RxNorm

Why Should Pharmacists Care?

Olivier Bodenreider
National Library of Medicine, NIH, DHHS
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Learning objectives

1- Explain the key elements, benefits, and limitations of RxNorm
2- Practice accessing RxNorm (RxNorm dataset, RxNav, APIs)
3- Identify companion resources linked to RxNorm
4- Identify issues with analyzing drugs in observational datasets
Question 1: Which type of information is in scope for RxNorm?
Question 2: Which use cases are covered by RxNorm?
Self-Assessment Question 1

Which type of information is in scope for RxNorm?

- A. Drug names
- B. Drug codes
- C. Pricing information
- D. Drug-drug interactions
- E. Indications
Self-Assessment Question 2

Which use cases are covered by RxNorm?

- A. E-prescribing
- B. Information exchange
- C. Formulary development
- D. Reference value sets
- E. Analytics
National Library of Medicine (NLM)

- World’s largest biomedical library
- Maintains and makes available a vast print collection
- **Produces electronic information resources** on a wide range of topics that are searched billions of times each year by millions of people around the globe
- Supports and conducts research, development, and training in biomedical informatics and health information technology

https://www.nlm.nih.gov/about/
NLM strategic plan (2006-2016)*

- **Goal 1.** Seamless, Uninterrupted Access to Expanding Collections of Biomedical Data, Medical Knowledge, and Health Information
- **Goal 2.** Trusted Information Services that Promote Health Literacy and the Reduction of Health Disparities Worldwide
- **Goal 3.** Integrated Biomedical, Clinical, and Public Health Information Systems that Promote Scientific Discovery and Speed the Translation of Research into Practice
- **Goal 4.** A Strong and Diverse Workforce for Biomedical Informatics Research, Systems Development, and Innovative Service Delivery

Overview

- RxNorm basics
- Applications for using RxNorm
  - RxNav, RxClass, RxMix
- Follow-along examples
- Analyzing observational data with RxNorm
RxNorm basics
Interoperability among drug vocabularies

- Exchange of information requires standardized names
  - Ordering drugs
  - Checking interactions
  - Inventory management
- No standard naming conventions for drugs
- Integrating drug vocabularies
- Unique identifiers for drugs
- Specify relations among drug entities
Source vocabularies in RxNorm

(terms in thousands, as of March 2017)
## Normalization Lexical level

<table>
<thead>
<tr>
<th>Name</th>
<th>Code</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>WARFARIN (COUMADIN) NA 1MG TAB</td>
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<td>VANDF</td>
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<td>warfarin 1 mg oral tablet</td>
<td>3617</td>
<td>MMSL</td>
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<tr>
<td>WARFARIN NA 1MG TAB,UD</td>
<td>4014039</td>
<td>VANDF</td>
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<td>NDDF</td>
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<td>MTHSPL</td>
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<tr>
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<td>MTHSPL</td>
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<td>GS</td>
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<td>Warfarin sodium 1mg tablet (product)</td>
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<td>SNOMEDCT_US</td>
</tr>
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<td>Warfarin Sodium Tab 1 MG</td>
<td>6749</td>
<td>MDDB</td>
</tr>
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<td>Warfarin Sodium, 1 mg oral tablet</td>
<td>3617</td>
<td>MMSL</td>
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<tr>
<td>WARFARIN SODIUM@1 mg@ORAL@TABLET</td>
<td>14198</td>
<td>NDDF</td>
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**Warfarin Sodium 1 MG Oral Tablet (855288)**
Normalized form

<table>
<thead>
<tr>
<th>Strength</th>
<th>Ingredient</th>
<th>Dose form</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 MG</td>
<td>Warfarin Sodium</td>
<td>Oral Tablet</td>
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</tbody>
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Clinical drug component

<table>
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<tr>
<th>Strength</th>
<th>Ingredient</th>
<th>Dose form</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Warfarin Sodium</td>
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Clinical drug form

<table>
<thead>
<tr>
<th>Strength</th>
<th>Ingredient</th>
<th>Dose form</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Warfarin Oral Tablet</td>
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<table>
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<th>Ingredient</th>
<th>Dose form</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Warfarin Sodium</td>
<td></td>
</tr>
</tbody>
</table>
Relations among drug entities

Ingredient
Azithromycin

C. Drug Comp.
Azithromycin 250 MG
Azithromycin Oral Tablet

C. Drug Form
Azithromycin Oral Tablet

C. Drug
Azithromycin 250 MG Oral Tablet

G. Pack
{6 (Azithromycin 250 MG Oral Tablet) } Pack

B. Drug Comp.
A. 250 MG [Zithromax]

B. Drug Form
A. Oral Tablet [Zithromax]

B. Drug
Zithromax 250 MG Oral Tablet

B. Pack
Z-PAK

Brand Name
Zithromax
What RxNorm does NOT contain

- Non-prescription drugs (limited coverage of OTC drugs)
- Non-drug entities (e.g., supplies)
- Drug classes / drug-class membership
- Indications, adverse events
- Drug-drug interactions
- Pricing information
- Dosing information

Available through services (APIs)
RxNorm – Why Should Pharmacists Care?  
Part 2

RxNorm in action
Example  Mapping NDCs to ATC drug classes

- NDCs are attached to a clinical drug (SCD) or a branded (drug)
- Branded drugs are mapped to clinical drugs
- Clinical drugs are linked to their ingredient
- Many drug classification systems link classes to ingredient-level drugs (e.g., ATC, NDF-RT, EPC, MeSH pharmacologic action)
A02 BC Proton pump inhibitors

<table>
<thead>
<tr>
<th>ATC code</th>
<th>Name</th>
<th>DDD</th>
<th>U</th>
<th>Adm. R</th>
<th>Note</th>
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</thead>
<tbody>
<tr>
<td>A02BC05</td>
<td>Esomeprazole</td>
<td>30</td>
<td>mg</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>mg</td>
<td>P</td>
<td></td>
</tr>
</tbody>
</table>


A new RxNav web application has replaced the Java version. Please help us to improve your site experience by providing us feedback at this link.

RxClass

The RxClass Browser is a web application for exploring and navigating through the class hierarchies to find the RxNorm drug members associated with each class.

https://rxnav.nlm.nih.gov/
RxNav

- Drug-centric browser
  - RxNorm
    - Prescribable subset
  - RxTerms
  - NDF-RT
  - Pill images
  - Drug-drug interactions
- Supports navigation to the rich RxNorm and NDF-RT graphs
- Links to other drug resources
  - DailyMed, MedlinePlus, NLM Drug Information Portal
- Drug-centric “class view”
- Leverages the drug APIs
RxClass

- Class-centric browser for RxNorm drugs
  - ATC
  - DailyMed (Mechanism of action, Physiologic effect, Chemical structure, FDA classes)
  - MeSH (Pharmacologic actions)
  - NDF-RT (VA classes, Diseases for indications/contra-indications)

- Supports search by drug or by class

- Features
  - Display and navigation
    - All the drugs for a class
    - All the classes for a drug
  - Compute similarity among drug classes (based on shared drug members)
Application programming interfaces (APIs)

- Expose the content of RxNorm, RxTerms and NDF-RT (and other resources)
  - Logical structure, not storage format
  - Up-to-date information (monthly updates of RxNorm)
  - Additional features
    - Normalized and approximate matching; spelling correction
    - Drug-drug interactions checking (from DrugBank)
    - Link to drug classes (from ATC, DailyMed, MeSH, NDF-RT)
    - Archive of NDCs since 2007
    - Optimized graph traversal (pre-computed)
- For use in applications
  - Web services
  - SOAP, REST (XML, JSON)
  - Independent of any programming language
RxMix

- Graphical interface to the drug APIs
  - RxNorm, NDF-RT, RxTerms, RxImageAccess, Interactions, RxClass, MedEx, DailyMed
- Handles interoperability between functions
- Helps users compose complex queries
  - *Find all the NDC codes for a given allergy class (e.g., barbiturates)*
- Supports batch execution
RxNorm use cases

- E-prescribing
  - *NCPDP SCRIPT standard for e-prescribing requires RxNorm*

- Information exchange
  - *DoD and VA rely on RxNorm to mediate drug information across their electronic medical record systems*

- Formulary development
  - *CMS uses RxNorm in their Formulary Reference File, as part of the guideline for Medicare drug benefits*

- Reference value sets
  - *The drug value sets used in clinical quality measures for Meaningful Use are defined in reference to RxNorm*

- Analytics
  - *OHDSI, the Observational Health Data Sciences and Informatics research group, uses RxNorm to analyze prescription data*
Follow-along examples
Follow-along examples

- Using *RxNav*
  - Find the ATC class for NDC 0186-5040-31 (Nexium 40 mg delayed-released capsule)
    - NDC → RxNorm branded drug → RxNorm ingredient → ATC ingredient → ATC class

- Using *RxClass*
  - Find all RxNorm ingredients from the same class as *esomeprazole*
    - Search classes by ingredient (or just click on a class in RxNav)
  - Find other classes with similar ingredients
    - Similar classes feature

- Using *RxMix* (Complete workflow)
Web applications

- Documentation
- RxNav
- RxClass
  - https://mor.nlm.nih.gov/RxClass/
- RxMix
A. ALIMENTARY TRACT AND METABOLISM
A02. DRUGS FOR ACID RELATED DISORDERS
A02B. DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)
A02BC. Proton pump inhibitors

<table>
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<tr>
<th>ATC code</th>
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<th>U</th>
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<td></td>
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</table>

Esomeprazole (283742) → Esomeprazole (A02BC05)


00186504031

0186-5040-31

Nexium (esomeprazole magnesium)
30 Delayed-Release Capsules
Rx only

Each delayed-release capsule contains 40 mg esomeprazole.

AstraZeneca
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<tr>
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<td>esomeprazole</td>
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<tr>
<td></td>
<td>Esomeprazole</td>
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<table>
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<th>Precise Ingredient</th>
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<tr>
<td>H1</td>
<td>Esomeprazole magnesium</td>
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<td>H2</td>
<td>Esomeprazole magnesium dihydrate</td>
</tr>
<tr>
<td>H3</td>
<td>Esomeprazole sodium</td>
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<tr>
<td>H4</td>
<td>Esomeprazole Strontium</td>
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<table>
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<tr>
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<tr>
<td>H1</td>
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<td>H2</td>
<td>Vimovo</td>
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<td>H2</td>
<td>Esomeprazole 2.5 MG</td>
</tr>
<tr>
<td>H3</td>
<td>Esomeprazole 20 MG</td>
</tr>
<tr>
<td>H4</td>
<td>Esomeprazole 40 MG</td>
</tr>
<tr>
<td>H5</td>
<td>Esomeprazole 5 MG</td>
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<tr>
<td>H6</td>
<td>Esomeprazole Strontium 24.85 MG</td>
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<td>Esomeprazole 10 MG Granules for Oral Suspension</td>
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<tr>
<td>H2</td>
<td>Esomeprazole 2.5 MG Granules for Oral Suspension</td>
</tr>
<tr>
<td>H3</td>
<td>Esomeprazole 20 MG / Naproxen 375 MG Delayed Release Oral Tablet</td>
</tr>
<tr>
<td>H4</td>
<td>Esomeprazole 20 MG / Naproxen 500 MG Delayed Release Oral Tablet</td>
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<tr>
<td>H5</td>
<td>Esomeprazole 20 MG Delayed Release Oral Capsule</td>
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<tr>
<td>H6</td>
<td>Esomeprazole 40 MG / (NexIUM)</td>
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<table>
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<tr>
<th>SCDGPCK</th>
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<tr>
<td>H1</td>
<td>Esomeprazole Injectable Product</td>
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<td>Esomeprazole Injectable Product</td>
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<td>H3</td>
<td>Esomeprazole Injectable Product</td>
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<tr>
<td>H4</td>
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<td>Esomeprazole Injectable Product</td>
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<td>H6</td>
<td>Esomeprazole Injectable Product</td>
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<table>
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<td>H2</td>
<td>Injectable Product</td>
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<td>H3</td>
<td>Oral Product</td>
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<td>H4</td>
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<td>H6</td>
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<table>
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<th>Branded Dose Form Group</th>
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<td>H2</td>
<td>NexIUM Injectable Product</td>
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<tr>
<td>H3</td>
<td>NexIUM Oral Product</td>
</tr>
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<td>H5</td>
<td>Vimovo Oral Product</td>
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<tr>
<td>H6</td>
<td>Vimovo Oral Product</td>
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Esomeprazole (A02BC05)

Esomeprazole (283742) → Esomeprazole (A02BC05)


00186504031

0186-5040-31
<table>
<thead>
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<th>Property</th>
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<tbody>
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<td>ATC</td>
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</table>
Esomeprazole (A02BC05)

Esomeprazole 40 MG Delayed Release Oral Capsule [Nexium] (606731)

Esomeprazole 40 MG Delayed Release Oral Capsule (606730)

Esomeprazole (283742)
### Finding all PPI drugs in ATC

dexrabeprazole not on the U.S. market

<table>
<thead>
<tr>
<th>ATC code</th>
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<th>Adm.R</th>
<th>Note</th>
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<td>40</td>
<td>mg O</td>
<td></td>
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<td>pantoprazole</td>
<td>40</td>
<td>mg O</td>
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<td>A02BC03</td>
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<td>mg P</td>
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<td>mg O</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>A02BC54</td>
<td>rabeprazole, combinations</td>
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</table>

[Link to ATC/DDD Index](https://www.whocc.no/atc_ddd_index/)
# RxClass

Exploring drug classes and their RxNorm drug members

## Class Browser

- **Anatomical Therapeutic Chemical (ATC1-4)**
  - **ALIMENTARY TRACT AND METABOLISM**
    - **ANABOLIC AGENTS FOR SYSTEMIC USE** (9)
    - **ANTIDIARRHEALS, INTESTINAL ANTI-INFLAMMATORY/ANTINFECTIVE AGENTS** (12)
    - **ANTIEMETICS AND ANTIULCERANTS** (13)
    - **ANTIOBESITY PREPARATIONS, EXCL. DIET PRODUCTS** (12)
    - **APPETITE STIMULANTS** (6)
    - **BILE AND LIVER THERAPY** (13)
    - **DIGESTIVES, INCL. ENZYMES** (7)
    - **DRUGS FOR ACID RELATED DISORDERS** (35)
      - **HISTAMINE 2-RECEPTOR ANTAGONISTS (H2-RA)** (12)
      - **PROTON PUMP INHIBITORS** (6)
      - **OTHER DRUGS FOR ACID RELATED DISORDERS** (9)
    - **DRUGS FOR CONSTIPATION** (35)
    - **DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS** (44)
    - **DRUGS USED IN DIABETES** (61)
    - **MINERAL SUPPLEMENTS** (39)
    - **OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS** (32)

## Search

- By class name
- By RxNorm drug name
- Ingredient drug only

## Proton pump inhibitors

**class:** Proton pump inhibitors / id: A02BC / class type: ATC1-4 / show context

### 6 RxNorm generic drugs in ATC / similar classes

<table>
<thead>
<tr>
<th>Type</th>
<th>RXCUI</th>
<th>RxNorm Name</th>
<th>Relation</th>
<th>All classes</th>
</tr>
</thead>
<tbody>
<tr>
<td>IN</td>
<td>816346</td>
<td>dexlansoprazole</td>
<td>DIRECT</td>
<td>Show</td>
</tr>
<tr>
<td>IN</td>
<td>283742</td>
<td>Esomeprazole</td>
<td>DIRECT</td>
<td>Show</td>
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<td>IN</td>
<td>17128</td>
<td>lansoprazole</td>
<td>DIRECT</td>
<td>Show</td>
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<td>IN</td>
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<td>Show</td>
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<td>A02BC07</td>
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<td>A02BC53</td>
<td>lansoprazole, combinations</td>
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</tr>
<tr>
<td>A02BC54</td>
<td>rabeprazole, combinations</td>
<td></td>
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</tbody>
</table>

Classes in other drug classification systems
# RxClass

Exploring drug classes and their RxNorm drug members

## Class Browser

- **Class:** Proton pump inhibitors / id: A02BC / class type: ATC1-4 / show context

## 6 RxNorm generic drugs in ATC1-4

<table>
<thead>
<tr>
<th>Type</th>
<th>RXCUI</th>
<th>RxNorm Name</th>
<th>Relation</th>
<th>All classes</th>
</tr>
</thead>
<tbody>
<tr>
<td>IN</td>
<td>816346</td>
<td>Dexlansoprazole</td>
<td>DIRECT</td>
<td></td>
</tr>
<tr>
<td>IN</td>
<td>283742</td>
<td>Esomeprazole</td>
<td>DIRECT</td>
<td></td>
</tr>
<tr>
<td>IN</td>
<td>17128</td>
<td>Lansoprazole</td>
<td>DIRECT</td>
<td></td>
</tr>
<tr>
<td>IN</td>
<td>7646</td>
<td>Omeprazole</td>
<td>DIRECT</td>
<td></td>
</tr>
<tr>
<td>IN</td>
<td>40790</td>
<td>Pantoprazole</td>
<td>DIRECT</td>
<td></td>
</tr>
<tr>
<td>IN</td>
<td>114579</td>
<td>Rabeprozole</td>
<td>DIRECT</td>
<td></td>
</tr>
<tr>
<td>Class</td>
<td>Similarity Score</td>
<td>Venn</td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------------------------------------</td>
<td>------------------</td>
<td>------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proton Pump Inhibitors in DailyMed (has_EPC)</td>
<td>0.93</td>
<td>Venn</td>
<td></td>
<td></td>
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<tr>
<td>Proton Pump Inhibitors in MeSH</td>
<td>0.93</td>
<td>Venn</td>
<td></td>
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<tr>
<td>Proton Pump Inhibitors in DailyMed (has_MoA)</td>
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<td>Venn</td>
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<tr>
<td>Proton Pump Interactions in DailyMed (has_MoA)</td>
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<td>Venn</td>
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<td>Cation Transporter Interactions in DailyMed (has_MoA)</td>
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<tr>
<td>DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL</td>
<td>0.40</td>
<td>Venn</td>
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<tr>
<td>REFLUX DISEASE (GORD) in ATC</td>
<td>0.40</td>
<td>Venn</td>
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<tr>
<td>Paraneoplastic Endocrine Syndromes in NDFRT (may_treat)</td>
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<tr>
<td>RxNorm Name</td>
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<tr>
<td>------------</td>
<td>--------</td>
<td>-------------</td>
<td></td>
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</tr>
<tr>
<td>dexlansoprazole</td>
<td>816346</td>
<td>Both</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esomeprazole</td>
<td>283742</td>
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<tr>
<td>lansoprazole</td>
<td>17128</td>
<td>Both</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omeprazole</td>
<td>7646</td>
<td>Both</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pantoprazole</td>
<td>40790</td>
<td>Both</td>
<td></td>
<td></td>
</tr>
<tr>
<td>rabeprazole</td>
<td>114979</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Amantadine</td>
<td>620</td>
<td>Class2 only</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rimantadine</td>
<td>9386</td>
<td>Class2 only</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Class1: Proton pump inhibitors (A02BC) in ATC
Class2: Proton Pump Inhibitors (N0000000147) in DailyMed (has_MoA)
# Class1 Only: 0
# Class2 Only: 2
# Both: 0
Equivalence Score: 0.70
Inclusion Score: -1.0
# Class Browser

- Anatomical Therapeutic Chemical (ATC1-4)
- Established Pharmacologic Classes (EPC) [from DailyMed]
- MeSH Pharmacologic Actions (MESHPA)
- Disease
- Chemical Structure (Chem) [from DailyMed]
- Mechanism of Action (MoA) [from DailyMed]
- Antibody Interactions (37)
- Enzyme Interactions (297)
- Immunologic and Biological Factor Interactions (40)
- Membrane Transporter Interactions (90)
  - ATP-Binding Cassette (ABC) Transporter Interactions (40)
  - Fatty Acid Transporter Interactions (1)
  - Ion Channel Interactions (24)
  - Ion Transporter Interactions (39)
    - Anion Transporter Interactions (9)
    - Anionporter Interactions (1)
    - Cation Transporter Interactions (14)
      - Organic Cation Transporter Interactions (6)
  - Proton Pump Interactions (8)
    - Proton Pump Inhibitors (8)
      - M2 Protein Inhibitors (2)
  - Symporter Interactions (14)
  - Monosaccharide Transporter Interactions (3)
  - Neurotransmitter Transporter Interactions (14)
  - Physicochemical Activity (121)
  - Receptor Interactions (383)
    - Unknown Cellular or Molecular Interaction (0)
  - Physiologic Effect (PE) [from DailyMed]
  - Pharmacokinetics (PK)
  - VA Classes (VA)

## Proton pump inhibitors

- class: Proton Pump Inhibitors / id: N0000000147 / class type: MOA / show context

### 8 RxNorm generic drugs for has MoA in DailyMed / similar classes

<table>
<thead>
<tr>
<th>Type</th>
<th>RXCUI</th>
<th>RxNorm Name</th>
<th>Relation</th>
<th>All classes</th>
</tr>
</thead>
<tbody>
<tr>
<td>IN</td>
<td>620</td>
<td>Amantadine</td>
<td>INDIRECT</td>
<td></td>
</tr>
<tr>
<td>IN</td>
<td>816346</td>
<td>doxepinprazole</td>
<td>DIRECT</td>
<td></td>
</tr>
<tr>
<td>IN</td>
<td>283742</td>
<td>Esomeprazole</td>
<td>DIRECT</td>
<td></td>
</tr>
<tr>
<td>IN</td>
<td>17128</td>
<td>lansoprazole</td>
<td>DIRECT</td>
<td></td>
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<tr>
<td>IN</td>
<td>7646</td>
<td>Omeprazole</td>
<td>DIRECT</td>
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<tr>
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<td>40790</td>
<td>pantoprazole</td>
<td>DIRECT</td>
<td></td>
</tr>
<tr>
<td>IN</td>
<td>114979</td>
<td>rabeprazole</td>
<td>DIRECT</td>
<td></td>
</tr>
<tr>
<td>IN</td>
<td>9386</td>
<td>Rimantadine</td>
<td>INDIRECT</td>
<td></td>
</tr>
</tbody>
</table>
Automating the mapping from NDC to ATC using RxMix
**Introduction**

RxMix is an interface for building applications that allows users to combine functions of the RxNorm, RxTerms, NDF-RT, RxClass, Interactions and RxImageAccess APIs. It allows users to run either interactively or in batch mode.

**Sample RxMix configurations**

- Find drug interaction brands for Morphine (RXCUI = 7052)
- Find allergy drugs for Proton Pump Inhibitors (NUI =N0000000147)

**APIs**

- RxNorm
- NDF-RT
- RxTerms
- RxImageAccess
- Interaction
- RxClass
- DailyMed
- MedEx

**References**

<table>
<thead>
<tr>
<th>TAG</th>
<th>DEFINITION</th>
</tr>
</thead>
<tbody>
<tr>
<td>mcInput</td>
<td>The physical sample acquisition date</td>
</tr>
<tr>
<td>rtInput</td>
<td>Only return an RXCUI if it contains an RXNORM vocabulary term.</td>
</tr>
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</table>
Esomeprazole (A02BC05)

<table>
<thead>
<tr>
<th>ATC code</th>
<th>Name</th>
<th>DDD</th>
<th>U</th>
<th>Adm.R</th>
<th>Note</th>
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</thead>
<tbody>
<tr>
<td>A02BC05</td>
<td>esomeprazole</td>
<td>30 mg</td>
<td>O</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>30 mg</td>
<td>P</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Esomeprazole (283742)

Esomeprazole 40 MG Delayed Release Oral Capsule (606730)

Esomeprazole 40 MG Delayed Release Oral Capsule [Nexium] (606731)

rxnorm:findRxcuiById ("NDC", "0186-5040-31", 0) ⇒ 606731
RxMix

Create applications from RxNorm, RxTerms, NDF-RT, and RxImageAccess APIs

WORKFLOW

No Workflow Defined

Select Function

findRxculByld

Optional Parameters

id_string: NDC

Add to Workflow

ADD

Add the selected function to workflow (Add)

LOAD

From workflow library

From my workflows

INPUT

NDC:

Basic Instructions

1. BUILD workflow using Select Function, then Add to Workflow (or select a button in LOAD section to load a workflow)
2. Enter INPUT value for interactive mode (or input file name for batch mode)

Introduction

RxMix is an interface for building applications that allows users to combine functions of the RxNorm, RxTerms, NDF-RT, RxClass, Interactions and RxImageAccess APIs. It allows users to run either interactively or in batch mode.

Sample RxMix configurations

- Find drug interaction brands for Morphine (RXCUI = 7052)
- Find allergy drugs for Proton Pump Inhibitors (NUI = N0000000147)

APIs

- NDF-RT
- RxTerms
- RxClass
- Interaction
- RxImageAccess
- MedEx

References

<table>
<thead>
<tr>
<th>TAG</th>
<th>DEFINITION</th>
</tr>
</thead>
<tbody>
<tr>
<td>acqDate</td>
<td>The physical sample acquisition date</td>
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</tbody>
</table>
**RxMix**

Create applications from RxNorm, RxTerms, NDF-RT, and RxImageAccess APIs

**WORKFLOW**

RxNorm, findRxNormByNDC

**Build**

Select Function

No function selected

**Load**

From workflow library

Remove Last, Save

From my workflows

**Input**

**Basic Instructions**

1. BUILD workflow using Select Function, then Add to Workflow (or select a button in LOAD section to load a workflow)

2. Enter INPUT value for interactive mode (or input file name for batch mode)

**Execute**

Clear, Run Interactive

**Output**

RXCUI

606731

...
### IN

<table>
<thead>
<tr>
<th>UMLSCUI</th>
<th>term_type</th>
<th>name</th>
<th>RXCUI</th>
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<tr>
<td>C0957846</td>
<td>IN</td>
<td>Esomeprazole</td>
<td>283742</td>
</tr>
</tbody>
</table>
Esomeprazole (283742)

Esomeprazole 40 MG Delayed Release Oral Capsule (606731)

Esomeprazole 40 MG Delayed Release Oral Capsule [Nexium] (606731)

rxclass:getClassByRxNormDrugId ("283742", "ATC", "ALL") → A02BC, Proton pump inhibitors
<table>
<thead>
<tr>
<th>UMLACUI</th>
<th>term_type</th>
<th>name</th>
<th>RXCUI</th>
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</thead>
<tbody>
<tr>
<td>C0937846</td>
<td>IN</td>
<td>Exonoprazole</td>
<td>283742</td>
</tr>
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</table>
A02BC, DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD);
A02, DRUGS FOR ACID RELATED DISORDERS;
A, ALIMENTARY TRACT AND METABOLISM
RxMix
Create applications from RxNorm, RxTerms, NDF-RT, and RxImageAccess APIs

WORKFLOW
RxNorm:findRxnormByIId
RxNorm:findRxnormByIId
RxClass:getClassByRxnormDrugId
Rxnorm:getRelatedByName
RxClass:getClassByRxnormDrugId

Select Function
getClassGraph

Add to Workflow

LOAD
From workflow library
Remove Last
Save

LOAD
From my workflows

OUTPUT

relaSource term_type drugName RXCUI rela clasId name classType
ATC IN Esomeprazole 283742 - A02BC Proton pump inhibitors ATC1-4
ATC MIN Esomeprazole / Naproxen 994302 - MI1AE Proton pump inhibitors ATC1-4

Basic Instructions
1. BUILD workflow using Select Function, then Add to Workflow
2. Enter INPUT value for interactive mode (or select a button in LOAD section to load a workflow)

EXECUTE
Clear
Run Interactive
Analyzing observational data with RxNorm
Source of observational data (drugs)

- Surescripts transactions
- Data from payers
  - Medicaid
  - Medicare Part D
- Commercial health analytics companies
  - Truven (120M patients)
  - PharMetrics Plus (100M patients)
  - Ambulatory EMR (35M patients)
  - Open Claims (250M patients)
- Networks of clinical data warehouses
  - PCORnet, OHDSI, Health Facts, ...
- Reagan-Udall Foundation for the FDA
  - IMEDS Research Lab (temporarily suspended)
Common use cases

- Pharmaco-epidemiology
  - Assess exposure to drugs (by ingredient or class)
  - Assess prescribed daily dose
  - Identify potentially inappropriate medications
    - Elderly (Beers)
    - Pregnant women (Briggs)

- Outcomes research
  - Comparative effectiveness
  - Pharmacovigilance and drug safety

- “Learning Health System”
**Prescribed vs. defined daily dose**

- **Dataset**
  - Surescripts feed
  - All prescriptions to ER patients
  - For 3 months in 2011 in a Bethesda hospital
- **Reference for defined daily dose: ATC**
- **Methods**
  - RxNorm clinical drug → RxNorm ingredient ↔ ATC ingredient → ATC defined daily dose ↔ prescribed daily dose
  - Restricted to systemic drugs (based on dose form)
- **Findings**
  - Confirmed feasibility
  - 25% of the prescriptions exactly match the ATC DDD
  - 50% of the prescriptions within 66-150% of the ATC DDD
  - 75% of the prescriptions within 50-200% of the ATC DDD

[Bodenreider, AMIA, 2014]
**Methods Example**

- **RxNorm**
  - Amoxicillin 500 MG Oral Capsule (308191)
  - Amoxicillin (723)
  - Oral Capsule

- **ATC/DDD Index**
  - amoxicillin (J01CA04)
  - 0
  - 1 g

- **Surescripts**
  - Amoxicillin 500 MG Oral Capsule (308191)
  - 40 capsules
  - 10 days
  - 40 x 500 mg / 10 = 2 g

**J ANTIINFECTIVES FOR SYSTEMIC USE**

**J01 ANTI-INFECTIVES FOR SYSTEMIC USE**

**J01C BETA-LACTAM ANTI-INFECTIVES, PENICILLINS**

**J01CA Penicillins with extended spectrum**
Results

Prescription classification

Frequency of drugs by level-1 ATC group in the Surescripts prescription dataset  N=86,578

- ALIMENTARY TRACT AND METABOLISM (A)
- BLOOD AND BLOOD FORMING ORGANS (B)
- CARDIOVASCULAR SYSTEM (C)
- DERMATOLOGICALS (D)
- GENITO URINARY SYSTEM AND SEX HORMONES (G)
- SYSTEMIC HORMONAL PREP., EXCL. SEX HORMONES AND INSULINS (H)
- ANTINFECTIVES FOR SYSTEMIC USE (J)
- ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS (L)
- MUSCULO-SKELETAL SYSTEM (M)
- NERVOUS SYSTEM (N)
- ANTIPARASITIC PRODUCTS, INSECTICIDES AND REPELLENTS (P)
- RESPIRATORY SYSTEM (R)
- SENSORY ORGANS (S)
- VARIOUS (V)

Top drugs:
- Atorvastatin
- Simvastatin
- Lisinopril
- Metoprolol
- Amlodipine
- Furosemide
- Atenolol
- Hydrochlorothiazide
- Zolpidem
- Sertraline
- Escitalopram
- Alprazolam
- Clonazepam
- Gabapentin
- Quetiapine
- Oxycodone
- Fluoxetine
- Duloxetine
86.1% of the prescriptions are within 33%-300% of the ATC DDD

76.1% of the prescriptions are within 50%-200% of the ATC DDD

49.5% of the prescriptions are within 66%-150% of the ATC DDD

28.6% of the prescriptions exactly match the ATC DDD

10.4% < 33% of the ATC DDD

3.5% > 300% of the ATC DDD
Issues

- No normalization of drugs in claims data
- NDCs contain clinically irrelevant details and need to be aggregated
- Many NDCs are obsolete and need to be mapped to current drugs for analysis
- Many drug classification systems link ingredients to classes, leading to ambiguous associations
Key Takeaways

- **Use standards!**
  - Because it is a standard drug terminology (in the U.S.), RxNorm can help integrate, exchange and analyze prescription data

- **Try it ay home!**
  - RxNav and RxClass are useful tools for exploring RxNorm drugs and classes from several drug classification systems
  - RxMix helps automate mapping across drug entities for non-programmers

- **Participate in research activities!**
  - Pharmacists are increasingly involved in research, especially with observational data from claims and electronic health records
Self-Assessment Question 1

Which type of information is in scope for RxNorm?

- ✔ A. Drug names
- ✔ B. Drug codes
- ✗ C. Pricing information
- ✗ D. Drug-drug interactions
- ✗ E. Indications
Self-Assessment Question 2

Which use cases are covered by RxNorm?

- ☑ A. E-prescribing
- ☑ B. Information exchange
- ☑ C. Formulary development
- ☑ D. Reference value sets
- ☑ E. Analytics
Medical Ontology Research

Contact: olivier@nlm.nih.gov
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U.S. National Library of Medicine