Processes and Approaches for Using the ATC Classification Systems and Non-Unique Drug Names for Classifying Drugs

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• Thanks to the audience for attending
Agenda

• The ATC classification system
  – How to utilize ATC classification in Drug Safety and Clinical Trials

• Non-Unique Drug Names
  – Challenges for coding, autocoding, dictionary versioning
  – How to select the best match from the multiple non-unique drug names
Background

• The WHO Collaboration Centre for international Drug Monitoring, the Uppsala Monitoring Centre (UMC) has been responsible for the WHO Programme since 1978.

• The WHO Drug Dictionary was developed for coding medicinal products within the WHO International Programme for Drug Monitoring in 1968.

• The WHO Drug Dictionary incorporates other international standards:
  – WHO INN for substance names
  – WHO ATC for classification of drug use
  – WHO Herbal ATC and nomenclature for herbal products and substances
ATC Classification Main Groups

A  Alimentary tract and metabolism
B  Blood and blood forming organs
C  Cardiovascular system
D  Dermatologicals
G  Genito-urinary system & sex hormones
H  Systemic hormonal preparations, excl. sex hormones and insulins
J  Antiinfectives for systemic use
L  Antineoplastics and immunomodulating agents
M  Musculo-skeletal system
N  Nervous system
P  Anti-parasitic products, insecticides and repellents
R  Respiratory system
S  Sensory organs
V  Various
Principal for ATC classifications

• Basic principle: Medicinal products are classified according to the main therapeutic use of main active ingredient
ATC Structure

• LEVEL 1: Main Group
  A ALIMENTARY TRACT AND METABOLISM

• LEVEL 2: Therapeutic Subgroup
  A02 DRUGS FOR ACID RELATED DISORDERS

• LEVEL 3: Chemical/Pharmacological/Therapeutic subgroups
  A02B DRUGS FOR PEPTIC ULCER AND GORD

• LEVEL 4: Chemical/Pharmacological/Therapeutic subgroups
  A02BC Proton pump inhibitors

• LEVEL 5: Chemical Substance
  A02BC01 Omeprazole
Use of the ATC system in the WHO Drug Dictionaries

• Purpose of introducing ATC into WHO Drug is to automatically provide high level information about the drug name. Analysis, aggregation of statistics
  – To identify interactions
• Understanding of the use of a product
  – E.g. compare with indication when coding concomitant medication with non-unique names.
More than One ATC Code Per Drug

• Each drug has a minimum of ATC codes, often only one

• Drugs can be used for several indications and it’s sometimes difficult to know why a drug was prescribed or used

• There is no ”Primary ATC code”
ATC Structure - Multiaxiality

• LEVEL 1: Main Group
  C CARDIOVASCULAR SYSTEM
  N NERVOUS SYSTEM

• LEVEL 2: Therapeutic Subgroup
  C02 ANTIHYPERTENSIVES
  N02 ANALGESICS

• LEVEL 3: Chemical/Pharmacological/Therapeutic subgroups
  C02A ANTIADRENERGIC AGENTS, CENTRALLY ACTING
  N02C ANTIMIGRAINE PREPARATIONS

• LEVEL 4: Chemical/Pharmacological/Therapeutic subgroups
  C02AC Imidazoline receptor agonists
  N02CX Other antimigraine preparations

• LEVEL 5: Chemical Substance
  C02AC01 Clonidine
  N02CX02 Clonidine
Non-Unique Drug Names

Background

- Currently there are ~200,000 entries total in WHODDE B-2
  - ~160,000 of the entries are unique drug names that correspond to the same ingredient(s)
  - ~37,000 entries are non-unique names or same name entries
    - The drug code is added to the name in order to make the name field unique
    - 16,000 drugs with non-unique drug names
      - ~8% of the drugs, but many very common drugs

- This does not optimize the use of TMS for coding and presents problems for autocoding and dictionary versioning
TMS WHODrug Forum

• Members and Co-Chairs from the TMS focus group, representatives from the WHO-UMC and DBMS Consulting

• Our objective is to provide TMS users who have implemented the WHODrug dictionary with options to better manage the issue of non-unique drug names when:
  – Installing and versioning the WHODrug dictionary
  – Autocoding
  – Classifying
  – Searching for and selecting the best match
Drug Names That Can Autocode

• TROMBYL: ‘Normal entries’
• A preferred name that also appears in trade names with variations of the ingredients and salts:
  AMPICILLIN
  AMPICILLIN /00000502/
  AMPICILLIN /00000503/

• A verbatim like ‘Ampicillin’ should autocode to the preferred name entry, not to a trade name.

• There are approximately 800 drugs with preferred name entries that fall into this category.
Trade Names That Cannot Autocode

ACTRON /00020001/
ACTRON /00109201/
ACTRON /00321701/
ACTRON /00391201/
ACTRON /00727101/
# Trade Names That Cannot Autocode

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Name Specifier</th>
<th>Drug Code</th>
<th>MaHolder</th>
<th>Country</th>
<th>Ingredients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actron</td>
<td></td>
<td>003912 01 026</td>
<td>Bayer</td>
<td>France</td>
<td>Acetylsalicylic acid Caffeine Paracetamol</td>
</tr>
<tr>
<td>Actron</td>
<td></td>
<td>001092 01 461</td>
<td>Bayer</td>
<td>Mexico</td>
<td>Ibuprofen</td>
</tr>
<tr>
<td>Actron</td>
<td></td>
<td>003217 01 053</td>
<td>Bayer</td>
<td>United States</td>
<td>Ketoprofen</td>
</tr>
<tr>
<td>Actron</td>
<td></td>
<td>000200 01 158</td>
<td>Bayer</td>
<td>Spain</td>
<td>Paracetamol</td>
</tr>
<tr>
<td>Actron</td>
<td>/Old form/</td>
<td>007271 01 001</td>
<td>Miles Martin</td>
<td>Spain</td>
<td>Acetylsalicylic acid Caffeine Citric acid Paracetamol Sodium bicarbonate</td>
</tr>
</tbody>
</table>
Issues

• **Coding Issues**: ~15,000 of the WHODD names are non-unique

• **Autocoding Issues**: Non-unique names cannot autocode and require further investigation

• **Dictionary Versioning Issues**: More terms are requiring reclassification during the versioning process

• **Additional Issues**: TMS “learning” feature enables the system to automatically code VTAs
Constraints

• Need to balance the accuracy with the coder-friendliness of the WHODrug dictionary

• Coders must code all of the data before study lock; they cannot leave terms uncoded

• WHODrug does not provide the Country or drug form in the B2 format
Assumptions

• Trade names will continue to be added to WHODrug when drugs are developed for different countries

• Drug names are not deleted that are no longer used; if a product is withdrawn, it will still need to remain in the dictionary.

• Non-unique drugs are differentiated by Country and/or drug form and/or ingredients and/or ATC

• Majority of companies using TMS use the WHODrug B2 format, which does not include country or drug form
Reduce Number of Non-Unique Drugs

• How can we reduce the number of terms requiring classification to the non-unique drug names?

• What guidelines and rules can be established to best load/update WHODrug, to code, and manage the terminology in TMS?
Establish Coding Rules

• Code/Autocode to the preferred name entry like ‘Ampicillin’, if a PN is available

• Code/Autocode to the base substance

• Collect the Generic name

• Code/Autocode to the term without salt in the case of drug names that are non-unique due to the salt variation like ‘Prilosec – Omeprazole’, which is a single substance with chemical variation with Minor therapeutic difference
  • Omeprazole (without salt)
  • Omeprazole magnesium (salt)
Coding When the Coding Rules Do Not Apply

• How do we select the best match?

• What data would help us classify the non-unique drug name to the correct dictionary term?

• What is the least common denominator?

• How can we provide the additional information when:
  – Collecting the VT?
  – Autocoding the VT?
  – Manually coding?

• Can additional data be included in or with the VT?
Differentiators

• **Ingredients:** If you have ingredients, don’t need to go further.

• **Country:** If you have a drug name in several forms, identify what country they come from.

• **Drug Form:** There are cases where you have multiple drug forms in one country.

• **Indication:** If you have the indication information, it can be used to identify ATC terms and can be used to identify some better matches.
Coding Using Country

• Questions:
  – Can the country or form be captured on the CRF?
  – Can you accurately use the country of the site to establish the country where the drug is produced?

• Advantage:
  – Allows you to select the best match by geographic region

• Disadvantage:
  – Additional information may not be available or limited.
  – Need multiple domains if the country is not part of the VT
  – WHODrug does not include country information in the B2 Format
Coding Using Ingredient

• **Questions:**
  – Can you collect the active ingredients?

• **Advantage:**
  – Allows you to select the best match by ingredient without having to look further

• **Disadvantage:**
  – Data managers need to limit the number of queries to sites
  – The patient does not usually know the ingredients
  – The investigator may not have this information either
Coding Using Drug Form & Indication

Drug Form
  – **Advantage:**
    • Allows you to select the best match by drug form alone or in combination with country
  – **Disadvantage:**
    • WHODrug does not include drug form information in the B2 Format

Indication
  – **Advantage:**
    • If you have the indication information, it can be used to identify ATC and can be used to identify some better matches
  – **Disadvantage:**
    • VTs don’t normally include the indication, although some TMS user combine this with the VT in a derivation procedure for coding (VT + Route + Indication)
Possible Options

• Use a similar algorithm for WHODrug Format C format loading for B2.
  – Requires establishing domain VTA rules for each of the multiple sets of Drug Recnums
  – Drug Names could be defaulted based on country or Preferred Name derivation
  – Create Global VTAs where a single drug exists with a Drug Code appended if the WHODDD Type is being used.

• If the goal of coding is ONLY to derive Preferred Names and NOT ATCs, then it is possible to create a Global VTA if all the Preferred Names are the same, even if the Drug Recnums are different

• Possible enhancements to TMS to allow “single” VTA coding (formerly called VTI functionality), which is similar to HLC at the VT coding level instead

• Derive a specific match based on Site/Investigator/Patient location or country, and use this in a derived question or Search Object.
TMS WHODrug Users’ Needs

• Be able to identify which non-unique drug name is the most recent and current entry
• Identify what distinguishes the non-unique drug names from each other on a drug name basis
• Collect the country, formulation, ingredients, or indication with the source VT
• Use the country, formulation, ingredients, or indication combined with the VT during classification
• Be able to view the country, formulation, ingredients, or indication information in the classification and approval screens when selecting the correct non-unique drug name
• Flag a preferred match for drug names with salt variations
• Avoid using multiple domains
• Increase the autocoding hit rate
• Reduce the number of terms that require re-coding after dictionary versioning
Wednesday, 10 October
10:30am – noon
Session 26 – TMS WHODrug Forum

• Discuss optimized processes to manually code, autocode, and version the dictionary for non-unique drug names

• Analyze how we can:
  – Implement technical or terminology changes
  – Work together on acceptable work-around alternatives
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