MTN-017: Adverse Events and MedDRA

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Outline

• General description of AE reporting/MedDRA coding process
• Cases
• MTN-017 “Cheat Sheet”
What is MedDRA?

• Extensive and highly specific standardized medical terminology dictionary developed by the ICH
• Facilitate sharing of regulatory information internationally for medical products.
• Most recent version is 16.1
- Verbatim term: Abdominal pain
  MedDRA preferred: “Abdominal pain”

- Verbatim term: Rectal Friability
  MedDRA preferred: UNCODABLE

- Verbatim term: “Tenesmus”
  Needs: ANATOMICAL SITE

- Verbatim term: “Scant rectal blood”
  MedDRA preferred: “Rectal Hemorrhage”
Case 1

• 24 year old male on oral Truvada (Period 1) reports anal pain at his end period visit. It is described as a burning/tingling sensation. He has a prior history of perianal HSV and reports that this is consistent with previous episodes.
• An Grade 2 Adverse Event of “Anal HSV” is reported on the AE CRF and faxed to SCHARP

• Meddra preferred term: Proctitis Herpes
• “Anal HSV”
  – maps to a Meddra preferred term of “Proctitis Herpes”
  – Proctitis - defined as inflammation of rectal mucosa. From the standpoint of MedDRA – also includes anal mucosa.
  – Appropriate if evidence of HSV involving anal mucosa
  – Clinical syndrome of HSV proctitis is a rare entity

• “Perianal HSV”
  – more accurately captures this adverse event
  – Maps to “genital herpes”
<table>
<thead>
<tr>
<th>Verbatim Term</th>
<th>Meddra Preferred Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perianal HSV</td>
<td>Genital Herpes</td>
</tr>
<tr>
<td>Anal HSV</td>
<td>Proctitis Herpes</td>
</tr>
<tr>
<td>Anal HSV Ulcer</td>
<td>Proctitis Herpes</td>
</tr>
<tr>
<td>Rectal HSV</td>
<td>Proctitis Herpes</td>
</tr>
</tbody>
</table>
Take home points

• Important to specify anatomic location
• Distinguish between anal and perianal involvement of HSV
Case 2

• 40 year old male on daily reduced glycerin tenofovir gel presents for his mid-period visit. Reports that his stools are softer and somewhat mushier.
• A verbatim term of “soft stool” is reported.

• This maps to a MedDRA preferred term of “Diarrhoea”.
• Definition of diarrhea?
  – WHO definition – three or more loose, liquid stools per day

• Alternative is to report as “change in stool consistency” without further detail which will map to “abnormal faeces”

• Any mention of “soft”, “loose”, or “softer” will cause the verbatim term to map to “diarrhoea”

• MedDRA preferred term of “frequent bowel movements” does exist
Take home points

• Certain details will impact MedDRA coding.

• Terms such “loose” or “soft” stool will map to “diarrhoea”

• Diarrhea related to procedure maps to “post procedure diarrhoea”
<table>
<thead>
<tr>
<th>Verbatim Term</th>
<th>MedDRA Preferred Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft Stools</td>
<td>Diarrhoea</td>
</tr>
<tr>
<td>Change in Stool Consistency (Softer)</td>
<td>Diarrhoea</td>
</tr>
<tr>
<td>Change in Stool Consistency</td>
<td>Abnormal Faeces</td>
</tr>
<tr>
<td>Change in Stool Consistency (mushier)</td>
<td>Abnormal Faeces</td>
</tr>
<tr>
<td>Increased stool frequency</td>
<td>Frequent Bowel Movements</td>
</tr>
<tr>
<td>Loose stool related to study product application</td>
<td>Post procedural diarrhoea</td>
</tr>
</tbody>
</table>
Case 3

• 34 yo male on RAI associated tenofovir gel. Reports some “gas pain”
• A verbatim term of “gas pain” is reported

• MedDRA preferred term: Flatulence
What is flatulence?

• The presence of too much air or gas being present in the stomach or intestines
• The process of flatus being passed through the anus
<table>
<thead>
<tr>
<th>Verbatim Term</th>
<th>MedDRA Preferred Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gas pain</td>
<td>Flatulence</td>
</tr>
<tr>
<td>Gas</td>
<td>Flatulence</td>
</tr>
<tr>
<td>Flatulence</td>
<td>Flatulence</td>
</tr>
<tr>
<td>Abdominal Bloating</td>
<td>Abdominal Distension</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>Abdominal pain</td>
</tr>
<tr>
<td>Abdominal pain due to bloating</td>
<td>Abdominal Distension</td>
</tr>
</tbody>
</table>
Take Home Points

• Overlap may exist between some medDRA preferred terms
• Opt for the term that captures the underlying cause of the adverse event
Case 4

• 45 yo participant on RAI associated tenofovir gel undergoes anoscopic examination. Reports recent history of receptive anal sex.

• Anoscopy reveals presence of punctate areas of breakdown and disruption involving the rectal mucosa
• A verbatim term of “rectal mucosal disruption” is reported

• MedDRA code does not exist for the term “epithelial disruption” and this would most likely generate a query

• DAIDS toxicity table – addendum 3 lists “epithelial disruption” and “endoscopic colorectal mucosal abnormality” but this will likely trigger a query
Anus vs. Rectum
<table>
<thead>
<tr>
<th>Verbatim Term</th>
<th>Meddra Preferred Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal mucosal disruption</td>
<td>Not codable</td>
</tr>
<tr>
<td>Epithelial disruption</td>
<td>Not codable</td>
</tr>
<tr>
<td>Rectal mucosal abrasion</td>
<td>Mucosal excoriation</td>
</tr>
<tr>
<td>Anal mucosal abrasion</td>
<td>Anal injury</td>
</tr>
<tr>
<td>Anal erosion</td>
<td>Anal erosion</td>
</tr>
<tr>
<td>Anal ulcer</td>
<td>Anal ulcer</td>
</tr>
</tbody>
</table>
Take home points

• “Mucosal disruption” or “epithelial disruption” will likely trigger query
• Preference for a more specific terms such as “abrasion”, “excoriation” or “ulcer”
• Specify anatomy/site
MTN-017 Cheat Sheet

• Approximately 136 adverse event verbatim terms obtained from prior gel studies, DAIDS toxicity table – addendum 3, MTN-017, and Anorectal Exam CRF

• Categories mirror rectal DAIDS tox table
  – Anal
  – Colorectal
  – Other GI
  – STI
  – Problem Verbatim terms
# MTN-017 Cheat Sheet

<table>
<thead>
<tr>
<th>Verbatim term</th>
<th>Meddra Preferred Term (PT)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANAL</strong></td>
<td></td>
</tr>
<tr>
<td>Anal abscess</td>
<td>Anal abscess</td>
</tr>
<tr>
<td>Bowen's disease</td>
<td>Bowen's disease</td>
</tr>
<tr>
<td>Anal bruising</td>
<td>Contusion</td>
</tr>
<tr>
<td>Anal discharge</td>
<td>Rectal discharge</td>
</tr>
<tr>
<td>Anal edema</td>
<td>Oedema</td>
</tr>
<tr>
<td>Anal erythema</td>
<td>Erythema</td>
</tr>
<tr>
<td>Anal fissure</td>
<td>Anal fissure</td>
</tr>
<tr>
<td>Anal fistula</td>
<td>Anal fistula</td>
</tr>
<tr>
<td>Anal hemorrhoids</td>
<td>Haemorrhoids</td>
</tr>
<tr>
<td>Anal intraepithelial neoplasia 1 (biopsy)</td>
<td>Anogenital dysplasia</td>
</tr>
<tr>
<td>PROBLEMATIC VERBATIM TERMS</td>
<td>COMMENTS</td>
</tr>
<tr>
<td>----------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Tenesmus</td>
<td>The term is missing anatomic location (for example, this could be bladder or rectal tenesmus).</td>
</tr>
<tr>
<td>Abdominal pain secondary to abdominal bloating</td>
<td>The reported term should be abdominal bloating. The pain should be listed as a sx of the bloating in the comments field.</td>
</tr>
<tr>
<td>Anal carcinoma in situ</td>
<td>3&quot; and &quot;Anal carcinoma in situ&quot; are the same. However &quot;anal carcinoma in situ&quot; will map to &quot;anal cancer stage 0&quot; while &quot;anal intraepithelial neoplasia 3&quot; maps to &quot;anogenital dysplasia&quot;. Preference would be to report as &quot;anal intraepithelial neoplasia 3&quot; if possible.</td>
</tr>
<tr>
<td>Anal HSV</td>
<td>Proctitis herpes</td>
</tr>
<tr>
<td>Anal ulcer HSV</td>
<td>Anal ulcer HSV will map to &quot;Proctitis herpes&quot;. Alternatively &quot;perianal herpes&quot; maps to &quot;genital herpes&quot;.</td>
</tr>
</tbody>
</table>
Future plans

• Spreadsheet will be available soon on www.mtnstopshiv.org website
• Will implement regular updates
• Updates in medDRA coding (new version out next month) may also impact spreadsheet
• Email me at hok2@upmc.edu with questions or suggestions
Acknowledgments

- Ross Cranston
- Javier Lama
- Jeanna Piper
- Karen Patterson
- Yevgeny Grigoriev
- Elaine Dinnie
Questions? Suggestions?