The RxNorm Time Machine

*Issues in using RxNorm for analytics*

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Disclaimer

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Analytics use cases

◆ Example
  ● Evolution of the prescription of opioid drugs over time

◆ Implementation
  ● Claims databases (e.g., Medicare VRDC, Truven)
    ■ NDC ↔ RxCUI [↔ drug class]
  ● Clinical data warehouses
    ■ [Compendia ID ↔] RxCUI [↔ drug class]

◆ Requires to make sense of obsolete codes
  ● Obsolete NDCs mapped to current drugs
  ● Identity criteria for obsolete RxCUIs (ingredient + strength + dose form)
NDCs and RxCUIs turnover rate

◆ NDC
  ● High
  ● Changes in
    ● Manufacturer
    ● Packaging

◆ RxCUI
  ● Low
  ● Changes in normal forms (ingredient / strength / dose form [+ QnF, QlD])
  ● Terminology updates (code changes due to editorial policies)
E-prescribing vs. analytics

◆ E-prescribing
  ● Restrict to currently marketed drugs
  ● Restrict to drugs marketed in a given region

◆ Analytics
  ● All drugs ever marketed
  ● All drugs marketed in all regions

RxNorm

RxNorm APIs

◆ Terminology updates
  (code changes due to editorial policies)
RxNorm dataset (Full monthly)

- Limited support for analytics
- Obsolete RxNorm concepts and relations still present in the RxNorm dataset
  - Concepts marked obsolete
    - SUPPRESS=Y and SUPPRESS=O
  - Non-prescribable entities (unquantified forms)
    - SUPPRESS=E
- Obsolete NDCs are removed from the set of NDCs curated by RxNorm (SAB=RXNORM)
- No cumulative history metadata
  - With start and end data for each RxCUI and NDC
- Retired RxCUI data (File = RXNCUI.RRF)
  - Used as the basis for remapping RxCUIs
RxNav

- Biased towards e-prescribing
  - Until very recently

- Only active RxNorm concepts and NDCs can be retrieved
  - Support for remapped concepts

- Only active concepts can be linked to other concepts
RxNorm API support for analytics

◆ NDC

● `getNDCStatus(NDC, startDate, endDate, latest_only)`
  - Indicate if an NDC is Active, Obsolete, Alien, or Unknown
    - Optionally restricted to a given time interval
  - RxNorm versions when the NDC was active
  - Original RxCUI(s) the NDC was associated with
    - All RxCUIs vs. latest RxCUI

● `getAllHistoricalNDCs(RxCUI, active_only)`
  - Return all NDCs ever associated with a given RxCUI
    - Optionally restricted to active NDCs
  - RxNorm versions when the NDC was active
- **getNDCStatus** (00364666854)

  ```json
  {
  "ndcStatus": {
    "status": "Obsolete",
    "comment": "RxCUI (312656) is still active",
    "ndcHistory": [{
      "activeRxcui": "312656",
      "originalRxcui": "312656",
      "startDate": "200706",
      "endDate": "201101"
    }]
  }
  ```

  312656 Promazine 50 MG/ML Injectable Solution

- **getNDCStatus** (00143314501)

  ```json
  {
  "ndcStatus": {
    "status": "Active",
    "comment": "",
    "ndcHistory": [{
      "activeRxcui": "1116191",
      "originalRxcui": "1116191",
      "startDate": "201108",
      "endDate": "201709"
    },
    {
      "activeRxcui": "1116191",
      "originalRxcui": "198918",
      "startDate": "200706",
      "endDate": "201107"
    }
  ]
  }
  ```

  1116191 ePHEDrine sulfate 25 MG Oral Capsule

  RXCUI = 198918 is obsolete and has been remapped to RXCUI = 1116191
getAllHistoricalNDCs(1668240)

RXCUI = 351772 is obsolete and has been remapped to RXCUI = 1668240

1668240
Zithromax 500 MG Injection
RxNorm API support for analytics

◆ RxCUI

- \textit{getRxculStatus}(RxCUI)
  - Indicate if an RxCUI is Active, Alien, Quantified, Remapped, Retired, or Unknown
  - Last RxNorm versions when active (for Remapped RxCUIs)
  - RxCUI, name and type of the current active RxNorm concept

- \textit{RxculHistory}*(RxCUI)
  - Indicate if an RxCUI is Active, Retired, Never Active, Non-RxNorm, Unknown
  - Return the canonical representation of any RxNorm concept
    - Identity: ingredient, strength, dose form (+ QnF, QlD)
    - Metadata: source, start and end date
- **getRxcuiStatus(198918)**

  RXCUI = 198918 is obsolete and has been remapped to RXCUI = 1116191

- **getRxcuiStatus(1805014)**

  RxCUI = 1805014 has been quantified and is remapped to multiple concepts
New RxNav support for obsolete concepts

- **New Status tab in RxNav**
  - Displays the canonical representation and metadata of all active and inactive RxNorm concepts
  - Powered by the *RxcuiHistory* API
Zithromax 500 MG Injection [RxCUI = 1668240]

Active Concept

Properties

<table>
<thead>
<tr>
<th>Title</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RxCUI</td>
<td>1668240</td>
</tr>
<tr>
<td>Concept Name</td>
<td>Azithromycin 500 MG Injection [Zithromax]</td>
</tr>
<tr>
<td>Pack Alias</td>
<td></td>
</tr>
<tr>
<td>Term Type</td>
<td>SBD</td>
</tr>
<tr>
<td>Dose Form</td>
<td>Injection</td>
</tr>
<tr>
<td>Dose Form RxCUI</td>
<td>1649574</td>
</tr>
<tr>
<td>Multiple Ingredient</td>
<td>No</td>
</tr>
<tr>
<td>Branded</td>
<td>Yes</td>
</tr>
<tr>
<td>Quantity Factor</td>
<td></td>
</tr>
<tr>
<td>Quality Distinction</td>
<td></td>
</tr>
<tr>
<td>SCD</td>
<td>Azithromycin 500 MG Injection</td>
</tr>
</tbody>
</table>

Ingredients

Active Ingredient(AI) & Active Moiety(AM), as well as non-normalized numerator and denominator values, will be available in the future.

<table>
<thead>
<tr>
<th>Base</th>
<th>AI</th>
<th>AM</th>
<th>Boss</th>
<th>Numerator Value</th>
<th>Numerator Units</th>
<th>Denominator Value</th>
<th>Denominator Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin</td>
<td></td>
<td></td>
<td></td>
<td>500</td>
<td>MG</td>
<td></td>
<td></td>
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</table>

Metadata

<table>
<thead>
<tr>
<th>Title</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Status</td>
<td>Active</td>
</tr>
<tr>
<td>Source</td>
<td>RXNORM</td>
</tr>
<tr>
<td>Start Date</td>
<td>11-2015</td>
</tr>
<tr>
<td>End Date</td>
<td></td>
</tr>
<tr>
<td>Is Current</td>
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</table>
Retired Concept

Properties

<table>
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<tr>
<th>Title</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RxCUI</td>
<td>857094</td>
</tr>
<tr>
<td>Concept Name</td>
<td>Acetaminophen 325 MG / Hydrocodone Bitartrate 5 MG Oral Tablet [Procet 5/325]</td>
</tr>
<tr>
<td>Pack Alias</td>
<td></td>
</tr>
<tr>
<td>Term Type</td>
<td>SBD</td>
</tr>
<tr>
<td>Dose Form</td>
<td>Oral Tablet</td>
</tr>
<tr>
<td>Dose Form RxCUI</td>
<td>317541</td>
</tr>
<tr>
<td>Multiple Ingredient</td>
<td>Yes</td>
</tr>
<tr>
<td>Branded</td>
<td>Yes</td>
</tr>
<tr>
<td>Quantity Factor</td>
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<tr>
<td>Quality Distinction</td>
<td></td>
</tr>
<tr>
<td>SCD</td>
<td>Acetaminophen 325 MG / Hydrocodone Bitartrate 5 MG Oral Tablet</td>
</tr>
</tbody>
</table>

Ingredients

Active Ingredient(AI) & Active Moiety(AM), as well as non-normalized numerator and denominator values, will be available in the future.

<table>
<thead>
<tr>
<th>Base</th>
<th>AI</th>
<th>AM</th>
<th>BosS</th>
<th>Numerator Value</th>
<th>Numerator Units</th>
<th>Denominator Value</th>
<th>Denominator Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocodone</td>
<td>Hydrocodone Bitartrate</td>
<td></td>
<td></td>
<td>5</td>
<td>MG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>Acetaminophen</td>
<td></td>
<td></td>
<td>325</td>
<td>MG</td>
<td></td>
<td></td>
</tr>
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</table>

Metadata

<table>
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<tr>
<th>Title</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Status</td>
<td>Retired</td>
</tr>
<tr>
<td>Source</td>
<td>RXNORM</td>
</tr>
<tr>
<td>Start Date</td>
<td>08-2009</td>
</tr>
<tr>
<td>End Date</td>
<td>02-2013</td>
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<tr>
<td>Is Current</td>
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</table>
## Non-RxNorm Concept

### Properties

<table>
<thead>
<tr>
<th>Title</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RxCUI</td>
<td>1023000</td>
</tr>
<tr>
<td>Concept Name</td>
<td>Hyperlipemia</td>
</tr>
<tr>
<td>SCID</td>
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</tr>
</tbody>
</table>

### Metadata

<table>
<thead>
<tr>
<th>Title</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Status</td>
<td>Non-RxNorm</td>
</tr>
<tr>
<td>Source</td>
<td>NDFRT</td>
</tr>
<tr>
<td>Start Date</td>
<td>11-2010</td>
</tr>
<tr>
<td>End Date</td>
<td>09-2017</td>
</tr>
<tr>
<td>Is Current</td>
<td>False</td>
</tr>
</tbody>
</table>
Summary

◆ The update model of the RxNorm dataset is biased towards e-prescribing, and does not fully support analytics

- Obsolete NDCs are removed from the set of NDCs curated by RxNorm
- Obsolete RxCUIs and relations persist
  - No metadata for obsolete RxCUIs
Support for analytics ("Time Machine") built through the RxNorm API

- NDC
  - NDC → RxCUI(s) + metadata
    - For each NDC ever curated by RxNorm
  - RxCUI → all NDCs ever associated with this RxCUI
    - Including through remapping of RxCUIs

- RxCUI
  - RxCUI → status (including remapping)
  - RxCUI → definitional properties and metadata (for all active and obsolete RxNorm concepts)

Displayed in RxNav (new Status tab)

Canonical representation of RxNorm drugs
  - Can also support a similarity function for drugs
Acknowledgments

◆ RxNav team (development)
  ● Lee Peters
  ● Richard Rice

◆ External collaborators (use cases)
  ● getRxcuiStatus
    ▪ Indian Health Service
    ▪ Value Set Authority Center
  ● getNDCStatus
    ▪ Boston Children’s Hospital/Harvard Medical School (Dr. Ken Mandl)
  ● getAllHistoricalNDCs, RxcuiHistory
    ▪ Greater Plains Collaborative PCORnet (Dr. Jim Campbell)
Medical Ontology Research

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