other information listed in SmPC)

  - Other feedback states that company’s internal experts have assigned this indication coding and the fact that the equivalent information is not stated in section 4.1 of the SmPC is irrelevant
Example – more indications than listed in SmPC

**Company version:**
- Prophylaxis
- Urinary tract infection
- Intra-abdominal infection
  - Soft tissue infection
- Acute bacterial exacerbation of chronic bronchitis
- Orbital osteomyelitis
- Meningitis due to anaerobic bacteria
- Arthritis infective
- Osteomyelitis of jaw
- Device related infection
- Prosthesis related infection
- Unspecified infection of bone, upper arm

**SmPC Section 4.1**
This medicinal product is indicated for the treatment of the infections listed below in adults and children, including neonates (from birth):
- Community acquired pneumonia
- Acute exacerbations of chronic bronchitis
- Complicated urinary tract infections, including pyelonephritis
- Soft-tissue infections: cellulitis, erysipelas and wound infections
- Intra-abdominal infections (see section 4.4)
- Prophylaxis against infection in gastrointestinal (including oesophageal), orthopaedic, cardiovascular, and gynaecological surgery (including caesarean section)

**EMA version:**
- Prophylaxis
- Urinary tract infection
- Intra-abdominal infection
  - Soft tissue infection
- Acute bacterial exacerbation of chronic bronchitis
- Community acquired pneumonia
  - Pyelonephritis
  - Cellulitis
  - Erysipelas
  - Wound infection

Kept MedDRA code
Removed MedDRA code
Added MedDRA code
Example – less indications than listed in SmPC

**SmPC Section 4.1**
Ampicillin is a broad-spectrum penicillin, indicated for the treatment of a wide range of bacterial infections caused by Ampicillin-Sensitive organisms. Such indications include infections of the upper and lower respiratory tract including bronchitis and pneumonia, genito-urinary tract and the gastro-intestinal tract, gynaecological infections, septicaemia, peritonitis, endocarditis, meningitis and enteric fever. Specific indications include ear, nose and throat infections and soft tissue infections and gonorrhoea.

**Company version:**
- Bacterial infection

**EMA version:**
- Bacterial infection
- Upper respiratory tract infection
- Lower respiratory tract infection
  - Bronchitis
  - Pneumonia
- Genitourinary tract infection
- Gastrointestinal bacterial infection
  - Gynaecological infection
  - Septicaemia
- Peritonitis/Peritonitis bacterial
- Endocarditis/Endocarditis bacterial
- Meningitis/Meningitis bacterial
  - Enteric fever
- Ear, nose and throat infection
  - Soft tissue infection
  - Gonorrhoea

Kept MedDRA code
Removed MedDRA code
Added MedDRA code
SmPC Section 4.1
Treatment of osteoporosis in postmenopausal women and in men at increased risk of fracture. In postmenopausal women, a significant reduction in the incidence of vertebral and nonvertebral fractures but not hip fractures has been demonstrated. Treatment of osteoporosis associated with sustained systemic glucocorticoid therapy in women and men at increased risk for fracture.
Example – details not listed in SmPC

Company version:
- Idiopathic pulmonary arterial hypertension
- Secondary pulmonary arterial hypertension

SmPC Section 4.1
Treatment of pulmonary arterial hypertension (PAH) classified as WHO functional class II and III, to improve exercise capacity

EMA version:
- Pulmonary arterial hypertension

Kept MedDRA code
Removed MedDRA code
Added MedDRA code
SmPC Section 4.1
Isoflurane is indicated as a general anaesthetic by inhalation.

Company version:
- Monitored anaesthesia care sedation
- Induction and maintenance of anaesthesia

EMA version:
- General anesthesia

Kept MedDRA code
Removed MedDRA code
Added MedDRA code
Indications coding guidance

- Guidance under revision
- XEVMPD updates for ISO IDMP compliance, aim to make migration easier
- ISO suggests the following should be coded:
  - Disease/symptom/procedure
  - Disease status
  - Comorbidity/concurrent conditions
  - Intended effect
  - Timing/duration
  - Also population specifics (age/age range/gender) and others (second line treatment etc)
Future considerations

• Wider applications of Article 57 and IDMP (EXCHANGE of medicinal product information amongst regulators/ worldwide data sources/MAHs and to reliably TRACE use of medicines)

• MedDRA aspects- need to consider how to reconcile indication coding in an ICSR with authorised product information
  • Analysis of off label use/misuse etc
  • Other analysis- contraindicated prescribing
  • Wider drug utilisation studies

• Guidance updates and how best to involve Industry in dialogue
THANK YOU

Questions

Examples
Indication Coding: An Industry Perspective

European MedDRA Users Group, Paris
16 April 2015

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Agenda

This presentation will cover:

• Introduction to Indication coding
  – Variables impacting Indication coding

• SmPC indication coding
  – Background
  – Coding guidelines
  – Industry perspective
    • Results of an informal survey
    • Recommendations
Disclaimer

The views expressed in this presentation are the views of the speaker and, while acknowledging input from both Regulators and Industry, they do not represent any official Regulator or Company position.
Introduction

• In this presentation, ‘indication’ refers to the intended use of a medicinal product or its therapeutic indication in a Regulatory context

• Depending on the Regulatory stage, data collection methods, systems, processes and personnel involved, there can be considerable variation in the way indications are expressed, coded and analysed

• This presentation will briefly review some general aspects of indication coding and will then focus on the current and future requirements, guidelines and challenges involved in the coding of SmPC indications using MedDRA
## Variables Impacting Indication Coding - Wording

<table>
<thead>
<tr>
<th>Indications may be expressed as...</th>
<th>Example texts</th>
<th>MedDRA coding impact PT (SOC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>The medical condition or disease to be treated</td>
<td>Pain</td>
<td>Pain (Gen)</td>
</tr>
<tr>
<td>The medical condition or disease to be prevented</td>
<td>Pain prevention</td>
<td>Pain prophylaxis (Surg)</td>
</tr>
<tr>
<td>The intended effect</td>
<td>Analgesia Anaesthesia</td>
<td>Analgesic therapy (Surg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anaesthesia (NS)</td>
</tr>
<tr>
<td>A therapy</td>
<td>Pain relief</td>
<td>Analgesic therapy (Surg)</td>
</tr>
<tr>
<td>A procedure</td>
<td>Anaesthesia induction Anaesthesia maintenance Anaesthesia procedure</td>
<td>Induction of anaesthesia (Surg) Maintenance of anaesthesia (Surg) Anaesthesia procedure (Surg)</td>
</tr>
<tr>
<td>A drug class or type of action</td>
<td>Analgesic Anaesthetic</td>
<td>No direct coding</td>
</tr>
</tbody>
</table>
Other Variables Impacting Indication Coding

- Level of detail available - Varies with Regulatory stage
  - Highest level of detail for regulatory submissions, e.g. SmPC/XEVM FD
  - Less detail in Clinical Trials
  - Lowest level of detail and data quality in spontaneous PV
- Data source, collection method, systems & processes
  - Electronic vs paper vs audio collection
  - IT aspects: autoencoders; field length, format, system limitations, e.g. ability to split text
  - Guidelines for data collection, processing & coding
- Personnel involved in data processing and coding
  - Dedicated Coders
  - Other Pharmaceutical professionals – Scientists, Physicians
  - Healthcare professionals – Physicians, Nurses, Admins ...
  - Public

This rest of this presentation will focus on the area which currently presents the greatest challenges to industry - the coding of SmPC indications
Background to SmPC Indication Coding

• The SmPC (Summary of Product Characteristics) contains a narrative description of the indications, and associated qualifiers, for the product’s intended use
• Since July 2012, it became mandatory to code the SmPC indications to MedDRA for submission to the EMA
• Coded SmPC indications are submitted to the EMA electronically and stored in their XEVMPD (Extended EudraVigilance Medicinal Product Dictionary) database
• The EMA is currently conducting a QA review of XEVMPD data, including indication coding, and informing companies of any resulting code changes
Examples of SmPC Indication Text

- SmPC text includes all proposed indications (in any EU language) and may include other qualifiers in addition to the basic indications, e.g. eligible populations, disease severity, demographics

Example:

- ‘...Infections of the upper and lower respiratory tract, e.g. exacerbations of chronic bronchitis, purulent middle ear infection, acute or recurrent sinusitis, etc., caused by streptococcus, pneumococcus (penicillin-sensitive) or staphylococci and Haemophilus not producing penicillinase...

- Or...

- ‘..Λοιμώξεις του ανώτερου και κατώτερου αναπνευστικού: π.χ. παροξύνσεις χρόνιας βρογχίτιδας, μέση πυώδης ωτίτιδα, οξεία ή υποτροπιάζουσα παραρρινοκολπίτιδα, κλπ., που οφείλονται σε στρεπτοκόκκους, πνευμονοκόκκους (ευαίσθητους στην πενικιλλίνη) ή σταφυλοκόκκους και αιμόφιλους που δεν παράγουν πενικιλλινάση...
SmPC Indication Coding Guidelines

- Efforts should be made to capture the most granular and comprehensive level of information available in MedDRA.
- Multiple terms can be used to code the medical concepts of indication(s), the signs, symptoms or intended effects.
- Low Level Terms (LLT) must be specified.
- The indication(s) is/are to be coded using the English term and corresponding code.
- Each (new or updated) indication is to be coded using MedDRA in its latest current version. The next official MedDRA version can also be used.
- It is not necessary to update medicinal product entries when a new MedDRA version is released.
- For coding instructions, please refer to MedDRA Term Selection: Points to Consider Document.
- The use of qualifiers (e.g. underlying disease comorbidities, population specifics) will be possible with the implementation of the ISO IDMP standards.
Examples of SmPC Indication Coding

• Example of indication text (excluding qualifiers)
  – ‘…relief of headache, migraine, backache, toothache, rheumatic and muscular pains and period pains. It also relieves discomfort during flu, inflammatory diseases of upper respiratory tract (colds) and lowers temperature’

• Possible MedDRA terms?:
  – Headache, Migraine, Backache, Toothache, Rheumatism, Muscular pain, Period pains, Discomfort, Influenza, Upper respiratory tract inflammation, Cold, High temperature

• Example qualifiers
  – Currently not able to code these using MedDRA
SmPC Indication Coding - Industry Challenges

• Many companies find SmPC coding challenging
  – Complex data
    • Narrative with multiple conditions & qualifiers
    • May need translation before coding
    • Not easy to automate coding
  – SmPC data traditionally processed within Regulatory department
    • MedDRA expertise and software may be elsewhere
  – Perceived lack of clear, detailed coding guidelines
    • MTS:PTC not detailed enough; EMA guidelines still evolving
  – EMA performing QA on data in XEVMPD
    • Some coded data being recoded in XEVMPD
    • Codes then differ between XEVMPD and company database

• Informal survey conducted to assess industry status
  – Results shown (n=7) in next few slides
Survey Results: Coding Guidelines

• Coding guidelines variable, but generally based on MTS:PTC or EMA XEVMPD documents
  – 3 based on or use MTS:PTC
  – 2 based on or use EMA XEVMPD guidelines
  – 1 aligned to both PTC and EVPRM
  – 1 has no specific guidelines

• General feeling that both PTC and EMA guidelines are inadequate
Survey Results: Workload, Resources & Processes

• Average number of terms coded per SmPC
  – 4 (Range 1- >100)

• Which group performs the coding?
  – PV (x3)
  – Labelling
  – Central + Local Regulatory
  – QA
  – Central coding group

• Coding process
  – Manual (x5)
  – Some automation plus manual (x2)
Survey Results:
Main Challenges

- Translations
- Multiple conditions (n>100 in some cases)
- Diagnoses, conditions, comorbidities, aetiologies etc.
  - how much to code?
- LLT too granular or repetitive sometimes
  - PT or hierarchy would be better in some cases to ensure all intended scope is included
- MedDRA not specific enough for some terms
  - Prophylaxis
  - Surgeries/procedures
  - Grades, severities...
- MedDRA not suitable in current form for coding qualifiers, demographics and other patient related textual information
  - Need to be able to code these for IDMP in the future
  - Will MedDRA be able to accommodate this or will another terminology be needed?
Survey Results:
Examples of Difficult Terms

• Treatment of most painful and febrile conditions
• Prophylactic vaccination for rotavirus immunisation
• Prophylaxis of postoperative, pancreatic complications following pancreatic surgery
• Alternative oral treatment for Clostridium difficile for prophylaxis in those patients in whom infection with Gram-positive organisms would constitute a hazard
• Bone metastases in primary breast cancer
• CE in MR-Angiography (children older than 6 years)
• Chronic lymphocytic leukaemia (2nd line)
• Hyperprolactinaemic ovulatory disturbance
• Stroke Prevention in Atrial Fibrillation
Survey Results:
Impact of XEVMPD QA on Coding (1)

• Some XEVMPD codes are being changed as a result of the ongoing QA process, and companies are being informed of the changes.
• Of those who have received QA feedback (n=3), average of 60% of SmPCs had some changes to coding, but re-coding not consistent.
• Time-consuming and difficult for companies to track and synchronise changes made in XEVMPD with own database.
  – Reports of changes could be improved.
• Companies feel they own the data and should have more control over changes, so there should be dialogue before making changes.
• Companies concerned regarding risks of company database and XEVMPD being out of sync.
Survey Results: Impact of XEVMPD QA on Coding (2)

• Example 1:
  – Company coded: Induction and Maintenance of Anesthesia and Monitored Anesthesia Care Sedation
  – EMA changed coding to Anesthesia (2 countries), General anesthesia (2 countries), while coding not changed for many other countries

• Example 2
  – Company coded: Asthma
  – EMA coded: Bronchospasm, Pain, Spasms, Biliary dyskinesia
Recommendations for Improvement?

• Need greater MedDRA expertise for SmPC coding to increase initial coding quality and consistency
  – Suggest increased training for Regulatory departments and/or better utilisation of company/CRO expertise used for AE/other MedDRA coding
• Need clearer guidance for SmPC coding
  – Update MTS:PTC
  – Update EMA/XEVMPD guidelines
• Need clearer understanding of use cases to ensure relevant coding
  – E.g. Off-label use, signal detection for same indications?
• Need better dialogue with EMA regarding coding changes
• Consider how to code qualifiers for IDMP (from July 2016)
  – Upgrade MedDRA or make other Controlled Vocabularies available?
Thank You