

Analyzing Opioid Prescriptions in Medicare

Part D: Issues, Tools, and Techniques

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- No relationships with commercial interest
- The views and opinions expressed do not necessarily state or reflect those of the U.S. Government, and they may not be used for advertising or product endorsement purposes



Learning objectives

- Summarize the process for linking National Drug Codes (NDCs) to RxNorm in the Medicare Part D data set
- List issues in identifying opioid drugs in drug classification systems, such as ATC
- Demonstrate how to calculate the daily dose and morphine equivalents for oral and other dosage forms

Self-Assessment Question 1

- Which type of information can be found in claims data, such as Medicare Part D dataset?
 - A. Patient name and address
 - B. ATC class (from the Anatomical Therapeutic Chemical drug classification)
 - C. “NDC codes” (from the National Drug Code directory)
 - D. Days supply
 - E. Quantity dispensed

Self-Assessment Question 2

- TRUE/FALSE: Medications can belong to only one ATC class?
 - A. True
 - B. False

Self-Assessment Question 3

- Conversion to oral morphine milligram equivalent
 - A. Enables comparison between daily doses of opioid drugs
 - B. Can be done by multiplying the unit strength by a factor, regardless of the dose form
 - C. Is required for characterizing the global evolution of opioid doses over time
 - D. Is required for characterizing differences in opioid doses dispensed across geographic areas
 - E. All of the above

Outline

- Introduction
 - RxNorm and the Medicare Part D dataset
 - Use case (analysis of opioid prescriptions)
 - *Follow-along activity with RxNav*
- How to link NDCs to RxNorm and ATC?
 - Identifying opioid drugs from a drug class – ATC
 - How to handle obsolete NDCs
 - *Follow-along activity with RxClass*
- Calculating the daily dose in oral morphine milligram equivalent
- Discussion of results from larger-scale analysis



Introduction



RxNorm

<https://www.nlm.nih.gov/research/umls/rxnorm/>

- Standard drug terminology
- Developed by the National Library of Medicine
- Integrates 13 drug vocabularies (interoperability)
- Scope
 - Prescription drugs (U.S. market)
 - Only terminology (not a drug knowledge base)
- Updated monthly
- Use cases
 - E-prescribing
 - Information exchange
 - Formulary development
 - Reference value sets
 - *Analytics*



Normalization **Lexical level**

Name	Code	Source
WARFARIN (COUMADIN) NA 1MG TAB	4005203	VANDF
warfarin 1 mg oral tablet	3617	MMSL
WARFARIN NA 1MG TAB,UD	4014039	VANDF
WARFARIN NA 1MG TAB,UD [VA Product]	N0000161787	NDFRT
WARFARIN SODIUM 1 mg ORAL TABLET	14198	NDDF
WARFARIN SODIUM 1 mg ORAL TABLET	60429-784	MTHSPL
Warfarin Sodium 1 MG Oral Tablet	104045	MMX
WARFARIN SODIUM 1 mg ORAL TABLET	63629-4017	MTHSPL
WARFARIN SODIUM 1 mg ORAL TABLET [Warfarin Sodium]	53808-0985	MTHSPL
Warfarin Sodium 1 MILLIGRAM In 1 TABLET ORAL TABLET	15330-100	MTHSPL
WARFARIN SODIUM 1.09 MG ORAL TABLET	281572	MTHFDA
Warfarin Sodium 1mg Oral tablet	933	GS
Warfarin sodium 1mg tablet (product)	319733000	SNOMEDCT_US
Warfarin Sodium Tab 1 MG	6749	MDDB
Warfarin Sodium, 1 mg oral tablet	3617	MMSL
WARFARIN SODIUM@1 mg@ORAL@TABLET	14198	NDDF
[...]		



Warfarin Sodium 1 MG Oral Tablet (855288)



RxNorm drug model

Definitional features

Generic drug entities

Branded drug entities

Ingredient/Brand name

[Navigational entities]

Drug Comp. = Ingredient + strength

Drug Form = Ingredient + dose form

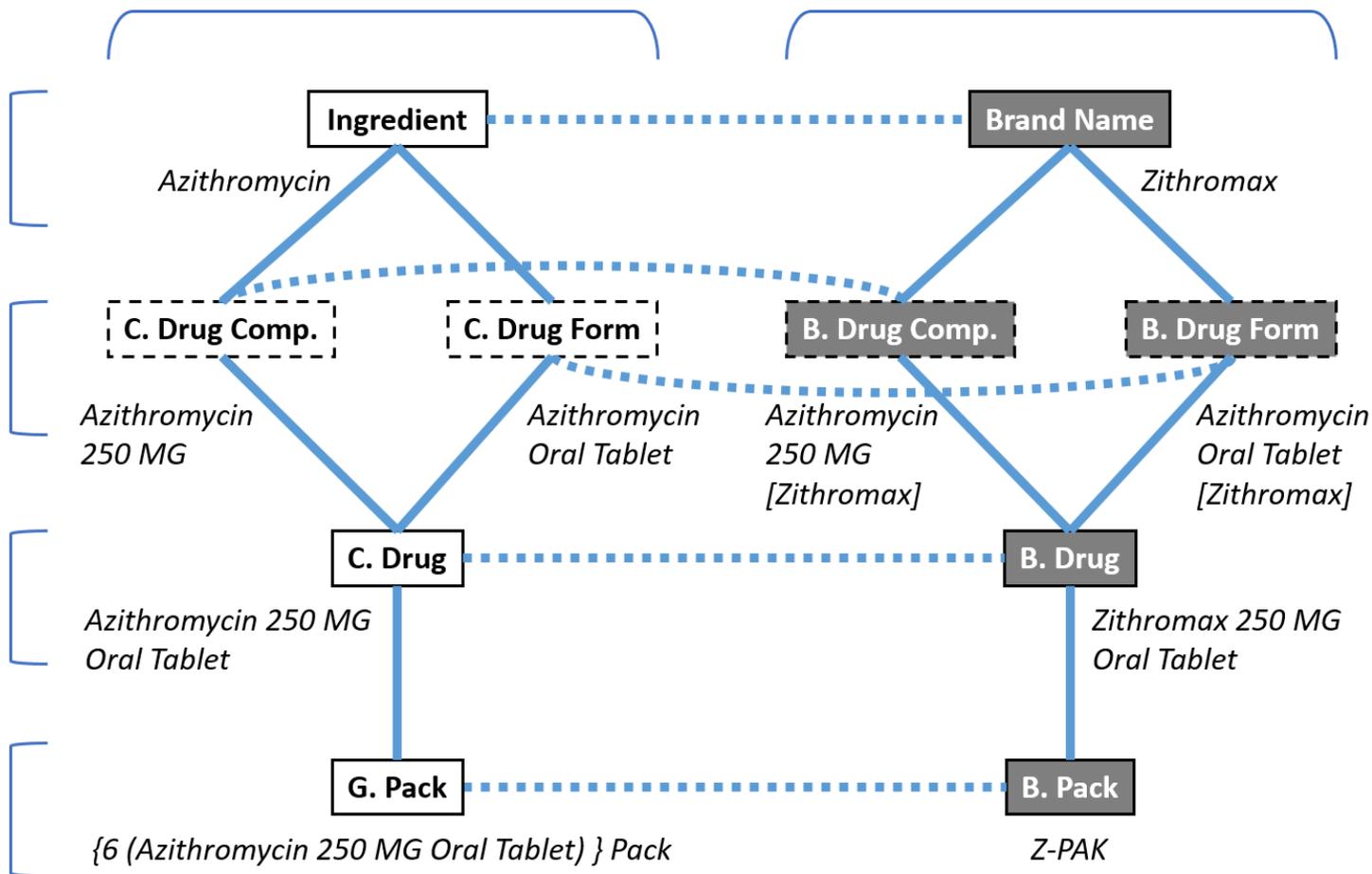
[Drug products (individual)]

Ingredient + strength + dose form

(+ optionally Quantity Factor and Quality Distinction)

[Drug products (collective)]

Collections of generic/branded drugs







Azithromycin [RxCUI = 18631]

- RxNorm Graph**
- RxNorm Properties**
- NDC
- RxTerms
- NDF-RT
- Pill Images
- Class View
- Interaction View
- Status

Views

- Classic**
- Simple
- Table

Filters

- H
- V
- Rx
- S
- Group
- Form

Links



Legend

- MIN
- Pack
- Multi

[Download](#)

IN/MIN	Ingredient (1)
H Rx S	Azithromycin

PIN	Precise Ingredient (3)
Rx S	AZITHROMYCIN ANHYDROUS
Rx S	Azithromycin Dihydrate
Rx S	Azithromycin Monohydrate

BN	Brand Name (3)
H Rx S	AzaSite
H Rx S	Zithromax
H Rx S	Zmax

SCDC	Clinical Drug Component (8)
H Rx S	Azithromycin 10 MG/ML
H Rx S	Azithromycin 1000 MG
H Rx S	Azithromycin 20 MG/ML
H Rx S	Azithromycin 250 MG
H Rx S	Azithromycin 33.3 MG/ML



SBDC	Branded Drug Component (8)
H Rx S	Azithromycin 10 MG/ML [AzaSite]
H Rx S	Azithromycin 1000 MG [Zithromax]
H Rx S	Azithromycin 20 MG/ML [Zithromax]
H Rx S	Azithromycin 250 MG [Zithromax]
H Rx S	Azithromycin 33.3 MG/ML [Zmax]

SCD/GPCK	Clinical Drug or Pack (14)
H Rx S	Azithromycin 10 MG/ML Ophthalmic Solution
H Rx S	Azithromycin 1000 MG Powder for Oral Suspension
H Rx S	Azithromycin 20 MG/ML Oral Suspension
S	Azithromycin 250 MG Oral Capsule
H Rx S	Azithromycin 250 MG Oral Tablet

SBD/BPCK	Branded Drug or Pack (11)
H Rx S	AzaSite 1 % Ophthalmic Solution
P H Rx S	TRI-PAK
P H Rx S	Z-PAK
H Rx S	Zithromax 1 GM Powder for Oral Suspension
H Rx S	Zithromax 20 MG/ML Oral Suspension

SCDG	Clinical Dose Form Group (6)
H Rx S	Azithromycin Injectable Product
H Rx S	Azithromycin Ophthalmic Product
H Rx S	Azithromycin Oral Liquid Product
H Rx S	Azithromycin Oral Powder Product
H Rx S	Azithromycin Oral Product

DFG	Dose Form Group (6)
HV Rx S	Injectable Product
HV Rx S	Ophthalmic Product
HV Rx S	Oral Liquid Product
HV Rx S	Oral Powder Product
HV Rx S	Oral Product

SBDG	Branded Dose Form Group (8)
H Rx S	AzaSite Ophthalmic Product
H Rx S	Zithromax Injectable Product
H Rx S	Zithromax Oral Liquid Product
H Rx S	Zithromax Oral Powder Product
H Rx S	Zithromax Oral Product

RxNav

- Browser for RxNorm
 - Graph: various types of drug entities in RxNorm for a given drug
 - Properties: names and codes (from non-proprietary sources)
 - NDC (only for clinical and branded drugs and packs)
- Additional information
 - Pill images (from the NLM C3PI collection)
 - Class view (link to drug classification systems)
 - Drug-drug interactions
 - Status (information about active and obsolete drugs)

*Not in scope for RxNorm,
but handled by RxNav*

Center for Medicare and Medicaid (CMS)

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Learn about your health care options

CMS.gov

Centers for Medicare & Medicaid Services

- Medicare
- Medicaid/CHIP
- Medicare-Medicaid Coordination
- Private Insurance
- Innovation Center
- Regulations & Guidance
- Research, Statistics, Data & Systems
- Outreach & Education

Medicare
Covers: people age 65 or older, people under age 65 with certain disabilities, and people of all ages with End-Stage Renal Disease.
3 parts:

- Part A Hospital Insurance
- Part B Medical Insurance
- Part D Prescription Drug Coverage

Covering more Americans

Making Americans healthier by preventing illness

Coordinating better care & lowering costs

CMS news

CMS covers 100 million people...



Center for Medicare and Medicaid (CMS) data

<https://www.resdac.org/cms-data>

- Available through the CMS Virtual Research Data Center (VRDC)
 - At a cost
 - Cloud-based environment – data cannot be downloaded
- Longitudinal data available
 - From 1999 for demographics, hospitalization and ambulatory data
 - From 2006 from drug coverage

Category	Program
Beneficiary Enrollment and Demographics	Medicare
Beneficiary Surveys	Qualified Entity Program
Facility Characteristics	Medicaid
Medicaid Utilization	Medicare Advantage
Medicare Utilization	Privacy Level
Physician and Professional Provider Characteristics	Research Identifiable Files
Prescription Drugs	Limited Data Sets
Prospective Payment Systems	Public Use Files
Quality of Care	
Resident Assessments	

Medicare Part D dataset

<https://www.resdac.org/cms-data/files/pde/data-documentation>

- Main variables in the Drug Event File
 - Beneficiary information (ID and demographics)
 - Date on which the prescription was filled
 - Drug: identified by NDC (11-digit format)
 - Quantity Dispensed
 - Days Supply
 - Cost information
- Related information for the NDC (provided by First Databank)
 - Brand name, generic name, strength, dosage form code, and dosage form description



Use case: Analysis of opioid prescriptions

- Identify prescriptions corresponding to opioids in the Medicare part D dataset
- For each opioid drug, calculate the trend of dispensation over time (“number of prescriptions”)
- For all opioids, calculate the trend of total (or daily) dose dispensed in oral morphine milligram equivalents
- Out of scope for this tutorial
 - Analyze differences by prescriber
 - Analyze comorbidities (e.g., depression, anxiety)
 - Analyze adverse effects (e.g., emergency room visit for opioid overdose)

In practice: Analysis of opioid prescriptions

- Identify drugs of interest
 - Find Opioid class
 - Get drug members (with RxNorm identifiers)
 - Get NDCs for RxNorm drugs
 - Get active NDCs
 - Get historical NDCs
 - Extract strength information for these drugs
- Extract dispensation information for these NDCs
 - Quantity dispensed
 - Days supply
- Calculate oral morphine milligram equivalent for each prescription

RxNav follow-along activity

- Search for **oxycodone**
- Explore branded drugs
 - Select **12 HR OxyCONTIN 10 MG Extended Release Oral Tablet**
 - Click on the NDC tab to explore NDCs
- Go back to the Graph tab
 - Select **oxycodone** again
 - Check ATC classes under the Class View tab
- Click on **Natural opium alkaloids** to go to RxClass

<https://mor.nlm.nih.gov/RxNav/>





String

oxyco|



oxyCODONE

oxyCODONE Hydrochloride

oxyCODONE terephthalate

OxyCONTIN

Acetaminophen / oxyCODONE

Aspirin / oxyCODONE

Aspirin / oxyCODONE Hydrochloride / oxyCODONE terephthalate

desoxycorticosterone

desoxycorticosterone acetate

desoxycorticosterone pivalate

Ibuprofen / oxyCODONE



RxNorm Graph

RxNorm Properties

NDC

RxTerms

NDF-RT

Pill Images

Class

Views

- Classic
- Simple
- Table

Filters

- H
- V
- Rx
- S
- Group
- Form

Links



Legend

- MIN
- Pack
- Multi

Download

IN/MIN

Ingredient

SCDC

Clinical Drug Component

SCD/GPCK

Clinical Drug or Pack

SBD/BPCK

Branded Drug or Pack

SCDG

Clinical Dose Form Group

DFG

Dose Form Group

SBDG

Branded Dose Form Group



String



oxyCODONE [RxCUI = 7804]

- RxNorm Graph
- RxNorm Properties**
- NDC
- RxTerms
- NDF-RT
- Pill Images
- Class View
- Interaction View
- Status

Views

- Classic**
- Simple
- Table

Filters

- H
- V
- Rx
- S
- Group
- Form

Links



Legend

- MIN**
- Pack**
- Multi**

Download

IN/MIN	Ingredient (6)
H Rx S	oxyCODONE
M H Rx M	Acetaminophen / oxyCODONE
M H Rx M	Aspirin / oxyCODONE
M H Rx M	Ibuprofen / oxyCODONE
M	Naloxone / oxyCODONE

SCDC	Clinical Drug Component (27)
S	oxyCODONE 10 MG
H Rx S	oxyCODONE 13.5 MG
H Rx S	oxyCODONE 18 MG
S	oxyCODONE 20 MG
H Rx S	oxyCODONE 27 MG

SCD/GPCK	Clinical Drug or Pack (71)
H Rx M	12 HR Acetaminophen 325 MG / oxyCODONE Hydrochloride 7.5 MG Extended Release Oral Tablet
M	12 HR Naloxone Hydrochloride 10 MG / oxyCODONE Hydrochloride 20 MG Extended Release Oral Tablet
M	12 HR Naloxone Hydrochloride 20 MG / oxyCODONE Hydrochloride 40 MG Extended Release Oral Tablet
M	12 HR Naloxone Hydrochloride 5 MG / oxyCODONE Hydrochloride 10 MG Extended Release Oral Tablet
M	12 HR Naltrexone hydrochloride 1.2 MG / oxyCODONE Hydrochloride 10 MG Extended Release Oral Capsule

SCDG	Clinical Dose Form Group (16)
H Rx M	Acetaminophen / oxyCODONE Oral Liquid Product
H Rx M	Acetaminophen / oxyCODONE Oral Product
H Rx M	Acetaminophen / oxyCODONE Pill
H Rx M	Aspirin / oxyCODONE Oral Product
H Rx M	Aspirin / oxyCODONE Pill

PIN	Precise Ingredient (2)
H Rx S	oxyCODONE Hydrochloride
H Rx S	oxyCODONE terephthalate



DFG	Dose Form Group (5)
HV Rx S	Injectable Product
HV Rx S	Oral Liquid Product
HV Rx S	Oral Product
HV Rx S	Pill
HV Rx S	Rectal Product

BN	Brand Name (17)
H Rx M	Endocet
H Rx M	Endodan Reformulated May 2009
H Rx S	Oxaydo
H Rx S	Oxecta
H Rx S	OxyCONTIN

SBDC	Branded Drug Component (44)
H Rx M	Acetaminophen 300 MG / oxyCODONE Hydrochloride 10 MG [Primlev]
H Rx M	Acetaminophen 300 MG / oxyCODONE Hydrochloride 5 MG [Primlev]
H Rx M	Acetaminophen 300 MG / oxyCODONE

SBD/BPCK	Branded Drug or Pack (44)
H Rx S	12 HR OxyCONTIN 10 MG Extended Release Oral Tablet
H Rx S	12 HR OxyCONTIN 15 MG Extended Release Oral Tablet
H Rx S	12 HR OxyCONTIN 20 MG Extended Release Oral Tablet

SBDG	Branded Dose Form Group (35)
H Rx M	Endocet Oral Product
H Rx M	Endocet Pill
H Rx M	Endodan Reformulated May 2009 Oral Product
H Rx M	Endodan Reformulated May 2009 Pill
H Rx S	Oxaydo Oral Product





12 HR OxyCONTIN 10 MG Extended Release Oral Tablet [RxCUI = 1049504]

- RxNorm Graph**
- RxNorm Properties
- NDC
- RxTerms
- NDF-RT
- Pill Images
- Class View
- Interaction View
- Status

Views

- Classic**
- Simple
- Table

Filters

- H
- V
- Rx
- S
- Group
- Form

Links**Legend**

- MIN
- Pack
- Multi

[Download](#)

IN/MIN	Ingredient (1)
H Rx S	oxyCODONE

PIN	Precise Ingredient (1)
H Rx S	oxyCODONE Hydrochloride

BN	Brand Name (1)
H Rx S	OxyCONTIN

SCDC	Clinical Drug Component (1)
H Rx SM	oxyCODONE Hydrochloride 10 MG



SBDC	Branded Drug Component (1)
H Rx S	oxyCODONE Hydrochloride 10 MG [OxyCONTIN]

SCD/GPCK	Clinical Drug or Pack (1)
H Rx S	Abuse-Deterrent 12 HR oxyCODONE Hydrochloride 10 MG Extended Release Oral Tablet

SBD/BPCK	Branded Drug or Pack (1)
H Rx S	12 HR OxyCONTIN 10 MG Extended Release Oral Tablet

SCDG	Clinical Dose Form Group (2)
H Rx S	oxyCODONE Oral Product
H Rx S	oxyCODONE Pill

DFG	Dose Form Group (2)
HV Rx S	Oral Product
HV Rx S	Pill

SBDG	Branded Dose Form Group (2)
H Rx S	OxyCONTIN Oral Product
H Rx S	OxyCONTIN Pill



String

Abuse-Deterrent 12 HR Oxycodone Hydro



OxyCONTIN 10 MG Extended Release Oral Tablet [RxCUI = 1049504]

Show NDCs Information

RxNorm Graph

RxNorm Properties

NDC

RxTerms

NDF-RT

Pill Images

Class View

Interaction View

Status

Views

- Classic
- Simple
- Table

Filters

- H
- V
- Rx
- S
- Group
- Form

Links



Legend

- MIN
- Pack
- Multi

Download

IN/MIN

Ingredient (1)

 H Rx S oxyCODONE

PIN

Precise Ingredient (1)

 H Rx S oxyCODONE Hydrochloride

BN

Brand Name (1)

 H Rx S OxyCONTIN

SCDC

Clinical Drug Component (1)

 H Rx SM oxyCODONE Hydrochloride 10 MG

SBDC

Branded Drug Component (1)

 H Rx S oxyCODONE Hydrochloride 10 MG [OxyCONTIN]

SCD/GPCK

Clinical Drug or Pack (1)

 H Rx S Abuse-Deterrent 12 HR oxyCODONE Hydrochloride 10 MG Extended Release Oral Tablet

SBD/BPCK

Branded Drug or Pack (1)

 H Rx S 12 HR OxyCONTIN 10 MG Extended Release Oral Tablet

SCDG

Clinical Dose Form Group (2)

 H Rx S oxyCODONE Oral Product H Rx S oxyCODONE Pill

DFG

Dose Form Group (2)

 HV Rx S Oral Product HV Rx S Pill

SBDG

Branded Dose Form Group (2)

 H Rx S OxyCONTIN Oral Product H Rx S OxyCONTIN Pill



String

Abuse-Deterrent 12 HR Oxycodone Hydro



12 HR OxyCONTIN 10 MG Extended Release Oral Tablet [RxCUI = 1049504]

RxNorm Graph

RxNorm Properties

NDC

RxTerms

NDF-RT

Pill Images

Class View

Interaction View

Status

Views

- Current NDC

- Historical NDC

[Download](#)

NDC9	NDC11	NDC10	SPL_SET_ID	LABELER	PACKAGING	NDC9 PROPERTIES	PILL IMAGES
43063-354	43063035402	43063-354-02	46345ce2-4038-4928-916d-f3764bddf456	PD-Rx Pharmaceuticals, Inc.	2 in 1 BOTTLE, PLASTIC	Show	
43063-354	43063035410	43063-354-10	46345ce2-4038-4928-916d-f3764bddf456	PD-Rx Pharmaceuticals, Inc.	10 in 1 BOTTLE, PLASTIC	Show	
59011-410	59011041010	59011-410-10	bdfde235-d717-4855-a3c8-a13d26dadede	Purdue Pharma LP	100 in 1 BOTTLE	Show	
59011-410	59011041020	59011-410-20	bdfde235-d717-4855-a3c8-a13d26dadede	Purdue Pharma LP	10 in 1 BLISTER PACK; 2 in 1 CARTON	Show	

S/N 123456789012

LOT NO VARNISH

EXP LOT/EXP

Attention Dispenser: Accompanying Medication Guide must be provided to the patient upon dispensing.

NDC 59011-410-10

OxyContin® 

(oxycodone hydrochloride)
extended-release tablets

10 mg

100 Tablets Rx Only

Purdue Pharma L.P.

Dispense in a tight, light-resistant container.
Store at 25°C (77°F); excursions permitted between 15°-30°C (59°-86°F).

U.S. Patent Nos.: 6,488,968; 7,129,248; 7,674,799;
7,674,800; 7,683,072; 8,174,383; 8,309,060;
8,337,898; 8,808,741; 8,821,929; 8,894,987;
8,894,988; 9,060,976; and 9,073,933.



3 59011-410-10 1



String

oxycodone



oxyCODONE [RxCUI = 7804]

RxNorm Graph

RxNorm Properties

NDC

RxTerms

NDF-RT

Pill Images

Class View

Interaction View

Status

Views

- Classic
- Simple
- Table

Filters

- H
- V
- Rx
- S
- Group
- Form

Links



Legend

- MIN
- Pack
- Multi

Download

IN/MIN

Ingredient (6)

H Rx S	oxyCODONE
M H Rx M	Acetaminophen / oxyCODONE
M H Rx M	Aspirin / oxyCODONE
M H Rx M	Ibuprofen / oxyCODONE
M	Naloxone / oxyCODONE

SCDC

Clinical Drug Component (27)

S	oxyCODONE 10 MG
H Rx S	oxyCODONE 13.5 MG
H Rx S	oxyCODONE 18 MG
S	oxyCODONE 20 MG
H Rx S	oxyCODONE 27 MG

SCD/GPCK

Clinical Drug or Pack (71)

H Rx M	12 HR Acetaminophen 325 MG / oxyCODONE Hydrochloride 7.5 MG Extended Release Oral Tablet
M	12 HR Naloxone Hydrochloride 10 MG / oxyCODONE Hydrochloride 20 MG Extended Release Oral Tablet
M	12 HR Naloxone Hydrochloride 20 MG / oxyCODONE Hydrochloride 40 MG Extended Release Oral Tablet
M	12 HR Naloxone Hydrochloride 5 MG / oxyCODONE Hydrochloride 10 MG Extended Release Oral Tablet
M	12 HR Naltrexone hydrochloride 1.2 MG / oxyCODONE Hydrochloride 10 MG Extended Release Oral Capsule

SCDG

Clinical Dose Form Group (16)

H Rx M	Acetaminophen / oxyCODONE Oral Liquid Product
H Rx M	Acetaminophen / oxyCODONE Oral Product
H Rx M	Acetaminophen / oxyCODONE Pill
H Rx M	Aspirin / oxyCODONE Oral Product
H Rx M	Aspirin / oxyCODONE Pill

PIN

Precise Ingredient (2)

H Rx S	oxyCODONE Hydrochloride
H Rx S	oxyCODONE terephthalate



BN

Brand Name (17)

H Rx M	Endocet
H Rx M	Endodan Reformulated May 2009
H Rx S	Oxaydo
H Rx S	Oxecta
H Rx S	OxyCONTIN

SBDC

Branded Drug Component (44)

H Rx M	Acetaminophen 300 MG / oxyCODONE Hydrochloride 10 MG [Primlev]
H Rx M	Acetaminophen 300 MG / oxyCODONE Hydrochloride 5 MG [Primlev]
H Rx M	Acetaminophen 300 MG / oxyCODONE

SBD/BPCK

Branded Drug or Pack (44)

H Rx S	12 HR OxyCONTIN 10 MG Extended Release Oral Tablet
H Rx S	12 HR OxyCONTIN 15 MG Extended Release Oral Tablet
H Rx S	12 HR OxyCONTIN 20 MG Extended Release Oral Tablet

SBDG

Branded Dose Form Group (35)

H Rx M	Endocet Oral Product
H Rx M	Endocet Pill
H Rx M	Endodan Reformulated May 2009 Oral Product
H Rx M	Endodan Reformulated May 2009 Pill
H Rx S	Oxaydo Oral Product



String



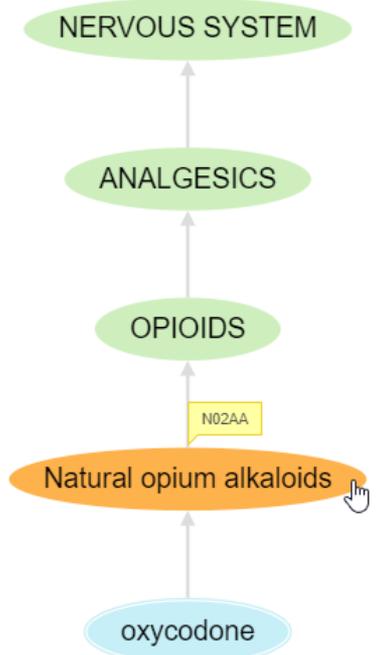
oxyCODONE [RxCUI = 7804]

- RxNorm Graph
- RxNorm Properties
- NDC
- RxTerms
- NDF-RT
- Pill Images
- Class View**
- Interaction View
- Status

Views

- ATC**
- MESH
- Drug
- Disease
- DF
- CHEM
- MoA
- PK
- PE

Hide Legend



Legend



How to link NDCs to RxNorm and ATC?

Identifying opioid drugs from a drug class

- ATC – Anatomical Therapeutic Chemical drug classification system



WHO Collaborating Centre for
Drug Statistics Methodology

News

ATC/DDD Index

Updates included in the
ATC/DDD Index

ATC/DDD methodology

ATC

DDD

ATC/DDD alterations,
cumulative lists

ATC/DDD Index and
Guidelines

Use of ATC/DDD

Courses

N NERVOUS SYSTEM

N02 **ANALGESICS**

N02A **OPIOIDS**

N02AA **Natural opium alkaloids**

N02AB **Phenylpiperidine derivatives**

N02AC **Diphenylpropylamine derivatives**

N02AD **Benzomorphan derivatives**

N02AE **Oripavine derivatives**

N02AF **Morphinan derivatives**

N02AG **Opioids in combination with antispasmodics**

N02AJ **Opioids in combination with non-opioid analgesics**

N02AX **Other opioids**

N02AA **Natural opium alkaloids**

ATC code Name

N02AA01 [morphine](#)

N02AA02 [opium](#)

N02AA03 [hydromorphone](#)

N02AA04 [nicomorphine](#)

N02AA05 [oxycodone](#)

N02AA08 [dihydrocodeine](#)

N02AA10 [papaveretum](#)

N02AA51 [morphine, combinations](#)

N02AA53 [hydromorphone and naloxone](#)

N02AA55 [oxycodone and naloxone](#)

N02AA56 [oxycodone and naltrexone](#)

N02AA58 [dihydrocodeine, combinations](#)

N02AA59 [codeine, combinations excl. psycholeptics](#)

N02AA79 [codeine, combinations with psycholeptics](#)

Issues: Obsolete NDCs

oxycodone [N02AA05]



oxyCODONE [7804]



*Abuse-Deterrent 12 HR oxyCODONE
Hydrochloride 10 MG Extended Release
Oral Tablet* [1860157]



*12 HR OxyCONTIN 10 MG Extended
Release Oral Tablet* [1049504]



4 Current NDCs

59011041010
43063035410
59011041020
43063035402

131 Obsolete NDCs

10544059120
10544059130
16590067710
16590067715
16590067720

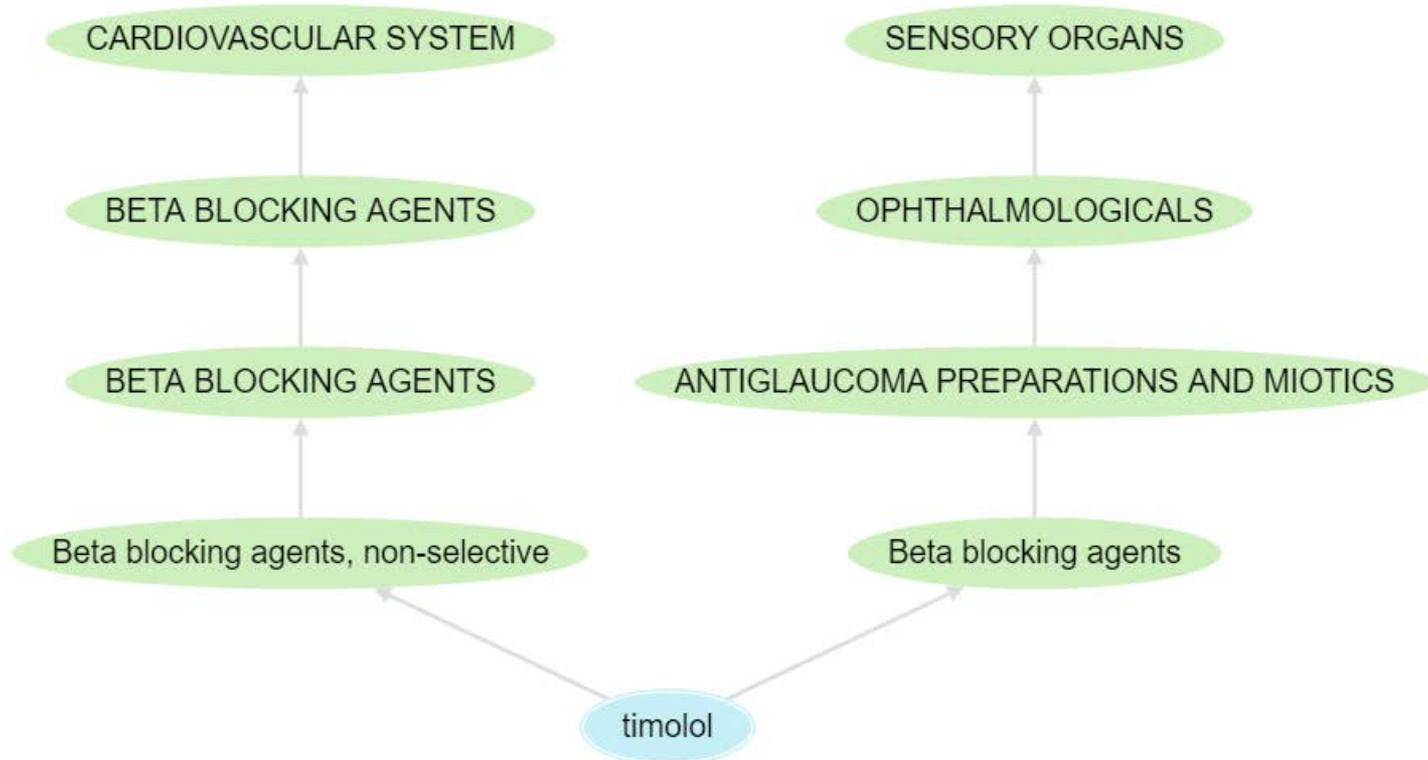
[...]

N NERVOUS SYSTEM					
N02 ANALGESICS					
N02A OPIOIDS					
N02AA Natural opium alkaloids					
ATC code	Name	DDD	U	Adm.R	Note
N02AA05	<u>oxycodone</u>	75	mg	O	
		30	mg	P	

*Obsolete NDCs can be queried
under Historical NDCs in RxNav*



Issues: Multiple ATC classes



RxClass follow-along activity

- Search for **OPIOIDS** in ATC
 - Navigate to the subclass **Natural opium alkaloids** (N02AA)
 - Explore the members of this class
- Click on **Oxycodone** to go to RxNav
 - Navigate to **12 HR OxyCONTIN 10 MG Extended Release Oral Tablet**
 - In the NDC tab, check Historical NDCs

<https://mor.nlm.nih.gov/RxClass/>

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 \(MoA\) \[from DailyMed\]](#)
- > [Physiologic Effect \(PE\) \[from DailyMed\]](#)
- > [Pharmacokinetics \(PK\)](#)
- > [VA Classes \(VA\)](#)



Class Name



ATC1-4

OPIOIDS

- Opioids in combination with antispasmodics
- Opioids in combination with non-opioid analgesics
- Other opioids

CHEM

- Receptors, Opioid (receptors, opioids)
- Receptors, Opioid, delta (receptors, delta opioids)
- Receptors, Opioid, kappa (receptors, kappa opioids)
- Receptors, Opioid, mu (receptors, mu opioids)

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- > GENITO URINARY SYSTEM AND SEX HORMONES (156)
- > MUSCULO-SKELETAL SYSTEM (124)
- > NERVOUS SYSTEM (413)
 - > ANALGESICS (66)
 - > ANTIMIGRAINE PREPARATIONS (16)
 - > OPIOIDS (28)
 - Benzomorphan derivatives (2)
 - Diphenylpropylamine derivatives (3)
 - Morphinan derivatives (2)
 - Natural opium alkaloids (8)
 - Opioids in combination with antispasmodics (0)
 - Opioids in combination with non-opioid analgesics (5)
 - Orpavine derivatives (1)
 - Other opioids (5)
 - Phenylpiperidine derivatives (2)
 - > OTHER ANALGESICS AND ANTIPYRETICS (22)
 - > ANESTHETICS (41)
 - > ANTI-PARKINSON DRUGS (27)
 - > ANTIEPILEPTICS (39)
 - > OTHER NERVOUS SYSTEM DRUGS (32)
 - > PSYCHOANALEPTICS (85)
 - > PSYCHOLEPTICS (130)
 - > RESPIRATORY SYSTEM (208)
 - > SENSORY ORGANS (167)
 - > SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES




 by class name/id

 by RxNorm drug name/id

 ingredient drug only

[Edit Drug Sources](#)

OPIOIDS

 class: **OPIOIDS** / id: **N02A** / class type: **ATC1-4** / [show context](#)

 28 RxNorm generic drugs in ATC / [similar classes](#)

Type	RXCUI	RxNorm Name	Relation	All classes
MIN	817579	Acetaminophen / Codeine	INDIRECT	Show
MIN	352362	Acetaminophen / Tramadol	INDIRECT	Show
MIN	135095	Aspirin / Codeine	INDIRECT	Show
IN	1819	Buprenorphine	INDIRECT	Show
IN	1841	Butorphanol	INDIRECT	Show
MIN	710303	Codeine / Ibuprofen	INDIRECT	Show
IN	3290	Dextromoramide	INDIRECT	Show
IN	22713	dezocine	INDIRECT	Show

- > GENITO URINARY SYSTEM AND SEX HORMONES (156)
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 - > SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES




 by class name/id

 by RxNorm drug name/id

 ingredient drug only

[Edit Drug Sources](#)

 class: **Natural opium alkaloids** / id: **N02AA** / class type: **ATC1-4** / [show context](#)


8 RxNorm generic drugs in ATC / similar classes

Type	RXCUI	RxNorm Name	Relation	All classes
IN	23088	dihydrocodeine	DIRECT	Show
IN	3423	Hydromorphone	DIRECT	Show
IN	7052	Morphine	DIRECT	Show
MIN	1545902	Naloxone / Oxycodone	DIRECT	Show
MIN	1806700	Naltrexone / Oxycodone	DIRECT	Show
IN	7676	Opium	DIRECT	Show
IN	7804	Oxycodone	DIRECT	Show
IN	7894	Papaveretum	DIRECT	Show

- > GENITO URINARY SYSTEM AND SEX HORMONES (157)
- > MUSCULO-SKELETAL SYSTEM (124)
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 - > PSYCHOANALEPTICS (85)
 - > PSYCHOLEPTICS (130)
 - > RESPIRATORY SYSTEM (209)
 - > SENSORY ORGANS (168)
 - > SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS (50)



Q

by class name/id
 by RxNorm drug name/id
 ingredient drug only
[Edit Drug Sources](#)

Natural opium alkaloids

class: **Natural opium alkaloids** / id: **N02AA** / class type: **ATC1-4** / [show context](#)



8 RxNorm generic drugs in ATC / similar classes

Type	RXCUI	RxNorm Name	Source Id	Source Name	Relation	All classes
IN	23088	dihydrocodeine	N02AA08	dihydrocodeine	DIRECT	Show
IN	3423	Hydromorphone	N02AA03	hydromorphone	DIRECT	Show
IN	7052	Morphine	N02AA01	morphine	DIRECT	Show
MIN	1545902	Naloxone / Oxycodone	N02AA55	oxycodone and naloxone	DIRECT	Show
MIN	1806700	Naltrexone / Oxycodone	N02AA56	oxycodone and naltrexone	DIRECT	Show
IN	7676	Opium	N02AA02	opium	DIRECT	Show
IN	7804	Oxycodone	N02AA05	oxycodone	DIRECT	Show
IN	7894	Papaveretum	N02AA10	papaveretum	DIRECT	Show

- > GENITO URINARY SYSTEM AND SEX HORMONES (157)
- > MUSCULO-SKELETAL SYSTEM (124)
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- > RESPIRATORY SYSTEM (209)
- > SENSORY ORGANS (168)
- > SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES




 by class name/id

 by RxNorm drug name/id

 ingredient drug only

[Edit Drug Sources](#)

 class: **Natural opium alkaloids** / id: **N02AA** / class type: **ATC1-4** / [show context](#)


8 RxNorm generic drugs in ATC / similar classes

Type	RXCUI	RxNorm Name	Source Id	Source Name	Relation	All classes
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MIN	1806700	Naltrexone / Oxycodone	N02AA56	oxycodone and naltrexone	DIRECT	Show
IN	7676	Opium	N02AA02	opium	DIRECT	Show
IN	7894	Oxycodone	N02AA05	oxycodone	DIRECT	Show
IN	7894	Papaveretum	N02AA10	papaveretum	DIRECT	Show





oxyCODONE [RxCUI = 7804]

- RxNorm Graph
- RxNorm Properties**
- NDC
- RxTerms
- NDF-RT
- Pill Images
- Class View
- Interaction View
- Status

Views

- Classic**
- Simple
- Table

Filters

- H
- V
- Rx
- S
- Group
- Form

Links



Legend

- MIN
- Pack
- Multi

[Download](#)

IN/MIN	Ingredient (6)
H Rx S	oxyCODONE
M H Rx M	Acetaminophen / oxyCODONE
M H Rx M	Aspirin / oxyCODONE
M H Rx M	Ibuprofen / oxyCODONE
M	Naloxone / oxyCODONE

SCDC	Clinical Drug Component (27)
S	oxyCODONE 10 MG
H Rx S	oxyCODONE 13.5 MG
H Rx S	oxyCODONE 18 MG
S	oxyCODONE 20 MG
H Rx S	oxyCODONE 27 MG

SCD/GPCK	Clinical Drug or Pack (71)
H Rx M	12 HR Acetaminophen 325 MG / oxyCODONE Hydrochloride 7.5 MG Extended Release Oral Tablet
M	12 HR Naloxone Hydrochloride 10 MG / oxyCODONE Hydrochloride 20 MG Extended Release Oral Tablet
M	12 HR Naloxone Hydrochloride 20 MG / oxyCODONE Hydrochloride 40 MG Extended Release Oral Tablet
M	12 HR Naloxone Hydrochloride 5 MG / oxyCODONE Hydrochloride 10 MG Extended Release Oral Tablet
M	12 HR Naltrexone hydrochloride 1.2 MG / oxyCODONE Hydrochloride 10 MG Extended Release Oral Capsule

SCDG	Clinical Dose Form Group (16)
H Rx M	Acetaminophen / oxyCODONE Oral Liquid Product
H Rx M	Acetaminophen / oxyCODONE Oral Product
H Rx M	Acetaminophen / oxyCODONE Pill
H Rx M	Aspirin / oxyCODONE Oral Product

PIN	Precise Ingredient (2)
H Rx S	oxyCODONE Hydrochloride
H Rx S	oxyCODONE terephthalate



DFG	Dose Form Group (5)
HV Rx S	Injectable Product
HV Rx S	Oral Liquid Product
HV Rx S	Oral Product
HV Rx S	Pill
HV Rx S	Rectal Product

BN	Brand Name (17)
H Rx M	Endocet
H Rx M	Endodan Reformulated May 2009
H Rx S	Oxaydo
H Rx S	Oxecta
H Rx S	OxyCONTIN

SBDC	Branded Drug Component (44)
H Rx M	Acetaminophen 300 MG / oxyCODONE Hydrochloride 10 MG [Primlev]
H Rx M	Acetaminophen 300 MG / oxyCODONE Hydrochloride 5 MG [Primlev]
H Rx M	Acetaminophen 300 MG / oxyCODONE

SBD/BPCK	Branded Drug or Pack (44)
H Rx S	12 HR OxyCONTIN 10 MG Extended Release Oral Tablet
H Rx S	12 HR OxyCONTIN 15 MG Extended Release Oral Tablet
H Rx S	12 HR OxyCONTIN 20 MG Extended Release

SBDG	Branded Dose Form Group (35)
H Rx M	Endocet Oral Product
H Rx M	Endocet Pill
H Rx M	Endodan Reformulated May 2009 Oral Product
H Rx M	Endodan Reformulated May 2009 Pill
H Rx S	Oxaydo Oral Product





12 HR OxyCONTIN 10 MG Extended Release Oral Tablet [RxCUI = 1049504]

- RxNorm Graph
- RxNorm Properties
- NDC
- RxTerms
- NDF-RT
- Pill Images
- Class View
- Interaction View
- Status

Views

- Classic
- Simple
- Table

Filters

- H
- V
- Rx
- S
- Group
- Form

Links



Legend

- MIN
- Pack
- Multi

Download

IN/MIN	Ingredient (1)
H Rx S	oxyCODONE

PIN	Precise Ingredient (1)
H Rx S	oxyCODONE Hydrochloride

BN	Brand Name (1)
H Rx S	OxyCONTIN

SCDC	Clinical Drug Component (1)
H Rx SM	oxyCODONE Hydrochloride 10 MG



SBDC	Branded Drug Component (1)
H Rx S	oxyCODONE Hydrochloride 10 MG [OxyCONTIN]

SCD/GPCK	Clinical Drug or Pack (1)
H Rx S	Abuse-Deterrent 12 HR oxyCODONE Hydrochloride 10 MG Extended Release Oral Tablet

SBD/BPCK	Branded Drug or Pack (1)
H Rx S	12 HR OxyCONTIN 10 MG Extended Release Oral Tablet

SCDG	Clinical Dose Form Group (2)
H Rx S	oxyCODONE Oral Product
H Rx S	oxyCODONE Pill

DFG	Dose Form Group (2)
HV Rx S	Oral Product
HV Rx S	Pill

SBDG	Branded Dose Form Group (2)
H Rx S	OxyCONTIN Oral Product
H Rx S	OxyCONTIN Pill



String

Abuse-Deterrent 12 HR Oxycodone Hydro

 **12 HR OxyCONTIN 10 MG Extended Release Oral Tablet** [RxCUI = 1049504]

RxNorm Graph

RxNorm Properties

NDC

RxTerms

NDF-RT

Pill Images

Class View

Interaction View

Status

Views

Current NDC

Historical
NDC

Download

RxCui	Status	NDC11	Start Date	End Date	Current
211692	indirect	10544059120	201003	201012	No
211692	indirect	10544059130	201003	201012	No
211692	indirect	16590067772	200903	201012	No
211692	indirect	48692003010	200706	201012	No
211692	indirect	48692003020	200706	201012	No
211692	indirect	48692003025	200706	201012	No
211692	indirect	48692060010	200706	201012	No
211692	indirect	48692060025	200706	201012	No
211692	indirect	48692060030	200706	201012	No
211692	indirect	48692061010	200706	201012	No
211692	indirect	48692061030	200706	201012	No
211692	indirect	48692062010	200706	201012	No
211692	indirect	48692062012	200706	201012	No
211692	indirect	48692062030	200706	201012	No
211692	indirect	48692069030	200706	201012	No
211692	indirect	48692088010	200706	201012	No
211692	indirect	48692088025	200706	201012	No
211692	indirect	54868381300	200706	201012	No
211692	indirect	54868381301	200706	201012	No
211692	indirect	54868381302	200706	201012	No
211692	indirect	54868381303	200709	201012	No

Calculating the daily dose in oral morphine milligram equivalent

Why converting to MME?

- Opioids have widely different potency levels
 - Fentanyl is about 100 times more potent than morphine
- Difficult to
 - Compare doses across drugs
 - Compare doses over time for multiple drugs
 - Aggregate results
- Reference: 1 mg of morphine administered orally
- Use case: How do these two drugs compare?
 - *12 HR OxyCONTIN 10 MG Extended Release Oral Tablet* (twice a day)
 - *72 HR fentaNYL 0.012 MG/HR Transdermal System*

MME conversion factor

<https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Opioid-Morphine-EQ-Conversion-Factors-Aug-2017.pdf>

- Conversion factor for each drug
 - Available from CMS
 - Compiled from CDC data

Opioid Oral Morphine Milligram Equivalent (MME) Conversion Factors^{1,2}

<u>Type of Opioid (strength units)</u>	<u>MME Conversion Factor</u>
Buprenorphine film/tablet ³ (mg)	30
Buprenorphine patch ⁴ (mcg/hr)	12.6
Buprenorphine film (mcg)	0.03
Butorphanol (mg)	7
Codeine (mg)	0.15
Dihydrocodeine (mg)	0.25
Fentanyl buccal or SL tablets, or lozenge/troche ⁵ (mcg)	0.13
Fentanyl film or oral spray ⁶ (mcg)	0.18
Fentanyl nasal spray ⁷ (mcg)	0.16
Fentanyl patch ⁸ (mcg)	7.2
Hydrocodone (mg)	1
Hydromorphone (mg)	4

Levorphanol tartrate (mg)	11
Meperidine hydrochloride (mg)	0.1
Methadone ⁹ (mg)	3
>0, <= 20	4
>20, <=40	8
>40, <=60	10
>60	12
Morphine (mg)	1
Opium (mg)	1
Oxycodone (mg)	1.5
Oxymorphone (mg)	3
Pentazocine (mg)	0.37
Tapentadol ¹⁰ (mg)	0.4
Tramadol (mg)	0.1



Issues

- MME/day requires computation of the daily dose from
 - Quantity Dispensed
 - Days Supply
 - Strength (+ quantity factor in some cases)
- Some drugs are not covered (no longer on the market)
 - See earlier references for Nalbuphine and Propoxyphene
- Conversion is relatively straightforward in most cases, but
 - Transdermal systems
 - Conversion for strength in micrograms
 - But strength in mg in RxNorm
 - Conversion accounts for the duration of the patch
 - But only the concentration strength (+ duration) is provided in RxNorm
 - Injectables
 - Use presentation strength, not concentration strength as in RxNorm

Example #1

- Drug: NDC = 59011041010
 - 12 HR OxyCONTIN 10 MG Extended Release Oral Tablet [1049504]
 - Ingredient: Oxycodone
 - Strength: 10 MG
- Dispensation information
 - Quantity Dispensed: 20
 - Days Supply: 10
- MME conversion factor: 1.5

- MME/day: $MME(mg) = 10 * \frac{20}{10} * 1.5 = 30 mg$

Example #2

- Drug: NDC = 00781724055
 - 72 HR fentaNYL 0.012 MG/HR Transdermal System [577057]
 - Ingredient: Fentanyl
 - (Concentration) strength: 0.012 MG/HR
 - Quantity factor: 72 HR
- Dispensation information
 - Quantity Dispensed: 4
 - Days Supply: 12
- MME conversion factor*: 100 (1 mg parenteral Fentanyl = 100 mg oral Morphine)

- MME/day: $MME(mg) = 72 * 0.012 * \frac{4}{12} * 100 = 28.8 mg$



Discussion of (preliminary) results from larger-scale analysis

Our MEDICARE dataset

- 20% random sample of Part D enrollees
 - 10.7 million beneficiaries (patients)
 - ~2.3 billion prescriptions
- Continuous enrollment (no gaps) between initial enrollment and end of study (death or 12/31/2015)
 - Required for outcomes research
 - 4.9 million beneficiaries (> 50% loss)
 - ~1 billion prescriptions
 - 41 million opioid prescriptions



Opioids in ATC

- NDC codes -> RxNorm -> ATC classes
- 3 ATC classes
 - **N02A OPIOIDS**
 - N07BC Drugs used in opioid dependence
 - N01AH Opioid anesthetics
 - R05DA Opium alkaloids and derivatives [Respiratory system*]

Opioids present in the Medicare dataset

BUPRENORPHINE
BUTORPHANOL
CODEINE
DIHYDROCODEINE
FENTANYL
HYDROCODONE
HYDROMORPHONE
MEPERIDINE (PETHIDINE)
METHADONE
MORPHINE
NALBUPHINE
OPIUM
OXYCODONE
PENTAZOCINE
PROPOXYPHENE (DEXTROP.)
TAPENTADOL
TRAMADOL

N NERVOUS SYSTEM

N02 **ANALGESICS**

N02A **OPIOIDS**

N02AA **Natural opium alkaloids**

N02AB **Phenylpiperidine derivatives**

N02AC **Diphenylpropylamine derivatives**

N02AD **Benzomorphan derivatives**

N02AE **Oripavine derivatives**

N02AF **Morphinan derivatives**

N02AG **Opioids in combination with antispasmodics**

N02AJ **Opioids in combination with non-opioid analgesics**

N02AX **Other opioids**

N NERVOUS SYSTEM

N01 **ANESTHETICS**

N01A **ANESTHETICS, GENERAL**

N01AH **Opioid anesthetics**

★ ATC code	Name
N01AH01	fentanyl
N01AH02	alfentanil
N01AH03	sufentanil
N01AH04	phenoperidine
N01AH05	anileridine
N01AH06	remifentanil
N01AH51	fentanyl, combinations

N NERVOUS SYSTEM

N07 **OTHER NERVOUS SYSTEM DRUGS**

N07B **DRUGS USED IN ADDICTIVE DISORDERS**

N07BC **Drugs used in opioid dependence**

★ ATC code	Name	DDD
N07BC01	buprenorphine	8
N07BC02	methadone	25
N07BC03	levacetylmethadol	25
N07BC04	lofexidine	1.4
N07BC05	levomethadone	
N07BC06	diamorphine	
N07BC51	buprenorphine, combinations	8

R RESPIRATORY SYSTEM

R05 **COUGH AND COLD PREPARATIONS**

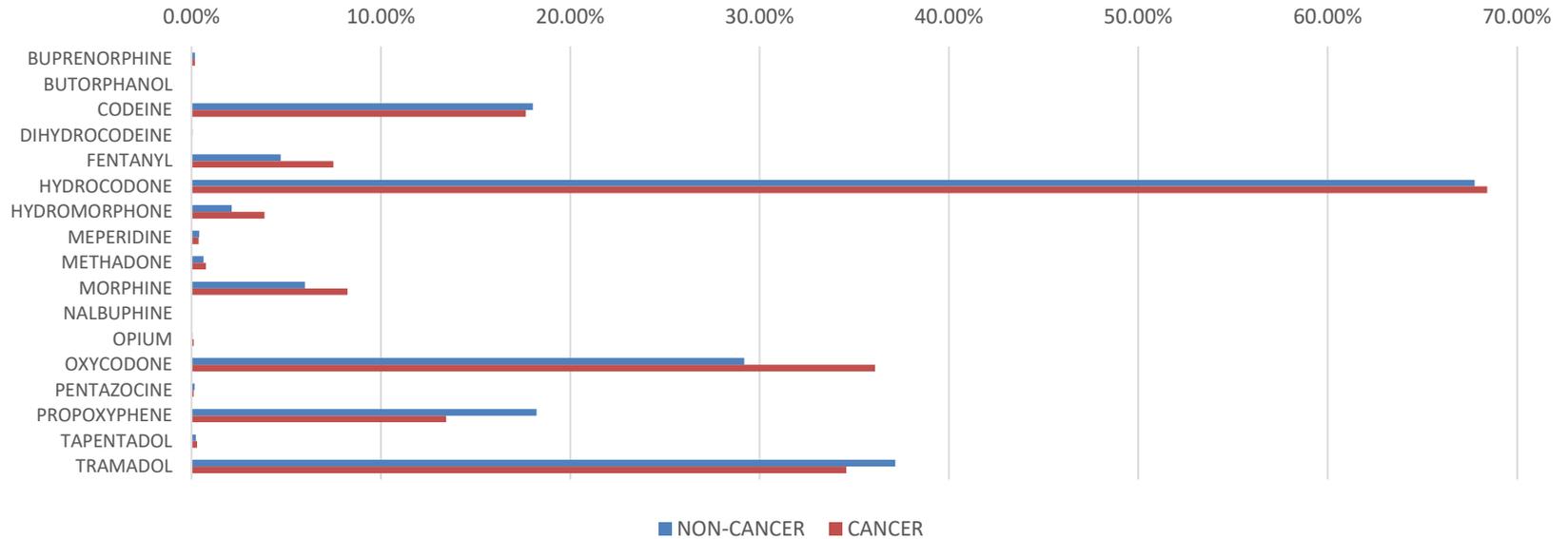
R05D **COUGH SUPPRESSANTS, EXCL. COMBINATIONS**

R05DA **Opium alkaloids and derivatives**

★ ATC code	Name
R05DA01	ethylmorphine
R05DA03	hydrocodone
R05DA04	codeine
R05DA05	opium alkaloids with morphine
R05DA06	normethadone
R05DA07	noscapine
R05DA08	pholcodine
R05DA09	dextromethorphan
R05DA10	thebacin
R05DA11	dimemorfan
R05DA12	acetyldihydrocodeine
R05DA20	combinations

Opioid prescriptions

Proportion of patients with opioid prescription (by drug)

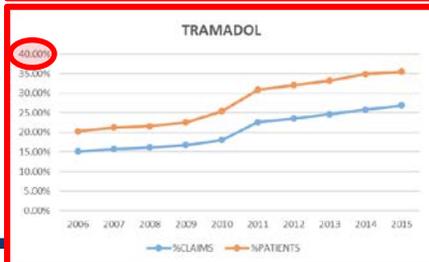
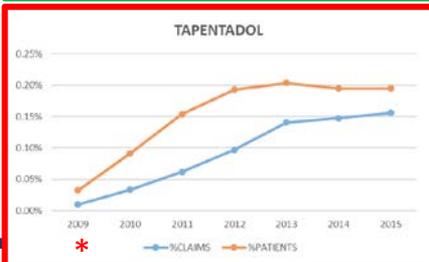
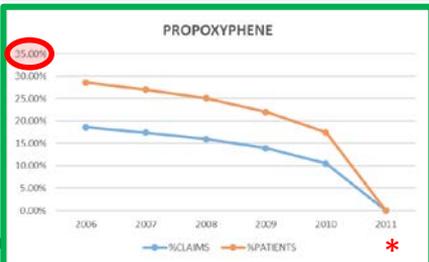
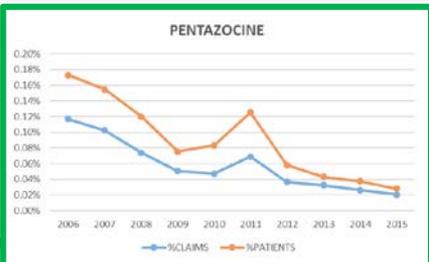
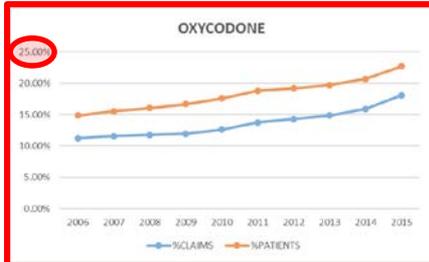
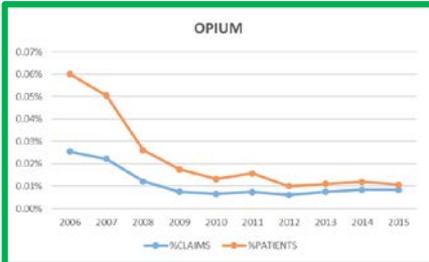
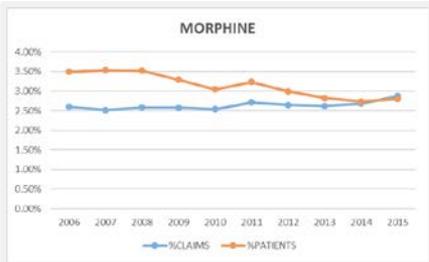
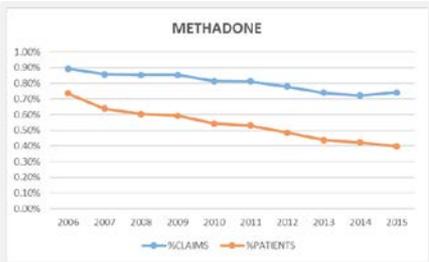
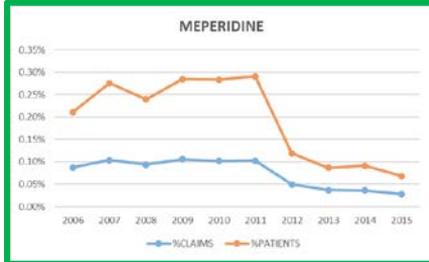
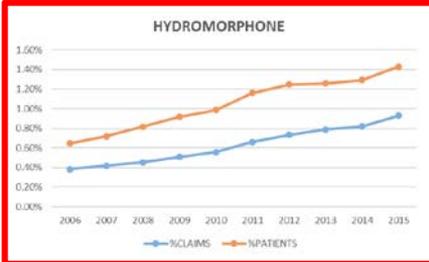
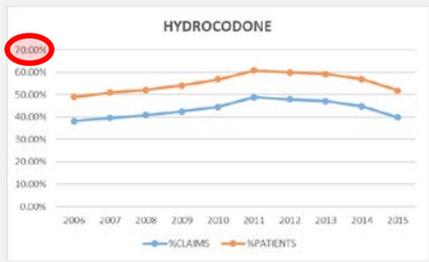
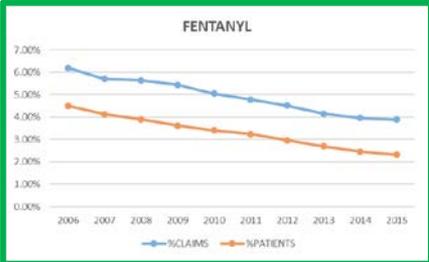
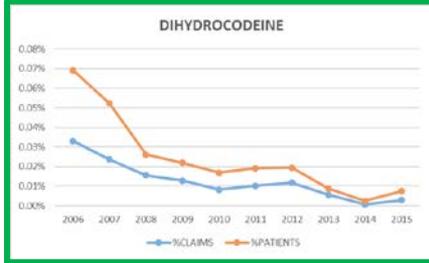
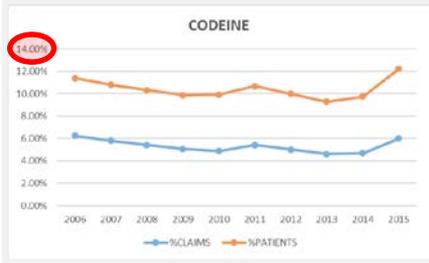
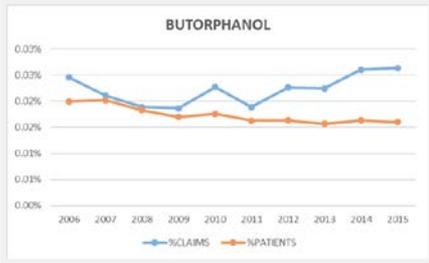
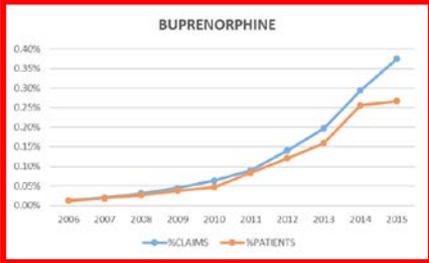


28,871,494 claims
2,436,397 patients

11,504,312 claims
1,118,652 patients

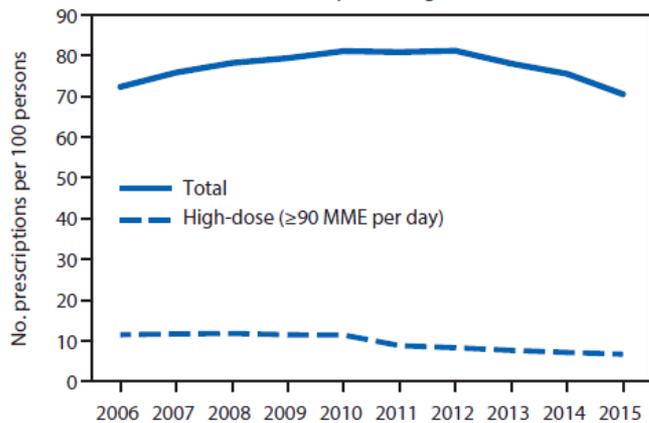
* 856,656 claims
post-ODU excluded



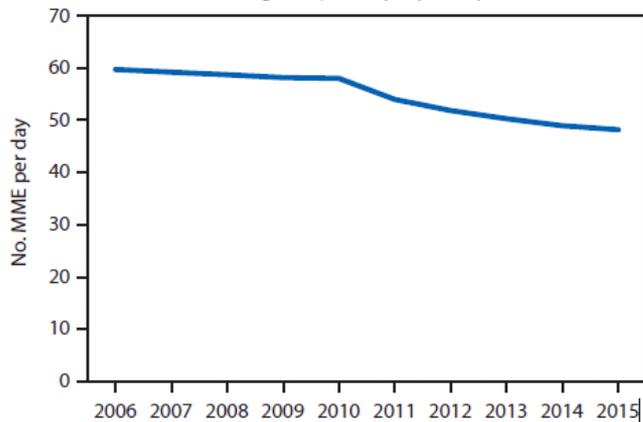


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Annual prescribing rate

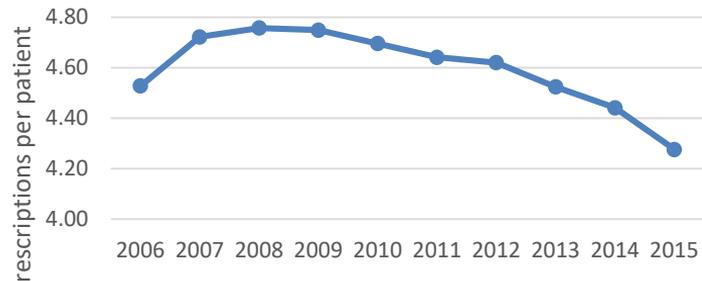


Average daily MME per prescription

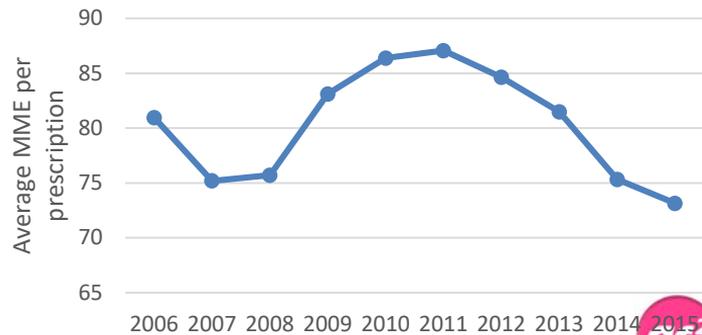


Medicare data

Annual prescribing rate
[among opioid patients]



Average daily MME per prescription



KEY TAKEAWAYS

1) DRUG ANALYTICS

are a key element of current healthcare analytics efforts and are facilitated by the availability of datasets (e.g., Medicare Part D) and tooling (e.g., RxNav, RxClass).

2) PHARMACISTS

can/should be involved in drug analytics, not only by providing domain expertise, but in doing some of the informatics work (“pharmacoinformatics”).



Self-Assessment Question 1

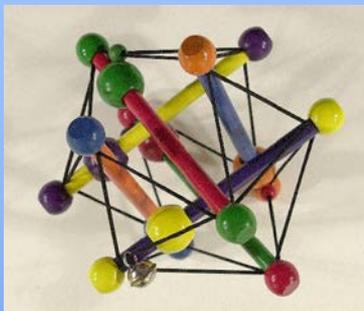
- Which type of information can be found in claims data, such as Medicare Part D dataset?
 - A. Patient name and address
 - B. ATC class (from the Anatomical Therapeutic Chemical drug classification)
 - C. “NDC codes” (from the National Drug Code directory)
 - D. Days supply
 - E. Quantity dispensed

Self-Assessment Question 2

- TRUE/FALSE: Medications can belong to only one ATC class?
 - A. True
 - B. False

Self-Assessment Question 3

- Conversion to oral morphine milligram equivalent
 - A. Enables comparison between daily doses of opioid drugs
 - B. Can be done by multiplying the unit strength by a factor, regardless of the dose form
 - C. Is required for characterizing the global evolution of opioid doses over time
 - D. Is required for characterizing differences in opioid doses dispensed across geographic areas



Medical Ontology Research



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