RxNav
*Interfaces to drug information sources*

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Acknowledgments

- Stuart Nelson
- Kelly Zeng
- Lee Peters
- Ramez Ghazzaoui
Outline

◆ **RxNorm**
  - Drug vocabulary integration
  - Drug vocabulary standardization

◆ **Visualizing drug information: RxNav**

◆ **Processing drug information: RxNorm API**

◆ **Integrating drug information sources**

◆ **Applications**
RxNorm

Overview
Motivation

◆ 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
Drug vocabulary integration

RxNorm
UMLS-like approach

- 9 source vocabularies
- Synonymous names grouped into an RxNorm concept
- Unique identifiers (RxCUI)
- RRF format

Differences
- RxNorm creates its own names
- Principled use of names relationships
- Limited scope: drug names
<table>
<thead>
<tr>
<th>Source Vocabularies in RxNorm</th>
<th>Count (in thousands, as of July 2008)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gold Standard Alchemy</td>
<td>15</td>
</tr>
<tr>
<td>Master Drug Data Base</td>
<td>60</td>
</tr>
<tr>
<td>(Medi-Span, Wolters Kluwer Health)</td>
<td>12</td>
</tr>
<tr>
<td>Multum MediSource Lexicon</td>
<td>67</td>
</tr>
<tr>
<td>Micromedex DRUGDEX</td>
<td>11</td>
</tr>
<tr>
<td>FDA National Drug Code Directory</td>
<td>79</td>
</tr>
<tr>
<td>FDA Structured Product Labels</td>
<td></td>
</tr>
<tr>
<td>Nat’l Drug Data File (First DataBank Inc.)</td>
<td>91*</td>
</tr>
<tr>
<td>SNOMED Clinical Terms (drug information)</td>
<td></td>
</tr>
<tr>
<td>Veterans Health Administration Nat’l Drug File</td>
<td>42</td>
</tr>
</tbody>
</table>
RxNorm concept

Ingredient

Acetaminophen

Acetaminophen
Paracetamol
APAP
Paracetamol product
Acetaminophen (product)
Acetaminophen (substance)
Acetaminophen product

SNOMED CT
MeSH
Multum
NDDF
...

161

MMSL:5005
SNOMEDCT:387517004
SNOMEDCT:90332006
NDDF:001605
MTHSPL:36209119
MMSL:4119
MMSL:d00049
VANDF:4017513
MMSL:4992
MMSL:52845
MTHFDA:50612
UMLS: C0000970
Drug vocabulary standardization

RxNorm
Normalization

◆ Lexical level
  • Conventions for representing strength, units, etc.

◆ Structural level
  • Generic vs. Brand names
  • Atomic elements: Ingredient, Strength, Dose form
  • Combinations
  • Principle set of relationships among the different types
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>GS</td>
<td>Digoxin 0.25mg/1mL Solution for injection</td>
</tr>
<tr>
<td>GS</td>
<td>Digoxin 500mcg/2mL Solution for injection</td>
</tr>
<tr>
<td>MDDB</td>
<td>'Digoxin Inj 0.25 MG/ML</td>
</tr>
<tr>
<td>MMSL</td>
<td>digoxin 250 mcg/mL (0.25 mg/mL) injectable solution</td>
</tr>
<tr>
<td>MMSL</td>
<td>Digoxin, 250 mcg/mL (0.25 mg/mL) injectable solution</td>
</tr>
<tr>
<td>MMX</td>
<td>Digoxin 0.25 MG/ML Injection Solution</td>
</tr>
<tr>
<td>MTHFDA</td>
<td>DIGOXIN 0.25 MG INTRAMUSCULAR INJECTION, SOLUTION</td>
</tr>
<tr>
<td>MTHFDA</td>
<td>DIGOXIN 250 MCG INTRAMUSCULAR INJECTION</td>
</tr>
<tr>
<td>MTHFDA</td>
<td>DIGOXIN 250 MCG INTRAVENOUS INJECTION</td>
</tr>
<tr>
<td>MTHSPL</td>
<td>digoxin 0.25 MILLIGRAM In 1.0 MILLILITER INTRAVENOUS INJECTION</td>
</tr>
<tr>
<td>MTHSPL</td>
<td>Digoxin 250 MICROGRAM In 1 MILLILITER INTRAVENOUS INJECTION, SOLUTION</td>
</tr>
<tr>
<td>NDDF</td>
<td>DIGOXIN 250 mcg/mL INJECTION AMPUL (ML)</td>
</tr>
<tr>
<td>NDDF</td>
<td>DIGOXIN 250 mcg/mL INJECTION DISPOSABLE SYRINGE (ML)</td>
</tr>
<tr>
<td>NDDF</td>
<td>DIGOXIN@250 mcg/mL@INJECTION@AMPUL (ML)</td>
</tr>
<tr>
<td>SNOMEDCT</td>
<td>Digoxin 250micrograms/mL injection solution 2mL ampule</td>
</tr>
<tr>
<td>SNOMEDCT</td>
<td>Digoxin 500micrograms/2mL injection</td>
</tr>
<tr>
<td>VANDF</td>
<td>DIGOXIN 0.25MG/ML INJ</td>
</tr>
<tr>
<td>[...]</td>
<td>[...]</td>
</tr>
</tbody>
</table>

**Digoxin 0.25 MG/ML Injectable Solution**
Normalization Structural level

- **Structural level**
  - Generic vs. Brand names
  - Atomic elements: Ingredient, Strength, Dose form
  - Combinations
  - Principle set of relationships among the different types
Normalized form

- **Strength**: 4mg/ml
- **Ingredient**: Fluoxetine
- **Dose form**: Oral Solution

Semantic clinical drug component

Semantic clinical drug form

Semantic clinical drug
Generic vs. Brand

- **Generic**
  - Ingredient (IN)
  - Clinical drug form (SCDF)
  - Clinical drug component (SCDC)
  - Clinical drug (SCD)

- **Brand**
  - Brand name (BN)
  - Branded drug form (SBDF)
  - Branded drug component (SBDC)
  - Branded drug (SBD)

*tradename_of*
Relations among drug entities
Relations among drug entities (revisited)

Brand Name: Zyrtec

C. Drug Component: Cetirizine 5MG

C. Drug Form: Cetirizine Oral Tablet

C. Drug: Cetirizine 5 MG Oral Tablet

B. Drug Component: Cetirizine 5MG [Zyrtec]

B. Drug Form: Cetirizine Oral Tablet [Zyrtec]

B. Drug: Zyrtec 5 MG Oral Tablet

Ingredient: Cetirizine
RxNorm database

- **9 data sources**
  - Gold Standard Alchemy
  - Master Drug Data Base
  - Multum MediSource Lex.
  - Micromedex DRUGDEX
  - FDA National Drug Code Directory
  - FDA Structured Product Labels
  - National Drug Data File Plus Source Vocabulary
  - SNOMED Clinical Terms
  - VA National Drug File

- **Content**
  - 4,109 ingredients
  - 9,845 brand names
  - 13,380 clinical drug comp.
  - 14,036 branded drug comp.
  - 18,245 clinical drugs
  - 14,769 branded drugs
  - 8,193 clinical drug forms
  - 11,520 branded drug forms
  - 104 dose forms

(as of July 1, 2008; excluding obsolete data)
Recent changes

◆ Generic/Branded Pack

- Collection of drugs prescribed as one unit
  - Z-PAK =
    {6 (Azithromycin 250 MG Oral Tablet [Zithromax])} Pack [Z-PAKS]
  - Nordette-28 =
    {21 (Ethinyl Estradiol 0.03 MG / Levonorgestrel 0.15 MG Oral Tablet) / 7
    (Inert Ingredients 1 MG Oral Tablet)} Pack [Nordette 28 Day]
  - Triphasil-21 =
    {6 (Ethinyl Estradiol 0.03 MG / Levonorgestrel 0.05 MG Oral Tablet) / 10
    (Ethinyl Estradiol 0.03 MG / Levonorgestrel 0.125 MG Oral Tablet) / 5
    (Ethinyl Estradiol 0.04 MG / Levonorgestrel 0.075 MG Oral Tablet)} Pack
    [Triphasil 21 Day]

Active GPCK forms 217
Active BPCK forms 279
Generic/Branded packs

**Ingredient**
- **Azithromycin**

**C. Drug Component**
- Azithromycin 250 MG

**C. Drug Form**
- Azithromycin Oral Tablet

**C. Drug**
- Azithromycin 250 MG Oral Tablet

**Brand Name**
- **Zithromax**

**B. Drug Component**
- Azithromycin 250 MG

**B. Drug Form**
- Azithromycin Oral Tablet [Zithromax]

**B. Drug**
- Zithromax 250 MG Oral Tablet

**B. Pack**
- Z-PAK

**G. Pack**
- {6 (Azithromycin 250 MG Oral Tablet) } Pack
Visualizing drug information

RxNav
RxNav

◆ **Visualization and navigation**
  - RxNorm browser
  - Spelling correction
  - Search on names and codes (including proprietary)
  - Standalone application
    - RxNorm database at NLM
    - Local RxNorm database

◆ **Drug information processing**
  - API to the RxNorm database
  - Web services
RxNav demo

Processing drug information

RxNorm Application Programming Interface
RxNorm API

- Made available in March 2008
- Based on Web Services
  - SOAP
  - Independent of any programming language
- Used by RxNav and MyMedicationList
- Enable access to all information displayed in RxNav
- Documentation
List of functions 1/2

◆ Housekeeping functions
  • getRxNormVersion()
  • getIdTypes()
  • getRelaTypes()
  • getTermTypes()

◆ Find RxNorm concepts
  • By name: findRxcuiByString( searchString )
  • By code: findRxcuiById( idType, id )
  • Help: getSpellingSuggestions( searchString )
List of functions 2/2

◆ Get RxNorm concept properties
  ● getRxConceptProperties( rxcui )
  ● getNDCs( rxcui )

◆ Get RxNorm concept relations
  ● By rel.: getRelatedByRelationship( rxcui, rel-list )
  ● By type: getRelatedByType( rxcui, type-list )
  ● All: getAllRelatedInfo( rxcui )

◆ Convenience function
  ● getDrugs( name )
Documentation

◆ Java

```java
import java.net.URL;
import BeanService.*;
import gov.nih.nlm.mor.axis.services.RxNormDBService.*;

String rxhost = "http://mor.nlm.nih.gov";
String rxURI = rxhost + "/axis/services/RxNormDBService";

// Locate the RxNorm API web service
URL rxURL = new URL(rxURI);
DBManagerService rxnormService = new DBManagerServiceLocator();
DBManager dbmanager = rxnormService.getRxNormDBService(rxURL);
```

◆ Coming up soon: Perl, .NET
Implementation Perl client

Method: getRxNormVersion()

Arg1:
- findRxInfoById(idType, id)
- findRxInfoByString(term)
- getRelatedInfo(rxcui)

Arg2:
- getDrugs(name)
- getIds(types)
- getNDCs(rxcui)
- getRelaTypes()

Comment:
- getRxConceptProperties(rxcui)
- getRxNormVersion()
- getSpellingSuggestion(term)
- getTermTypes()

Method: getRxConceptProperties(rxcui)

Arg1: 58930

Arg2:

Search Clear

<table>
<thead>
<tr>
<th>STR</th>
<th>Zyrtec</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUPPRESS</td>
<td>N</td>
</tr>
<tr>
<td>TTY</td>
<td>BN</td>
</tr>
<tr>
<td>SY</td>
<td></td>
</tr>
<tr>
<td>RXCUI</td>
<td>58930</td>
</tr>
<tr>
<td>LAT</td>
<td>ENG</td>
</tr>
<tr>
<td>CUI</td>
<td>C0162723</td>
</tr>
</tbody>
</table>
Implementation .NET client
Coming up soon

◆ Get proprietary information in a given source
  - Subject to UMLS intellectual property restrictions
  - Requires a “ticket” (similar to UMLSKS API)
  - Use cases
    - Access to exact names and codes in a given source
    - Support for mapping across drug vocabularies through RxNorm
      - Code in Multum → code in First Data Bank

◆ Multi-ingredient search
Integrating drug information sources

Link out
FDA Standard product labels

For a FDA View of this Label, click here

Zyrtec (cetirizine hydrochloride) Tablet, Film Coated
Zyrtec (cetirizine hydrochloride) Tablet, Chewable
Zyrtec (cetirizine hydrochloride) Syrup
[Pfizer Labs]

Drug Label Sections

- Description
- Clinical Pharmacology
- Indications & Usage
- Contraindications
- Warnings
- Precautions
- Adverse Reactions
- Overdosage
- Dosage & Administration
- How Supplied
- Patient Counseling Information
- Supplemental Patient Material
- Boxed Warning
- Patient Package Insert
- Highlights
- Full Table of Contents

DESCRIPTION

Cetirizine hydrochloride, the active component of ZYRTEC® tablets and syrup, is an orally active and selective H1-receptor antagonist. The chemical name is (±) - [2· [4-[ (4-chlorophenyl]phenylmethyl] -1 - piperazinyl] ethoxy]acetic acid, dihydrochloride. Cetirizine hydrochloride is a racemic compound with an empirical formula of C21H26ClN2O3·2HCl. The
Coming up soon

- Currently no clinical information
  - In RxNorm
  - Processable through RxNav
    - Textual information available through the links to DailyMed and MedlinePlus Drugs

- Clinical information available in other sources
  - E.g., MedlinePlus drugs, NDF-RT
  - Soon to be integrated in RxNav
MedlinePlus Drugs

Cetirizine

(see ti’ ra zee)

Contents of this page:
- Why is this medication prescribed?
- How should this medicine be used?
- Other uses for this medicine
- What special precautions should I follow?
- What special dietary instructions should I follow?
- What should I do if I forget a dose?
- What side effects can this medication cause?
- What storage conditions are needed for this medicine?
- In case of emergency/exercise
- What other information should I know?
- Brand names
- Brand names of combination products

Why is this medication prescribed?
Cetirizine is used to temporarily relieve the symptoms of hay fever (allergy to pollen, dust, or other substances in the air) and allergy to other substances (such as dust mites, animal dander, cockroaches, and molds). These symptoms include sneezing, runny nose, itchy, red, watery eyes, and itching nose or throat. Cetirizine is also used
National Drug File Reference Terminology

- Developed by the Veterans Health Administration
- Part of the VA clinical information system
- Non-terminological information
  - Pharmacologic class (isa)
  - Indications (may_treat, may_diagnose, may_prevent)
  - Contraindications (drug_contraindicated_for)
  - Mechanism of action (mechanism_of_action_of)
  - Drug-drug interactions (contraindicated_with)
  - Physiology (has_physiologic_effect)
  - Metabolism (metabolic_site_of, metabolizes, pharmacokinetics_of)
NDF-RT Examples

◆ Cetirizine

- `drug_contraindicated_for` Drug Allergy
- `may_treat` Rhinitis, Allergic, Perennial
- `may_treat` Urticaria
- `has_physiologic_effect` Decreased Histamine Activity
Applications
Applications

◆ Terminology integration and standardization (RxNorm) enables interoperability and mapping across vocabularies

◆ Specific applications
  - Data integration
  - Medication reconciliation
  - Personal Health Record
  - E-prescribing / CPOE
  - CDA R2
Medication Record for:
Bodenreider Olivier

### Current Medications

<table>
<thead>
<tr>
<th>Name of Medication</th>
<th>Start Date</th>
<th>Stop Date</th>
<th>Amount Each Time</th>
<th>Frequency</th>
<th>Instruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfamethoxazole 400 MG / Trimethoprim 80 MG Oral</td>
<td>06/27/2008</td>
<td>07/05/2008</td>
<td>1</td>
<td>Twice a Day</td>
<td></td>
</tr>
<tr>
<td>Lipitor 10 MG Oral Tablet</td>
<td>06/27/2008</td>
<td>07/26/2008</td>
<td>1</td>
<td>Once a Day</td>
<td></td>
</tr>
</tbody>
</table>

### Previous Medications

<table>
<thead>
<tr>
<th>Name of Medication</th>
<th>Start Date</th>
<th>Stop Date</th>
<th>Amount Each Time</th>
<th>Frequency</th>
<th>Instruction</th>
</tr>
</thead>
</table>

http://mml.nlm.nih.gov/

[Zeng, AMIA 2008]
Quality control in RxNorm

◆ Multiple equivalent paths between RxNorm entities

\[
\text{getRelatedByRelationship}(r, \text{consists of}) \circ \text{getRelatedByRelationship}(*, \text{has ingredient}) \\
\equiv \\
\text{getRelatedByRelationship}(r, \text{inverse isa}) \circ \text{getRelatedByRelationship}(*, \text{has ingredient})
\]
Examples of application

◆ Quality control in RxNorm: Results
  ● 35,000 pairs of paths investigated
  ● Few discrepancies detected
  ● Types of errors
    ■ Obsolete brand names
    ■ Obsolete branded drug forms
    ■ Erroneous relations
  ● Discrepancies reported to the RxNorm team

[Peters, AMIA 2008]
References

RxNorm

RxNav and RxNorm API