

Implemented MedDRA Version 18.0 Complex Changes

(January 2015)

MedDRA User Submitted Requests:

1. **Add New HLT *Patient positioning* to HLGT *Therapeutic procedures and supportive care NEC***

Submitter rationale: Several PTs could be linked more appropriately in one group, such as PT *Beach chair position*, PT *Trendelenburg position* and new PTs - PT *Supine position*, PT *Prone position* and PT *Fowler's position*. (Note: these three PTs were added in MedDRA Version 17.0).

Terminology Impact: If approved, PT *Lithotomy position* would be moved under HLT *Patient positioning* in addition to the PTs proposed in the submitter's rationale.

Implementation Status: This proposal will be implemented as requested. HLT *Patient positioning* will be added to provide a better grouping for therapeutic positioning concepts such as PT *Beach chair position*, PT *Fowler's position*, PT *Lithotomy position*, PT *Prone position*, PT *Trendelenburg position* and PT *Supine position*. These PTs will be moved to HLT *Patient positioning*.

2. **Add new HLGT *Product therapeutic and non-therapeutic uses* to SOC *General disorders and administration site conditions***

Add a new HLT *Underdoses* to new HLGT *Product therapeutic and non-therapeutic uses*

Move HLT *Overdoses* from HLGT *Medication errors* in SOC *Injury, poisoning and procedural complications* to new HLGT *Product therapeutic and non-therapeutic uses*

Submitter rationale: HLGT *Medication errors* contains terms which are not medication errors. Consequently, routine data retrieval by this HLGT is not indicative or informative of actual occurrence of medication errors. Specifically, HLGT *Medication errors* contains HLT *Overdoses* which contributes significant noise to signal detection due to PT *Overdose* and PT *Intentional overdose*; the HLGT also contains other terms which are not a medication error, such as PT *Intentional underdose*. This is a proposal to address these terms in HLGT *Medication errors* which do not represent medication errors, in order to improve the accuracy of MedDRA hierarchy for both coding and retrieval purposes.

Implementation Status: The MSSO reviewed the feedback received from this proposal and, in collaboration with the ICH M1 Points to Consider Working Group, developed a structure to better organize product use concepts including medication error, overdose, and underdose concepts, as well misuse concepts and off label use concepts as described in Item 3 below. The following points describe the approach taken. Please see the table below which illustrates the placement of these terms. For the sake of brevity, not all LLTs are shown in the table. It should be noted that definitions of misuse may not always include the concept of therapeutic use; misuse may be closer to the concept of abuse in some regions Section 3.16 in the *MedDRA Term Selection: Points to Consider* document, Release 4.9 based on MedDRA Version 18.0 (available on 1 March 2015) will be updated to reflect the potential interpretations of misuse.



- A new HLGT *Product use issues* will be added to SOC *Injury, poisoning and procedural complications*. The name of the new HLGT will be rephrased to HLGT *Product use issues* instead of proposed HLGT *Product therapeutic and non-therapeutic uses* because the definitions and categories of “therapeutic” and “non-therapeutic” may differ between different regulatory regions and may be subject to misinterpretation. Placing new HLGT *Product use issues* in SOC *Injury, poisoning and procedural complications* instead of SOC *General disorders and administration site conditions* allows grouping of related product use concepts (medication errors, misuse, off label use, overdoses, and underdoses) in one location to facilitate coding and retrieval, without the need for extensive multi-axial links.
- A new HLT *Product issue issues NEC* will be added under HLGT *Product use issues* to accommodate a mix of misuse, intentional use, and other non-specific use concepts. This new HLT will have two new PT concepts:
 - A new PT *Product use issue* will be added to accommodate non-specific product use concepts that are not specifically identified as medication errors, off label use, misuse etc.
 - PT *Intentional product use issue* will be added to accommodate use issue concepts that are known to be intentional but are not specifically identified as being misuse or off label use.

Please see the table below for existing PTs moved to HLT *Product issue issues NEC*.



- Two new HLTs – HLT *Overdoses NEC* and HLT *Underdoses NEC* - will be added to new HLGT *Product use issues* to group related concepts in SOC *Injury, poisoning and procedural complications*. The “NEC” qualifier is needed because not all overdose and underdose terms are in these two



new HLTs; there are additional accidental overdose and underdose terms in HLT *Maladministrations*. Existing HLT *Overdoses* will be merged to new HLT *Overdoses NEC*.

- Non-specific LLTs under PT *Off label use* and PT *Intentional product misuse* that do not specifically state or imply misuse or off label use will be moved to a broader concept, non-specific PT. For example, LLT *Intentional dose decrease* and LLT *Intentional dose increase* will be moved to from PT *Intentional product misuse* to new PT *Product use issue*. LLT *Drug use for unapproved indication* will be moved from PT *Off label use* to new PT *Product use issue*. Please see the table below for more information.

| SOC Injury, poisoning and procedural complications | |  New  Existing | | *Not all LLTs are shown | |
|--|----------------|---|----------------------------|---|--|
| HLGT | HLT | PT | LLT* | Notes | |
| Product use issues | | | | | |
| | Off label uses | | | | |
| | | Off label use | Off label use | Moved from HLT <i>Therapeutic procedures NEC</i> in SOC <i>Surgical and medical procedures</i> | |
| | | | Off label dosing | | |
| | | | Off label dosing frequency | | |
| | | Off label use of device | Off label use of device | Primary link to HLT <i>Device issues NEC</i> in SOC <i>General disorders and administration site conditions</i> | |
| | Overdoses NEC | Intentional overdose | | HLT <i>Overdoses</i> merged to new HLT | |
| | | Overdose | | Non-specific term. Moved from HLT <i>Overdoses</i> | |
| | | Prescribed overdose | | Non-specific. May describe a medication error or off label use scenario. Moved from HLT <i>Overdoses</i> . | |
| | | | | | |
| | Product use | Intentional | Intentional product | | |

| SOC Injury, poisoning and procedural complications |  New | | *Not all LLTs are shown | |
|--|--|---|---|---|
| |  Existing | | | |
| HLGT | HLT | PT | LLT* | Notes |
| | issues NEC | product use issue | use issue | |
| | | | Intentional dose decrease | Move from PT <i>Intentional product misuse</i> |
| | | | Intentional dose increase | Move from PT Intentional product misuse |
| | | | Intentional use beyond labeled administration duration | |
| | | | Intentional use beyond labeled duration | Move from PT Intentional product misuse |
| | | | Intentional use beyond labelled administration duration | |
| | | | Intentional use beyond labelled duration | Moved from PT <i>Intentional product misuse</i> |
| | | | Intentional use by incorrect route | Moved from PT <i>Intentional product misuse</i> |
| | | | Intentional use for unlabeled indication | Moved from PT <i>Off label use</i> |
| | | | Intentional use for unlabelled indication | Moved from PT <i>Off label use</i> |
| | | Drug administered to patient of inappropriate age | Drug administered to patient of inappropriate age | PT moved from HLT <i>Maladministrations</i> because most cases are intentional, not accidental |
| | | | Adult product administered to child | Moved from PT <i>Off label use</i> |
| | | | Adult use of a child product | |
| | | | Child product given to infant | Moved from PT <i>Off label use</i> |
| | | | Drug use in unapproved age group | |
| | | | Inappropriate age at vaccine administration | |

| SOC Injury, poisoning and procedural complications |  New | | *Not all LLTs are shown | |
|--|--|----------------------------|--|--|
| |  Existing | | | |
| HLGT | HLT | PT | LLT* | Notes |
| | | Intentional product misuse | Intentional product misuse | Moved from HLT <i>Therapeutic procedures NEC</i> in SOC <i>Surgical and medical procedures</i> |
| | | | Drug misuse | Non-current |
| | | | Intentional drug misuse | |
| | | | Intentional misuse | |
| | | | Intentional misuse by dose change | |
| | | | Intentional misuse in dosing frequency | |
| | | Product use issue | Product use issue | |
| | | | Drug use for unapproved dosing regimen | |
| | | | Drug use for unapproved indication | Moved from PT <i>Off label use</i> |
| | | | Drug use for unapproved schedule | |
| | | | Drug use in unapproved population | Moved from PT <i>Off label use</i> |
| | | | Drug use via unapproved administration route | Moved from PT <i>Off label use</i> |
| | | | Medically prescribed prolongation of labeled treatment duration | |
| | | | Medically prescribed prolongation of labelled treatment duration | |
| | | | Product use in unapproved indication | |

| SOC Injury, poisoning and procedural complications |  New  Existing | | *Not all LLTs are shown | |
|--|---|---|-------------------------|---|
| HLGT | HLT | PT | LLT* | Notes |
| | | Contraindicated drug administered | | This term does not specify or imply medication error, off label use or misuse. Moved from HLT <i>Maladministrations</i> . |
| | Underdoses NEC | Intentional underdose | | Moved from HLT <i>Maladministrations</i> . |
| | | Prescribed underdose | | Non-specific. May describe a medication error or off label use scenario. Moved from HLT <i>Maldministrations</i> . |
| | | Underdose | | Moved from HLT <i>Maladministrations</i> . |
| Medication errors | | | | |
| | Maladministrations | | | Not all PTs are shown. |
| | | Accidental overdose | | Moved from HLT <i>Overdoses</i> |
| | | Accidental underdose | | |
| | | Radiation overdose Radiation underdose | | Moved from HLT <i>Overdoses</i> . Radiation overdose and underdose are assumed to be accidental. |

3. Add new HLT *Off label uses*

Submitter rationale: The new EU legislation extends the definition of an adverse drug reaction to include use inside and outside of the terms of the marketing authorisation. Therefore there is a need to code and aggregate cases of 'off label use' where this has been reported and to specify the type of 'off label use' more precisely. Additional PTs are required to provide this specificity of coding.

MSSO Note: This request was previously suspended from MedDRA Version 17.0. If this change were implemented, any PT and LLTs added or moved under the proposed HLT *Off label uses* would have to be carefully considered in order to make clear distinctions between the concepts of off label use, misuse, medication errors, and intentional vs unintentional use. See section 3.16 of the *MedDRA Term Selection: Points to Consider* document.

Implementation Status: This proposal will be implemented as requested. HLT *Off label uses* will be added to new HLG *Product use issues* in SOC *Injury, poisoning and procedural complications* to group related product use concepts (medication errors, misuse, off-label use, overdoses, and underdoses) in one location to facilitate coding and retrieval. Please see item 2 for an explanation of the structure that will be implemented in MedDRA Version 18.0 to better organize these product use concepts.

The following changes are proposed by the MSSO:

4. Merge HLT *Abdominal hernias, site unspecified* and HLT *Abdominal cavity hernias NEC* with new HLT *Abdominal hernias NEC* in HLG *Abdominal hernias and other abdominal wall conditions*

MSSO Rationale: The MSSO proposes grouping all abdominal hernia terms together by merging *HLT Abdominal hernias, site unspecified* and *HLT Abdominal cavity hernias NEC* with new *HLT Abdominal hernias NEC* in HLG *Abdominal hernias and other abdominal wall conditions*. Adding *HLT Abdominal hernias NEC* would streamline existing concepts and broaden the scope of this new HLT.

Terminology Impact: If approved, the PTs under *HLT Abdominal cavity hernias NEC* and *HLT Abdominal hernias, site unspecified* would move under new *HLT Abdominal hernias NEC*.

Implementation Status: This proposal will be implemented as requested.

5. Add new HLT *Limb fractures* under HLG *Fractures* in SOC *Musculoskeletal and connective tissue disorders* and merge existing HLTs - *HLT Lower limb fractures* and *HLT Upper limb fractures* under new HLT *Limb fractures*.

Add new HLT *Limb fractures and dislocations* under HLG *Bone and joint injuries* in SOC *Injury, poisoning and procedural complications*. Merge existing HLTs - *HLT Lower limb fractures and dislocations* and *HLT Upper limb fractures and dislocations* under new HLT *Limb fractures and dislocations*.

MSSO Rationale: These proposals will remove redundancy and dispersion of limb fractures in SOC *Musculoskeletal and connective tissue disorders* and *Limb fractures and dislocations* in SOC *Injury, poisoning and procedural complications*.

Terminology Impact: If implemented, PTs from *HLT Fractures NEC* which clearly pertain to limb fractures would be moved to new *HLT Limb fractures* including:

- PT *Greenstick fracture*
- PT *Epiphyseal fracture*
- PT *Limb fracture*

- PT *Osteochondral fracture*
- PT *Torus fracture*

In SOC *Injury, poisoning and procedural complications*, PTs from HLT *Fractures and dislocations NEC* which clearly pertain to limb fractures and dislocations would be moved to HLT *Limb fractures and dislocations* including:

- PT *Greenstick fracture*
- PT *Limb fracture*
- PT *Osteochondral fracture*
- PT *Torus fracture*

Additionally, PTs from HLT *Bone and joint injuries NEC* which clearly pertain to limb fractures and dislocations would be moved to HLT *Limb fractures and dislocations* including:

- PT *Epiphyseal fracture*

Note: All PTs listed above would be primary to SOC *Injury, poisoning and procedural complications* and secondary to SOC *Musculoskeletal and connective tissue disorders*.

Implementation Status: This proposal will be implemented as requested.