DUR Board Meeting
September 5, 2018
Brynhild Haugland Room

North Dakota Medicaid
DUR Board Meeting Agenda
Brynhild Haugland Room
State Capitol
600 East Boulevard Avenue
Bismarck, ND
September 5, 2018
1:00 pm

1. Administrative items
    - Travel vouchers

2. Old business
    - Review and approval of 06/2018 meeting minutes
    - Budget update
    - Review top 15 therapeutic categories/top 25 drugs
    - Prior authorization/PDL update
    - Second review of Daxbia
    - Second review of dermatophytosis (Tinea infections) agents
    - Second review of eosinophilic asthma agents
    - Second review of migraine prophylaxis (CGRP Inhibitors)
    - Second review of Millipred DP
    - Second review of Rytary
    - Sanford Update

3. New business
    - Review of glyburide and Avandia
    - Review of Lucemyra
    - Review of Palynziq
    - Review of Roxybond
    - Review of Siklos
    - Utilization review of concomitant sedative/hypnotic and benzodiazepine agents
    - Update on CAR T-cell Therapies
    - Retrospective DUR criteria recommendations
    - Upcoming meeting date/agenda.
        - Next meeting is December 5, 2018 in the Lecture Room A of the Heritage Center

4. Adjourn

Please remember to silence all cellular phones during the meeting.

Drug Utilization Review (DUR) Meeting Minutes
June 6, 2018

Members Present: Katie Kram, Tanya Schmidt, Zach Marty, LeNeika Roehrich, Andrea Honeyman, Carlotta McCleary, Peter Woodrow, Jeffrey Hostetter

Members Absent: Gaylord Kavlie, Laura Schield, Michael Quast, Michael Booth, Wendy Brown, Russ Sobotta

Medicaid Pharmacy Department: Brendan Joyce, Alexi Murphy, Gary Betting

Old Business

T. Schmidt served as Chair in the absence of W. Brown, and called the meeting to order at 1:00 p.m. Chair T. Schmidt asked for a motion to approve the minutes of the March meeting. K. Kram moved that the minutes be approved and L. Roehrich seconded the motion. Chair T. Schmidt called for a voice vote to approve the minutes. The motion passed with no audible dissent.

Review Top 15 Therapeutic Categories/Top 25 Drugs

B. Joyce presented the quarterly review of the top 15 therapeutic classes by total cost of claims, top 25 drugs based on number of claims, and top 25 drugs based on claims cost for the 1st quarter of 2018.

PDL Update

A. Murphy shared with the Board all of changes made to the Preferred Drug List since the most recent 2018 version of the Preferred Drug List was posted. Changes included classifying Epipen (epinephrine) and Epipen Jr (epinephrine) as preferred agents, ritonavir, Azasite (azithromycin), and Advair HFA (fluticasone/salmeterol) being classified as a non-preferred agents, and PDL category criteria updates to hepatitis C treatments and for partial opioid antagonists for opioid dependence.

Second Review of Chemotherapy Induced Nausea and Vomiting Agents

A motion and second was made at the March meeting to place the chemotherapy induced nausea and vomiting agents, Anzemet and Zuplenz on prior authorization along with other agents used for the treatment of chemotherapy induced nausea and vomiting. The topics were brought up for a second review. There was no public comment. A motion to approve amended form and prior authorization criteria was made by K. Kram and seconded by J. Hostetter. Chair T. Schmidt called for a voice vote and the motion passed with no audible dissent.

Second Review of Biosimilar Agents

A motion and second was made at the March meeting to generate prior authorization criteria for biosimilar agents. The topic was brought up for a second review. There was no public comment. Chair T. Schmidt called for a voice vote and the motion passed with no audible dissent.

Second Review of Topical Corticosteroid Agents

A motion and second was made at the March meeting to place non-preferred topical corticosteroid agents on prior authorization. The topics were brought up for a second review. There was no public comment. Chair T. Schmidt called for a voice vote and the motion passed with no audible dissent.

Second Review of Dupixent
A motion and second was made at the March meeting to place Dupixent on prior authorization. The topics were brought up for a second review. Chair T. Schmidt called for a voice vote and the motion passed with no audible dissent.

Second Review of Gocovri and Tussicaps (Non-Preferred Dosage Forms)
A motion and second was made at the March meeting to place Eucrisa on prior authorization. The topics were brought up for a second review. There was no public comment. Chair T. Schmidt called for a voice vote and the motion passed with no audible dissent.

Discussion of First Fill of Narcotics
B. Joyce presented information on national quality measure updates regarding first fills of narcotics. These measures will require the first fill of narcotics to be for a 7 day supply or less, which will result in North Dakota Medicaid adjusting the claims processing edit for first fills of narcotics from a limit of 14 days to 7 days. The Board vocalized no issues with this change.

New Business

Rytary
T. DeRuiter and A. Murphy reviewed Rytary with the Board. A motion was made by K. Kram to create this new PA criteria class and manage these medications through prior authorization. The motion was seconded by J. Hostetter. This topic will be reviewed at the next meeting

Daxbia
T. DeRuiter and A. Murphy reviewed Daxbia with the Board. A motion was made by K. Kram to manage the medications through prior authorization. The motion was seconded by L. Roehrich. This topic will be reviewed at the next meeting

Millipred DP
T. DeRuiter and B. Joyce reviewed Millipred DP with the Board. A motion was made by J. Hostetter to manage the medication through prior authorization. The motion was seconded by P. Woodrow. This topic will be reviewed at the next meeting

Eosinophilic Asthma Agents
T. DeRuiter and B. Joyce reviewed the eosinophilic asthma agents Cinqair, Fasenra, and Nucala with the Board. Ted Sheedy of GlaxoSmithKline spoke regarding clinical trial data of Nucala. A motion was made by K. Kram to manage the medication through prior authorization. The motion was seconded by J. Hostetter. This topic will be reviewed at the next meeting

Dermatophytosis (Tinea infections) Agents
T. DeRuiter and B. Joyce reviewed agents used for the treatment of tinea infections with the Board. A motion was made by P. Woodrow to manage the medication through prior authorization. The motion was seconded by K. Kram. This topic will be reviewed at the next meeting

Migraine Prophylaxis (CGRP Inhibitors)

T. DeRuiter and B. Joyce reviewed the class of CGRP inhibitors for migraine prophylaxis with the Board. A motion was made by K. Kram to manage the medication through prior authorization. The motion was seconded by J. Hostetter. This topic will be reviewed at the next meeting

Review of GLP-1 Receptor Agonist Utilization

T. DeRuiter and B. Joyce reviewed the utilization of GLP-1 receptor agonist agents with the Board. The presented information showed utilization of the available GLP-1 receptor agonists during the 1st quarter 2018 as compared to the utilization of the same agents during 3rd quarter 2017. The data was presented in terms of number of monthly prescriptions for and number of patients receiving each GLP-1 receptor agonist.

Medication Therapy Management (MTM) Program Update

A. Murphy updated the Board on the status of the state MTM program. The Board was informed that the program would be starting up within the next few months and will focus on proper use of inhaled asthma products, compliance with mental health medications, diabetes treatment, and transitioning care between inpatient and outpatient facilities.

Retrospective Drug Utilization Review (RDUR) Criteria Recommendations

The recommended RDUR criteria enclosed in the packet were developed from product information provided by the manufacturers and are usually consistent with new indications, new drugs added, and new warnings. These proposed criteria will be added to the current set of criteria and will be used in future DUR cycles. J. Hostetter moved to approve the new criteria and K. Kram seconded the motion. The motion passed with no audible dissent.

Adjournment and Upcoming Meeting Date

J. Hostetter moved to adjourn the meeting at and K. Kram seconded. Chair T. Schmidt adjourned the meeting at 2:35 pm. The next DUR Board meeting will be held September 5, 2018 at 1:00 pm in the Brynhild Haugland Room at the State Capitol.

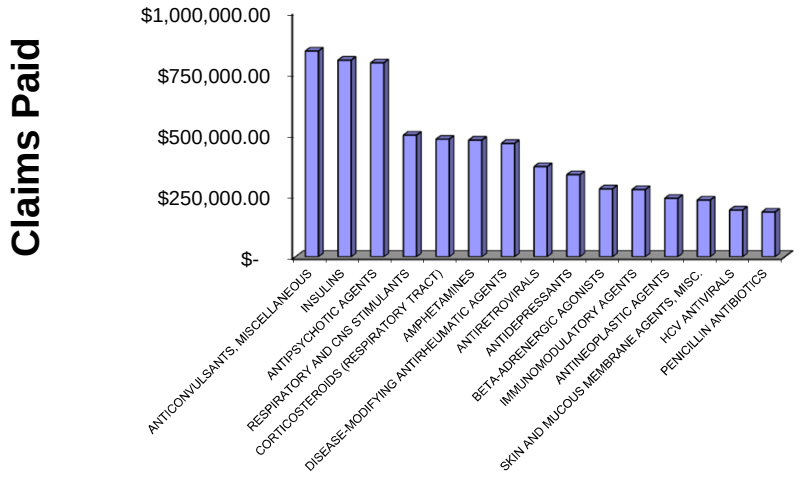
NORTH DAKOTA MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 04/01/2018 - 06/30/2018

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTICONVULSANTS, MISCELLANEOUS	8,294	$ 840,324.50	$ 101.32	5.94%
INSULINS	1,789	$ 803,137.88	$ 448.93	1.28%
ANTIPSYCHOTIC AGENTS	6,326	$ 792,155.56	$ 125.22	4.53%
RESPIRATORY AND CNS STIMULANTS	3,731	$ 497,602.56	$ 133.37	2.67%
CORTICOSTEROIDS (RESPIRATORY TRACT)	1,958	$ 481,136.71	$ 245.73	1.40%
AMPHETAMINES	3,063	$ 477,427.20	$ 155.87	2.19%
DISEASE-MODIFYING ANTIRHEUMATIC AGENTS	125	$ 463,945.45	$ 3,711.56	0.09%
ANTIRETROVIRALS	516	$ 368,969.53	$ 715.06	0.37%
ANTIDEPRESSANTS	14,776	$ 335,901.08	$ 22.73	10.57%
BETA-ADRENERGIC AGONISTS	3,376	$ 278,095.81	$ 82.37	2.42%
IMMUNOMODULATORY AGENTS	41	$ 275,118.58	$ 6,710.21	0.03%
ANTINEOPLASTIC AGENTS	269	$ 239,282.44	$ 889.53	0.19%
SKIN AND MUCOUS MEMBRANE AGENTS, MISC.	255	$ 232,218.06	$ 910.66	0.18%
HCV ANTIVIRALS	12	$ 191,481.60	$ 15,956.80	0.01%
PENICILLIN ANTIBIOTICS	4,152	$ 183,253.77	$ 44.14	2.97%
Total Top 15	48,683	$ 6,460,050.73	$ 132.70	34.84%

Total Rx Claims From 04/01/2018 - 06/30/2018	139,731

Top 15 Therapeutic Classes
Based on Total Cost of Claims

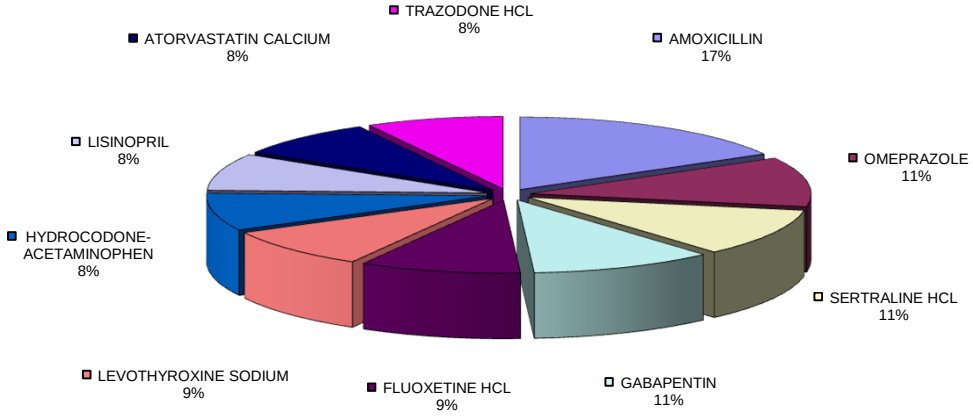


TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 04/01/2018 - 06/30/2018

Drug	AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
AMOXICILLIN	PENICILLIN ANTIBIOTICS	4,080	$ 150,202.46	$ 36.81	2.92%
OMEPRAZOLE	PROTON-PUMP INHIBITORS	2,678	$ 52,547.58	$ 19.62	1.92%
SERTRALINE HCL	ANTIDEPRESSANTS	2,565	$ 49,749.76	$ 19.40	1.84%
GABAPENTIN	ANTICONVULSANTS, MISCELLANEOUS	2,561	$ 91,351.90	$ 35.67	1.83%
FLUOXETINE HCL	ANTIDEPRESSANTS	2,248	$ 32,970.94	$ 14.67	1.61%
LEVOTHYROXINE SODIUM	THYROID AGENTS	2,161	$ 42,123.65	$ 19.49	1.55%
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	2,021	$ 62,192.87	$ 30.77	1.45%
LISINOPRIL	ANGIOTENSIN-CONVERTING ENZYME INHIBITORS	1,998	$ 46,065.99	$ 23.06	1.43%
ATORVASTATIN CALCIUM	HMG-COA REDUCTASE INHIBITORS	1,998	$ 55,173.27	$ 27.61	1.43%
TRAZODONE HCL	ANTIDEPRESSANTS	1,924	$ 29,229.52	$ 15.19	1.38%
MONTELUKAST SODIUM	LEUKOTRIENE MODIFIERS	1,881	$ 34,512.03	$ 18.35	1.35%
METHYLPHENIDATE ER	RESPIRATORY AND CNS STIMULANTS	1,849	$ 327,065.34	$ 176.89	1.32%
VYVANSE	AMPHETAMINES	1,689	$ 374,960.52	$ 222.00	1.21%
ALBUTEROL SULFATE	BETA-ADRENERGIC AGONISTS	1,673	$ 78,095.31	$ 46.68	1.20%
ESCITALOPRAM OXALATE	ANTIDEPRESSANTS	1,637	$ 32,032.49	$ 19.57	1.17%
CLONIDINE HCL	CENTRAL ALPHA-AGONISTS	1,630	$ 29,855.46	$ 18.32	1.17%
AZITHROMYCIN	MACROLIDE ANTIBIOTICS	1,630	$ 43,901.87	$ 26.93	1.17%
METFORMIN HCL	BIGUANIDES	1,533	$ 22,449.21	$ 14.64	1.10%
AMOXICILLIN-CLAVULANATE POTASS	PENICILLIN ANTIBIOTICS	1,495	$ 59,181.40	$ 39.59	1.07%
OSELTAMIVIR PHOSPHATE	NEURAMINIDASE INHIBITOR ANTIVIRALS	1,468	$ 160,909.80	$ 109.61	1.05%
PROAIR HFA	BETA-ADRENERGIC AGONISTS	1,406	$ 112,504.25	$ 80.02	1.01%
RISPERIDONE	ANTIPSYCHOTIC AGENTS	1,360	$ 19,732.39	$ 14.51	0.97%
QUETIAPINE FUMARATE	ANTIPSYCHOTIC AGENTS	1,347	$ 25,352.12	$ 18.82	0.96%
VITAMIN D3	VITAMIN D	1,333	$ 20,330.15	$ 15.25	0.95%
LAMOTRIGINE	ANTICONVULSANTS, MISCELLANEOUS	1,302	$ 19,337.12	$ 14.85	0.93%
TOTAL TOP 25		47,467	$ 1,971,827.40	$ 41.54	33.97%

Total Rx Claims From 04/01/2018 - 06/30/2018	139,731

Top 10 Drugs
Based on Number of Claims

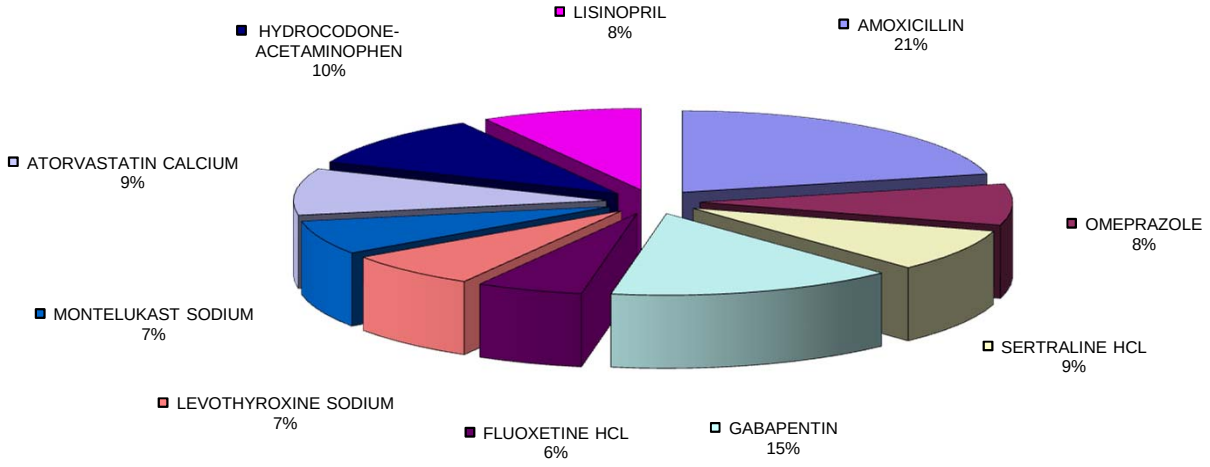


TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 04/01/2018 - 06/30/2018

Drug	AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
AMOXICILLIN	PENICILLIN ANTIBIOTICS	2,788	$ 122,517.84	$ 43.94	2.00%
OMEPRAZOLE	PROTON-PUMP INHIBITORS	2,579	$ 46,713.49	$ 18.11	1.85%
SERTRALINE HCL	ANTIDEPRESSANTS	2,553	$ 48,364.92	$ 18.94	1.83%
GABAPENTIN	ANTICONVULSANTS, MISCELLANEOUS	2,408	$ 85,100.37	$ 35.34	1.72%
FLUOXETINE HCL	ANTIDEPRESSANTS	2,157	$ 31,575.27	$ 14.64	1.54%
LEVOTHYROXINE SODIUM	THYROID AGENTS	2,137	$ 40,278.25	$ 18.85	1.53%
MONTELUKAST SODIUM	LEUKOTRIENE MODIFIERS	2,005	$ 38,657.95	$ 19.28	1.43%
ATORVASTATIN CALCIUM	HMG-COA REDUCTASE INHIBITORS	2,002	$ 52,858.42	$ 26.40	1.43%
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	1,932	$ 59,411.72	$ 30.75	1.38%
LISINOPRIL	ANGIOTENSIN-CONVERTING ENZYME INHIBITORS	1,907	$ 47,448.92	$ 24.88	1.36%
TRAZODONE HCL	ANTIDEPRESSANTS	1,871	$ 26,692.90	$ 14.27	1.34%
METHYLPHENIDATE ER	RESPIRATORY AND CNS STIMULANTS	1,671	$ 296,224.81	$ 177.27	1.20%
ESCITALOPRAM OXALATE	ANTIDEPRESSANTS	1,549	$ 32,211.08	$ 20.79	1.11%
METFORMIN HCL	BIGUANIDES	1,518	$ 23,182.01	$ 15.27	1.09%
CLONIDINE HCL	CENTRAL ALPHA-AGONISTS	1,503	$ 27,756.22	$ 18.47	1.08%
VYVANSE	AMPHETAMINES	1,492	$ 345,116.56	$ 231.31	1.07%
PROAIR HFA	BETA-ADRENERGIC AGONISTS	1,370	$ 116,518.28	$ 85.05	0.98%
RISPERIDONE	ANTIPSYCHOTIC AGENTS	1,318	$ 20,043.33	$ 15.21	0.94%
QUETIAPINE FUMARATE	ANTIPSYCHOTIC AGENTS	1,315	$ 23,124.78	$ 17.59	0.94%
VITAMIN D3	VITAMIN D	1,285	$ 19,417.31	$ 15.11	0.92%
LAMOTRIGINE	ANTICONVULSANTS, MISCELLANEOUS	1,273	$ 18,739.40	$ 14.72	0.91%
FLUTICASONE PROPIONATE	CORTICOSTEROIDS (EENT)	1,248	$ 24,830.53	$ 19.90	0.89%
ARIPIPRAZOLE	ANTIPSYCHOTIC AGENTS	1,212	$ 30,239.54	$ 24.95	0.87%
CETIRIZINE HCL	SECOND GENERATION ANTIHISTAMINES	1,207	$ 53,813.67	$ 44.58	0.86%
DULOXETINE HCL	ANTIDEPRESSANTS	1,193	$ 25,894.09	$ 21.71	0.85%
TOTAL TOP 25		43,493	$ 1,656,731.66	$ 38.09	31.13%

Total Rx Claims From 04/01/2018 - 06/30/2018	139,731

Top 10 Drugs
Based on Total Claims Cost



Added to PA	Category
ACZONE	Acne
AMCINONIDE	Topical Steroids
AMLODIPINE-VALSARTAN	Combination
ANZEMET	Chemo Induced Nausea/Vomiting
APEXICON E	Topical Steroids
ARNUITY ELLIPTA	Steroid Inhaler
Auvi Q	Epinephrine pens
BETAMETHASONE DIPROPIONATE	Topical Steroids
BETAMETHASONE VALERATE	Topical Steroids
BONJESTA	Diclegis/Bonjesta
CAPTOPRIL	ACE Inhibitors
CAPTOPRIL-HYDROCHLOROTHIAZIDE	Combination
Cinryze	Hereditary Angioedema
CLENPIQ	Bowel Prep Agents
CLOBETASOL EMOLLIENT	Topical Steroids
CLOBETASOL PROPIONATE EMOLLIENT FOAM	Topical Steroids
CLOBETASOL PROPIONATE FOAM	Topical Steroids
CLOCORTOLONE PIVALATE	Topical Steroids
CORDRAN	Topical Steroids
DESOXIMETASONE	Topical Steroids
DIFLORASONE DIACETATE	Topical Steroids
doptelet	> $3000
EUCRISA	Eucrisa
FLUOCINOLONE ACETONIDE	Topical Steroids
FLUOCINONIDE	Topical Steroids
FLURANDRENOLIDE	Topical Steroids
FLUTICASONE PROPIONATE	Topical Steroids
FLUVASTATIN ER	Statins
FLUVASTATIN SODIUM	Statins
FULPHILA	Biosimilars
GOCOVRI	Extended Release Amantadine
HALOBETASOL PROPIONATE	Topical Steroids
HALOG	Topical Steroids
HYDROCORTISONE BUTYRATE	Topical Steroids
HYDROCORTISONE VALERATE	Topical Steroids
IDELVION	Antihaemophilia
JADENU	Jadenu
JADENU SPRINKLE	Jadenu
JUVISYNC	Combination
KEVZARA PEN	Cytokine Modulators
LONHALA MAGNAIR	COPD
LUCEMYRA	> $3000
MAKENA	> $3000

MEFLOQUINE HCL	Malaria
METAXALONE	Skelaxin
MIRCERA	Biosimilars
OLUMIANT	Cytokine Modulators
OSMOLEX ER	Extended Release Amantadine
PALYNZIQ	> $3000
PANDEL	Topical Steroids
PREDNICARBATE	Topical Steroids
PRESTALIA	Combination
PROVENTIL HFA	Rescue Inhalers
RETACRIT	Biosimilars
RETIN-A MICRO PUMP	Acne
SERNIVO	Topical Steroids
SORILUX	Plaque Psoriasis
Tavalisse	> $3000
TAZAROTENE	Acne
TELMISARTAN-AMLODIPINE	Combination
TOPICORT	Topical Steroids
TRANDOLAPRIL-VERAPAMIL ER	Combination
TRETINOIN	Acne
TRIAMCINOLONE ACETONIDE	Topical Steroids
TRIANEX	Topical Steroids
TUSSICAPS	Tussicaps
ULTRAVATE	Topical Steroids
ZARXIO	Biosimilars
ZUPLENZ	Chemo Induced Nausea/Vomiting

Removed from PA	**Category**
ACTIVASE	Activase
ADVAIR HFA	Steroid/LABA Inhalers
BILTRICIDE	Biltricide
calcipotriene cream	Plaque Psoriasis
CARDURA XL	BPH
CATHFLO ACTIVASE	Activase
CELECOXIB	NSAIDs
DARAPRIM	> $3000
DIFFERIN	Acne
EPIPEN 2-PAK	epinephrine pens
EPIPEN JR	epinephrine pens
ESZOPICLONE	Sedative/Hypnotic
FLOVENT DISKUS	Steroid Inhalers
HETLIOZ	Sedative/Hypnotic
INTRON A	Interferon - Hep C
JUBLIA	Onychomycosis
MYTESI	Fulyzaq

NAPROXEN SODIUM CR	NSAIDs
NORTHERA	Northera
PROGLYCEM	> $3000
PROMACTA	> $3000
Sorilux (calcipotriene) Foam	Plaque Psoriasis
TUDORZA PRESSAIR	COPD
VALSARTAN-HYDROCHLOROTHIAZIDE	combination
VENTOLIN HFA	Rescue Inhalers
XIFAXAN	IBS
XOPENEX HFA	Rescue Inhalers
ZALEPLON	Sedative/Hypnotic
ZETONNA	Steroid Inhalers
ZYCLARA	Actinic Keratosis

Non-Preferred Dosage Forms
Prior Authorization Criteria

Criteria:

- The prescriber must submit medical justification explaining why the patient cannot use the preferred product (subject to clinical review)
- Patient must have FDA indication
- Patient must not have contraindications to requested product
- Patient must have failed a therapeutic course of all preferred agents
    - Trial must have been within the last 2 years
    - Trials must have been at least 30 days in duration unless otherwise indicated
    - A failure is defined as product was not effective at maximum tolerated dose or patient has a documented intolerance or adverse reaction to inactive ingredients where the non-preferred product is expected to have a different result and other alternatives (e.g. medications in same class) are not an option for the patient

Daxbia (Cephalexin):

Preferred	Non-Preferred
Cephalexin	Dexbia (Cephalexin)

Oral Steroids:

Additional Criteria:

- Emflaza: See Emflaza Criteria on this document
- Rayos: Trial of 12 weeks with 2AM dosing of prednisone

Preferred	Non-Preferred
Budesonide EC	DEXPAK (dexamethasone)
Cortisone	EMFLAZA (deflazacort)
Dexamethasone	MILLIPRED (Prednisolone)
Hydrocortisone	Prednisolone sodium phosphate ODT
Methylprednisone	Prednisolone sodium phosphate 10mg/5ml, 20mg/5ml solution
Prednisolone sodium phosphate 5mg/5ml, 15mg/5ml, 25mg/5ml	RAYOS (prednisone)
Prednisone	TAPERDEX (dexamethasone)
	UCERIS (budesonide)

Rytary (Carbidopa/Levodopa):

Additional Criteria: Patient is not in a long term care facility

Preferred	Non-Preferred
Carbidopa/Levodopa	RYTARY (carbidopa/levodopa)
Carbidopa/Levodopa ER	
Carbidopa/Levodopa/Entacapone	

Emflaza Criteria:

- Patient must be 5 years of age or older
- Patient must have diagnosis of Duchenne muscular dystrophy (DMD) confirmed by the documented presence of abnormal dystrophin or a confirmed mutation of the dystrophin gene
- **Additional Initial Criteria: Approval 6 months**
    - Onset of weakness before 5 years of age
    - Must be prescribed by or in consultation with a physician who specializes in the treatment of Duchenne Muscular Dystrophy (DMD) and/or neuromuscular disorders
    - Serum creatinine kinase activity at least 10 times the upper limit of normal (ULN) prior to initiating treatment
    - Inadequate treatment response, intolerance, or contraindication to a 6-month trial of prednisone
    - Obtain a baseline motor milestone score from ONE the following assessments:
        - 6-minute walk test (6MWT)
        - North Star Ambulatory Assessment (NSAA)
        - Motor Function Measure (MFM)
        - Hammersmith Functional Motor Scale (HFMS)
    - Patient must have ONE of the following significant intolerable adverse effects supported by documentation:
        - Cushingoid appearance
        - Central (truncal) obesity
        - Undesirable weight gain (>10% of body weight gain increase over 6-month period)
        - Diabetes and/or hypertension that is difficult to manage
        - Severe behavioral adverse effect
- **Additional Renewal Criteria: Approval 1 year**
    - Patient must have ONE of the following:
        - Improvement in motor milestone score from baseline from ONE the following assessments:
        - 6MWT – improvement of 20 meters from baseline
        - NSAA – improvement of 2 points from baseline
        - MFM – improvement of 2 points from baseline
        - HFMS – improvement of 2 points from baseline
    - Patient must have had improvement of adverse effects experienced on prednisone supported by documentation:
        - Cushingoid appearance
        - Central (truncal) obesity
        - Undesirable weight gain (>10% of body weight gain increase over 6-month period)
        - Diabetes and/or hypertension that is difficult to manage
        - Severe behavioral adverse effect

health information designs

Non-Preferred Dosage Forms
Prior Authorization Form

Fax Completed Form to:
855-207-0250
For questions regarding this Prior authorization, call
866-773-0695

Prior Authorization Vendor for ND

ND Medicaid requires that patients receiving a prescription for non-preferred dosage form of a preferred agent must meet the following prior authorization criteria:

- The prescriber must submit medical justification explaining why the patient cannot use the preferred product (subject to clinical review)
- Patient must have FDA approved indication for use
- Patient must not have contraindications to requested product
- Patient must have failed a therapeutic course of all preferred agents within the last 2 years
  - Trials must have been at least 30 days in duration unless otherwise indicated
  - A failure is defined as product was not effective at maximum tolerated dose or patient has a documented intolerance or adverse reaction to inactive ingredients where the non-preferred product is expected to have a different result and other alternatives (e.g. medications in same class) are not an option for the patient

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name	Specialist involved in therapy (if not treating physician)		
Prescriber NPI	Telephone Number	Fax Number	
Address	City	State	Zip Code

Requested Drug and Dosage:	**Diagnosis for this request:**

List all failed medications:	**Start Date:**	**End Date:**

• **Does the patient have any contraindications to therapy with the requested agent?**	□ YES □ NO
• **Is medical justification explaining why the patient cannot use the preferred product attached?** *(please attach any relevant documentation to the request)*	□ YES □ NO

□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*

Prescriber (or Staff) / Pharmacy Signature**	Date

**: *By completing this form, I hereby certify that the above request is true, accurate and complete. That the request is medically necessary, does not exceed the medical needs of the member, and is clinically supported in the patient's medical records. I also understand that any misrepresentations or concealment of any information requested in the prior authorization request may subject me to audit and recoupment.*

Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
TELEPHONE NUMBER	FAX NUMBER	DRUG	NDC #

Topical Antifungals
Prior Authorization Criteria

Approval Duration

Onychomycosis: 1 year
Dermatophytosis: 1 month

Criteria:

- Patient must have an FDA approved diagnosis confirmed by potassium hydroxide (KOH) preparation.
- Patient must have failed a trial of 3 preferred agents including at least one oral agent (terbinafine, fluconazole, or itraconazole) for the length of recommended treatment time for patient's particular infection.
- The prescriber must submit medical justification explaining why the patient cannot use a preferred product cannot be used if requested product ingredient is available in a preferred formulation (subject to clinical review).
- **Additional Criteria for Treatment of Onychomycosis:**
    - There must have been enough time since treatment cessation to assess healthy toenail outgrow (≥ 6 months)

Preferred	Non-Preferred
Ciclopirox cream	Ciclopirox gel
Ciclopirox shampoo	Ciclopirox solution
Ciclopirox suspension	KERYDIN (tavaborole)
Clotrimazole cream	Ketoconazole foam
Econazole cream	MENTAX (butenafine) CREAM
ERTACZO (sertraconazole) CREAM	Naftifine cream
EXELDERM CREAM (sulconazole)	NAFTIN (naftifine) GEL
EXELDERM SOLUTION (sulconazole)	Nystatin – triamcinolone cream
JUBLIA (efinaconazole)	Nystatin – triamcinolone ointment
Ketoconazole cream	Oxiconazole cream
Ketoconazole shampoo	OXISTAT (oxiconazole) LOTION
LUZU (luliconazole) CREAM	PENLAC (ciclopirox)
MENTAX (butenafine) CREAM	
Miconazole	
Nystatin cream	
Nystatin ointment	
Nystatin powder	
VUSION (miconazole/zinc oxide/white petrolatum)	

health information designs

Topical Antifungals
Prior Authorization Form

Fax Completed Form to:
855-207-0250
For questions regarding this Prior authorization, call
866-773-0695

Prior Authorization Vendor for ND

ND Medicaid requires that patients receiving a prescription for a non-preferred topical antifungal agent must meet the following criteria:

Criteria for all agents:

- Patient must have an FDA approved diagnosis confirmed by potassium hydroxide (KOH) preparation.
- Patient must have failed a trial of 3 preferred agents including at least one oral agent (terbinafine, fluconazole, or itraconazole) for the length of recommended treatment time for patient's particular infection.
- The prescriber must submit medical justification explaining why the patient cannot use a preferred product cannot be used if requested product ingredient is available in a preferred formulation.

Additional criteria for treatment of onychomycosis:

- There must have been enough time since treatment cessation to assess healthy toenail outgrow (≥ 6 months)

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name	Specialist involved in therapy (if not treating physician)		
Prescriber NPI	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage:	**Diagnosis for this request:**		
List all failed medications:		**Start Date:**	**End Date:**
Additional Qualifications for Coverage (e.g. medical justification explaining inability to meet required trials)			
□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*			
Prescriber (or Staff) / Pharmacy Signature**		Date	
**: *By completing this form, I hereby certify that the above request is true, accurate and complete. That the request is medically necessary, does not exceed the medical needs of the member, and is clinically supported in the patient's medical records. I also understand that any misrepresentations or concealment of any information requested in the prior authorization request may subject me to audit and recoupment.*			

Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
TELEPHONE NUMBER	FAX NUMBER	DRUG	NDC #

Eosinophilic Asthma Agents

- All agents will now only be approved when requested via medical billing only.

Migraine Prophylaxis (CGRP Inhibitors)
Prior Authorization Criteria

Approval Duration

Initial Approval: 3 months
Renewal Approval: 1 year

Criteria:

- **Initial**
  - Patient must experience 4 or more migraine days per month.
  - Prescriber must submit documentation of treatment failure of a 2 month trial of two preferred agents from different therapeutic classes.
    - Documentation must include clinical notes regarding failure to reduce migraine frequency.
- **Renewal**
  - Patient must experience a reduction in migraines of at least 50%

Preferred	Non-Preferred
Amitriptyline	AIMOVIG (erenumab-aooe)
Atenolol	
BOTOX (Onabotulinumtoxin A)	
Divalproex Sodium	
Metoprolol	
Nadolol	
Propranolol	
Timolol	
Topiramate	
Venlafaxine	

health information designs

Migraine Prophylaxis (CGRP Inhibitors) Prior Authorization Form

Fax Completed Form to: 855-207-0250
For questions regarding this Prior authorization, call 866-773-0695

Prior Authorization Vendor for ND

ND Medicaid requires that patients receiving a prescription for a CGRP inhibitor must meet the following criteria:

Initial Requests:

- Patient must experience 4 or more migraine days per month.
- Prescriber must submit documentation of treatment failure of a 2 month trial of two preferred agents from different therapeutic classes. Documentation must include clinical notes regarding failure to reduce migraine frequency.

Renewal Requests: Patient must experience a reduction in migraines of at least 50%

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name	Specialist involved in therapy (if not treating physician)		
Prescriber NPI	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage:	**Diagnosis for this request:**		
Number of experienced migraine days per month:			
List all failed medications:		**Start Date:**	**End Date:**
Additional Qualifications for Coverage (e.g. medical justification explaining inability to meet required trials)			
□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*			
Prescriber (or Staff) / Pharmacy Signature**		Date	
**: *By completing this form, I hereby certify that the above request is true, accurate and complete. That the request is medically necessary, does not exceed the medical needs of the member, and is clinically supported in the patient's medical records. I also understand that any misrepresentations or concealment of any information requested in the prior authorization request may subject me to audit and recoupment.*			

Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
TELEPHONE NUMBER	FAX NUMBER	DRUG	NDC #

Medicaid Expansion

Top Line Performance Metrics

- Generic Fill Rate (GFR) decreased 0.2 percentage points to 86.2%

	Medicaid Expansion			Medicaid - Ages 35-65	
Description	1/18 - 6/18	1/17 - 6/17	Change	1/18 - 6/18	Change
Avg Members per Month	20,333	20,087	1.2%		
Number of Unique Patients	15,352	15,517	-1.1%		
Pct Members Utilizing Benefit	75.5%	77.2%	-1.7		
Total Days	5,523,788	5,381,086	2.7%		
Total Rxs	219,680	217,070	1.2%		
Average Member Age	39.3	39.1	0.5%	49.0	0.2%
Nbr Rxs PMPM	1.80	1.80	0.0%	2.64	0.6%
Generic Fill Rate	86.2%	86.3%	-0.2	85.2%	-0.5
Home Delivery Utilization	0.0%	0.0%	0.0	0.2%	0.0
Member Cost %	0.4%	0.3%	0.1	0.5%	0.0
Specialty Percent of Plan Cost	26.6%	21.4%	5.2	45.9%	1.6
Formulary Compliance Rate	99.7%	98.7%	1.0	98.9%	-0.2

Key Statistics: Specialty Detailed

- You have 331 unique specialty patients, an increase of 29 specialty patients

Medicaid Expansion						
	Non-Specialty			Specialty		
Description	1/18 - 6/18	1/17 - 6/17	Change	1/18 - 6/18	1/17 - 6/17	Change
Avg Members per Month	20,333	20,087	1.2%	20,333	20,087	1.2%
Number of Unique Patients	15,325	15,495	-1.1%	331	302	9.6%
Pct Members Utilizing Benefit	75.4%	77.1%	-1.8	1.6%	1.5%	0.1
Total Days	5,491,061	5,350,425	2.6%	32,727	30,661	6.7%
Total Rxs	218,492	215,968	1.2%	1,188	1,102	7.8%
Percent of Total Rxs	99.46%	99.49%	0.0	0.54%	0.51%	0.0
Nbr Rxs PMPM	1.79	1.79	-0.1%	0.010	0.009	6.5%
Generic Fill Rate	86.5%	86.6%	-0.2	30.0%	29.6%	0.4
Member Cost %	0.5%	0.4%	0.1	0.0%	0.1%	0.0

Specialty	
Medicaid - Ages 35-65	
1/18 - 6/18	Change
0.04	4.0%
17.9%	4.9
0.0%	0.0

Top 10 Indications

- The highest trend is in Multiple Sclerosis at 22.1%

REPRESENT

68.2%

OF YOUR TOTAL PLAN COST

Top Indications by Plan Cost

1/18 - 6/18							1/17 - 6/17			
Rank	Peer Rank	Indication	Rxs	Patients	Generic Fill Rate	Peer Generic Fill Rate	Rank	Rxs	Patients	Generic Fill Rate
1	2	DIABETES	17,019	2,158	38.7%	42.0%	1	15,744	2,047	38.2%
2	3	INFLAMMATORY CONDITIONS	840	213	59.2%	50.3%	3	884	216	59.6%
3	6	PAIN/INFLAMMATION	29,470	6,670	94.9%	96.6%	2	32,462	7,144	94.1%
4	4	ASTHMA	8,836	2,513	25.5%	23.4%	5	8,229	2,403	25.2%
5	8	MENTAL/NEURO DISORDERS	5,641	1,429	90.9%	91.3%	4	5,004	1,260	90.2%
6	7	HEPATITIS C	53	29	1.9%	1.7%	6	37	16	10.8%
7	9	MULTIPLE SCLEROSIS	107	27	1.9%	16.6%	8	98	20	11.2%
8	1	HIV	289	59	6.9%	12.1%	10	300	57	0.0%
9	19	ATTENTION DISORDERS	3,443	815	63.9%	77.6%	9	3,710	824	72.7%
10	14	DEPRESSION	24,043	5,437	98.1%	98.5%	7	22,439	5,290	97.7%
		Total Top 10:	**89,741**		**76.0%**			**88,907**		**76.8%**
		Differences Between Periods:	**834**		**-0.8%**					

Peer = Express Scripts Peer 'Medicaid - Ages 35-65' market segment

Top 25 Drugs

- Represent 44.5% of your total Plan Cost and comprise 13 indications
- 6 of your top 25 are specialty drugs

Top Drugs by Plan Cost								
				1/18 - 6/18		1/17 - 6/17		
Rank	Peer Rank	Brand Name	Indication	Rxs	Pts.	Prev Rank	Rxs	Pts.
1	40	NOVOLOG FLEXPEN	DIABETES	1,540	499	1	1,408	476
2	4	HUMIRA PEN*	INFLAMMATORY CONDITIONS	157	43	2	148	36
3	9	LYRICA	PAIN/INFLAMMATION	1,293	351	3	1,293	355
4	98	LEVEMIR FLEXTOUCH	DIABETES	1,005	316	5	904	306
5	11	LANTUS SOLOSTAR	DIABETES	1,286	408	7	834	276
6	50	EPCLUSA*	HEPATITIS C	17	9	4	16	7
7	2	MAVYRET*	HEPATITIS C	32	18			
8	16	ADVAIR DISKUS	ASTHMA	893	324	9	805	286
9	15	LATUDA	MENTAL/NEURO DISORDERS	268	88	12	231	81
10	20	VICTOZA 3-PAK	DIABETES	376	118	11	345	99
11	53	GILENYA*	MULTIPLE SCLEROSIS	36	9	24	19	5
12	49	XIFAXAN	GI DISORDERS	135	50	16	97	43
13	22	SYMBICORT	ASTHMA	815	312	13	708	273
14	56	COPAXONE*	MULTIPLE SCLEROSIS	31	8	25	22	4
15	90	VYVANSE	ATTENTION DISORDERS	780	213	15	765	205
16	183	ZUBSOLV	CHEMICAL DEPENDENCE	982	156	213	39	9
17	19	JANUVIA	DIABETES	488	134	20	429	116
18	35	CHANTIX	SMOKING CESSATION	489	271	21	446	260
19	72	NOVOLOG	DIABETES	310	81	17	375	104
20	36	SPIRIVA	COPD	446	146	19	495	145
21	158	CONTOUR NEXT TEST STRIP	DIAGNOSTIC AIDS	1,756	672	342	72	27
22	43	JARDIANCE	DIABETES	379	104	487	8	2
23	42	GABAPENTIN	PAIN/INFLAMMATION	6,617	1,801	26	6,509	1,810
24	59	PROAIR HFA	ASTHMA	2,448	1,211	31	2,087	1,111
25	13	ENBREL SURECLICK*	INFLAMMATORY CONDITIONS	27	7	10	53	16
			Total Top 25:	22,606			18,108	
			Differences Between Periods:	4,498				

*Specialty Drugs

Peer = Express Scripts Peer 'Medicaid - Ages 35-65' market segment

Top 25 Specialty Drugs

- Represent 21.6% of your total Plan Cost and comprise 7 indications

Top Specialty Drugs by Plan Cost								
				1/18 - 6/18		1/17 - 6/17		
Overall Rank	Overall Peer Rank	Brand Name	Indication	Rxs	Pts.	Overall Rank	Rxs	Pts.
2	4	HUMIRA PEN	INFLAMMATORY CONDITIONS	157	43	2	148	36
6	50	EPCLUSA	HEPATITIS C	17	9	4	16	7
7	2	MAVYRET	HEPATITIS C	32	18			
11	53	GILENYA	MULTIPLE SCLEROSIS	36	9	24	19	5
14	56	COPAXONE	MULTIPLE SCLEROSIS	31	8	25	22	4
25	13	ENBREL SURECLICK	INFLAMMATORY CONDITIONS	27	7	10	53	16
27	58	AUBAGIO	MULTIPLE SCLEROSIS	19	6	38	16	4
29	8	TRUVADA	HIV	70	23	33	66	16
30	76	ENBREL	INFLAMMATORY CONDITIONS	23	5	49	13	4
32	154	HUMIRA PEN CROHN-UC-HS START	INFLAMMATORY CONDITIONS	7	7	154	2	2
39	17	ATRIPLA	HIV	39	8	55	32	8
41	84	SPRYCEL	CANCER	9	2			
44	29	STRIBILD	HIV	27	5	48	26	7
45	542	ORKAMBI	CYSTIC FIBROSIS	4	1			
46	38	REVLIMID	CANCER	6	1			
47	52	ENOXAPARIN SODIUM	ANTICOAGULANT	104	45	56	101	64
49	70	VOSEVI	HEPATITIS C	3	1			
51	306	LONSURF	CANCER	9	2			
55	62	HUMIRA	INFLAMMATORY CONDITIONS	14	3	61	14	3
59	3	TRIUMEQ	HIV	22	6	111	12	4
65	139	XELJANZ	INFLAMMATORY CONDITIONS	13	3	89	11	2
69	92	IMATINIB MESYLATE	CANCER	6	2			
70	1	GENVOYA	HIV	18	5	29	42	12
77	55	IBRANCE	CANCER	4	1			
82	63	COSENTYX PEN (2 PENS)	INFLAMMATORY CONDITIONS	6	4			
			Total Top 25:	703			593	
			Differences Between Periods:	110				

Peer = Express Scripts Peer 'Medicaid - Ages 35-65' market segment

Advanced Opioid Management Activity

Sanford Health Plan - Medicaid

2018-01-01 - 2018-06-30

EXPRESS SCRIPTS®

Opioid Metrics

Opioids	All Patients			Cancer/PC*			Without Cancer/PC*		
	2017 (1-2Q)	2018 (1-2Q)	% Diff	2017 (1-2Q)	2018 (1-2Q)	% Diff	2017 (1-2Q)	2018 (1-2Q)	% Diff
Patients	4,341	3,564	-19.6%	49	38	-25.2%	4,292	3,526	- 19.5%
% Members	21.6%	17.5%	- 4.1%	0.2%	0.2%	0%	21.4%	17.3%	- 4.1%
% Patients	28.0%	23.2%	- 4.8%	0.3%	0.2%	- 0.1%	27.7%	23.0%	- 4.7%
New Patients	2,886	2,419	- 17.6%	19	20	5.1%	2,867	2,399	- 17.7%
Total Rx Count	14,036	10,808	- 25.9%	232	154	-40.4%	13,804	10,654	- 25.7%
% Rxs	6.3%	4.8%	- 1.5%	0.1%	0.1%	0%	6.2%	4.7%	- 1.5%
Rxs per Patient	3.23	3.03	- 6.3%	4.73	4.05	-15.4%	3.22	3.02	- 6.41%-
Total Plan Cost	$431,326	$277,967	- 43.2%	$11,875	$7,809	-41.3%	$419,451	$270,158	-43.2%
% of Total Plan Cost	2.4%	1.5%	- 0.9%	0.1%	0.0%	- 0.1%	2.4%	1.5%	- 0.9%
% Patients with long acting and short acting opioid use	5.3%	3.1%	-2.2%	12.2%	10.5%	- 1.7%	5.2%	3.0%	- 2.2%
Average days per patient SA:LA ratio (for patients taking both)	104:91	101:96	N/A	113:157	111:163	N/A	104:89	101:93	N/A
Prescribers per Patient	1.65	1.52	- 8.2%	1.73	1.76	1.7%	1.65	1.52	-8.2%
Pharmacies per Patient	1.29	1.25	-3.1%	1.27	1.24	-2.3%	1.29	1.25	-3.1%
Patients filling 3 drug combination**	23	25	8.3%	0	0	0%	23	25	8.3%

*Palliative Care

**(Benzodiazepines, Opioids and Skeletal Muscle Relaxants)

Long Acting Opioid Metrics

Long Acting Opioids	All Patients			Cancer/PC*			Without Cancer/PC*		
	2017 (1-2Q)	2018 (1-2Q)	% Diff	2017 (1-2Q)	2018 (1-2Q)	% Diff	2017 (1-2Q)	2018 (1-2Q)	% Diff
Patients	269	121	-75.8%	7	5	-33.3%	262	116	-77.2%
% Opioid Patients	6.2%	3.4%	- 2.8%	14.3%	13.2%	- 1.1%	6.1%	3.3%	- 2.8%
Days per Rx	25.68	24.24	-5.7%	26.79	29.70	10.3%	25.63	23.92	-6.9%
Days per Patient	93.67	96.17	2.6%	160.71	160.40	-0.1%	91.87	93.40	1.6%
Rxs per Patient	3.65	3.97	8.3%	6.00	5.40	-10.5%	3.58	3.91	8.8%
Total Rx Count	981	480	-68.5%	42	27	-43.4%	939	453	-69.8%
Total Plan Cost	$160,908	$75,750	-71.9%	$7,317	$5,001	-37.6%	$153,591	$70,750	-73.8%

*Palliative Care

Short Acting Opioid Metrics

Short Acting Opioids	All Patients			Cancer/PC*			Without Cancer/PC*		
	2017 (1-2Q)	2018 (1-2Q)	% Diff	2017 (1-2Q)	2018 (1-2Q)	% Diff	2017 (1-2Q)	2018 (1-2Q)	% Diff
Patients	4,301	3,552	- 19%	48	37	-25.8%	4,253	3,515	-19%
% Opioid Patients	99.1%	99.7%	0.6%	98.0%	97.4%	-0.6%	99.1%	99.7%	0.6%
New Patients	2,860	2,405	-17.2%	19	20	5.1%	2,841	2,385	-17.4%
Days per Rx	12.97	12.75	-1.7%	19.30	16.65	-14.7%	12.88	12.70	-1.4%
Days per Patient	39.37	37.07	- 6.0%	76.40	57.16	-28.8%	38.95	36.86	-5.5%
Rxs per Patient	3.04	2.91	-4.3%	3.96	3.43	-14.3%	3.02	2.90	- 4.0%
Days per New Patient First Fill	6.56	4.27	-42.2%	9.21	3.95	- 79.9%	6.55	4.28	-41.9%
Total Rx Count	13,055	10,328	-23.3%	190	127	-39.7%	12,865	10,201	-23.0%
Total Plan Cost	$270,418	$202,216	-28.6%	$4,558	$2,808	-47.5%	$265,860	$199,408	-28.5%
Patients getting more than 7 days supply	1,919	1,276	-40.2%	34	17	- 66.6%	1,885	1,259	-39.8%
% Patients getting more than 7 days supply	44.6%	35.9%	-8.7%	70.8%	45.9%	- 24.9%	44.3%	35.8%	-8.5%
Patients getting 7 days supply or less	2,382	2,276	-4.5%	14	20	35.2%	2,368	2,256	-4.8%
% Patients getting 7 days supply or less	55.4%	64.1%	8.7%	29.2%	54.1%	24.9%	55.7%	64.2%	8.5%

*Palliative Care

Antidotes/Addiction Treatment Metrics

Antidotes	All Patients			Cancer/PC*			Without Cancer/PC*		
	2017 (1-2Q)	2018 (1-2Q)	% Diff	2017 (1-2Q)	2018 (1-2Q)	% Diff	2017 (1-2Q)	2018 (1-2Q)	% Diff
Patients	12	19	45.1%	1	0	- 100%	11	19	53.3%
Rxs per Patient	1.50	1.11	-29.8%	1.00	0.00	- 100%	1.55	1.11	-33.0%
Total Rx Count	18	21	15.3%	1	0	- 100%	17	21	21.0%
Total Plan Cost	$2,340	$2,540	8.1%	$126	0	- 100%	$2,178	$2,540	15.3%

Addiction Treatment	All Patients			Cancer/PC*			Without Cancer/PC*		
	2017 (1-2Q)	2018 (1-2Q)	% Diff	2017 (1-2Q)	2018 (1-2Q)	% Diff	2017 (1-2Q)	2018 (1-2Q)	% Diff
Patients	134	191	35.0%	1	0	-100%	133	191	35.8%
Rxs per Patient	5.89	6.93	16.2%	6.00	0.00	-100%	5.89	6.93	16.2%
Total Rx Count	789	1,324	50.6%	6	0	-100%	783	1,324	51.3%
Total Plan Cost	$264,024	$317,166	18.2%	$1,519	$0	-100%	$262,505	$317,166	18.8%

*Palliative Care

Morphine Equivalent Dose (MEqD)

MEqD	
Number of Unique Opioid Patients That Hit >200mg Accumulated MEqD Edit At Least Once	31
% of Total Opioid Patients That Hit >200mg Accumulated MEqD Edit At Least Once	0.9%
Number of Opioid Claims That Hit >200mg Accumulated MEqD Edit	51
% of Total Opioid Claims That Hit >200mg Accumulated MEqD Edit	0.5%
Total Primary Coverage Reviews	20
Total Primary Approvals	19
Total Primary Denials	1
Total Appeals	0
Total Appeal Approvals	0
Total Appeal Denials	0
Total Rejects With A Subsequent Fill	47
Total Successful Reductions in Accumulated MEqD	0
Success Rate	0.0%
Average Rejected Accumulated MEqD Reduction (Reject vs 1st Fill)	0.0%
Median Rejected Accumulated MEqD Reduction (Reject vs 1st Fill)	0.0%

Data based on enrollment activity in the Express Scripts standard MEqD edit

Short Acting Edit

Short Acting 7 Day Edit	
Number of Unique Opioid Patients That Hit the 7 Day Short Acting Edit	388
% of Total Opioid Patients That Hit the 7 Day Short Acting Edit	10.9%
Number of Opioid Claims That Hit the 7 Day Short Acting Edit	424
% of Total Opioid Claims That Hit the 7 Day Short Acting Edit	3.9%
Total Primary Coverage Reviews	16
Total Primary Approvals	9
Total Primary Denials	7
Total Appeals	0
Total Appeal Approvals	0
Total Appeal Denials	0
Total Rejects With A Subsequent Fill	333
Total Successful Reductions to 7 Days Supply or Less	316
Success Rate	94.9%
Average Rejected Days Supply	16.40
Average Days Supply on 1st Subsequent Fill	7.29
Average Days Supply Reduction (Reject vs 1st Fill)	-55.5%
Median Days Supply Reduction (Reject vs 1st Fill)	-46.2%

Data based on enrollment activity in the Express Scripts standard Short Acting 7Day Edit

Long Acting Edit

Long Acting PA Edit	
Number of Unique Opioid Patients that Hit the Long Acting PA Edit	38
% of Total Opioid Patients that Hit the Long Acting PA Edit	1.1%
Number of Opioid Claims that Hit the Long Acting PA Edit	48
% of Total Opioid Claims that Hit the Long Acting PA Edit	0.4%
Total Primary Coverage Reviews	28
Total Primary Approvals	20
Total Primary Denials	8
Total Appeals	0
Total Appeal Approvals	0
Total Appeal Denials	0
Total Rejects With A Subsequent Fill	38
Total Successful Switches to a Short Acting Opioid	26
Success Rate	68.4%

Data based on enrollment activity in the Express Scripts standard Long Acting PA Edit

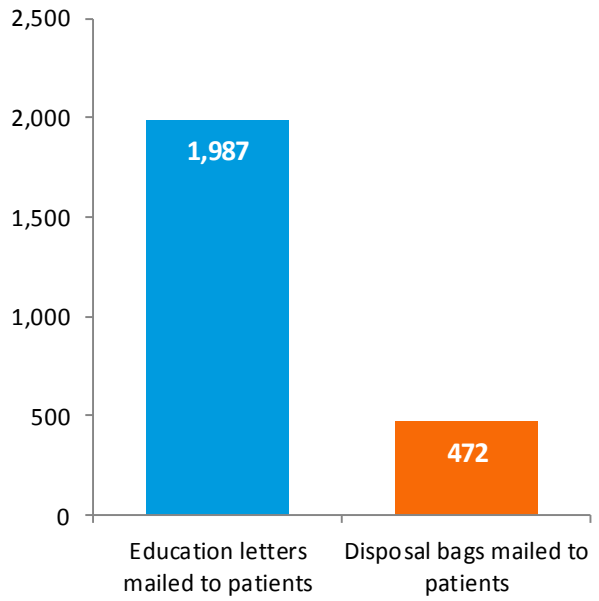
Member Interventions

Member outreach as part of Advanced Opioid Management Solution.

1987 Education letters mailed to patients

472 Disposal bags mailed to patients

264 Opioid alerts sent to Physicians

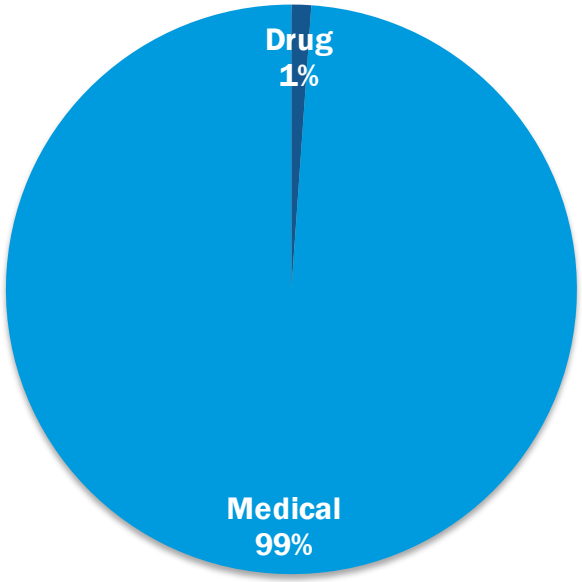


Advanced Opioid Management Savings Analysis

Drug Cost Savings	
Long Acting Edit	$1,167
Short Acting Edit	($136)
Total	$1,031

Medical Cost Avoidance	
Total	$91,726

Total Program Savings



Total Estimated Savings $92.8K

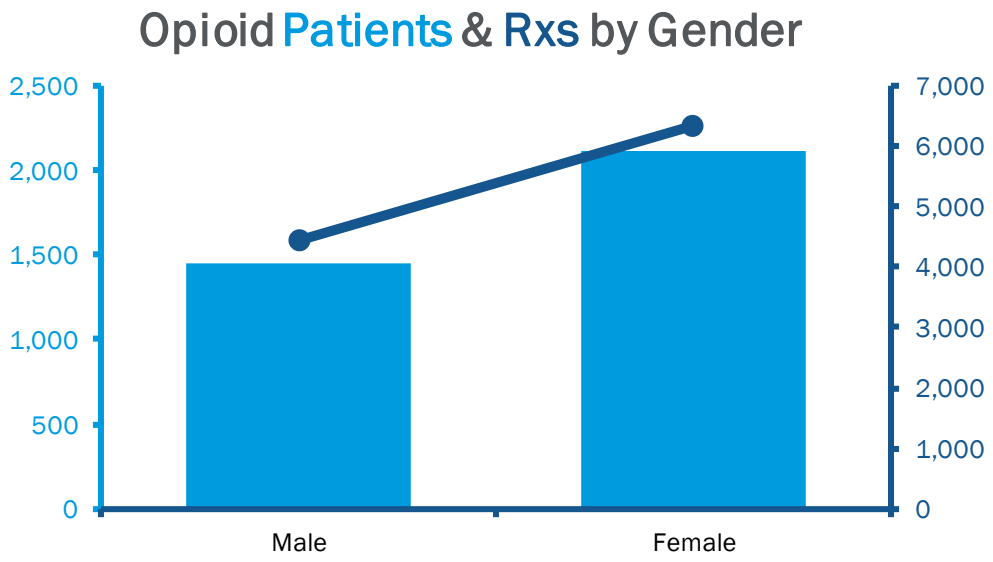
~ $0.76 PMPM Savings

Estimated Pharmacy plan savings $0.01 PMPM

Estimated Medical plan savings $0.75 PMPM

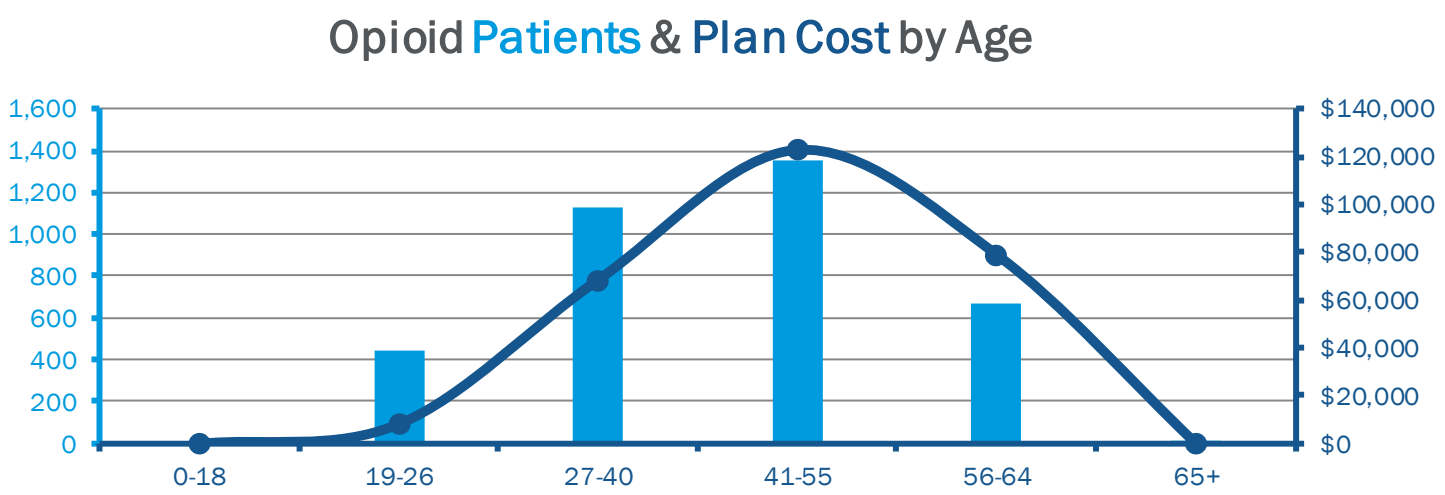
Gender Distribution

Gender	Patients Filling Opioids	% Patients filling Opioids	Opioid RXs /Opioid Patient
Male	1,449	40.7%	3.1
Female	2,115	59.3%	3.0



Age Distribution

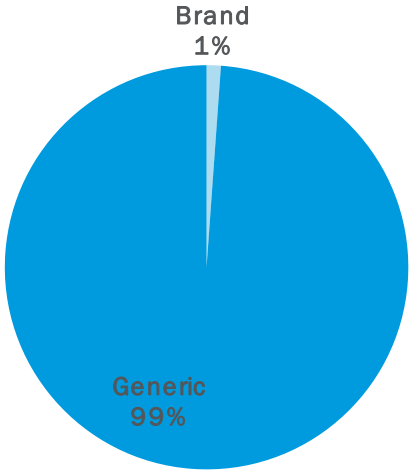
Age Range	Patients	Plan Cost	Female Patients	% Female
0-18	0	$0	0	0.0%
19-26	441	$8,154	289	65.5%
27-40	1,128	$68,338	685	60.7%
41-55	1,353	$122,555	783	57.9%
56-64	665	$78,832	372	55.9%
65+	3	$88	2	66.7%



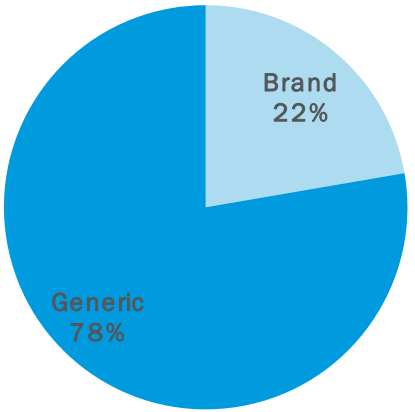
Brand vs Generic Utilization

	Opioid RXs	% Opioid RXs	Total Plan Cost	% Plan Cost	Cost/Rx
Brand Opioids	123	1.1%	$61,979	22.3%	$503.90
Generic Opioids	10,685	98.9%	$215,987	77.7%	$20.21

Brand vs Generic (by Rx Count)



Brand vs Generic (by Plan Cost)



Top 10 Opioids by Rx Count

Rank	Drug Name	Brand(A/B) Generic(G)	RX Count	% Opioid RXs	Overall Medication Rank by RX Count
1	HYDROCODONE-ACETAMINOPHEN	G	4,182	38.7%	6
2	TRAMADOL HCL	G	2,404	22.2%	22
3	OXYCODONE-ACETAMINOPHEN	G	1,680	15.5%	33
4	OXYCODONE HCL	G	1,157	10.7%	53
5	ACETAMINOPHEN-CODEINE	G	440	4.1%	111
6	MORPHINE SULFATE ER	G	236	2.2%	175
7	HYDROMORPHONE HCL	G	230	2.1%	178
8	FENTANYL	G	157	1.5%	223
9	NUCYNTA	A	51	0.5%	376
10	MORPHINE SULFATE	G	51	0.5%	377
		Top 10 Total	**10,588**		

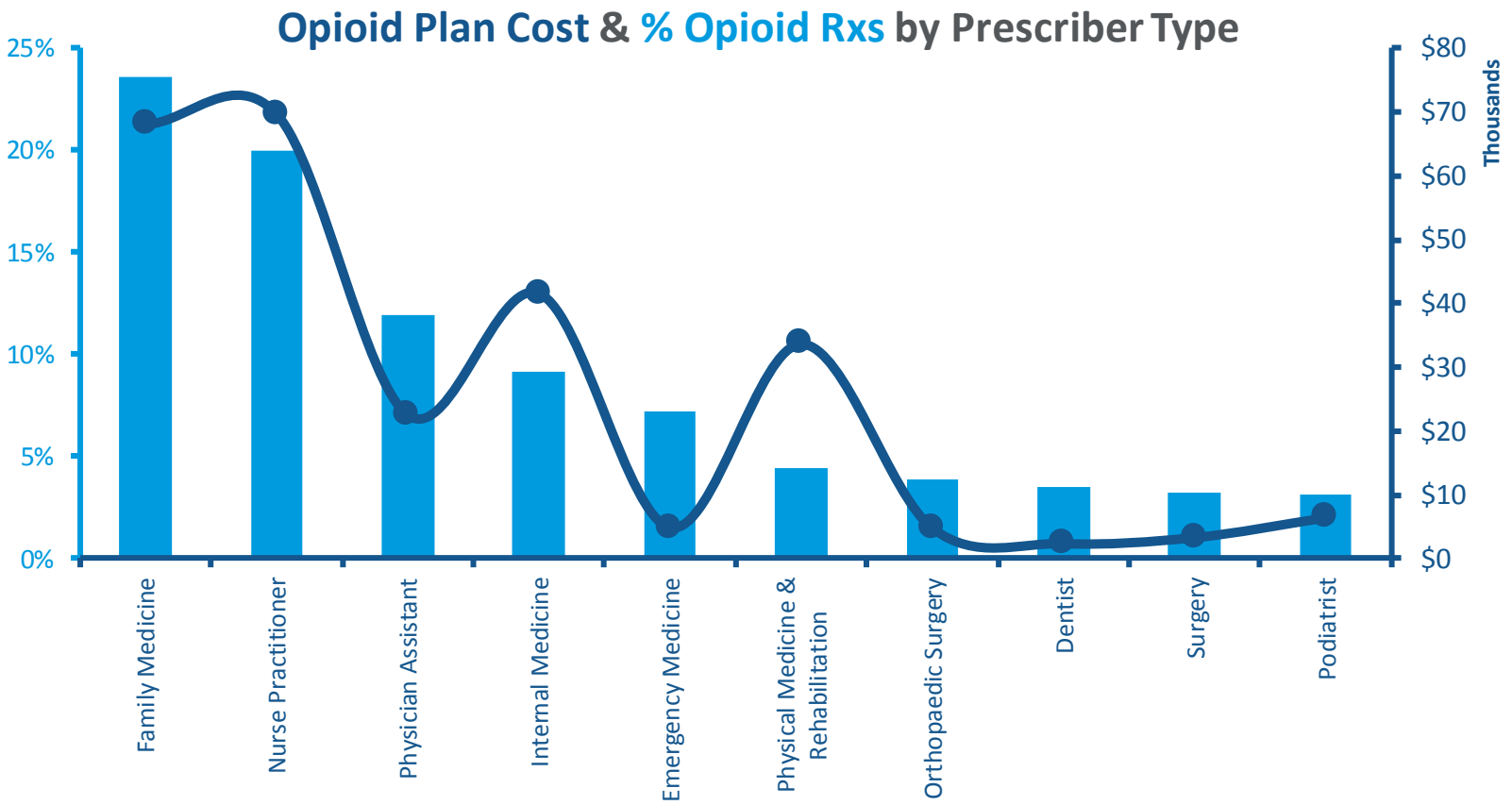
Top 10 Long Acting Opioids by Rx Count

Rank	Drug Name	Brand(A/B) Generic(G)	RX Count	% Opioid RXs	Overall Medication Rank by RX Count
1	MORPHINE SULFATE ER	G	236	2.2%	175
2	FENTANYL	G	157	1.5%	223
3	OXYCONTIN	A	39	0.4%	416
4	BUTRANS	A	18	0.2%	589
5	NUCYNTA ER	A	10	0.1%	721
6	METHADONE HCL	G	8	0.1%	784
7	TRAMADOL HCL ER	G	7	0.1%	808
8	OXYCODONE HCL ER	A	2	0.0%	1,081
9	EMBEDA	A	1	0.0%	1,162
10	DURAGESIC	B	1	0.0%	1,160
		Top 10 Total	**479**		

Top 10 Short Acting Opioids by Rx Count

Rank	Drug Name	Brand(A/B) Generic(G)	RX Count	% Opioid RXs	Overall Medication Rank by RX Count
1	HYDROCODONE-ACETAMINOPHEN	G	4,182	38.7%	6
2	TRAMADOL HCL	G	2,404	22.2%	22
3	OXYCODONE-ACETAMINOPHEN	G	1,680	15.5%	33
4	OXYCODONE HCL	G	1,157	10.7%	53
5	ACETAMINOPHEN-CODEINE	G	440	4.1%	111
6	HYDROMORPHONE HCL	G	230	2.1%	178
7	NUCYNTA	A	51	0.5%	376
8	MORPHINE SULFATE	G	51	0.5%	377
9	HYDROCODONE-IBUPROFEN	G	50	0.5%	379
10	TRAMADOL HCL-ACETAMINOPHEN	G	31	0.3%	476
		Top 10 Total	**10,276**		

Top Prescriber Types



Avandia and Actos[1-22]

Cardiovascular Effects

- Avandia (rosiglitazone) and Actos (pioglitazone) both increase the risk of HF (Boxed Warning for both products.
- Potential that Avandia use is associated with a higher risk of adverse cardiovascular events than Actos.
    - Based off of retrospective analyses of prescription data obtained from national databases, Avandia was associated with an increase in heart failure and all-cause mortality compared with Actos.
        - The largest study included 227,571 patients 65 years or older who initiated treatment with Avandia or Actos.
            - Avandia use was associated with a significantly ↑risk of stroke, HF, and all-cause mortality [HR of 1.27, 1.25, and 1.14, respectively].
- In September 2010, the FDA restricted Avandia to those already taking it and to new patients who cannot control their Type 2 diabetes with other medications, and instituted a REMS program.
    - RECORD study
        - *The Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycaemia in Diabetes study*: Designed to evaluate the effects of Avandia on cardiovascular events and mortality
            - 321 patients in the Avandia group and 323 in the control group, experienced the cardiovascular hospitalization or cardiovascular death.
                - ↑ Incidence of HF in 61 subjects assigned to Avandia compared with 29 in the control group [HR=2.10, 95% CI=1.35-3.27].
                - The effect of Avandia on MI was inconclusive due to the small number of events and possibly affected by greater statin use in the Avandia group [HR=1.14, 95% CI=0.80-1.63].
- In 2012, the FDA removed restrictions on Avandia and in 2015, the FDA removed the REMS requirement.
- **Risk of Myocardial Infarction:**
    - **Effect of Avandia on the risk of MI is uncertain.**
        - Some analyses have shown no or inconclusive evidence of Avandia use effecting MI risk, while many others have shown an increased risk of MI with Avandia use.
            - Ex 1: One meta-analysis of 42 trials of Avandia demonstrated an ↑in MI compared with placebo, metformin, sulfonylurea, or insulin (86 and 72 MIs in the Avandia and control groups respectively [HR=1.43, 95% CI=1.03-1.98]).
            - Ex 2: An independent meta-analysis performed by the manufacturers of Avandia showed similar findings [HR for events related to ischemia=1.31, 95% CI=1.01-1.70].
            - Ex. 3: The RECORD study showed inconclusive results for MI risk.
    - **Actos effects on MI risk**
        - Meta-analysis of 19 trials of Actos for the treatment of diabetes:
            - MI occurred in 1.5% of patients in the Actos group and 2% in the comparator group (placebo, metformin, sulfonylurea, rosiglitazone) [HR=0.81, 95% CI=0.64-1.02].
        - *Prospective Pioglitazone Clinical Trial in Macrovascular Events (PROactive)* trial
            - Patients with DM2 and high risk for macrovascular complications, managed with DM medications + either placebo or Actos.
            - Significant ↓in the incidence of all-cause mortality, MI, or stroke in the Actos treated group [HR=0.84, 95% CI=0.72-0.98].
            - Subanalysis showed Actos use in patients with previous MI results in a decreased incidence of fatal/nonfatal MI [HR=0.72, 95% CI=0.52-0.99].

Effects on Lipids

- Avandia and Actos have demonstrated differing effects on serum lipid concentrations in multiple studies, with most randomized trials finding that Actos produces a more favorable lipid profile.
    - Multiple randomized trials have shown that LDL levels typically remained constant when Actos added to a DM regimen while increases in LDL cholesterol levels ranging from 8 to 16 percent were noted in studies of Avandia.

        - In those same studies, HDL levels increased ~10% with both products, but reductions in serum TG were observed more often with Actos than with Avandia.
    - In the largest randomized trial that directly compared the two drugs, 735 patients with DLD and DM2 were assigned to receive either Avandia or Actos as monotherapy.
        - TG reductions were significantly greater in the Actos vs Avandia group [52 vs. 13 mg/dL].
        - HDL increases were greater in the Actos vs Avandia group [5.2 vs. 2.4 mg/dL]
        - LDL increases were greater in the Avandia vs Actos group [21.3 vs. 21.3 mg/dL

Current Utilization of Thiazoladinediones	
Agent	**Number of Patients**
Actos	24
Avandia	0

Glyburide and Other Sulfonylureas[23-28]

Hypoglycemia Risks:

- Incidence of hypoglycemia appears to be less common with shorter-acting than longer-acting sulfonylureas (SUs)
    - In a four-year, retrospective study of 14,000 patients 65 years or older with type 2 diabetes treated with different SUs, episodes of serious hypoglycemia were rare. The incidence was highest in those patients taking glyburide and lowest among those taking tolbutamide [19.9 vs. 3.5 episodes/1000 person-years].

Use in Chronic Kidney Disease:

- SU metabolites are renally excreted after undergoing metabolism. Agents such as glyburide and glimepiride have active metabolites that retain some hypoglycemic activity.
- Glipizide's metabolites are inactive.
- Therefore, the risk of hypoglycemia is higher in patients with chronic kidney disease in patients receiving a SU with active metabolites.

Cardiovascular Risk:

- Newer SUs, such as glipizide and glimepiride, are selective for the pancreatic SU receptors over the cardiac receptors (unlike glyburide)
    - Do not appear to be associated with ↑cardiovascular mortality compared with metformin or other diabetes medications, although direct controlled clinical trials have not been performed.
- Research:
    - Retrospective study using pharmaceutical data for 5795 subjects who received initial monotherapy with either a SU or metformin.
        - Evaluated deaths per 1000 person-years during the follow-up period
            - 61.4 for glyburide vs 39.6 for metformin
            - Risk of death or an acute ischemic event was greater for subjects exposed to higher doses of the SU, but not metformin
    - A meta-analysis of 47 trials comparing 2nd generation SUs (glimepiride and glipizide) with diet, placebo, or an active comparator, the SUs were not associated with ↑risk of overall mortality, CV mortality, MI, or stroke.
    - In a study of 1310 patients with DM who were hospitalized for MI, mortality rates were significantly ↓ in patients previously treated with a SU compared with other oral medications, insulin, or no medication [3.9, 6.4, 9.4, and 8.4% respectively].
        - Among the SU-treated patients, mortality was significantly lower in patients receiving second-generation sulfonylureas compared to glyburide.

Current Utilization of Sulfonylureas	
Agent	**Number of Patients**
Glipizide	82
Glimepiride	56
Glyburide	20

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PRODUCT DETAILS OF LUCEMYRA (LOFEXIDINE)

INDICATIONS AND USE:

- Opioid Withdrawal
    - Mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation in adults.
        - MoA: Central alpha-2 adrenergic agonist that reduces the release of norepinephrine and decreases sympathetic tone

DOSAGE AND ADMINISTRATION:

- Initial dosing is 0.54 mg 4 times daily, which may be titrated to symptoms
- **Max:** 0.72 mg/dose or 2.88 mg/day
- **Duration:** Administer during peak opioid withdrawal period (generally 5 to 7 days after last opioid use). May continue for up to 14 days if needed
- **Discontinuation:** Decrease dose gradually over 2 to 4 days.
- **Dose Adjustments**
    - **Renal impairment:**
        - eGFR 30-88.9 mL/minute/1.73 m^2: 0.36 mg/dose
        - eGFR <30 mL/minute/1.73 m^2: 0.18 mg/dose
    - **Hepatic impairment:**
        - Moderate impairment (Child-Pugh class B): 0.36 mg/dose
        - Severe impairment (Child-Pugh class C): 0.18 mg/dose

DOSAGE FORM AND STRENGTHS:

- 0.18 mg tablets

CONTRAINDICATIONS:

- None per label

WARNINGS AND PRECAUTIONS:

- **Cardiovascular effects:**
    - Syncope and Decreases in BP or HR
        - Reduce dose or interrupt therapy if clinically significant bradycardia and/or hypotension occur.
        - Avoid use in patients with severe coronary insufficiency, recent myocardial infarction, significant bradycardia, cerebrovascular disease, and chronic renal failure.
    - QT Prolongation
        - Avoid use in patients with congenital long QT syndrome.
- **Accidental opioid overdose**
    - Lofexidine is not a treatment for opioid use disorder, and it should be used only in conjunction with a comprehensive management program for the treatment of opioid use disorder.
    - Patients who had been treated with lofexidine may respond to lower opioid doses than previously used. This could result in potentially life-threatening opioid overdose.
- **Discontinuation of therapy**
    - Discontinuing lofexidine gradually to avoid severe withdrawal symptoms.
- **CYP2D6 poor metabolizers**
    - Exposure to lofexidine may be increased.

ADVERSE REACTIONS:

- **Most common (>10%)**
    - Orthostatic hypotension (29-42%), bradycardia (24-32%), hypotension (30%)
    - Insomnia (51-55%), dizziness (19-23%), sedation/drowsiness (12-13%)
    - Xerostomia (10-11%)

DRUG INTERACTIONS

- Most significant are those that :
    - Agents that significantly lower BP (bromperidol) or HR (ceritinib), or significantly prolong QT interval (e.g. hydroxychloroquine, macimorelin, mifepristone, promazine, etc.)

COST

Drug	Strength	Package Size	AWP Pkg Price	AWP Unit Price
LUCEMYRA	0.18 mg	36 Tablets	893.81	24.83
LUCEMYRA	0.18 mg	96 Tablets	2,383.49	24.83

CURRENT UTILIZATION

ND Medicaid Utilization (06/2018 – 07/2018)		
Label Name	**Rx Num**	**Total Reimb Amt**
LUCEMYRA	0	N/A

REFERENCES:

1. Facts & Comparisons eAnswers. Available at http://online.factsandcomparisons.com. Accessed on July 20. 2018.
2. Lucemyra (lofexidine) [prescribing information]. Louisville, KY: US WorldMeds, LLC; May 2018.

PRODUCT DETAILS OF PALYNZIQ (PEGVALIASE-PQPZ INJECTION)

INDICATIONS AND USE:

- To reduce blood phenylalanine concentrations in adult patients with phenylketonuria (PKU) who have uncontrolled blood phenylalanine concentrations >600 micromol/L on existing management

DOSAGE AND ADMINISTRATION:

- Initial: 2.5 mg once weekly for 4 weeks.
- After initial 4 weeks, double dose weekly to 40 mg weekly, then 10 mg once daily.
    - Followed by 20 mg once daily for 24 weeks, then can go to 40 mg daily has not been achieved on the 20 mg daily dose (if a 20% reduction of blood phenylalanine from baseline does not occur OR if blood phenylalanine concentration 600 micromol/L or less)
- If a response has not been achieved after administering 40 mg once daily for 16 weeks, discontinue therapy

DOSAGE FORM AND STRENGTHS:

- 2.5 mg/0.5 mL, 10 mg/0.5 mL, and 20 mg/mL prefilled syringes for SQ injection

CONTRAINDICATIONS:

- None per label

BOXED WARNING

- Anaphylaxis has been reported after administration and may occur at any time during treatment.
    - Administer the initial dose under the supervision of a healthcare provider
    - Prior to self-injection, confirm patient competency with self-administration

WARNINGS AND PRECAUTIONS:

- Anaphylaxis (see boxed warning)

ADVERSE REACTIONS:

- Most common (>10%)
    - **CNS**: HA (35-50%), fatigue (13-22%), anxiety (5-18%), dizziness (16-17%)
    - **Derm**: Skin changes (21-44%), pruritus (20-24%), alopecia (5-17%), Injection-site reaction (72-88%)
    - **GI**: Nausea (18-26%), vomiting (13-26%), ab pain (14-25%), diarrhea (9-22%)
    - **Hematologic**: Change in serum protein (<LLN: complement factor C3 8-84%; complement factor C4 48-62%), ↑ C-RP (64-68%), ↓ phenylalanin (16-61%)
    - **Hypersensitivity**: Anaphylaxis (9-84%), hypersensitivity reaction (53-69%)
    - **Immunologic**: Antibody development (100%; neutralizing antibodies to PAL enzyme activity: 88%)
    - **Muscoluskeletal**: Arthralgia (61-83%), ↑ creatine phosphokinase (18-43%)
    - **Respiratory**: Sore throat (13-23%), cough (9-22%), nasal congestion (4-18%)

DRUG INTERACTIONS

- No significant interactions

COST

Drug	Strength	Package Size	AWP Pkg Price	AWP Unit Price
PALYNZIQ	2.5 mg/0.5 mL	1 mL	585.60	585.60
PALYNZIQ	10 mg/0.5 mL	1 mL	585.60	585.60
PALYNZIQ	20 mg/1 mL	1 mL	585.60	585.60

CURRENT UTILIZATION

ND Medicaid Utilization (06/2018 – 07/2018)		
Label Name	**Rx Num**	**Total Reimb Amt**
PALYNZIQ	0	N/A

REFERENCES:

1. Facts & Comparisons eAnswers. Available at http://online.factsandcomparisons.com. Accessed on July 20. 2018.
2. Palynziq (pegvaliase-pqpz) [prescribing information]. Novato, CA: BioMarin Pharmaceutical Inc; May 2018.

PRODUCT DETAILS OF ROXYBOND (OXYCODONE ABUSE-DETERRENT TABLET)

INDICATIONS AND USE:

- Opioid agonist indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.
    - Only to be used when alternative treatment options….
        - Have not been tolerated, or are not expected to be tolerated,
        - Have not provided adequate analgesia or are not expected to provide adequate analgesia.
    - Formulated with inactive ingredients that make the tablet more difficult to manipulate for misuse and abuse: Difficult to prepare into solution and forms viscous material that does not pass through a needle easily.

DOSAGE AND ADMINISTRATION:

- Initial: 5 or 15 mg every 4-6 hours as needed and titrate to effect.
- Dosing ≥15 years of age:
    - 1 to 4 grams per total daily dose in equally divided doses
- Dosing for 1 to 14 years of age:
    - Usual: 25 to 50 mg/kg given in equally divided doses for 7-14 days
    - Severe infections: 50 to 100 mg/kg in equally divided doses
    - Otitis Media: 75 to 100 mg/kg in equally divided doses

DOSAGE FORM AND STRENGTHS:

- 5, 15, 30 mg tablets

CONTRAINDICATIONS:

- Significant respiratory depression
- Acute or severe bronchial asthma in an unmonitored setting or in absence of resuscitative equipment
- Known or suspected gastrointestinal obstruction, including paralytic ileus
- Hypersensitivity to oxycodone

BOXED WARNING

- Respiratory depression, addiction/abuse potential, accidental ingestion, neonatal opioid withdrawal, CYP3A4 interactions, risk when used with benzos.

WARNINGS AND PRECAUTIONS:

- See boxed warnings
- Avoid use in cachectic and debilitated patients
- May cause hypotension
- Use with caution in patients with mental health conditions, seizures, head trauma, abdominal conditions, and biliary tract impairment.

ADVERSE REACTIONS:

- Most common adverse reactions: dizziness, nausea, constipation, vomiting, headache, pruritus, insomnia, asthenia, and somnolence.

DRUG INTERACTIONS

- Other CNS depressants, CYP 3A4 inducers and inhibitors

COST

Drug	Strength	Package Size	AWP Price	AWP Unit Price
ROXYBOND	5 mg	100 tablets	667.00	8.00
ROXYBOND	15 mg	100 tablets	933.60	9.34
ROXYBOND	30 mg	100 tablets	1,244.40	12.44

CURRENT UTILIZATION

ND Medicaid Utilization (06/2018 – 07/2018)		
Label Name	**Rx Num**	**Total Reimb Amt**
ROXYBOND	0	N/A

REFERENCES:

1. Facts & Comparisons eAnswers. Available at http://online.factsandcomparisons.com. Accessed on July 20. 2018.
2. Roxybond (oxycodone) [prescribing information]. Basking Ridge, NJ: Daiichi Sankyo Inc; June 2017.

PRODUCT DETAILS OF SIKLOS (HYDROXYUREA)

INDICATIONS AND USE:

- Sickle cell anemia
  - To reduce the frequency of painful crises and to reduce the need for blood transfusions in patients with recurrent moderate to severe painful crises.

DOSAGE AND ADMINISTRATION:

- Dosing ≥2 years of age:
  - **Max:** 35 mg/kg/day (titrated to effect, every 2 weeks if blood labs in acceptable range)
  - Neutrophils ≥2,500 cells/mm^3; platelets ≥95,000/mm^3; hemoglobin >5.3 g/dL; and reticulocytes ≥95,000/mm^3 if hemoglobin is <9 g/dL
  - **Initial:** 20 mg/kg/day
    - **Renal impairment (CrCl <50 mL/min):** Reduce initial dose 50%

DOSAGE FORM AND STRENGTHS:

- 100 mg tablets

CONTRAINDICATIONS:

- Hypersensitivity to hydroxyurea or any component of its formulation

BOXED WARNING

- Bone marrow suppression: Hydroxyurea may cause severe myelosuppression. Monitor blood counts at baseline and throughout treatment. Interrupt treatment and reduce dose as necessary.
- Secondary malignancy: Hydroxyurea is carcinogenic. Advise sun protection and monitor patients for malignancies

WARNINGS AND PRECAUTIONS:

- Cutaneous vasculitic toxicity
  - Vasculitic ulcerations and gangrene have been reported in patients with myeloproliferative disorders during hydroxyurea treatment.
    - Avoid use in patients with leg ulcer wounds and d/c if this occurs.
- HIV-infected patients
  - Pancreatitis, hepatotoxicity, and peripheral neuropathy have occurred when hydroxyurea was administered with antiretroviral medications.
- Macrocytosis
  - Self-limiting macrocytosis may be seen early in treatment. Prophylactic folic acid supplementation is recommended
- Tumor lysis syndrome
  - Hyperuricemia may occur with antineoplastic treatment.
- Radiation therapy recipients
  - Patients with a history of radiation therapy are at risk for exacerbation of post irradiation erythema and myelosuppression
- Avoid use of live vaccines during hydroxyurea therapy

ADVERSE REACTIONS:

- **Common (>5%)**
  - Eczema (infants and children: 13%)
  - Macrocytosis (MCV >97: 42%)
  - Leg ulcer (7%), dermal ulcer (3%)
  - Acute mucocutaneous toxicity (5%)
  - Asthma (infants and children: 9%)

DRUG INTERACTIONS

- Live vaccines, Tacrolimus and pimecrolimus, Antiretroviral therapy, Other immunosuppressants, Other myelosuppressive agents

COST

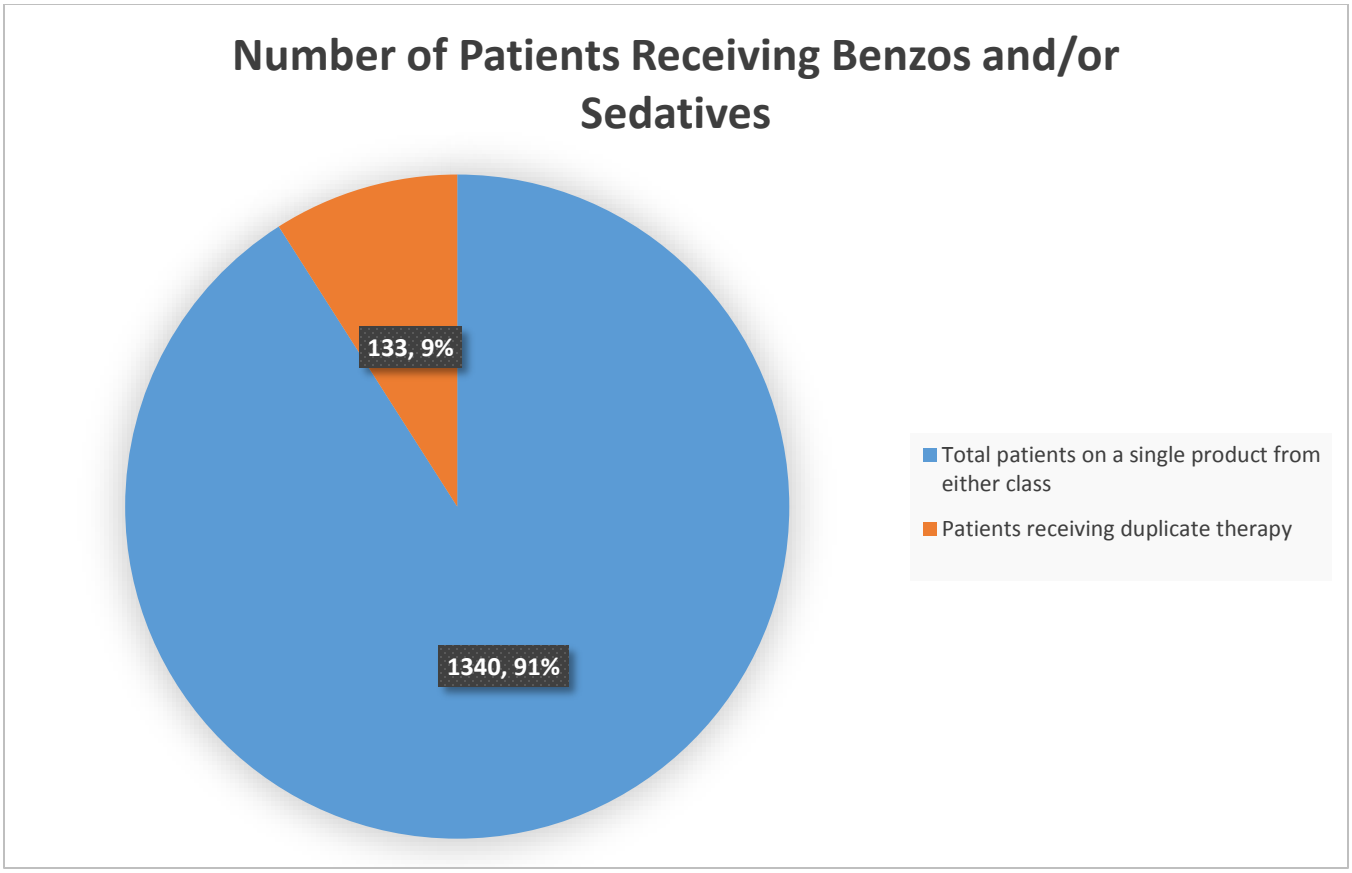
Drug	Strength	Package Size	AMP Pkg Price	AWP Unit Price
SIKLOS	100 mg	100 tablets	360.00	6.00

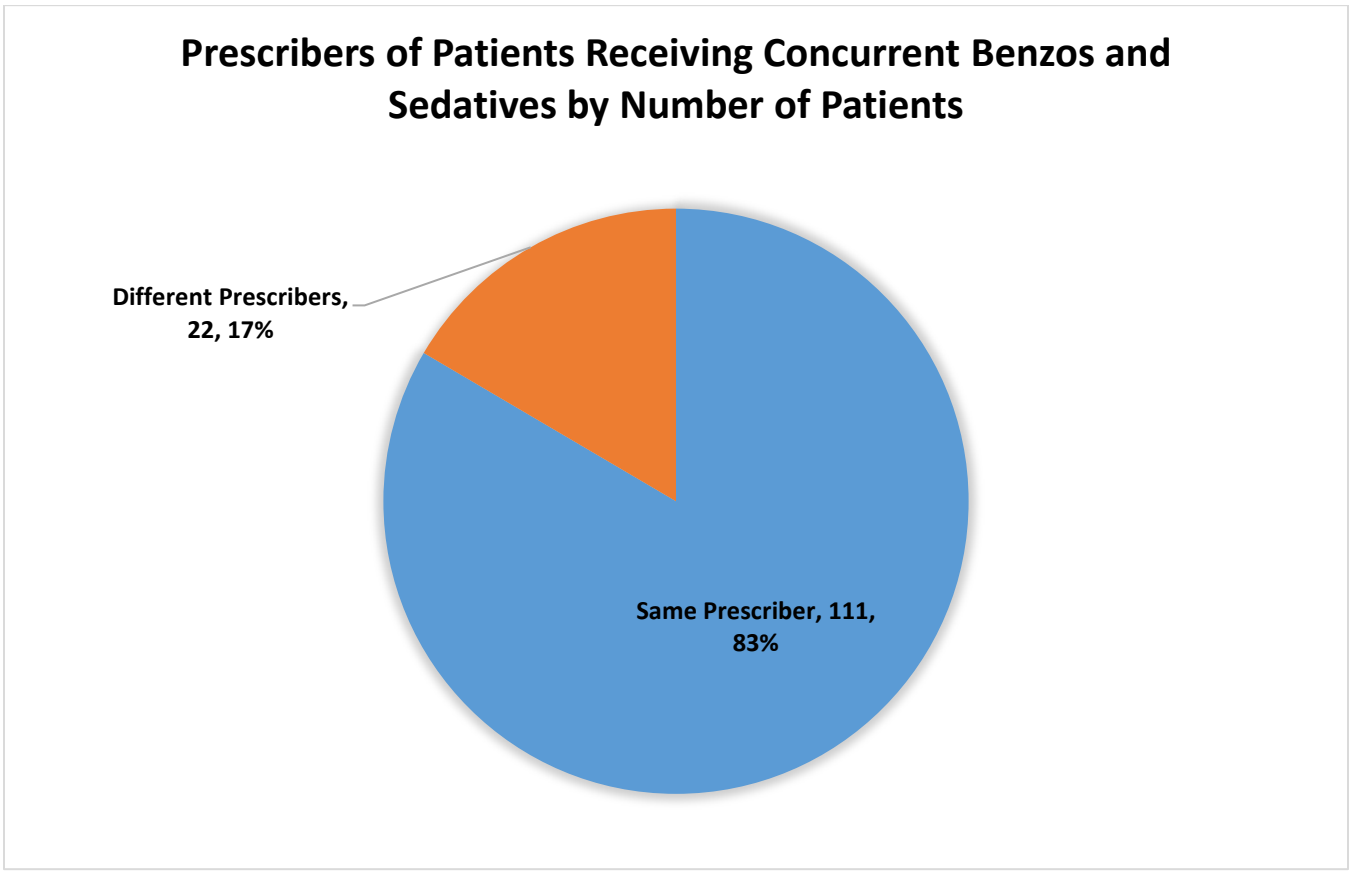
CURRENT UTILIZATION

ND Medicaid Utilization (06/2018 – 07/2018)		
Label Name	**Rx Num**	**Total Reimb Amt**
SIKLOS	0	N/A

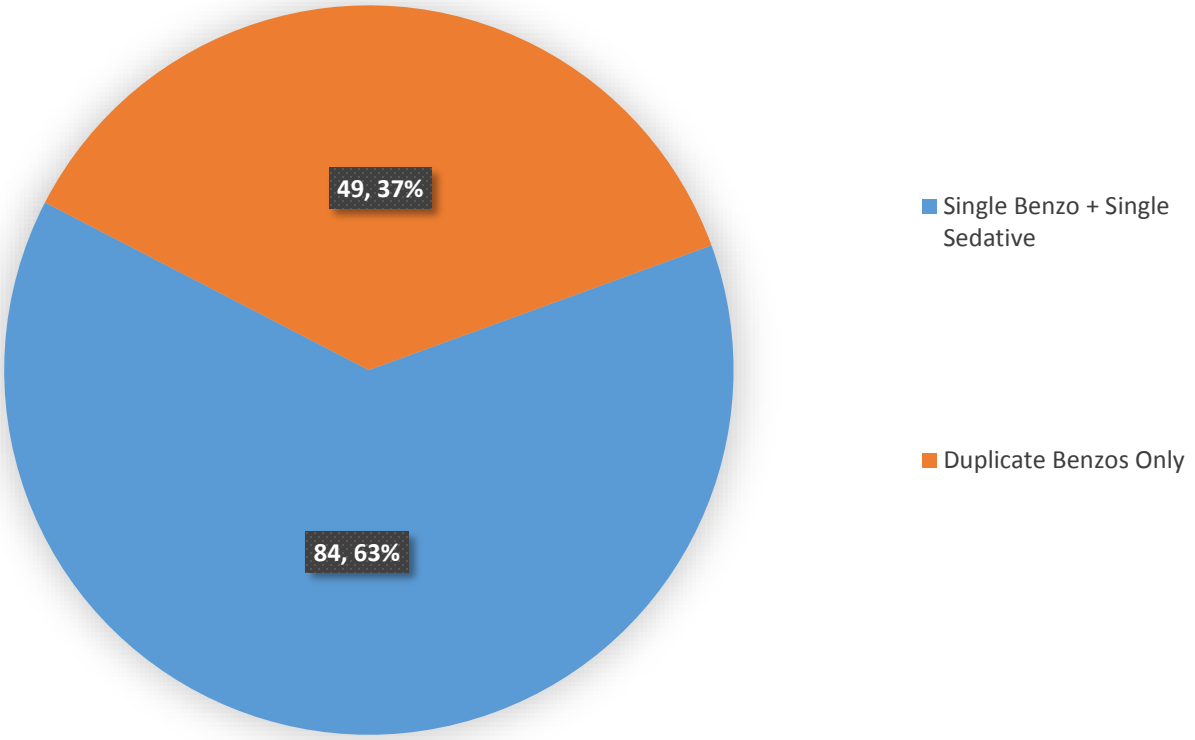
REFERENCES:

1. Facts & Comparisons eAnswers. Available at http://online.factsandcomparisons.com. Accessed on July 20. 2018.
2. Siklos (hydroxyurea) [prescribing information]. Bryn Mawr, PA: Medunik USA Inc; May 2018.

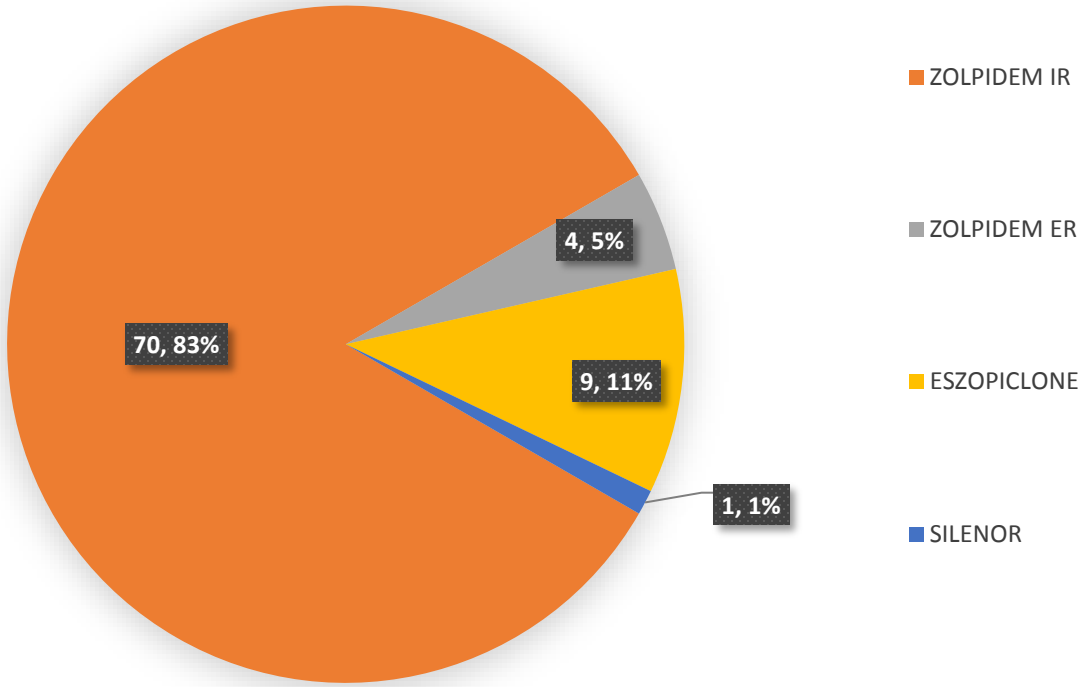

Number of Patients Receiving Benzos and/or Sedatives
133, 9%
1340, 91%
Total patients on a single product from either class
Patients receiving duplicate therapy


Prescribers of Patients Receiving Concurrent Benzos and Sedatives by Number of Patients
Different Prescribers, 22, 17%
Same Prescriber, 111, 83%

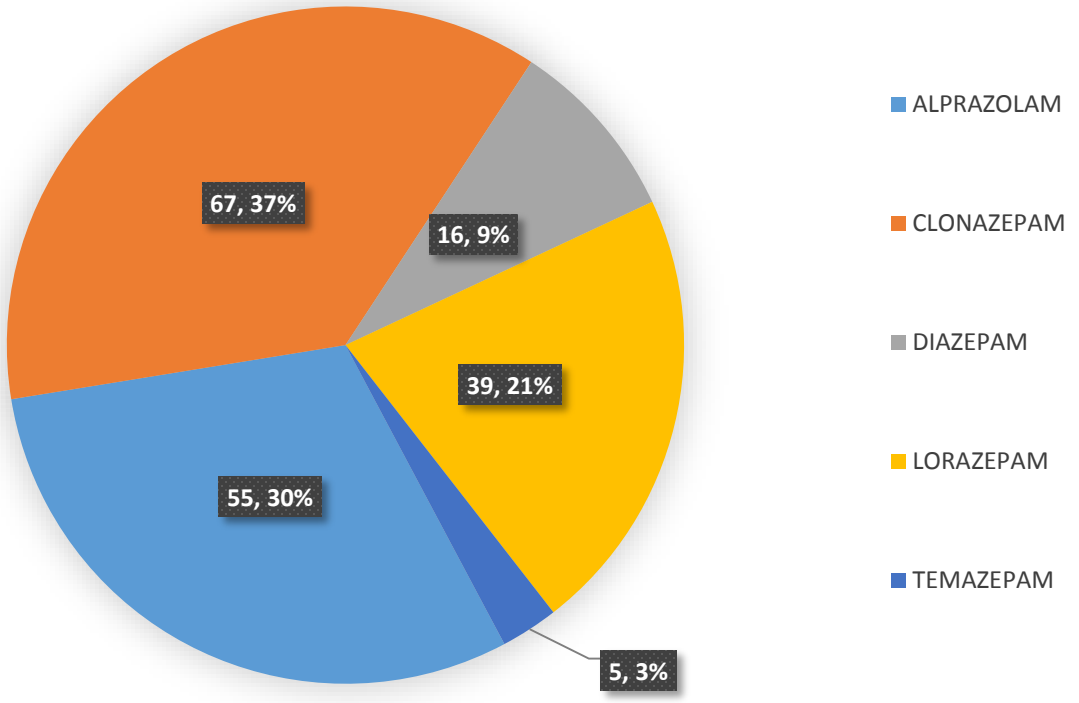
Benzo/Sedative Concurrent Use by Number of Patients



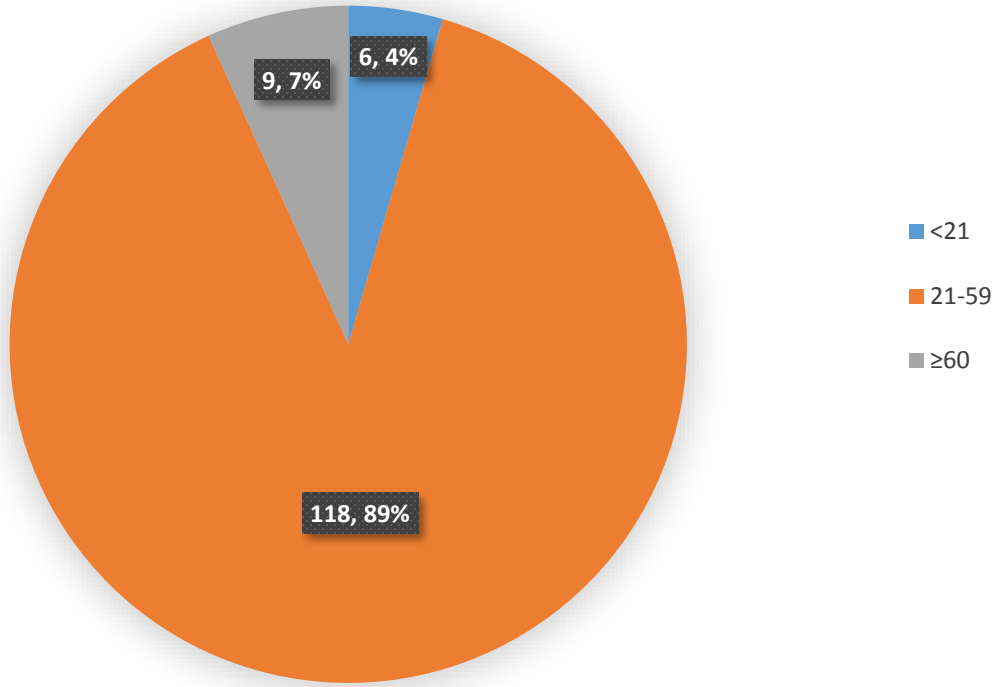
Most Common Sedatives Used Concurrently with Benzos by Number of Patients

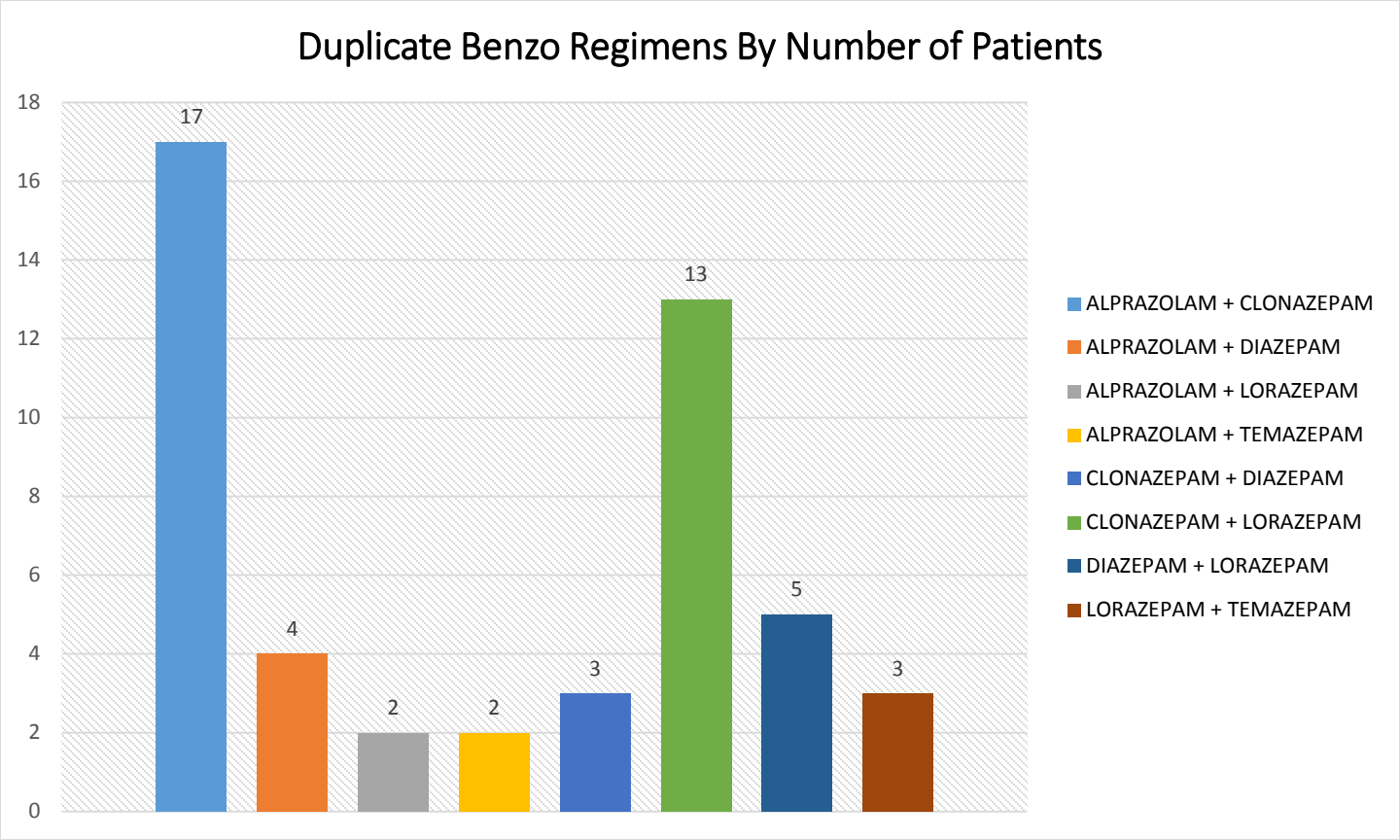


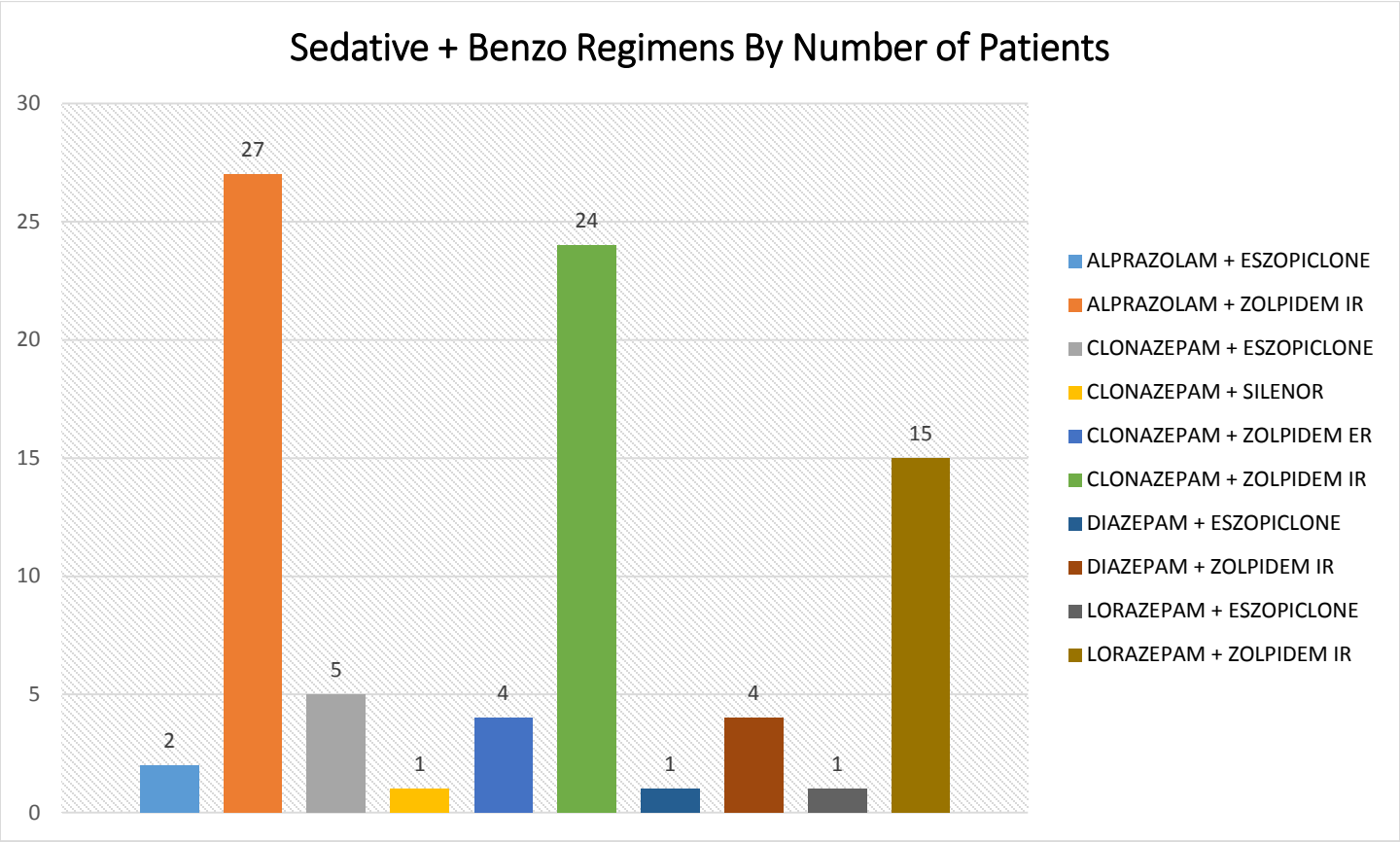
Most Common Benzos Used Concurrently with Sedatives by Number of Patients

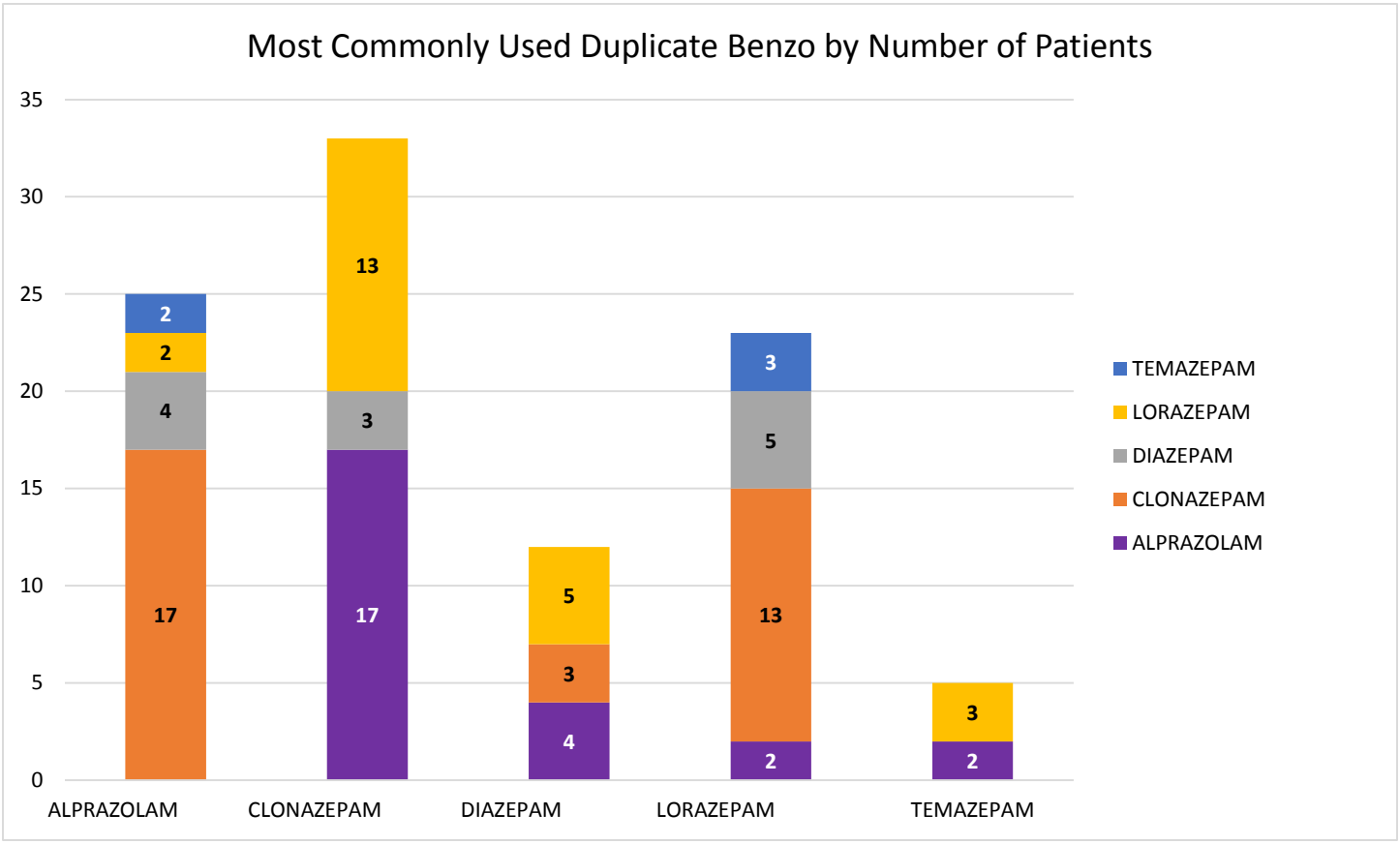


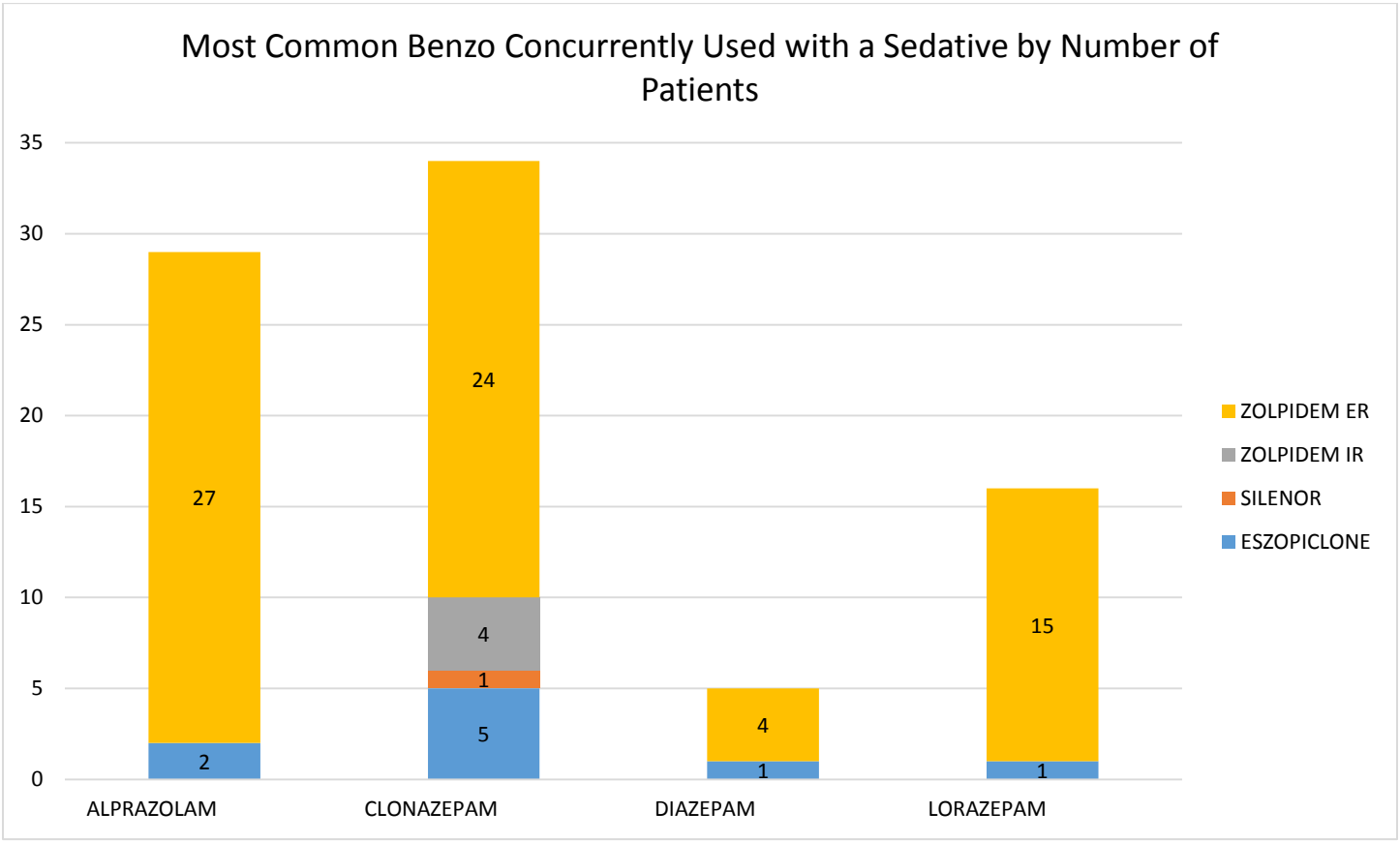
Number of Patients on Concurrent Benzos/Sedatives by Age Group




Duplicate Benzo Regimens By Number of Patients
18
16
14
12
10
8
6
4
2
0
17
4
2
2
3
13
5
3
ALPRAZOLAM + CLONAZEPAM
ALPRAZOLAM + DIAZEPAM
ALPRAZOLAM + LORAZEPAM
ALPRAZOLAM + TEMAZEPAM
CLONAZEPAM + DIAZEPAM
CLONAZEPAM + LORAZEPAM
DIAZEPAM + LORAZEPAM
LORAZEPAM + TEMAZEPAM


Sedative + Benzo Regimens By Number of Patients
30
25
20
15
10
5
0
2
27
5
1
4
24
1
4
1
15
ALPRAZOLAM + ESZOPICLONE
ALPRAZOLAM + ZOLPIDEM IR
CLONAZEPAM + ESZOPICLONE
CLONAZEPAM + SILENOR
CLONAZEPAM + ZOLPIDEM ER
CLONAZEPAM + ZOLPIDEM IR
DIAZEPAM + ESZOPICLONE
DIAZEPAM + ZOLPIDEM IR
LORAZEPAM + ESZOPICLONE
LORAZEPAM + ZOLPIDEM IR


Most Commonly Used Duplicate Benzo by Number of Patients
35
30
25
20
15
10
5
0
2
2
4
17
13
3
17
5
3
4
3
5
13
2
3
2
ALPRAZOLAM
CLONAZEPAM
DIAZEPAM
LORAZEPAM
TEMAZEPAM
TEMAZEPAM
LORAZEPAM
DIAZEPAM
CLONAZEPAM
ALPRAZOLAM


Most Common Benzo Concurrently Used with a Sedative by Number of Patients
35
30
25
20
15
10
5
0
27
2
24
4
1
5
4
1
15
1
ALPRAZOLAM
CLONAZEPAM
DIAZEPAM
LORAZEPAM
ZOLPIDEM ER
ZOLPIDEM IR
SILENOR
ESZOPICLONE

Overview of CAR T-Cell Immunotherapies

How they Work

- Chimeric antigen receptor (CAR) T-cell therapies
    - Unique compared to other chemotherapy agents in that the active product is actually genetically modified versions of a patient's own T-cells
    - Therapies work by reprogramming a patient's T cells to make it produce a CAR on its surface that allows it to target a specified antigen (transgene encoding)
        - CAR is an antibody fragment which recognizes and binds to a specific target "antigen"
        - After antigen binding, the CAR transmits a signal promoting T-cell proliferation, activation, secretion of inflammatory mediators, and ultimately destruction of antigen expressing cells

Preparation of the Active Product

- Because CAR T-cell immunotherapies are genetically enhanced versions of a patient's own T-cells, a multi-step process must take place prior to a patient being able to be treated with them.
    1. Patient's T-cells are removed from their blood using a process called leukapheresis
    2. T-cells are sent to a lab where they are genetically engineered to produce CD19 directed CARs
    3. The number of modified CAR T-cells is augmented by growing cells in the laboratory, which are then frozen
    4. Depending on the agent and the regimen chosen, the patient may be given lymphodepleting regimen*
    5. The patient's modified CAR T-cells are transfused into the patient's blood stream

Available Products

- Kymriah (tisagenlecleucel)
    - Indicated for the treatment of B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse in patients up to 25 years of age
    - Efficacy was proven in a trial including 63 pediatric and young adult patients with R/R B-cell precursor ALL.
        - 63% and 19% achieved CR or complete remission with incomplete blood count recovery (CRi) respectively.
        - The median DOR was not reached and the median time to onset of CR/CRi was 29 days.
- Yescarta (axicabtagene ciloleucel)
    - Indicated for the treatment of relapsed or refractory large B-cell lymphoma after 2 or more lines of systemic therapy (includes diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma).
    - Efficacy established in an open-label trial of 101 adult patients with relapsed or refractory aggressive B-cell non-Hodgkin lymphoma.
        - 51% achieved complete remission (CR) and 21% achieved partial remission
        - Median duration of response (DOR) of 9.2 months and a median time to response of 0.9 months
- Both products carry boxed warnings regarding the existence of a REMS program for each product as well as on the risk of potentially fatal or life-threatening cytokine release syndrome (CRS) and neurological toxicities associated with the products.
- Other warning include risk of serious viral, bacterial, and other infections; prolonged cytopenias,; Hypogammaglobulinemia; Hepatitis B virus (HBV) reactivation; and development of secondary malignancies or leukemia recurrence during treatment
- Most common adverse reactions (>10%), include blood pressure changes, tachycardia, headache, fatigue, delirium, hypophosphatemia, GI upset, acute renal failure, hypoxia, cough, myalgia and fever.

References:

1. Fischer, A. "FDA News Release: FDA approves CAR-T cell therapy to treat adults with certain types of large B-cell lymphoma". Press Announcements. United States Food and Drug Administration, 18 October 2017.
2. Fischer, A. "FDA approval brings first gene therapy to the United States". Press Announcements. United States Food and Drug Administration, 30 August 2017.
3. Kymriah (tisagenlecleucel) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2017.
4. Yescarta (axicabtagene ciloleucel) [prescribing information]. Santa Monica, CA: Kite Pharma Inc; October 2017.

NORTH DAKOTA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
3RD QUARTER 2018

Criteria Recommendations ***Approved*** ***Rejected***

1. Midostaurin / Overutilization _____ _____

Alert Message: The manufacturer's recommended dose of Rydapt (midostaurin) for patients with acute myeloid leukemia (AML) is 50 mg twice daily.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Midostaurin		Acute Myeloid Leukemia

Max Dose: 100mg/day

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Rydapt Prescribing Information, June 2018, Novartis Pharmaceuticals Corp.

2. Midostaurin / Overutilization _____ _____

Alert Message: The manufacturer's recommended dose of Rydapt (midostaurin) for patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHM) or mast cell leukemia (MCL) is 100 mg twice daily.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Midostaurin		Aggressive Systemic Mastocytosis (ASM) Mast Cell Leukemia

Max Dose: 200mg/day

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Rydapt Prescribing Information, June 2018, Novartis Pharmaceuticals Corp.

3. Midostaurin / Strong CYP3A4 Inducers _____ _____

Alert Message: Concurrent use of Rydapt (midostaurin), a CYP3A4 substrate, with a strong CYP3A4 inducer should be avoided as concomitant use may result in decreased midostaurin concentrations and reduced efficacy.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Midostaurin	Carbamazepine	Rifampin	
	Phenobarbital	Enzalutamide	
	Primidone		
	Phenytoin		

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Rydapt Prescribing Information, June 2018, Novartis Pharmaceuticals Corp.

4. Midostaurin / Strong CYP3A4 Inhibitors _____ _____

Alert Message: Concurrent use of Rydapt (midostaurin), a CYP3A4 substrate, with a strong CYP3A4 inhibitor may increase exposure to midostaurin and its active metabolites, increasing the risk of midostaurin toxicity. Consider alternative therapies that do not strongly inhibit CYP3A4 or monitor for increased risk of midostaurin-related adverse reactions.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Midostaurin	Clarithromycin	Nefazodone	
	Cobicistat	Ketoconazole	
	Conivaptan	Itraconazole	
	Ritonavir	Posaconazole	
	Saquinavir	Voriconazole	
	Indinavir		
	Nelfinavir		

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Rydapt Prescribing Information, June 2018, Novartis Pharmaceuticals Corp.

5. Midostaurin / Pregnancy / Pregnancy negating _____ _____

Alert Message: Rydapt (midostaurin) may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus.

Conflict Code: MC – Drug (Actual) Disease Precaution
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Midostaurin	Pregnancy	Miscarriage
		Abortion
		Delivery

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Rydapt Prescribing Information, April 2017, Novartis Pharmaceuticals Corp.

6. Midostaurin / Therapeutic Appropriateness _____ _____

Alert Message: Advise males with female sexual partners of reproductive potential that effective contraception should be used during treatment with Rydapt (midostaurin) and for 4 months after the last dose. Based on its mechanism of action and findings from animal reproduction studies, midostaurin may cause embryo-fetal toxicity.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Midostaurin		

Gender: Male

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Rydapt Prescribing Information, June 2018, Novartis Pharmaceuticals Corp.

7. Midostaurin / Therapeutic Appropriateness _____ _____

Alert Message: Based on its mechanism of action and findings from animal reproduction studies, Rydapt (midostaurin) may cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with midostaurin and for at least 4 months after the last dose.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Midostaurin		

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Rydapt Prescribing Information, June 2018, Novartis Pharmaceuticals Corp.

8. Midostaurin / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Rydapt (midostaurin) have not been established in pediatric patients.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Midostaurin		

Age Range: 0-17 yoa

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Rydapt Prescribing Information, June 2018, Novartis Pharmaceuticals Corp.

9. Midostaurin / Pulmonary Toxicity _____ _____

Alert Message: Cases of interstitial lung disease and pneumonitis, some fatal, have occurred in patients treated with Rydapt (midostaurin) as monotherapy or with chemotherapy. Monitor patients for pulmonary symptoms. Discontinue midostaurin in patients who experience signs and symptoms of interstitial lung disease or pneumonitis without an infectious etiology.

Conflict Code: MC – Drug (Actual) Disease Precaution
Drugs/Diseases

Util A	Util B	Util C
Midostaurin	Acute Interstitial Pneumonia Dyspnea	

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Rydapt Prescribing Information, June 2018, Novartis Pharmaceuticals Corp.

10. Neratinib / Overutilization _____ _____

Alert Message: The manufacturer's recommended dose of Nerlynx (neratinib) is 240 mg (6 tablets) orally once daily.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Neratinib		

Max Dose: 240 mg/day

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Nerlynx Prescribing Information, June 2018, Puma Biotechnology, Inc.

11. Neratinib / Diarrhea _____ _____

Alert Message: Nerlynx (neratinib) can cause severe diarrhea. Aggressively manage diarrhea occurring despite recommended prophylaxis with additional antidiarrheals, fluids, and electrolytes as clinically indicated. Withhold neratinib in patients who experience severe and/or persistent diarrhea. Permanently discontinue neratinib in patients experiencing Grade 4 diarrhea or Grade >/= 2 diarrhea that occurs after maximal dose reduction.

Conflict Code: MC - Drug (Actual) Disease Precaution
Drugs/Diseases

Util A	Util B	Util C
Neratinib	Diarrhea	

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Nerlynx Prescribing Information, June 2018, Puma Biotechnology, Inc.

12. Neratinib / Therapeutic Appropriateness-Hepatotoxicity _____ _____

Alert Message: Nerlynx (neratinib) has been associated with hepatotoxicity characterized by increased liver enzymes. Monitor liver function tests monthly for the first 3 months of treatment, then every 3 months while on treatment and as clinically indicated. Withhold neratinib in patients experiencing Grade 3 liver abnormalities and permanently discontinue neratinib in patients experiencing Grade 4 liver abnormalities.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Neratinib		

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Nerlynx Prescribing Information, June 2018, Puma Biotechnology, Inc.

13. Neratinib / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on findings from animal studies and its mechanism of action, Nerlynx (neratinib) can cause fetal harm when administered to a pregnant woman. In animal reproductive studies, administration of neratinib to pregnant rabbits during organogenesis caused abortions, embryo-fetal death and fetal abnormalities.

Conflict Code: Drug (Actual) Disease Precaution
Drugs/Diseases

Util A	Util B	Util C
Neratinib	Pregnancy	Miscarriage
		Abortion
		Delivery

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Nerlynx Prescribing Information, June 2018, Puma Biotechnology, Inc.

14. Neratinib / Therapeutic Appropriateness _____ _____

Alert Message: Nerlynx (neratinib) may cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with neratinib and for 1 month after the last dose. Females of reproductive potential should have a pregnancy test prior to starting treatment with neratinib.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Neratinib		

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Nerlynx Prescribing Information, June 2018, Puma Biotechnology, Inc.

15. Neratinib / Therapeutic Appropriateness _____ _____

Alert Message: Based on findings in animal reproductive studies, advise males receiving Nerlynx (neratinib) with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of neratinib.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Neratinib		

Gender: Male

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Nerlynx Prescribing Information, June 2018, Puma Biotechnology, Inc.

16. Neratinib / Proton Pump Inhibitors _____ _____

Alert Message: Concurrent use of Nerlynx (neratinib) with a proton pump inhibitor should be avoided as concomitant use of these agents may result in decreased neratinib exposure and efficacy. Drug interaction studies with neratinib and lansoprazole resulted in a decrease in neratinib Cmax and AUC of 71% and 65%, respectively.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Neratinib	Omeprazole	
	Esomeprazole	
	Lansoprazole	
	Rabeprazole	
	Dexlansoprazole	
	Pantoprazole	

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Nerlynx Prescribing Information, June 2018, Puma Biotechnology, Inc.

17. Neratinib / H2-Receptor Antagonists _____ _____

Alert Message: Concurrent use of Nerlynx (neratinib) with an H-2-receptor blocker should be avoided as concomitant use of these agents may result in decreased neratinib exposure and efficacy. The solubility of neratinib is pH dependent and its solubility decreases as gastric pH increases.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Neratinib	Cimetidine	
	Famotidine	
	Nizatidine	
	Ranitidine	

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Nerlynx Prescribing Information, June 2018, Puma Biotechnology, Inc.

18. Neratinib / Antacids _____ _____

Alert Message: Concurrent use of Nerlynx (neratinib) with an antacid may result in decreased neratinib exposure and efficacy. The solubility of neratinib is pH dependent and its solubility decreases as gastric pH increases. If concomitant use is warranted separate the dosing of neratinib and antacids by 3 hours.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Neratinib	Magnesium Hydroxide	
	Aluminum Hydroxide	
	Calcium Carbonate	

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Nerlynx Prescribing Information, June 2018, Puma Biotechnology, Inc.

19. Neratinib / Moderate & Strong CYP3A4 Inhibitors _____ _____

Alert Message: Concurrent use of Nerlynx (neratinib), a CYP substrate, with a moderate or strong CYP3A4 inhibitor should be avoided as concomitant use may result in increased neratinib plasma concentrations and neratinib toxicity.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B			Util C
Neratinib	Clarithromycin	Nefazodone	Erythromycin	Cimetidine
	Cobicistat	Ketoconazole	Ciprofloxacin	
	Conivaptan	Itraconazole	Crizotinib	
	Ritonavir	Posaconazole	Cyclosporine	
	Saquinavir	Voriconazole	Dronedarone	
	Indinavir	Diltiazem	Fluvoxamine	
	Nelfinavir	Verapamil	Imatinib	
	Atazanavir	Aprepitant	Clotrimazole	
	Tipranavir	Fluconazole	Idelalisib	

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Nerlynx Prescribing Information, June 2018, Puma Biotechnology, Inc.

20. Neratinib / Moderate & Strong CYP3A4 Inducers _____ _____

Alert Message: Concurrent use of Nerlynx (neratinib), a CYP3A4 substrate, with a moderate or strong CYP3A4 inducer should be avoided as concomitant use may result in decreased neratinib plasma concentrations and loss of neratinib efficacy.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B			Util C
Neratinib	Carbamazepine	Rifampin	Bosentan	
	Phenobarbital	Rifabutin	Efavirenz	
	Primidone	Rifapentine	Etravirine	
	Phenytoin	Mitotane	Modafinil	
	Enzalutamide	Nevirapine		

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Nerlynx Prescribing Information, June 2018, Puma Biotechnology, Inc.

21. Neratinib / Digoxin _____ _____

Alert Message: Concurrent use of Nerlynx (neratinib) with digoxin may result in increased digoxin concentrations and risk of digoxin toxicity due to neratinib inhibition of digoxin P-gp-mediated transport. In drug studies, concomitant use of digoxin with multiple oral doses of neratinib in healthy subjects increased the mean digoxin Cmax by 54% and the AUC by 32%. Dosage adjustment of digoxin may be required.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Neratinib	Digoxin	

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Nerlynx Prescribing Information, June 2018, Puma Biotechnology, Inc.

22. Neratinib / P-gp Substrates _____ _____

Alert Message: Concurrent use of Nerlynx (neratinib), a P-gp inhibitor, with a P-gp substrate may result in increased concentrations of the substrate. Monitor patient for P-gp substrate-related adverse reactions.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Neratinib	Dabigatran	
	Fexofenadine	
	Quinidine	
	Loperamide	
	Afatinib	
	Colchicine	
	Dapagliflozin	
	Edoxaban	
	Empagliflozin	
	Everolimus	
	Maraviroc	
	Methotrexate	
	Morphine	
	Paliperidone	
	Pazopanib	
	Ranolazine	
	Rivaroxaban	
	Saxagliptin	
	Sirolimus	
	Sitagliptin	
	Tacrolimus	
	Tolvaptan	
	Venetoclax	

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Nerlynx Prescribing Information, June 2018, Puma Biotechnology, Inc.

23. Abemaciclib / Overutilization _____ _____

Alert Message: Verzenio (abemaciclib) may be over-utilized. When used as monotherapy, the recommended maximum dose of abemaciclib is 200 mg twice daily.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Abemaciclib		Fulvestrant

Max Dose: 400 mg/day

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Verzenio Prescribing Information, Sept. 2017, Eli Lilly and Company.

24. Abemaciclib / Overutilization _____ _____

Alert Message: Verzenio (abemaciclib) may be over-utilized. When used in combination with fulvestrant, the recommended maximum dose of abemaciclib is 150 mg twice daily.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Abemaciclib		Fulvestrant

Max Dose: 300 mg/day

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Verzenio Prescribing Information, Sept. 2017, Eli Lilly and Company.

25. Abemaciclib / Severe Hepatic Impairment _____ _____

Alert Message: Patients with severe hepatic impairment should have the Verzenio (abemaciclib) dosing frequency reduced to one tablet once daily. In a single dose clinical study, the terminal half-life and the systemic exposure of abemaciclib plus its active metabolites doubled in subjects with severe hepatic impairment (Child-Pugh C) relative to those with normal liver function.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Abemaciclib		Cirrhosis
		Hepatic Fibrosis

Max Dose: 1 tablet per day

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Verzenio Prescribing Information, Sept. 2017, Eli Lilly and Company.
Center for Drug Evaluation and Research, NDA/BLA Multi-Discipline Review and Evaluation NDA 208716 Abemaciclib. February 1, 2016.

26. Abemaciclib / Ketoconazole _____ _____

Alert Message: Concurrent use of Verzenio (abemaciclib) with ketoconazole should be avoided due to the risk of abemaciclib toxicity. Ketoconazole is a potent CYP3A4 inhibitor and concomitant use with the CYP3A4 substrate, abemaciclib, is predicted to increase the AUC of abemaciclib by up to 16-fold.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Abemaciclib	Ketoconazole	

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Verzenio Prescribing Information, Sept. 2017, Eli Lilly and Company.

27. Abemaciclib / Strong CYP3A4 Inhibitors _____ _____

Alert Message: The concurrent use of Verzenio (abemaciclib), a CYP3A4 substrate, with a strong CYP3A4 inhibitor may increase the exposure of abemaciclib and its active metabolites, leading to abemaciclib toxicity. Refer to the official package labeling for the recommended abemaciclib dosage reduction when abemaciclib is used concomitantly with a strong CYP3A4 inhibitor. If the strong CYP3A4 inhibitor is discontinued, increase the abemaciclib dose (after 3-5 half-lives of the inhibitor) to the dose that was used before starting the strong inhibitor.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Abemaciclib	Clarithromycin	Indinavir	
	Nefazodone	Nelfinavir	
	Cobicistat	Itraconazole	
	Saquinavir	Posaconazole	
	Ritonavir	Voriconazole	

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Verzenio Prescribing Information, Sept. 2017, Eli Lilly and Company.

28. Abemaciclib / Strong CYP3A4 Inducers _____ _____

Alert Message: The concurrent use of Verzenio (abemaciclib), a CYP3A4 substrate, with a strong CYP3A4 inducer should be avoided due to the risk of decreased abemaciclib efficacy. In clinical studies, the co-administration of the strong CYP3A4 inducer rifampin with abemaciclib decreased the plasma concentrations of abemaciclib plus its active metabolites by 67% in healthy subjects.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Abemaciclib	Carbamazepine	Rifampin	
	Phenytoin	Mitotane	
	Phenobarbital	Enzalutamide	
	Primidone		

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Verzenio Prescribing Information, Sept. 2017, Eli Lilly and Company.

29. Abemaciclib / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on findings from animal studies and the mechanism of action, Verzenio (abemaciclib) can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Females of reproductive potential should have a negative pregnancy test prior to initiating treatment with abemaciclib and advised to use effective contraception during treatment with abemaciclib and for at least 3 weeks after the last dose.

Conflict Code: MC – Drug (Actual) Disease Precaution
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Abemaciclib	Pregnancy	Miscarriage
		Delivery
		Abortion

Gender: Female
Age Range: 18 – 50 yoa

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Verzenio Prescribing Information, Sept. 2017, Eli Lilly and Company.

30. Arnuity Ellipta / Overutilization (5-11 yoa) _____ _____

Alert Message: Arnuity Ellipta (fluticasone furoate inhalation) may be over-utilized. The manufacturer's recommended maximum dose in patients 5 to 11 years of age is 50 mcg once daily.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Fluticasone Furoate		

Age Range 5 – 11 yoa

References:
Arnuity Ellipta Prescribing Information, May 2018, GlaxoSmithKline.

31. Deutetrabenazine / Tetrabenazine _____ _____

Alert Message: Concurrent use of Austedo (deutetrabenazine) with Ingrezza (valbenazine) is contraindicated. Both deutetrabenazine and valbenazine are VMAT2 inhibitors and concomitant use may cause synergistic or additive toxicity.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Deutetrabenazine	Valbenazine	

References:
Austedo Prescribing Information, June 2018, Teva Pharmaceuticals.

32. Dexlansoprazole / Therapeutic Appropriateness - Age _____ _____

Alert Message: The safety and effectiveness of Dexilant (dexlansoprazole) have not been established in pediatric patients less than 12 years of age. Dexlansoprazole is not recommended in pediatric patients less than 12 years of age.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Dexlansoprazole		

Age Range: 0-11 yoa

References:
Dexilant Prescribing Information, June 2018, Takeda Pharmaceuticals.
Clinical Pharmacology. 2018, Elsevier/Gold Standard.

33. Dexlansoprazole / Overutilization _____ _____

Alert Message: The recommended dose of Dexilant (dexlansoprazole) for healing of erosive esophagitis (EE) is 60 mg once daily. For maintenance of healed EE and relief of associated heartburn or symptomatic non-erosive GERD, the recommended dose is 30 mg once daily.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Negate)**
Dexlansoprazole		Hepatic Impairment

Max Dose: 60 mg/day

References:
Dexilant Prescribing Information, June 2018, Takeda Pharmaceuticals.
Clinical Pharmacology. 2018, Elsevier/Gold Standard.

34. Alectinib / Overutilization _____ _____

Alert Message: The manufacturer's recommended daily dose of Alecensa (alectinib) is 600 mg taken twice daily for a total daily dose of 1200 mg.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Alectinib		

Max Dose: 1200 mg/day

References:
Alecensa Prescribing Information, June 2018, Genentech.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

35. Alectinib / Overutilization – Hepatic Impairment _____ _____

Alert Message: The recommended daily dose of Alecensa (alectinib) in patients with severe hepatic impairment (Child-Pugh C) is 450 mg twice daily. No dose adjustment is recommended for patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C (Include)
Alectinib		Cirrhosis
		Hepatic Fibrosis

Max Dose: 900 mg/day

References:
Alecensa Prescribing Information, June 2018, Genentech.

36. Alectinib / Therapeutic Appropriateness _____ _____

Alert Message: Alecensa (alectinib) can cause severe ALT, AST, or bilirubin elevation. Monitor liver function tests and total bilirubin every 2 weeks during the first 3 months of treatment, then once a month and as clinically indicated, with more frequent testing in patients who develop transaminase and bilirubin elevations. Based on the severity of the adverse reaction, modify therapy according to the manufacturer's instructions in the official prescribing information.

Conflict Code: TA -Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Alectinib		

References:
Alecensa Prescribing Information, June 2018, Genentech.

37. Alectinib / ILD Symptoms & Interstitial Pneumonitis _____ _____

Alert Message: Alecensa (alectinib) can cause interstitial lung disease (ILD)/pneumonitis. Promptly investigate for ILD/pneumonitis if patient presents with new or worsening respiratory symptoms such as dyspnea, fever, or cough. Immediately withhold treatment with alectinib in patients diagnosed with ILD/pneumonitis and permanently discontinue alectinib if no other potential causes of ILD/pneumonitis have been identified.

Conflict Code: MC – Drug (Actual) Disease Warning/Precaution
Drugs/Diseases

Util A	Util B	Util C
Alectinib	Dyspnea	
	Fever	
	Cough	
	Wheezing	
	Interstitial pneumonitis	

References:
Alecensa Prescribing Information, June 2018, Genentech.

38. Alectinib / Bradycardia _____ _____

Alert Message: Symptomatic bradycardia can occur with Alecensa (alectinib) therapy. In cases of non-life-threatening, symptomatic bradycardia withhold alectinib until recovery to asymptomatic bradycardia or to a heart rate of 60 bpm or above and evaluate concomitant medications known to cause bradycardia. If attributable to a concomitant medication, resume alectinib at a reduced dose (450 mg BID or 300 mg BID) upon recovery to asymptomatic bradycardia or to a heart rate of 60 bpm or above. If not attributed to a concomitant medication permanently discontinue alectinib. Permanently discontinue in case of recurrence or in cases of life-threatening bradycardia.

Conflict Code: MC – Drug (Actual) Disease Warning/Precaution
Drugs/Diseases

Util A	Util B	Util C
Alectinib	Bradycardia	

References:
Alecensa Prescribing Information, June 2018, Genentech.

39. Alectinib / Therapeutic Appropriateness _____ _____

Alert Message: Alecensa (alectinib) can cause severe myalgia and creatine phosphokinase (CPK) elevation. Assess CPK every 2 weeks during the first month of therapy and in patients reporting unexplained muscle pain tenderness or weakness. In case of severe CPK elevations (CPK > 5 times ULN), modify therapy according to the manufacturer's instructions in the official prescribing information.

Conflict Code: TA -Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Alectinib		

References:
Alecensa Prescribing Information, June 2018, Genentech.

40. Alectinib / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Alecensa (alectinib) can cause fetal harm in a pregnant woman based on its mechanism of action and findings in animals. Advise female patients of childbearing potential receiving alectinib to use effective contraceptive measures during treatment and for 1 week following final alectinib dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months following the final dose.

Conflict Code: MC – Drug (Actual) Disease Warning/Precaution
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Alectinib	Pregnancy	Miscarriage
		Delivery
		Abortion

Age Range 11-50 yoa
Gender: Female

References:
Alecensa Prescribing Information, June 2018, Genentech.

41. Tofacitinib IR / Overutilization _____ _____

Alert Message: Xeljanz (tofacitinib) may be over-utilized. The manufacturer's recommended maximum dose of tofacitinib, for patients with ulcerative colitis, is 10 mg twice daily.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Tofacitinib IR		Ulcerative Colitis

Max Dose: 20 mg/day

References:
Xeljanz/Xeljanz XR Prescribing Information, May 2018, Pfizer, Inc.
Clinical Pharmacology, 2018 Elsevier/Gold Standard.

42. Tofacitinib XR / Moderate, Severe Renal Insufficiency & Hepatic Impair. _____ _____

Alert Message: The manufacturer recommends that a patient receiving Xeljanz XR (tofacitinib extended-release) be switched to immediate-release tofacitinib 5 mg once daily if the patient has moderate or severe renal insufficiency or moderate hepatic impairment.

Conflict Code: MC – Drug (Actual) Disease Precaution
Drugs/Diseases

Util A	Util B	Util C
Tofacitinib XR	CKD 3, 4, &5	
	Hepatic Impairment	

References:
Xeljanz/Xeljanz XR Prescribing Information, May 2018, Pfizer, Inc.
Clinical Pharmacology, 2018 Elsevier/Gold Standard.

43. Tofacitinib XR / Strong CYP3A4 Inhibitors & Potent CYP2C19 Inhibitors _____ _____

Alert Message: The manufacturer recommends that a patient receiving Xeljanz XR (tofacitinib extended-release) be switched to immediate-release tofacitinib 5 mg once daily if the patient is receiving concurrent therapy with a strong CYP3A4 inhibitor or with one or more concomitant medications that cause both moderate CYP3A4 inhibition and potent CYP2C19 inhibition.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Tofacitinib XR	Nefazodone	Voriconazole	
	Saquinavir	Itraconazole	
	Ritonavir	Posaconazole	
	Nelfinavir	Cobicistat	
	Indinavir	Fluconazole	
	Clarithromycin	Fluvoxamine	
	Ketoconazole		

References:
Xeljanz/Xeljanz XR Prescribing Information, May 2018, Pfizer, Inc.
Clinical Pharmacology, 2018 Elsevier/Gold Standard.