

Coding dictionaries information: How to manage? How to use?

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Because health matters

Agenda

- General points
 - MedDRA
 - WHODD
- Load of data
- Macro to merge dictionaries with study datasets
- The reporting
- Next steps

General points : MedDRA

- What is MedDRA ?
- MedDRA definition and use
- MedDRA structure
 - Lowest Level Term
 - Preferred Term
 - High Level Term
 - High Level Group Term
 - System Organ Class
- MedDRA Multi-axiality

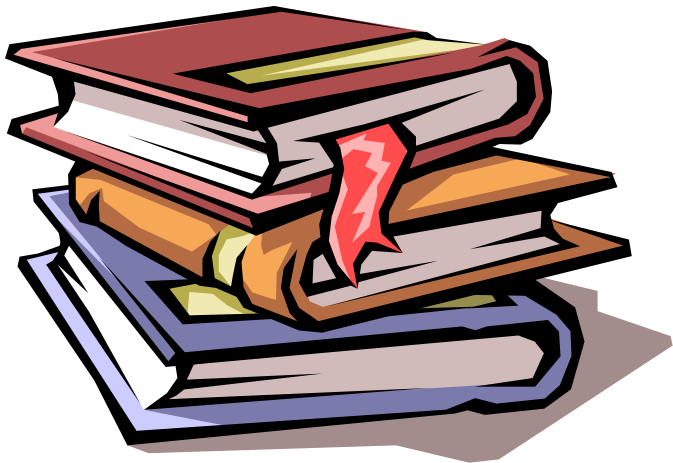
WHAT is MedDRA?

Med = **Medical**

D = **Dictionary** (*for*)

R = **Regulatory**

A = **Activities**



MedDRA definition and use

- **MedDRA definition**

- **MedDRA use**

- **Examples**

MedDRA structure

System Organ Class (SOC) (26)

High Level Group Term (HLGT) (333)

High Level Term (HLT) (1,699)

Preferred Term (PT) (18,641)

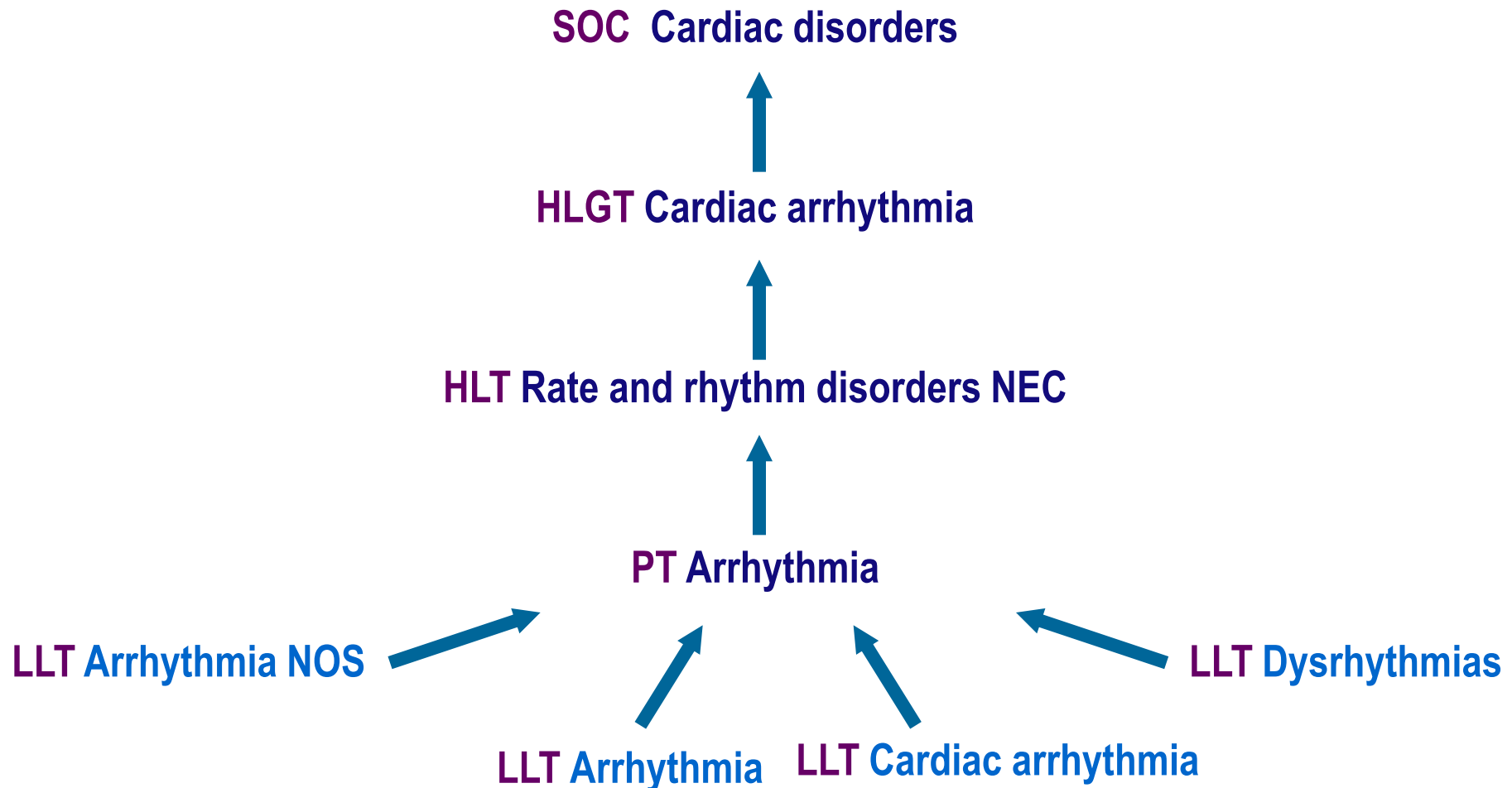
Lowest Level Term (LLT) (67,503)

Lowest Level Term

- Has one of the following relationships to PT
 - ✓ **Synonym**
 - ✓ **Lexical variant**
 - ✓ **Quasi-synonym**
- **Constitutes the entry level of the terminology and linked to a single PT**
- **Large terminology with > 65,000 terms (version 12.1)**

MedDRA Hierarchy (LLT)

Lowest Level Term (*Example*)

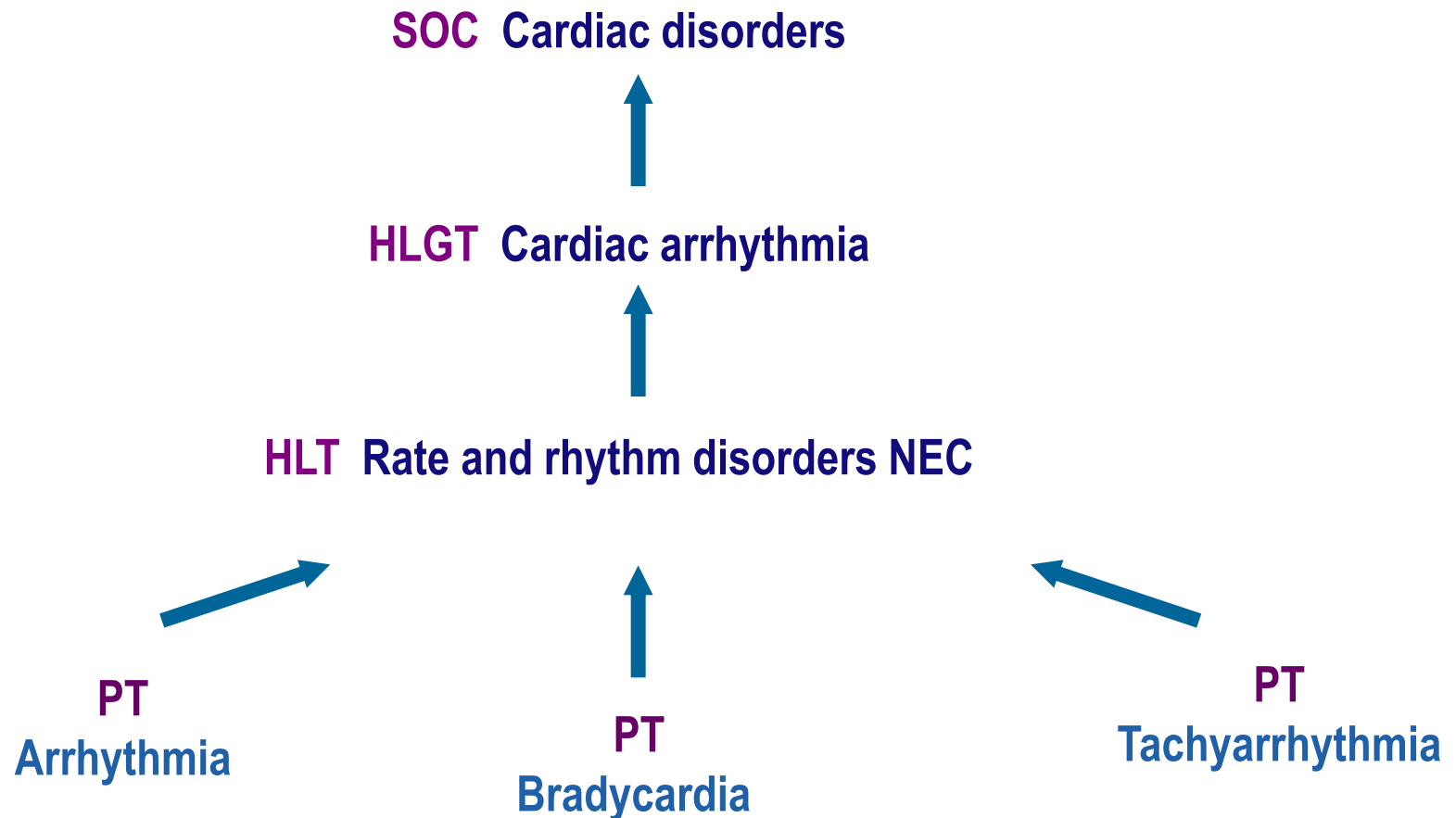


Preferred Term

- **PT represents a single unique medical concept**
- **Proposed level for reporting (FDA)**
- **No limit to the number of LLTs that can be linked to a single PT**
- **An identical LLT is created for every PT**

MedDRA Hierarchy (PT)

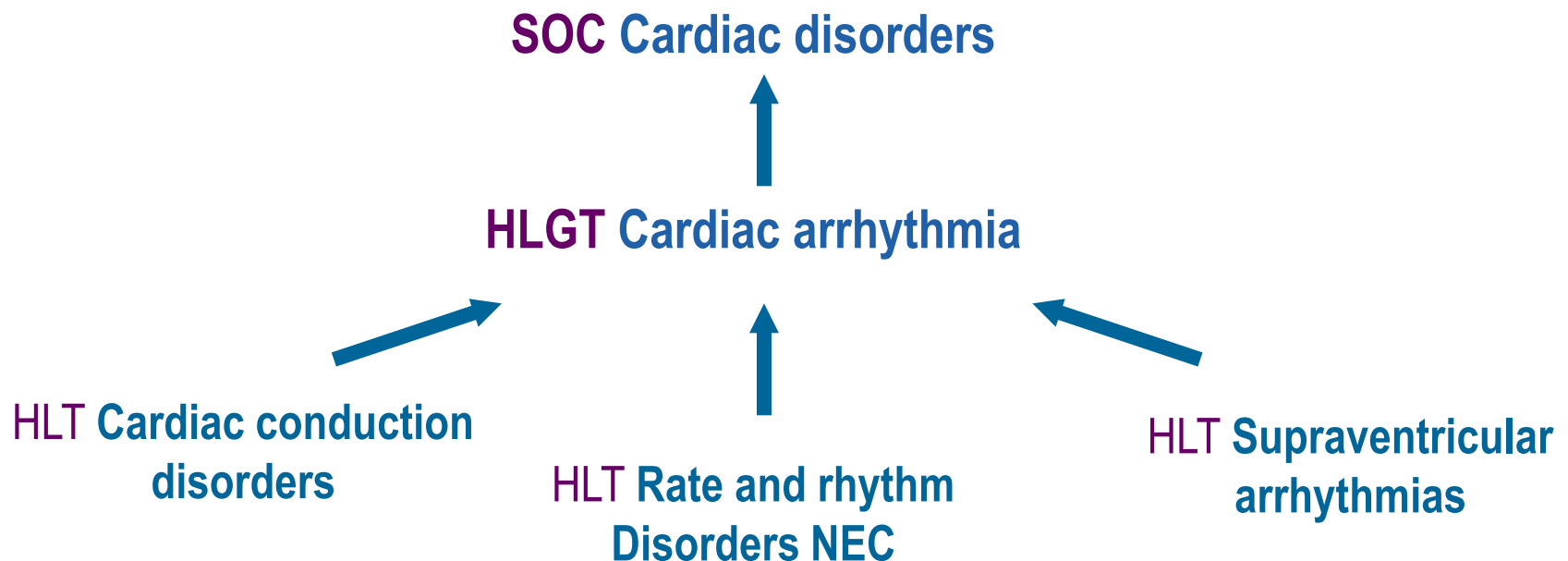
Preferred Term (*Example*)



MedDRA Hierarchy (HLT)

High Level Term

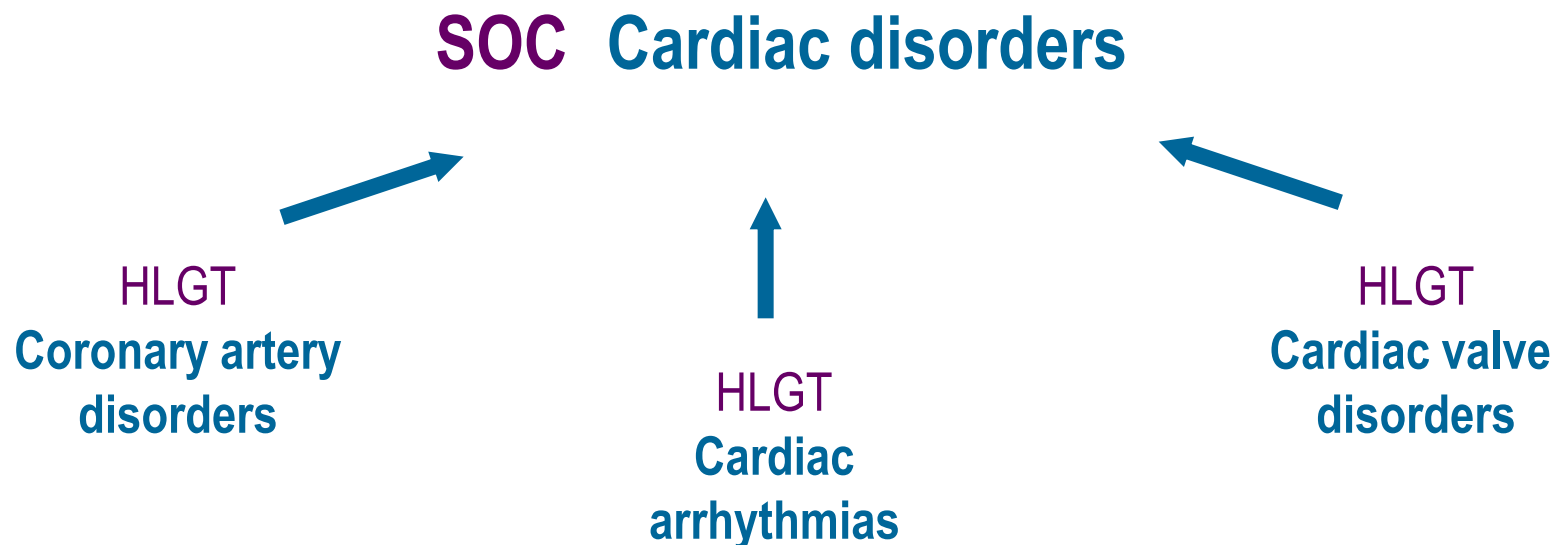
- Subordinate to HLGTs and super ordinate descriptor for the PTs linked to it
- Provides clinically relevant groupings



MedDRA Hierarchy (HLGT)

High Level Group Term

- Subordinate only to System Organ Classes and super ordinate descriptor for one or more HLTs
- Provides clinically relevant groupings



System Organ Class (SOC)

Highest level of the
hierarchy which provides
the broadest concepts for
Data retrieval

MedDRA Multi-axiality

SOC = Respiratory, thoracic and mediastinal disorders

HLGT = Respiratory tract infections

HLT = Viral upper respiratory tract infections

SOC = Infections and infestations

HLGT = Viral infectious disorders

HLT = Influenza viral infections

PT = Influenza

General points : WHODD

- WHODD definition : World Health Organization Drug Dictionaries
- WHODD use

WHODD structure

Main Items of WHODD used for coding:

- Drug name
- Drug record number
- Sequence 1
- Sequence 2
- ATC code : Anatomical Therapeutic Chemical Classification codes

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Load of data : MedDRA

- MedDRA is released twice a year updates (xx.0 and xx.1)
 - Current version 12.1
- Provide by MSSO
 - Text files (about ten)
- Coding information's will be available in 2 different datasets
 - SOC
 - SMQ

Load of data : WHODD

- WHODD is released twice a year updates (March, September)
 - Current version : SEPT2009
- Provide by UMC
 - Text files (about ten)
 - Format B2
- Coding information's will be available in 2 different datasets
 - ATC
 - ING

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Problematic

- CDM systems not suitable to handle all coding information's
 - Issue of system performance
 - Issue of DB size
 - Issue of DB structure
 - All variables not necessary for CDM
- Needs are growing
 - Safety need to be looked closer
 - New tools need to be implemented (SMQs)
- Merge between analysis dataset and dictionary
 - Biostatistics level and not at the CDM level anymore
 - SAS macros

Step 1 : identify analysis variables to remove

```
proc contents data=analysis_med out=contents noprint;
run;
data _null_;
attrib drop_items format=$200. label='Drop Items';
retain drop_items "";
set contents end=EOF;
if substr(upcase(name),1) in ('PT','PTN','LLTCUR'
                             , 'HLT','HLTN','HLGT','HLGTN'
                             , 'SOC','SOCN','SOCL','SMQL'
                             , 'ABBREV','DICTV','BODSYN','BODSYS','DECOD','DICTVS')
then do;
    drop_items = compbl(drop_items || ' ' || name);
end;
if EOF then do ;
    call symput('drop_items',drop_items);
end ;
run;
```

Step 2 : merge with the dictionary dataset

```
/* retrieve SOC path from dictionary */
proc sort data= meddra.SOC(where=(lltcur='Y')) out=SOC;
  %if %upcase(&ALLSOC) = Y %then %do ;
    where soc1fl in('Y','N');
  %end ;
  %if %upcase(&ALLSOC) = N %then %do ;
    where soc1fl='Y';
  %end ;
  by llt;
run;
/* Create dataset_SOC with SOC path */
proc sql;
  create table &data_out as
  select a.*
    ,b.*
  from analysis_med(drop=&drop_items) a left join soc b
  on a.&var_merg. = b.lltcd
  order by line_no
;
quit;
```

Step3 : call of the macro

```
%MEDDRA (  
  data_in      = work.ae_end  
  ,mod         = ae  
  ,data_out    = work.ae_soc_d  
  ,v_meddra    = information from the analysis dataset  
  ,var_dict    = aedictv  
  ,var_merg    = aelltcd  
  ,allsoc      = Y  
  ,v_adssds    = 4);
```

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The reporting : MedDRA

Number (%) of patients with TEAE(s) by Primary SOC, HLGT, HLT and PT Safety population

PRIMARY SYSTEM ORGAN CLASS

HLGT: High Level Group Term

HLT: High Level Term

Preferred Term n(%)

Trt A
(N=XX)

Trt B
(N=XX)

Any class	xxx (xx.x%)	xxx (xx.x%)
INFECTIONS AND INFECTIONS	xxx (xx.x%)	xxx (xx.x%)
HLGT : Bacterial infectious disorders	xxx (xx.x%)	xxx (xx.x%)
HLT : Bacterial infections nec	xxx (xx.x%)	xxx (xx.x%)
Cellulitis	xxx (xx.x%)	xxx (xx.x%)
HLT : Streptococcal infections	xxx (xx.x%)	xxx (xx.x%)
Pharyngitis streptococcal	xxx (xx.x%)	xxx (xx.x%)
HLGT : Fungal infectious disorders	xxx (xx.x%)	xxx (xx.x%)
HLT : Fungal infections nec	xxx (xx.x%)	xxx (xx.x%)
Vulvovaginal mycotic infection	xxx (xx.x%)	xxx (xx.x%)
HLT : Tinea infections	xxx (xx.x%)	xxx (xx.x%)
Tinea pedis	xxx (xx.x%)	xxx (xx.x%)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	xxx (xx.x%)	xxx (xx.x%)
HLGT: Breast neoplasm benign (incl nipple)	xxx (xx.x%)	xxx (xx.x%)
HLT: Breast and nipple neoplasms benign	xxx (xx.x%)	xxx (xx.x%)
Benign breast neoplasm	xxx (xx.x%)	xxx (xx.x%)
HLGT: Cutaneous neoplasms benign	xxx (xx.x%)	xxx (xx.x%)
HLT: Skin neoplasms benign	xxx (xx.x%)	xxx (xx.x%)
Acanthoma	xxx (xx.x%)	xxx (xx.x%)
Lentigo	xxx (xx.x%)	xxx (xx.x%)

TEAE: Treatment emergent adverse event, SOC: System organ class, HLGT: High level group term, HLT: High level term, PT: Preferred term

MedDRA <dictionary version xxx>

n (%) = number and percentage of patients with at least one TEAE

Note: Table sorted by SOC internationally agreed order and HLGT, HLT, PT by alphabetic order

PGM=SARxxx/YYYxxx/CSR/BS/PGM_RPT/STD_AE_HLGT.sas OUT=OUTPUT/ STD_AE_HLGT_i.rtf (DDMMMYYYY - HH:MM)

The reporting : MedDRA

Number (%) of patients with TEAE(s) by Primary SOC and PT by maximal intensity Safety population

Primary System Organ Class Preferred Term n(%)	Trt A (N=XX)			Trt B (N=XX)		
	Mild	Moderate	Severe	Mild	Moderate	Severe
Infections and infestations						
Nasopharyngitis	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Upper respiratory tract infection	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Sinusitis	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Influenza	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Gastroenteritis	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Diverticulitis	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Urinary tract infection	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Pharyngitis	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Bronchitis	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Rhinitis	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Cystitis	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

TEAE: Treatment emergent adverse event, SOC: System organ class, PT: Preferred term

MedDRA <dictionary version xxx>

n (%) = number and percentage of patients with at least one TEAE

Note: Table sorted by SOC internationally agreed order and PT sorted by decreasing frequency according to all TEAE summary (table STD_AE_SOCPT.doc)

In case of several occurrences for the same PT (respectively SOC), the maximal intensity is used

PGM=SARxxxx/YYYxxxx/CSR/BS/PGM_RPT/STD_AE_SOCPT_intensity.sas OUT=OUTPUT/ STD_AE_SOCPT_intensity_i.rtf (DDMMYYYY - HH:MM)

The reporting : WHODD

Concomitant medications - Number of patients by anatomic class and therapeutic class Randomized population

Anatomic Class	Trt A	Trt B
Therapeutic Class	(N=XX)	(N=XX)
Any concomitant medications	xx (xx.x%)	xx (xx.x%)
Anatomic Class1	xx (xx.x%)	xx (xx.x%)
Therapeutic class 1	xx (xx.x%)	xx (xx.x%)
Therapeutic class 2	xx (xx.x%)	xx (xx.x%)
Therapeutic class 3	xx (xx.x%)	xx (xx.x%)
Therapeutic class N	xx (xx.x%)	xx (xx.x%)
Anatomic Class2	xx (xx.x%)	xx (xx.x%)
Therapeutic class 1	xx (xx.x%)	xx (xx.x%)
Therapeutic class 2	xx (xx.x%)	xx (xx.x%)
Therapeutic class 3	xx (xx.x%)	xx (xx.x%)
Therapeutic class N	xx (xx.x%)	xx (xx.x%)
Anatomic ClassN	xx (xx.x%)	xx (xx.x%)
Therapeutic class 1	xx (xx.x%)	xx (xx.x%)
Therapeutic class 2	xx (xx.x%)	xx (xx.x%)
Therapeutic class 3	xx (xx.x%)	xx (xx.x%)
Therapeutic class N	xx (xx.x%)	xx (xx.x%)

ATC: Anatomical therapeutic chemical, IP: Investigational product

WHO-DD <dictionary version xxx>

Note: A medication can be counted in several ATC classes

Concomitant medications are those the patient used at any time during the TEAE period (from first IP intake up to XX)

Anatomic classes are sorted by decreasing frequency in treatment group XX. Therapeutic classes are sorted by decreasing frequency in treatment group XX within each medication class.

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Next steps

- A lot of things to implement
- MedDRA
 - SMQ
 - CMQ
- WHODD
 - Format C
 - SDQ
 - CDQ