RxNav
Browser and Application Programming Interfaces for Drug Information Sources

Olivier Bodenreider
Lister Hill National Center for Biomedical Communications
Bethesda, Maryland - USA
Acknowledgments

- Lee Peters
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Outline

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

- **Other drug information sources accessible through RxNav**
  - RxTerms
  - NDF-RT

- **Visualizing drug information:** RxNav

- **Processing drug information:** RxNorm API

- Applications
References

- RxNav and RxNorm APIs

- RxNorm

- RxTerms

- NDF-RT
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

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

**Differences**
- RxNorm creates its own names
- Principled use of named relationships
- Limited scope: drug names
Source vocabularies in RxNorm

- Gold Standard Alchemy
- Medi-Span Master Drug Data Base
- Multum MediSource Lexicon
- Micromedex RED CODE
- Medical Subject Headings
- FDA National Drug Code Directory
- FDA Structured Product Labels
- First DataBank NDDF Plus
- VHA National Drug File-Ref. Terminology
- SNOMED Clinical Terms (drug information)
- VHA National Drug File

RxNorm

(terms in thousands, as of January 2011)

- Gold Standard Alchemy: 23
- Medical Subject Headings: 66
- FDA Structured Product Labels: 86
- First DataBank NDDF Plus: 87
- VHA National Drug File-Ref. Terminology: 133*
- SNOMED Clinical Terms (drug information): 87*
- VHA National Drug File: 48

Total: 113
RxNorm concept

Ingredient

Acetaminophen

SNOMED CT
MeSH
Multum
NDDF
...

161

MMSL:5005
SNOMEDCT:387517004
SNOMEDCT:90332006
NDDF:001605
MTHSPL:362O9ITL9D
MMSL:4119
MMSL:d00049
VANDF:4017513
MMSL:4992
MMSL:52845
MTHFDA:50612
UMLS: C0000970

Acetaminophen
Paracetamol
APAP
Paracetamol product
Acetaminophen (product)
Acetaminophen (substance)
Acetaminophen product
Drug vocabulary standardization

RxNorm
Normalization

◆ Lexical level
  ● Conventions for representing names
    (strength, units, etc.)

◆ Structural level
  ● Conventions for representing types of drug entities and their interrelations
Normalization Lexical level

- GS Digoxin 0.25mg/1mL Solution for injection
- GS Digoxin 500mcg/2mL Solution for injection
- MDDB 'Digoxin Inj 0.25 MG/ML
- MMSL digoxin 250 mcg/mL (0.25 mg/mL) injectable solution
- MMSL Digoxin, 250 mcg/mL (0.25 mg/mL) injectable solution
- MMX Digoxin 0.25 MG/ML Injection Solution
- MTHFDA DIGOXIN 0.25 MG INTRAMUSCULAR INJECTION, SOLUTION
- MTHFDA DIGOXIN 250 MCG INTRAMUSCULAR INJECTION
- MTHFDA DIGOXIN 250 MCG INTRAVENOUS INJECTION
- MTHSPL digoxin 0.25 MILLIGRAM In 1.0 MILLILITER INTRAVENOUS INJECTION
- MTHSPL Digoxin 250 MICROGRAM In 1 MILLILITER INTRAVENOUS INJECTION, SOLUTION
- NDDF DIGOXIN 250 mcg/mL INJECTION AMPUL (ML)
- NDDF DIGOXIN 250 mcg/mL INJECTION DISPOSABLE SYRINGE (ML)
- NDDF DIGOXIN@250 mcg/mL@INJECTION@AMPUL (ML)
- SNOMEDCT Digoxin 250micrograms/mL injection solution 2mL ampule
- SNOMEDCT Digoxin 500micrograms/2mL injection
- VANDF DIGOXIN 0.25MG/ML INJ
- [...] [...]
Normalization Structural level

◆ Structural level
  ● Atomic elements
    ■ Ingredient
    ■ Strength
    ■ Dose form
  ● Generic vs. Brand names
  ● Principle set of relationships among the different types
**Normalized form**

<table>
<thead>
<tr>
<th>Strength</th>
<th>Ingredient</th>
<th>Dose form</th>
</tr>
</thead>
<tbody>
<tr>
<td>4mg/ml</td>
<td>Fluoxetine</td>
<td>Oral Solution</td>
</tr>
</tbody>
</table>

**Clinical drug component**

**Clinical drug form**

**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)

**Ingredient**
- Azithromycin

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

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

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

**B. Drug Component**
- Azithromycin 250 MG [Zithromax]

**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
RxNorm database

◆ 11 data sources
- Gold Standard Alchemy
- Medi-Span Master Drug Data Base
- Multum MediSource Lexicon
- Micromedex RED BOOK
- Medical Subject Headings
- FDA National Drug Code Directory
- FDA Structured Product Labels
- First DataBank NDDF Plus
- VHA NDF – RT
- SNOMED Clinical Terms
- VHA National Drug File

◆ Content
- 4,942 ingredients
- 14,667 brand names
- 19,862 clinical drugs
- 16,275 branded drugs
- 307 generic packs
- 388 branded packs
- 15,715 clinical drug comp.
- 14,680 branded drug comp.
- 8,478 clinical drug forms
- 12,188 branded drug forms
- 100 dose forms

(as of January 26, 2011; excluding obsolete data)
Other drug information sources accessible through RxNav

RxTerms
NDF-RT
RxTerms

- Drug interface terminology derived from RxNorm for prescription writing or medication history recording
  - Commonly used synonyms and abbreviations (e.g. HCTZ for hydrochlorothiazide)
  - “tall man” lettering recommended by FDA to avoid medication errors
    - ChlorproMAZINE
    - ChlorproPAMIDE
- Developed at NLM
National Drug File Reference Terminology

- Developed by the Veterans Health Administration
- Part of the VA clinical information system
- Available from the NCI web site (XML, OWL)
- Integrated in RxNorm since June 2010
Clinical information

- Pharmacologic class, Ingredients (isa)
- Therapeutic intent (may_treat, may_diagnose, may_prevent)
- Chemical ingredient (has_ingredient, has_active_metabolites)
- Mechanism of action (has_MoA)
- Physiologic effect (has_PE)
- Pharmacokinetics/Metabolism (has_PK, site_of_metabolism)
- Dose form (has_dose_form)
- Contraindications (CI_with, CI_MoA, CI_PE, induces)
- Drug-drug interactions
NDF-RT Examples

- **Clopidogrel**
  - *may_prevent* Cerebral Infarction
  - *may_prevent* Coronary Thrombosis
  - *may_prevent* Myocardial Infarction
  - *Cl_with* Blood Coagulation Disorders
  - *Cl_with* Drug Hypersensitivity
  - *Cl_with* Hemorrhage
  - *has_Ingredient* clopidogrel
  - *has_MoA* G-Protein-linked Receptor Interactions
  - *has_PE* Decreased Platelet Aggregation

- **CLOPIDOGREL BISULFATE 75MG TAB,UD**
  - *isa* PLATELET AGGREGATION INHIBITORS
Legend
- has PE: has physiologic effect
- CI with: contra-indicated with

Representation of the drug
Clopidogrel in NDF-RT

- has ingredient
- has physiologic effect
- contra-indicated with
  isa (stated)
Visualizing drug information

RxNav
RxNav

◆ Visualization and navigation
  ● RxNorm browser
    ■ Integrated with RxTerms and NDF-RT
  ● Auto-completion and spelling correction
  ● Search on names and codes (including proprietary)
  ● Standalone application
  ● Queries databases at NLM (RxNorm, RxTerms, NDF-RT)
  ● Links to external sources (DailyMed)

◆ Drug information processing
  ● API to the RxNorm database
  ● Web services (SOAP, REST)
RxNav demo

http://rxnav.nlm.nih.gov/
RxNorm Properties
RxCUI= 309362

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RxNorm Name</td>
<td>clopidogrel 75 MG Oral Tablet</td>
</tr>
<tr>
<td>RxCUI</td>
<td>309362</td>
</tr>
<tr>
<td>TTY</td>
<td>SCD</td>
</tr>
<tr>
<td>UMLSCUI</td>
<td>C0975741</td>
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<tr>
<td>Source</td>
<td>Gold Standard Alchemy</td>
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<td>MultiSource Lexicon</td>
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<td>Source</td>
<td>Metathesaurus FDA National Drug Code Directory</td>
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<td>Metathesaurus FDA Structured Product Labels</td>
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<tr>
<td>Source</td>
<td>National Drug Data File Plus Source Vocabulary</td>
</tr>
<tr>
<td>Source</td>
<td>National Drug File</td>
</tr>
<tr>
<td>Source</td>
<td>SNOMED Clinical Terms</td>
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<td>Veterans Health Administration National Drug File</td>
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RxCUI: 309362
Name: clopidogrel 75 MG Oral Tablet

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<td>Suppress</td>
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<td>Data Version</td>
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# CLOPIDOGREL BISULFATE 75MG TAB,UD

## Properties Table

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<tr>
<td>Display_Name</td>
<td>CLOPIDOGREL BISULFATE 75MG TAB,UD</td>
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<td>Print_Name</td>
<td>CLOPIDOGREL BISULFATE 75MG TAB UD</td>
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<tr>
<td>kind</td>
<td>DRUG_KIND</td>
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<td>Level</td>
<td>VA Product</td>
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<td>Status</td>
<td>Active</td>
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<td>Units</td>
<td>MG</td>
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<tr>
<td>Strength</td>
<td>75</td>
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<td>code</td>
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<td>VU1D</td>
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<td>UMLS_CUI</td>
<td>C0975741</td>
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<td>RxNorm_CUI</td>
<td>309362</td>
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<tr>
<td>RxNorm_Name</td>
<td>clopidogrel 75 MG Oral Tablet</td>
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<tr>
<td>VANDF_Record</td>
<td>&lt;VANDF_Record&gt;50.68*12795^&lt;VANDF_Record&gt;&lt;VA_File&gt;50.68&lt;VA_File&gt;&lt;VA_IEN&gt;12795&lt;VA_IEN&gt;</td>
</tr>
<tr>
<td>VA_National_For...</td>
<td>CLOPIDOGREL TAB</td>
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<tr>
<td>Kind</td>
<td>Subject</td>
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<td>------------</td>
<td>--------------------------</td>
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</tr>
<tr>
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<td>CLOPIDOGREL</td>
</tr>
<tr>
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<td>CLOPIDOGREL</td>
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<td>Dose Form</td>
<td>CLOPIDOGREL BISULFATE 75MG TAB,UD</td>
</tr>
<tr>
<td>Ingredient</td>
<td>CLOPIDOGREL</td>
</tr>
<tr>
<td>Mechanism of Action</td>
<td>CLOPIDOGREL</td>
</tr>
<tr>
<td>Physiologic Effect</td>
<td>CLOPIDOGREL</td>
</tr>
</tbody>
</table>
CLOPIDOGREL BISULFATE 75MG TAB,UD

Mechanism of Action

- Cellular or Molecular Interactions
  - Receptor Interactions
    - G-Protein-linked Receptor Interactions
      - CLOPIDOGREL
        - CLOPIDOGREL BISULFATE

Legend

- VA Product
- Drug
- Mechanism of Action
- In
- Isolated
- Contribute
- MECHANISM OF ACTION
- Im
- MECHANISM OF ACTION
- Drug
- In, MeA
- CL, MIA
- MECHANISM OF ACTION
CLOPIDOGREL BISULFATE 75MG TAB,UD
Pharmacokinetics

CLOPIDOGREL

CLOPIDOGREL BISULFATE

CLOPIDOGREL BISULFATE 75MG TAB,UD

Legend

VIA Product -- DRUG \arrow{has}\rightarrow DRUG -- PHARMACOKINETICS \arrow{has}\rightarrow PHARMACOKINETICS -- DRUG \arrow{has PK}\rightarrow PHARMACOKINETICS
CLOPIDOGREL BISULFATE 75MG TAB,UD
Drug Interactions

CLOPIDOGREL BISULFATE

CIMETIDINE [Significant]
OMEPRAZOLE [Significant]
WARFARIN [Significant]
Processing drug information

RxNorm Application Programming Interface
RxNorm APIs

- Made available in March 2008
- Based on Web Services
  - SOAP, REST
  - Independent of any programming language
- Used by *RxNav* and other applications
- Enable access to all information displayed in RxNav
- Documentation
- Testing environment (SOAP client demo)
List of functions (SOAP) 1/3

◆ Housekeeping functions
  ● getRxNormVersion()
  ● getIdTypes()
  ● getRelaTypes()
  ● getTermTypes()
  ● getSourceTypes()

◆ Find RxNorm concepts
  ● By name: findRxcuiByString( searchString, source-list, allSourcesFlag, searchType )
  ● By code: findRxcuiById( idType, id, allSourcesFlag )
  ● Help: getSpellingSuggestions( searchString )
  ● Versioning: findRemapped( rxcui )
Get RxNorm concept properties

- `getRxConceptProperties( rxcui )`
- `getStrength( rxcui )`
- `getQuantity( rxcui )`
- `getNDCs( rxcui )`
- `getUNII( rxcui )`
- `getProprietaryInformation( rxcui, source-list, proxyTicket* )`
List of functions (SOAP) 3/3

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

◆ Miscellaneous functions
  ● getDrugs( name )
  ● getDisplayTerms()
  ● getMultiIngredBrand( rxcui-list )
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);
```

◆ Perl, .NET
Implementation Perl client

RxNorm API demo

Method: getRxConceptProperties(rxcui)
Arg1: 58930
Arg2: 
Arg3: 
Arg4: 

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

![RxNorm API access](image)

Method: `getRxConceptProperties (rxcui)`

Argument 1: 58930

Argument 2: 

Returned data:

- **STR**: Zyrtec
- **RXCUI**: 58930
- **TTY**: BN
- **LAT**: ENG
- **SUPPRESS**: N
- **SY**: 
- **CUI**: C0162723
RESTful API

◆ Base URI
  ● http://rxnav.nlm.nih.gov/REST/

◆ List of resources
  ● http://rxnav.nlm.nih.gov/RxNormRestAPI.html
<table>
<thead>
<tr>
<th>RESTful resource</th>
<th>SOAP-based function</th>
</tr>
</thead>
<tbody>
<tr>
<td>/</td>
<td>(none)</td>
</tr>
<tr>
<td>/version</td>
<td>getRxNormVersion</td>
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<tr>
<td>/displaynames</td>
<td>getDisplayNames</td>
</tr>
<tr>
<td>/idtypes</td>
<td>getIdTypes</td>
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<tr>
<td>/relatetypes</td>
<td>getRelaTypes</td>
</tr>
<tr>
<td>/termtypes</td>
<td>getTermTypes</td>
</tr>
<tr>
<td>/rxcui?name=value&amp;srclst=value&amp;allsrc=value&amp;search=value</td>
<td>findRxcuiByString</td>
</tr>
<tr>
<td>/rxcui?idtype=value&amp;id=value&amp;allsrc=value</td>
<td>findRxcuiById</td>
</tr>
<tr>
<td>/rxcui/{rxcui}</td>
<td>(none)</td>
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<tr>
<td>/rxcui/{rxcui}/properties</td>
<td>getRxConceptProperties</td>
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<tr>
<td>/rxcui/{rxcui}/ndcs</td>
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<td>/brands?ingredientids=value</td>
<td>getMultiIngredBrand</td>
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<tr>
<td>/drugs?name=value</td>
<td>getDrugs</td>
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</tbody>
</table>

```xml
<?xml version="1.0" encoding="UTF-8" standalone="yes"?>
<rxnormdata>
  <idGroup>
    <name>bactrim</name>
    <rxcui>151399</rxcui>
  </idGroup>
</rxnormdata>
```
REST output  JSON


```
JSON output
{
   "idGroup" : {
      "rxcui" : "151399",
      "name" : "bactrim"
   }
}
```
RxNormNorm Recently released

- Managing variation in clinical drug names
- Use case: mapping of local formularies to RxNorm
- Extends the UMLS program norm
- Specific normalization rules
  - Expansion of abbreviations (e.g., tab to tablet)
  - Reformatting of specific elements (e.g., space between number and unit)
  - Removal of salt variants (e.g., succinate from metoprolol succinate)
New functions Coming up soon

- **RxMap**
  - Mapping lists of drug names / identifiers to RxNorm
  - Batch mode version of
    - findRxceuiByString()
    - findRxceuiById()

- **RxXMap**
  - Mapping across vocabularies through RxNorm
  - Combines
    - findRxceuiById()
    - getProprietaryInformation()
  - Requires UMLS license
New APIs Coming up soon

- **RxTerms**
  - SOAP + REST
  - List of RxTerms properties for a given RxCUI

- **NDF-RT**
  - SOAP + REST
  - Find NDF-RT entity by name, NUI, RxCUI
  - Get properties for a given NDF-RT drug entity
  - Get relations for a given NDF-RT drug entity
  - Find drug interactions
Applications
Examples of application

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

◆ Specific applications
  ● Information exchange (“meaningful use”)
  ● Medication lists
  ● Medication reconciliation
  ● E-prescribing / CPOE
  ● CDA R2
  ● Personal Health Record
Quality control in RxNorm

- Multiple equivalent paths between RxNorm entities

getRelatedByRelationship( \( r; \text{consists of} \)) \( \circ \) getRelatedByRelationship( \( *; \text{has ingredient} \))

\( \equiv \)

getRelatedByRelationship( \( r; \text{inverse isa} \)) \( \circ \) 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, JAMIA 2009]
Applications outside NLM

◆ RxSafe (OHSU)
  ● “improve medication safety for patients”
  ● http://www.ohsu.edu/RxSafe/

◆ My-Medi-Health (Vanderbilt)
  ● “Child-Centered Medication Management”
Usage statistics  All queries

Number of queries per month

- all queries
- REST queries
- 12 m sliding avg

Jan-08  Mar-08  May-08  Jul-08  Sep-08  Nov-08  Jan-09  Mar-09  May-09  Jul-09  Sep-09  Nov-09  Jan-10  Mar-10  May-10  Jul-10  Sep-10  Nov-10

Queries range from 0 to 3,500,000 per month.
Usage statistics  Interactive queries

Number of interactive queries per month

- 12 m sliding...
Contact: RXNAVINFO@LIST.NIH.GOV
Web: http://rxnav.nlm.nih.gov/

Olivier Bodenreider
Lister Hill National Center for Biomedical Communications
Bethesda, Maryland - USA