North Dakota Medicaid
Drug Utilization Review Board
Meeting
September 2, 2020
Via Teleconference

North Dakota Medicaid
DUR Board Meeting Agenda
Join Microsoft Teams Meeting

(Click on link)
Join by phone: 1 701-328-0950, Conference ID: 312 304 233#
September 2, 2020
1:00 pm

1. Administrative items
    - DHS announcements

2. Old business
    - Review and approval of June 2020 meeting minutes
    - Budget update
    - Review top 25 drugs for second quarter of 2020
    - Prior authorization/PDL update
    - Second review of Palforzia
    - Second review of Mytesti
    - Second review of antifibrinolytic agents
    - Second review of ACL inhibitors
    - Second review of cystic fibrosis agents

3. New business
    - Retrospective DUR criteria recommendations
    - Review of agents for the treatment of diabetic gastroparesis
    - Review of Ohriahnn (elagolix/estradiol/norethindrone)
    - Review of Dojolvi (triheptanoin)
    - Review of utilization data for select medication classes
    - Upcoming meeting date/agenda.
        - Next meeting is December 2, 2020
4. Adjourn

Please remember to silence all cellular phones during the meeting.

Drug Utilization Review (DUR) Meeting Minutes
June 3, 2020

Members Present: Andrea Honeyman, Tanya Schmidt, Jennifer Iverson, Gabriela Balf, Laura Schield, Jennifer Iverson, Mary Aaland, Peter Woodrow, Amy Werremeyer, Cory Miller

Medicaid Pharmacy Department: Alexi Murphy, Brendan Joyce, LeNeika Roerich

Old Business

Chair A. Honeyman called the meeting to order at 1:05 p.m. Chair A. Honeyman asked for a motion to approve the minutes of the March meeting. L. Schield moved that the minutes be approved, and T. Schmidt seconded the motion. The chair called for a voice vote to approve the minutes. The motion passed with no audible dissent.

Review Top 25 Drugs

T. DeRuiter and A. Murphy presented the quarterly review of the top 25 drugs based on total cost od claims, as well as the top 25 drugs based on the total number of claims for the 1st quarter of 2020.

PDL/PA Criteria Updates

A. Murphy shared with the Board all of changes made to the Preferred Drug List since the most recent version of the Preferred Drug List was posted. Notable changes included updates to the criteria for Hepatitis C Treatments and Insulin, as well as changes to coverage requirements for Xifaxan in the Diarrhea – Irritable Bowel Syndrome and Traveler's Diarrhea criteria. All PDL updates are listed in the handouts for the June 2020 DUR Board meeting. When a new version of the PDL is published and posted to the website, all updates/changes made since the last version are called out at the top of the document itself.

Update to Criteria for Medications Costing >$3,000

A. Murphy presented a proposed update to the prior authorization criteria for medications that cost >$3,000. The update included new renewal criteria which requires documentation indicating that the patient has experienced and maintained a clinical benefit since starting the requested medication. There was no public comment. Chair A. Honeyman called for a voice vote to approve the updated criteria, which passed with no audible dissent.

Second Review of Conjupri

A motion and second was made at the March 2020 DUR Board meeting to place Conjupri on prior authorization. The topic was brought up for a second review. Prior authorization criteria were presented to the Board by T. DeRuiter. There were no public comments. Chair A. Honeyman called for a voice vote to approve the updated criteria, which passed with no audible dissent.

New Business

Review of Cystic Fibrosis Agents

T. DeRuiter and A. Murphy presented a review of CFTR modulators for the treatment of cystic fibrosis to the Board. During public comment, J. Rusinak from Vertex Pharmaceuticals presented an overview of clinical information on the available CFTR modulators to the Board. A motion was made by L. Schield to manage these medications through prior authorization. The motion was seconded by P. Woodrow. Prior authorization criteria for these agents will be presented, reviewed, and voted on by the Board at the next meeting.

Review of ACL Inhibitors

T. DeRuiter and A. Murphy presented a review of ACL inhibitors to the Board. A motion was made by A. Werremeyer to manage these medications through prior authorization. The motion was seconded by P. Woodrow. Prior authorization criteria for these agents will be presented, reviewed, and voted on by the Board at the next meeting.

Review of Antifibrinolytic Agents

T. DeRuiter and A. Murphy presented a review of antifibrinolytic agents to the Board. A motion was made by T. Schmidt to manage these medications through prior authorization. The motion was seconded by P. Woodrow. Prior authorization criteria for these agents will be presented, reviewed, and voted on by the Board at the next meeting.

Review of Palforzia

T. DeRuiter and A. Murphy presented a review of Palforzia for use in patients with a peanut allergy. to the Board. A. Honeyman and M. Aaland inquired as to the recommended duration of use. S. Payne from Aimmune explained the recommendations on treatment duration to the Board. A motion was made by P. Woodrow to manage this medication through prior authorization. The motion was seconded by J. Iverson. Prior authorization criteria will be presented, reviewed, and voted on by the Board at the next meeting.

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 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. L. Schield moved to approve the new criteria and P. Woodrow seconded the motion. The motion passed with no audible dissent.

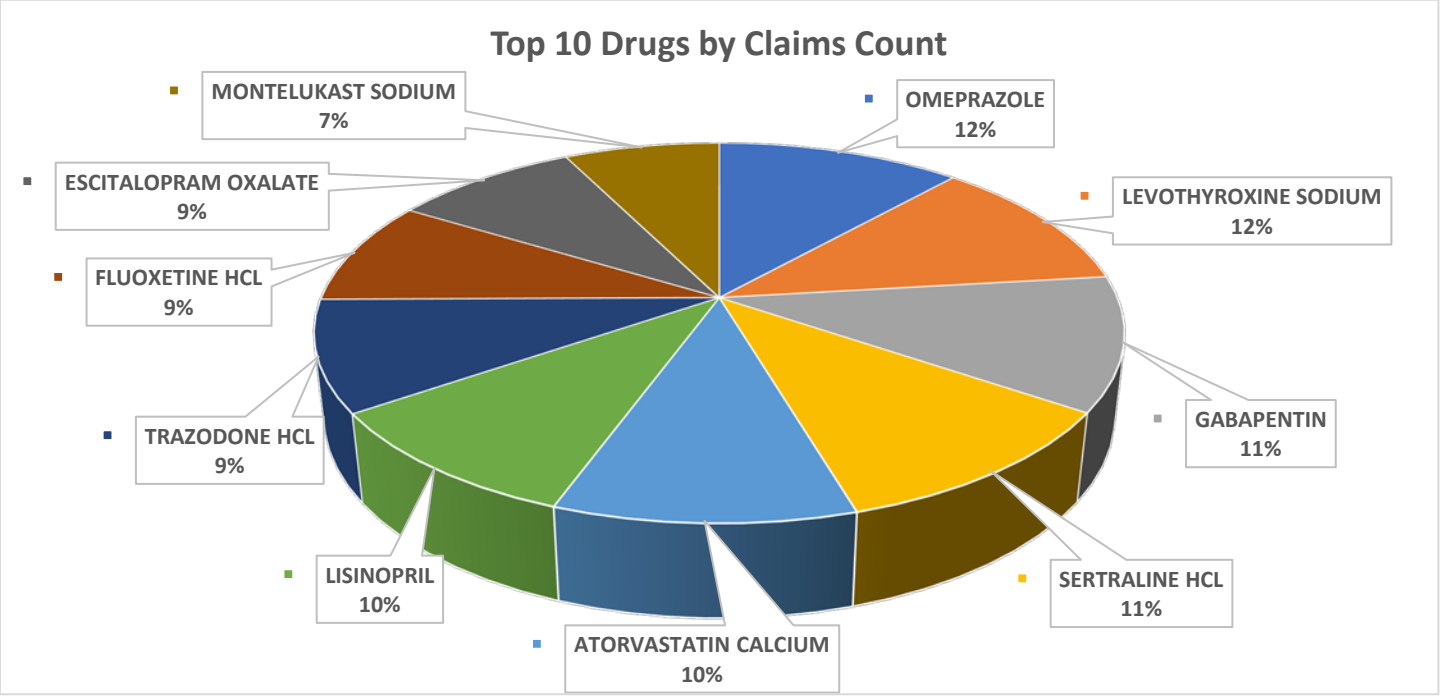
Adjournment and Upcoming Meeting Date

Chair A. Honeyman adjourned the meeting at 2:45 pm. The next DUR Board meeting will be held September 2, 2020 at 1:00 pm with location to be determined.

Top 25 Drugs Based on Number of Claims from 04/01/2020 – 06/30/2020

Drug	AHFS Class	Claims	Claims Cost	Cost Per Claim	% Total Claims
OMEPRAZOLE	PROTON-PUMP INHIBITORS	4,421	$57,716.90	$13.06	1.92%
LEVOTHYROXINE SODIUM	THYROID AGENTS	4,369	$81,280.27	$18.60	1.90%
GABAPENTIN	ANTICONVULSANTS, MISC	4,316	$70,284.45	$16.28	1.87%
SERTRALINE HCL	ANTIDEPRESSANTS	4,141	$55,929.71	$13.51	1.80%
ATORVASTATIN CALCIUM	STATINS	3,856	$54,671.99	$14.18	1.67%
LISINOPRIL	ACE INHIBITORS	3,733	$47,482.79	$12.72	1.62%
TRAZODONE HCL	ANTIDEPRESSANTS	3,587	$49,919.95	$13.92	1.56%
FLUOXETINE HCL	ANTIDEPRESSANTS	3,369	$46,725.57	$13.87	1.46%
ESCITALOPRAM OXALATE	ANTIDEPRESSANTS	3,365	$44,832.14	$13.32	1.46%
MONTELUKAST SODIUM	LEUKOTRIENE MODIFIERS	2,815	$40,149.52	$14.26	1.22%
METFORMIN HCL	BIGUANIDES	2,725	$34,036.58	$12.49	1.18%
BUPROPION XL	ANTIDEPRESSANTS	2,536	$46,535.48	$18.35	1.10%
DULOXETINE HCL	ANTIDEPRESSANTS	2,518	$43,984.52	$17.47	1.09%
HYDROCODONE-APAP	OPIATE AGONISTS	2,500	$40,685.84	$16.27	1.08%
PANTOPRAZOLE SODIUM	PROTON-PUMP INHIBITORS	2,490	$33,985.61	$13.65	1.08%
AMLODIPINE BESYLATE	DIHYDROPYRIDINES	2,285	$28,810.56	$12.61	0.99%
ARIPIPRAZOLE	ANTIPSYCHOTIC AGENTS	2,201	$34,545.56	$15.70	0.96%
CLONIDINE HCL	CENTRAL ALPHA-AGONISTS	2,180	$27,460.74	$12.60	0.95%
BUPRENORPHINE-NALOXONE	OPIATE PARTIAL AGONISTS	2,162	$124,696.96	$57.68	0.94%
VYVANSE	AMPHETAMINES	2,107	$537,697.83	$255.20	0.91%
LAMOTRIGINE	ANTICONVULSANTS, MISC	2,076	$28,404.11	$13.68	0.90%
VENLAFAXINE HCL ER	ANTIDEPRESSANTS	2,010	$33,804.42	$16.82	0.87%
CLONAZEPAM	BENZODIAZEPINES	1,994	$26,756.14	$13.42	0.87%
QUETIAPINE FUMARATE	ANTIPSYCHOTIC AGENTS	1,988	$28,299.07	$14.23	0.86%
CYCLOBENZAPRINE HCL	SKELETAL MUSCLE RELAXNT	1,925	$22,883.22	$11.89	0.84%

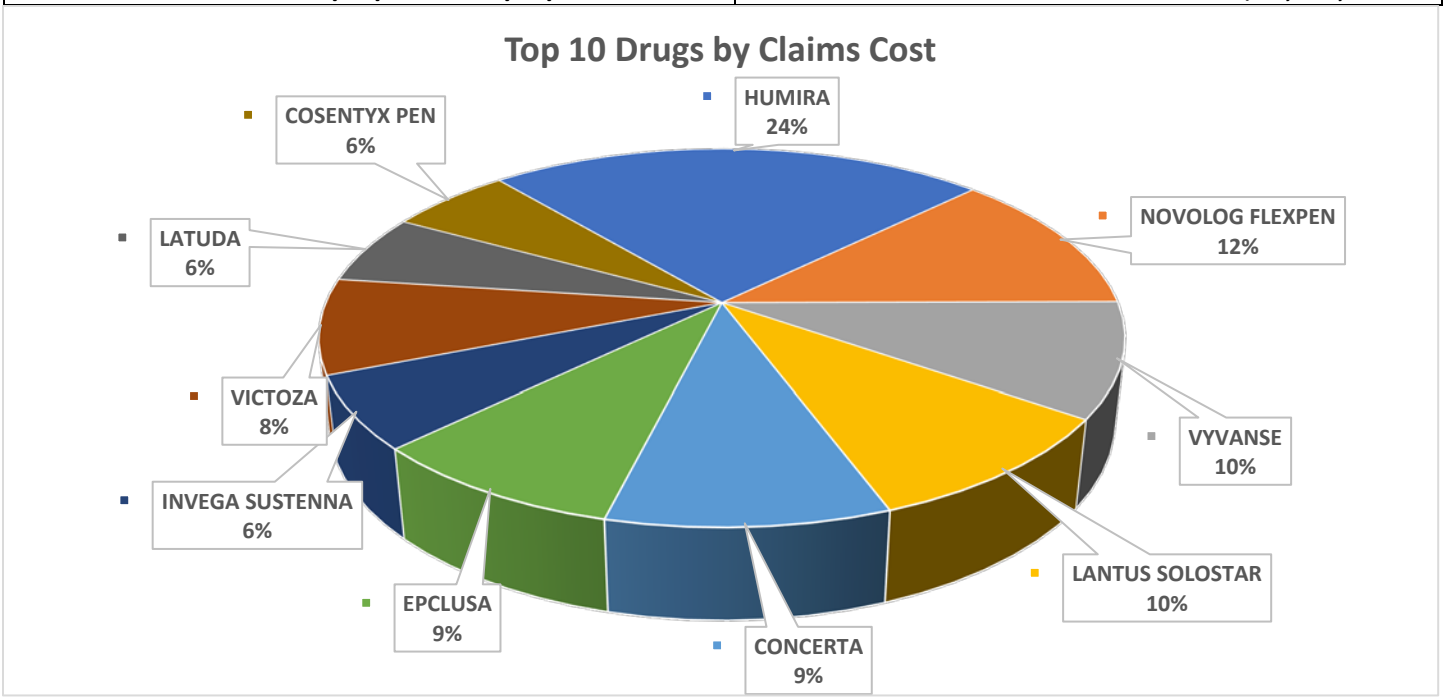
Total Claims From 04/01/2020 – 06/30/2020	**230,447**



Top 25 Drugs Based on Total Claims Cost from 04/01/2020 – 06/30/2020

Drug	AHFS Class	Claims Cost	Claims	Cost Per Claim	% Total Cost
HUMIRA	DMARDS	$1,309,696.32	212	$6,177.81	5.84%
NOVOLOG FLEXPEN	INSULINS	$672,750.01	1,142	$589.10	3.00%
VYVANSE	AMPHETAMINES	$537,697.83	2,107	$255.20	2.40%
LANTUS SOLOSTAR	INSULINS	$529,917.69	1,196	$443.07	2.36%
CONCERTA	AMPHETAMINES	$528,520.86	1,491	$354.47	2.36%
EPCLUSA	HCV ANTIVIRALS	$486,516.26	20	$24,325.81	2.17%
INVEGA SUSTENNA	ANTIPSYCHOTIC AGENTS	$341,027.25	155	$2,200.18	1.52%
VICTOZA	INCRETIN MIMETICS	$447,832.12	582	$769.47	2.00%
LATUDA	ANTIPSYCHOTIC AGENTS	$326,972.27	408	$801.40	1.46%
COSENTYX PEN	SKIN/MUCOUS MEMBRANE	$322,897.19	56	$5,766.02	1.44%
NORDITROPIN FLEXPRO	PITUITARY	$318,597.15	94	$3,389.33	1.42%
JARDIANCE	SGLT2 INHIB	$302,636.13	681	$444.40	1.35%
LEVEMIR FLEXTOUCH	INSULINS	$292,073.03	574	$508.84	1.30%
SYMBICORT	INHALED CORTICOSTEROIDS	$237,036.22	755	$313.96	1.06%
SABRIL	ANTICONVULSANTS, MISC	$230,220.79	12	$19,185.07	1.03%
XIFAXAN	ANTIBACTERIALS, MISC	$228,838.91	108	$2,118.88	1.02%
TRIKAFTA	CFTR CORRECTORS	$215,177.31	9	$23,908.59	0.96%
BIKTARVY	ANTIRETROVIRALS	$193,652.45	121	$1,600.43	0.86%
GENVOYA	ANTIRETROVIRALS	$193,495.86	130	$1,488.43	0.86%
ABILIFY MAINTENA	ANTIPSYCHOTIC AGENTS	$192,822.28	98	$1,967.57	0.86%
CONTOUR NEXT TEST STRIP	DIABETES MELLITUS	$189,195.98	1,649	$114.73	0.84%
NOVOLOG	INSULINS	$180,676.45	310	$582.83	0.81%
ELIQUIS	ANTICOAGULANTS	$157,740.03	385	$409.71	0.70%
BYDUREON PEN	INCRETIN MIMETICS	$155,519.00	248	$627.09	0.69%
FLOVENT HFA	INHALED CORTICOSTEROIDS	$155,257.85	668	$232.42	0.69%

Total Claims Cost From 04/01/2020 – 06/30/2020	$22,407,994.13



Top 15 Therapeutic Classes Based on Number of Claims from 04/01/2020 – 06/30/2020

Therapeutic Class Description	Claims	Claims Cost	Cost per Claim	% Total Claims
ANTIDEPRESSANTS	27,567	$570,724.84	$20.70	11.96%
ANTICONVULSANTS, MISC	13,019	$853,288.73	$65.54	5.65%
ANTIPSYCHOTIC AGENTS	8,986	$1,494,611.38	$166.33	3.90%
PROTON-PUMP INHIBITORS	7,387	$126,311.82	$17.10	3.21%
OPIATE AGONISTS	6,511	$131,054.36	$20.13	2.83%
NSAIDS	6,390	$90,885.56	$14.22	2.77%
HMG-COA REDUCTASE INHIBITORS	6,357	$91,192.10	$14.35	2.76%
BETA-ADRENERGIC BLOCKING AGENTS	5,631	$105,371.79	$18.71	2.44%
ANXIOLYTICS, SEDATIVES, AND HYPNOTICS	5,561	$90,345.20	$16.25	2.41%
ACE INHIBITORS	4,794	$68,150.76	$14.22	2.08%
THYROID AGENTS	4,648	$90,533.43	$19.48	2.02%
AMPHETAMINES	4,342	$689,297.87	$158.75	1.88%
NON-AMPHETAMINE STIMULANTS	3,982	$749,548.50	$188.23	1.73%
BIGUANIDES	3,960	$54,699.52	$13.81	1.72%
INSULINS	3,615	$1,845,924.41	$510.63	1.57%

Top 15 Therapeutic Classes Based on Claims Cost from 04/01/2020 – 06/30/2020

Therapeutic Class Description	Claims Cost	Claims	Cost/Claim	% Total Cost
INSULINS	$1,845,924.41	3,615	$510.63	8.24%
DMARDS	$1,767,487.97	373	$4,738.57	7.89%
ANTIPSYCHOTICS	$1,494,611.38	8,986	$166.33	6.67%
SKIN AND MUCOUS MEMBRANE AGENTS, MISC.	$932,354.99	437	$2,133.54	4.16%
ANTICONVULSANTS, MISC	$853,288.73	13,019	$65.54	3.81%
ANTIRETROVIRALS	$835,623.66	750	$1,114.16	3.73%
NON-AMPHETAMINE STIMULANTS	$749,548.50	3,982	$188.23	3.35%
INHALED CORTICOSTEROIDS	$704,831.50	3,069	$229.66	3.15%
AMPHETAMINES	$689,297.87	4,342	$158.75	3.08%
INCRETIN MIMETICS	$632,450.02	880	$718.69	2.82%
HCV ANTIVIRALS	$627,486.89	32	$19,608.97	2.80%
ANTIDEPRESSANTS	$570,724.84	27,567	$20.70	2.55%
ANTINEOPLASTIC AGENTS	$563,475.85	518	$1,087.79	2.51%
IMMUNOMODULATORY AGENTS	$443,496.65	61	$7,270.44	1.98%
URINARY ANTISPASMODICS	$368,465.70	1,614	$228.29	1.64%

PDL Update

ADDED TO PA	
Drug	**Class**
Ajovy Autoinjector	Prophylaxis of Migraine – CGRP Inhibitors
Arazlo	Acne - Retinoid
Asmanex HFA	Corticosteroids – Inhaled
Consensi	NSAIDs
Crinone	Progesterone
Cuvitru	Immune Globulins
Dexabliss	Steroids - Oral
Esperoct	Antihemophilic Factor Products
Gvoke Syringe	Glucose Rescue Medications
Halog Solution	Steroids - Topical
Harvoni Pallet	Hepatitis C Treatments
Helidac	Antibiotics - Resistance Prevention - H. pylori
Hizentra Syringe	Immune Globulins
Ingrezza Initiation Pack	Tardive Dyskinesia
Kynmobi	Parkinson's disease
Licart	NSAIDs
Lumify	Glaucoma - Alpha Adrenergics
Molindone	Antipsychotics
Nalocet	Opioid Analgesic – Short Acting
Nurtec ODT	Migraine Treatment - Non-Triptan Agents
Nuzyra	Antibiotics - Resistance Prevention - MRSA
Osmolex Er 332 Mg/Day Pack	Parkinson's disease
Oxervate	Medications >$3,000
Promacta Suspension	Thrombocytopenia
Reyvow	Migraine Treatment - Non-Triptan Agents
Riomet ER	Non-Preferred Dosage Form
Skyrizi	Cytokine Modulators
Sovaldi Pallets	Hepatitis C Treatments
Teriparatide	Osteoporosis
Tiglutik	Medications >$3,000
Trijardy XR	DPP4-Inhibitors/SGLT2 Inhibitors Combination
Udenyca	Hematopoietic, Colony Stimulating Factors
Xeljanz XR 22Mg	Cytokine Modulators
Xenleta	Antibiotics - Resistance Prevention - CAP
Zelnorm	Idiopathic Constipation
Zeposia	Multiple Sclerosis - Injectable Non-Interferons

Palforzia

Palforzia Prior Authorization Form

Group Criteria:

- **Initial Criteria:** *Approval Duration = 6 months*
  - The patient must have an FDA-approved indication for use (meets label recommendations for diagnosis and age)
  - The patient does not have any contraindications to treatment
  - The prescriber must be or be in consultation with an allergy and/or immunology specialist
  - The provider must attest that the patient has access to injectable epinephrine, and that the patient/caregiver has been instructed and trained on its appropriate use
  - The patient must not have any of the following:
    - Uncontrolled asthma
    - A history of eosinophilic esophagitis or another eosinophilic GI disease
    - Severe or life-threatening anaphylaxis in the 60 days prior to the request
  - The patient must have a clinical history of allergy to peanuts or peanut-containing foods AND one of the following:
    - The patient has had a serum immunoglobulin E (IgE) to peanut ≥0.35 kUA/L
    - Skin prick test (SPT) to peanut ≥ 3mm compared to control
    - Allergic reaction produced during a provider observed intake of peanuts
- **Renewal Criteria:** *Approval Duration = 6 months for continued up-titration or 12 months for maintenance the 300mg dose*
  - The patient must have been compliant with Palforzia, as evidenced by pharmacy records or pharmacy claims history showing on-time fills during the last 6 months
  - The patient must not have any of the following:
    - Uncontrolled asthma
    - Severe or persistent GI symptoms
    - Eosinophilic esophagitis
  - The patient must have experienced and maintained clinical benefit since starting treatment with Palforzia, as evidenced by the following:
    - The patient continues to have a peanut allergy and has been/is being monitored for resolution of their allergy
    - The patient has been able to tolerate the maintenance dose of Palforzia (300 mg daily)
      OR
    - The prescriber has submitted a plan to continue up-titration to a final dose of 300 mg daily and have not already requested a renewal PA for the up-titration period

PA REQUIRED
PALFORZIA (peanut allergen powder)

health information designs

Palforzia
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 Palforzia to meet criteria confirming the medication is being used according to its FDA-approved indication. Please fill out the following form in its entirety.

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:**

Does the patient have uncontrolled asthma?	□ YES	□ NO
Has the patient experienced severe or life-threatening anaphylaxis in the 60 days?	□ YES	□ NO
Does the patient have a history of eosinophilic esophagitis or another eosinophilic GI disease?	□ YES	□ NO
Has the patient/caregiver been educated on appropriate use of epinephrine?	□ YES	□ NO
RENEWAL ONLY: Does the patient continue to have a peanut allergy and has been/is being monitored for resolution of their allergy?	□ YES	□ NO
RENEWAL ONLY: Has the patient been able to tolerate the maintenance dose of Palforzia (300 mg daily)?	□ YES	□ NO

Additional Qualifications for Coverage (*if applicable*)

□ *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 #

Mytesi

General Prior Authorization Form

Group Criteria:

- **Initial Criteria:** *Approval Duration = 3 months*
  - The patient must have an FDA-approved indication for use (meets label recommendations for diagnosis and age)
  - The provider must submit medical documentation confirming that infectious and medication-induced etiologies of diarrhea have been ruled out
  - The patient must have had a 30-day trial of each preferred agent of a unique active ingredient, as evidenced by paid claims or pharmacy printouts
- **Renewal Criteria:** *Approval Duration = 12 months*
  - The patient must have experienced and maintained clinical benefit since starting treatment with Mytesi, as evidenced by medical documentation (e.g. chart notes) attached to the request (subject to clinical review)

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
Loperamide	LOMOTIL (diphenoxylate HCl/atropine)
Diphenoxylate HCl / atropine	MYTESTI (crofelemer)

Antifibrinolytic Agents

General Prior Authorization Form

Group Criteria:

- **Non-Preferred Agents Criteria:** *Approval Duration = 12 months*
  - The patient must have an FDA-approved indication for use (meets label recommendations for diagnosis and age)
  - The patient must have had a 30-day trial of each preferred agent, as evidenced by paid claims or pharmacy printouts.
  - Clinical justification must be provided explaining why the patient is unable to use all other products (subject to clinical review)

Product Specific Criteria:

- **Non-Solid Dosage Formulations:** The patient must be unable to ingest solid dosage form as evidenced by swallow study documentation

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
	LYSTEDA (tranexamic acid)
	AMICAR (aminocaproic acid) oral solution
	AMICAR (aminocaproic acid) tablet
	aminocaproic acid oral solution
	aminocaproic acid tablet
	tranexamic acid tablet

Lipid-Lowering Agents

General Prior Authorization Form

Additional Criteria for HMG-CoA (3-hydroxy-3-methylglutaryl-CoA) REDUCTASE INHIBITORS

Group Criteria:

- **Initial Criteria:** *Approval Duration = 3 months*
  - The patient must have an FDA-approved indication for use (meets label recommendations for diagnosis and age)
  - The patient must have LDL levels of >130 mg/dL after a 90-day trial of each of the following, as evidenced by paid claims or pharmacy printouts:
    - A lipid lowering agent other than a statin combined with either Crestor (rosuvastatin) ≥20 mg or Lipitor (atorvastatin) ≥ 40 mg
    - A PCSK9 Inhibitor combined with either Crestor (rosuvastatin) ≥20 mg or Lipitor (atorvastatin) ≥ 40 mg
  - The patient must currently be receiving a maximally tolerated statin (HMG-CoA reductase inhibitor) agent, as evidenced by paid claims or pharmacy printouts
  - Clinical justification must be provided explaining why the patient is unable to use all other products to lower their cholesterol (subject to clinical review)
- **Renewal Criteria:** *Approval Duration = 12 months*
  - The patient must currently be receiving a maximally tolerated statin (HMG-CoA reductase inhibitor) agent, as evidenced by paid claims or pharmacy printouts
  - The patient must have experienced and maintained clinical benefit since starting treatment with the requested medication, as evidenced by medical documentation (e.g. chart notes) attached to the request (subject to clinical review)

ACL (ATP Citrate Lyase) INHIBITORS	
PREFERRED AGENTS (NO PA REQUIRED)	**NON-PREFERRED AGENTS (PA REQUIRED)**
	NEXLETOL (bempedoic acid)
	NEXLIZET (bempedoic acid and ezetimibe)
MTP (Microsomal Triglyceride Transfer Protein) INHIBITOR	
PREFERRED AGENTS (NO PA REQUIRED)	**NON-PREFERRED AGENTS (PA REQUIRED)**
	JUXTAPID (lomitapide)
PCSK9 (Proprotien Convertase Subtilisin/Kexin Type 9) INHIBITORS	
PREFERRED AGENTS (NO PA REQUIRED)	**NON-PREFERRED AGENTS (PA REQUIRED)**
PRALUENT PEN (alirocumab) – Labeler 72733	PRALUENT PEN (alirocumab) – Labeler 00024
REPATHA PUSHTRONEX (evolocumab)	
REPATHA SURECLICK (evolocumab)	
REPATHA SYRINGE (evolocumab)	

CFTR Modulators

General Prior Authorization Form

Group Criteria: *Approval Duration = 12 months*

- The patient must have an FDA-approved indication for use (meets label recommendations for diagnosis and age).
- The patient must have a CFTR mutation that the requested medication is FDA-approved to treat, as evidenced by medical documentation (e.g. chart notes, genetic testing) that is attached to the request

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
Kalydeco (ivacaftor)	
Orkambi (lumacaftor/ivacaftor)	
Symdeko (tezacaftor/ivacaftor)	
Trikafta (elexacaftor/tezacaftor/ivacaftor)	

health information designs

General
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 medications to meet specific diagnosis and step-therapy requirements. Criteria for agents requiring prior authorization can be found at one of the following locations:

- The Preferred Drug List (PDL) available at www.hidesigns.com/assets/files/ndmedicaid/NDPDL.pdf
- Prior Authorization Criteria available at www.hidesigns.com/assets/files/ndmedicaid/2018/Criteria/PA_Criteria.pdf

*****Completed Medwatch form(s) must be attached to this request for failed trial(s) in which the active ingredient of the failed product is the same as the requested product*****

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)

□ Patient is pregnant: Due Date _____
□ Patient has inability to take or tolerate solid oral dosage forms (please attach swallow study)
□ Patient has feeding tube in place: (please state specific type of feeding tube _____)
□ Other: (please fill out below)

□ *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 #

REVIEW OF PHARMACOLOGIC TREATMENT OF DIABETIC GASTROPARESIS

Diabetic Gastroparesis:

- Diabetic gastroparesis is thought to result from impaired neural control of gastric function in patients with diabetes mellitus
    - It is not progressive, and treatment is directed toward alleviating symptoms
        - Primary treatment of gastroparesis:
            - Improved glycemic control
            - Dietary modification
            - Administration of prokinetic agents
            - Avoidance of medications that can delay gastric emptying (e.g. incretin mimetics)

Pharmacological Treatment

- Prokinetics: increase the rate of gastric emptying and should be administered 10 to 15 minutes before meals with an additional dose before bedtime in patients with persistent symptoms
    - **Metoclopramide (only Rx-only medication with FDA-approved indication for use)**
        - Oral tablet
        - ODT
        - Injection
        - Nasal (Gimoti)
    - Macrolide antibiotics (off-label)
        - Erythromycin
        - Azithromycin
    - *Investigational drugs*
        - *Domperidone*
        - *Cisapride*

Metoclopramide:

- **Indication**:
    - Relief of symptoms associated with acute and recurrent diabetic gastric stasis
- **Mechanism of action:**
    - Dopamine 2 receptor antagonist, 5-HT4 agonist, & a weak 5-HT3 receptor antagonist
        - Enhances the response to acetylcholine of tissue in upper GI tract
            - Causes enhanced motility and accelerated gastric emptying; increases lower esophageal sphincter tone
- **Boxed Warning:**
    - Treatment with metoclopramide can cause tardive dyskinesia (TD). The risk of developing TD increases with duration of treatment and total cumulative dose. Discontinue metoclopramide therapy in patients who develop signs or symptoms of TD. There is no known treatment for tardive dyskinesia. In some patients, symptoms lessen or resolve after metoclopramide treatment is stopped.

- **Contraindications:**
    - Hypersensitivity to metoclopramide or any component of the formulation
    - Situations where stimulation of GI motility may be dangerous (GI obstruction, perforation, or hemorrhage)
    - Pheochromocytoma or other catecholamine-releasing paragangliomas
    - Seizure disorders (eg, epilepsy)
    - History of tardive dyskinesia or dystonic reaction to metoclopramide
    - Concomitant use with other agents likely to increase extrapyramidal reactions

- **Warnings/Precautions**
  - Tardive dyskinesia
  - May cause extrapyramidal symptoms, generally manifested as acute dystonic reactions within the initial 24 to 48 hours of use
    - Avoid with Parkinson's disease
  - Use may be associated with neuroleptic malignant syndrome (NMS)
  - May cause QT prolongation and torsades de pointes in certain individuals (eg, heart failure patients with renal impairment)
  - Depression has occurred
  - May elevate blood pressure; avoid use in patients with hypertension
  - Elevates prolactin levels
  - Use with caution in patients who are at risk of fluid overload (heart failure, cirrhosis)

- **Dosing:**

	Solution	**Oral Tablet**	**ODT**	**Injection**	**Nasal**
Adult	5-10 mg 2-3 times daily (max of 40 mg/day)				One spray (15 mg) in 1 nostril
Pediatric	Off-label only				N/A
Renal Impairment	Use with caution in patients with moderate to severe renal impairment; dosage adjustment recommended				
Hepatic Impairment	Use caution in patients with moderate to severe hepatic impairment; dosage adjustment recommended				
In chronic therapy, limit course to ≤12 weeks. Consider a "drug holiday" or dose reduction (eg, 5 mg twice daily before the 2 main meals of the day) for ~2 weeks whenever clinically feasible or at least every 12 weeks (whichever is shorter) to evaluate efficacy and necessity of continued treatment					

- **Drug interactions:**
  - **Antipsychotics**
    - Potential for increased frequency and severity of TD, EPS, & NMS
  - **Strong CYP2D6 Inhibitors**
    - Increased plasma concentrations of metoclopramide
  - **MAOIs**
    - Increased risk of hypertension
  - **CNS Depressants**
    - Increased risk of CNS depression
  - **Drugs that Impair Gastrointestinal Motility**
    - Reduced efficacy
  - **Dopamine Agonists**
    - Decreased therapeutic effect of metoclopramide due to opposing effects on dopamine

COST

Drug	**Strength**	**Package Size**	**AWP Pkg Price**	**AWP Unit Price**
Metoclopramide	5 mg/ 5 mL	473 mL	$35.40	$0.07
Metoclopramide	5 mg tablet	100	$32.00	$0.32
Metoclopramide	10 mg tablet	1,000	$215.00	$0.21
Metoclopramide	5 mg/mL solution	2 mL (25 syr)	$33.30	$0.67
Metoclopramide	5 mg ODT	100	$949.30	$9.49
Metoclopramide	10 mg ODT	100	$949.30	$9.49
Gimoti	10 mL nasal spray	NA	NA	NA

CURRENT UTILIZATION

ND Medicaid Utilization (06/2019 – 06/2020)		
Label Name	**Rx Num**	**Total Reimb Amt**
Metoclopramide tablet	1,121	$14,949.91
Metoclopramide oral sln	75	$1,264.59
Metoclopramide ODT	0	-
Metoclopramide injection	1	$15.96
Gimoti	0	-

REFERENCES:

1. Facts & Comparisons eAnswers. Available at http://online.factsandcomparisons.com. Accessed on August 14. 2020.
2. UpToDate. Available at https://www.uptodate.com/contents/search. Accessed on August 14. 2020.
3. Reglan (metoclopramide) [prescribing information]. Baudette, MN: ANI Pharmaceuticals; August 2017.

REVIEW OF OHRIAHNN (elagolix/estradiol/norethindrone)

Indication:

- Management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women
    - Use should be limited to 24 months due to the risk of continued bone loss, which may not be reversible
- **Other agents used for this indication:**
    - Estrogen/progestin contraceptives
        - Oral contraceptive pills, vaginal ring, or transdermal patch
            - Little high-quality evidence supporting this practice, but many guidelines still recommend as first-line therapy
    - Progestin IUDs
        - Primarily levonorgestrel -releasing IUDs
            - Supporting data are mainly observational, but most guidelines support the use of LNG IUDs as a first-line agent
    - Progestin-only contraceptives
        - Little evidence for efficacy, but some guidelines support use
    - Tranexamic acid
        - Small studies have shown benefit

Mechanism of action

- Elagolix is a short-acting, gonadotropin-releasing hormone antagonist that suppresses pituitary and ovarian hormone function in a dose-dependent manner
    - Concentrations of luteinizing hormone, follicle stimulating hormone, estradiol, and progesterone are decreased during therapy, reducing bleeding associated with uterine fibroids
- Estradiol may reduce the bone loss associated with elagolix
- Norethindrone may protect the uterus from adverse endometrial effects of unopposed estrogen

Boxed Warning:

- Thromboembolic disorders and vascular events
    - Estrogen and progestin combinations increase the risk of thrombotic or thromboembolic disorders including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at increased risk for these events. Elagolix, estradiol, and norethindrone is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events, including women >35 years of age who smoke and women with uncontrolled hypertension

Contraindications:

- Hypersensitivity to any ingredient of the formulation
- Osteoporosis
- Current or history of breast cancer or other hormone-sensitive malignancies, and with increased risk for hormone-sensitive malignancies
- Hepatic impairment or disease
- Undiagnosed abnormal uterine bleeding
- Concurrent use of organic anion transporting polypeptide (OATP)1B1 inhibitors that are known or expected to significantly increase elagolix plasma concentrations
- Pregnancy
- Females at high risk of arterial, venous thrombotic, or thromboembolic disorders
    - Women >35 years of age who smoke
    - Current diagnosis of or history of deep vein thrombosis or pulmonary embolism, vascular disease, inherited or acquired hypercoagulopathies, uncontrolled hypertension, or headaches with focal neurological symptoms or have migraine headaches with aura if >35 years of age

Warnings/Precautions:

- Increased risk of thromboembolic disorders and vascular events
  - Discontinue use if an arterial or venous thrombotic event occurs or is suspected
- Retinal vascular thrombosis
  - Discontinue if unexplained loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions occur and immediately evaluate for retinal vein thrombosis
- May increase the risk for breast cancer and other hormone-sensitive malignancies
  - Discontinue if a hormone-sensitive malignancy is diagnosed
- Menstrual bleeding patterns may change
  - May alter the ability to detect pregnancy. Pregnancy testing should be conducted if pregnancy is suspected; discontinue use if pregnancy is confirmed
- Depression
  - May increase the risk of depression and mood changes. Consider risks and benefits of therapy if mood disturbances occur
- Bone mineral density loss
  - Associated with bone mineral density (BMD) loss; risk is increased with duration of use and may not be completely reversible following discontinuation. Evaluate BMD at baseline with dual-energy x-ray absorptiometry. Consider supplementation with calcium and vitamin D. Limit duration of treatment to 24 months to reduce the extent of BMD loss. Use caution in patients with risk factors for osteoporosis, including medications which may decrease BMD. Use is contraindicated in women with known osteoporosis.
- Gallbladder disease
  - May increase risk of gallbladder disease, especially in women with a history of cholestatic jaundice associated with past estrogen use or with pregnancy. Discontinue if jaundice occurs.
- Hypertension
  - Discontinue if BP rises significantly with use.
- Lipid effects
  - May adversely affect lipid levels, including serum triglycerides leading to pancreatitis.
- Diabetes
  - May impair glucose tolerance; closely monitor women with diabetes or prediabetes
- Alopecia
  - May cause alopecia. Reversibility is unknown; hair loss continued after discontinuation of therapy in most affected women. Consider discontinuation if alopecia occurs
- Drug-drug interactions
  - Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.
- Surgical patients
  - Whenever possible, discontinue 4 to 6 weeks prior to surgeries known to have an increased risk of thromboembolism or during periods of prolonged immobilization
- Tartrazine
  - Contains tartrazine (ie, FD&C Yellow No. 5), which may cause hypersensitivity reactions, especially in patients with aspirin hypersensitivity
- Laboratory changes
  - May change the results of some laboratory tests (eg, coagulation factors, lipids, glucose tolerance, binding proteins). Estrogens may raise serum concentrations of thyroxine-binding globulin, sex hormone-binding globulin, and cortisol-binding globulin. Females on thyroid replacement therapy may require higher doses of thyroid hormone while receiving estrogens

Dosing:

- **Adults:**
  - Elagolix 300 mg/estradiol 1 mg/norethindrone 0.5 mg every morning and elagolix 300 mg every evening
    - Maximum of 24 months of treatment
    - Not indicated for use in postmenopausal females****
- **Pediatric:**
  - Safety and efficacy have not been established
- **Renal Impairment**
  - No dosage adjustment necessary
- **Hepatic Impairment**
  - Contraindicated for use in mild, moderate or severe hepatic impairment

Drug interactions

- Strong CYP3A4 Inhibitors
- OATP1B1/1B3 inhibitors
- P-glycoprotein/ABCB1 substrates
- Related to mechanism:
  - Anticoagulants: diminished therapeutic effect of anticoagulants
  - Anastrozole diminished therapeutic effect
  - Increase in effects of other drugs
  - Simvastatin
  - Cyclosporin

COST

Drug	Strength	Package Size	AWP Pkg Price	AWP Unit Price
Oriahnn	300 mg – 300 mg – 1 mg	56 capsules	$1,088.97	$19.44
Tranexamic acid	650 mg oral tab	30 tablets	$156.60	$15.66
Mirena	52 mg	1 IUD	$1,144.21	$1,144.21
Ethinyl Estradiol and Levonorgestrel	0.02 mg – 0.1 mg	28 tablets	$105.48	$1.26

CURRENT UTILIZATION

ND Medicaid Utilization (06/2019 – 06/2020)		
Label Name	**Rx Num**	**Total Reimb Amt**
Oriahnn	0	-

REFERENCES:

1. Facts & Comparisons eAnswers. Available at http://online.factsandcomparisons.com. Accessed on August 14. 2020.
2. UpToDate. Available at https://www.uptodate.com/contents/search. Accessed on August 14. 2020.
3. Oriahnn (elagolix/estradiol/norethindrone) [prescribing information]. North Chicago, IL: AbbVie Inc; May 2020.
4. American College of Obstetricians and Gynecologists. ACOG practice bulletin. Alternatives to hysterectomy in the management of leiomyomas. Obstetrics and gynecology. 2008 Aug;112(2 Pt 1):387.

REVIEW OF DOJOLVI (triheptanoin)

Indication:

- As a source of calories and fatty acids for the treatment of molecularly confirmed long-chain fatty acid oxidation disorders (LC-FAOD) in adults and pediatric patients

Long-Chain Fatty Acid Oxidation Disorders (LC-FAOD)

- Fatty acid oxidation disorders (FAODs) are autosomal recessive disorders of metabolism resulting in failure of mitochondrial beta-oxidation or the carnitine-based transport of fatty acids into mitochondria
    - Leads to deficient energy production and produce widely variable clinical presentations ranging from mild hypotonia in adults to sudden death in infants
- Treatment of LC-FAOD:
    - Treatment involves avoidance of prolonged fasting, dietary fat restriction, and medium chain triglyceride supplementation
        - High cab diet, low in long-chain fats

Mechanism of action:

- It is a medium-chain triglyceride that provide a source of calories and fatty acids to bypass the long-chain fatty acid oxidation disorder enzyme deficiencies for energy production and replacement

Contraindications:

- There are no contraindications listed in the manufacturer's labeling

Warnings and Precautions:

- Avoid use in patients with pancreatic insufficiency; reduced absorption leading to insufficient supplementation of medium-chain fatty acids may occur
- Do not use PVC feeding tubes; the performance and functionality of feeding tubes may degrade over time depending on usage and environmental conditions

Dosing:

- **Adults:**
    - Patients not currently receiving a medium-chain triglyceride product
        - ~10% of the patient's total prescribed daily caloric intake (DCI) divided into at least 4 times daily orally initially
        - Increase dosage by ~5% of the patient's total prescribed DCI every 2 to 3 days until target dose of up to 35% of the patient's prescribed DCI is achieved
    - Patients switching from another medium-chain triglyceride product
        - Prior to initiation, discontinue any other medium-chain triglyceride products
        - Initiate at the last tolerated daily dosage of medium-chain triglyceride divided into at least 4 times daily orally
        - Increase dosage by ~5% of the patient's total prescribed DCI every 2 to 3 days until target dose of up to 35% of the patient's prescribed DCI is achieved
    - Formula for triheptanoin dose
        - Total daily dose (mL) = (Patient's DCI [kcal] x desired % of DCI) divided by 8.3 kcal/mL.
- **Pediatric:**
    - Same as adult
        - In neonates, may need increased dosage due to higher fat intake
- **Renal Impairment**
    - No dosage adjustment provided per labeling
- **Hepatic Impairment**
    - No dosage adjustment provided per labeling

Drug interactions

- Orlistat: may decrease active metabolite of Dojolvi

COST

Drug	Strength	Package Size	AWP Pkg Price	AWP Unit Price
Dojolvi	100 %	500 mL	$5,850.00	$11.70

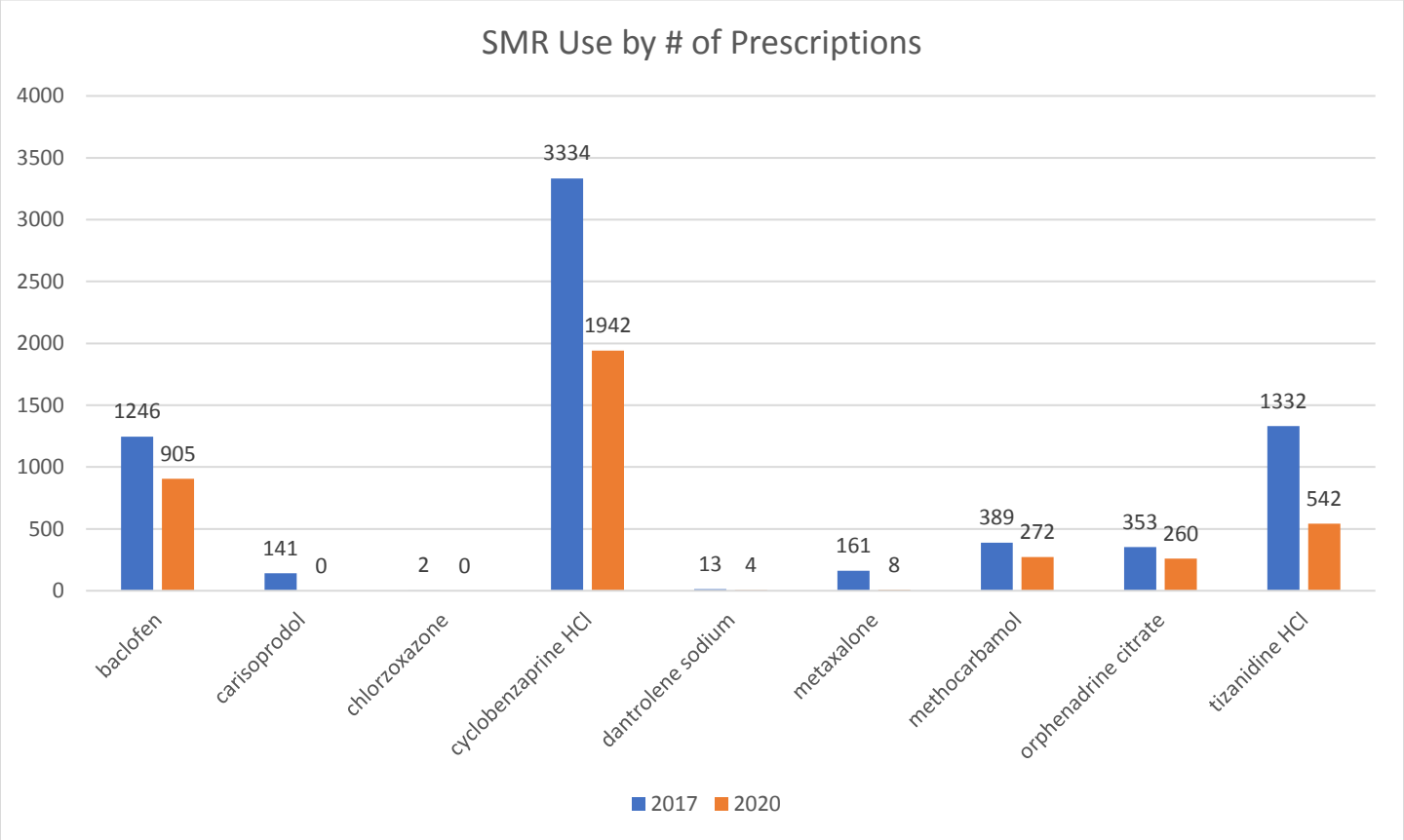
CURRENT UTILIZATION

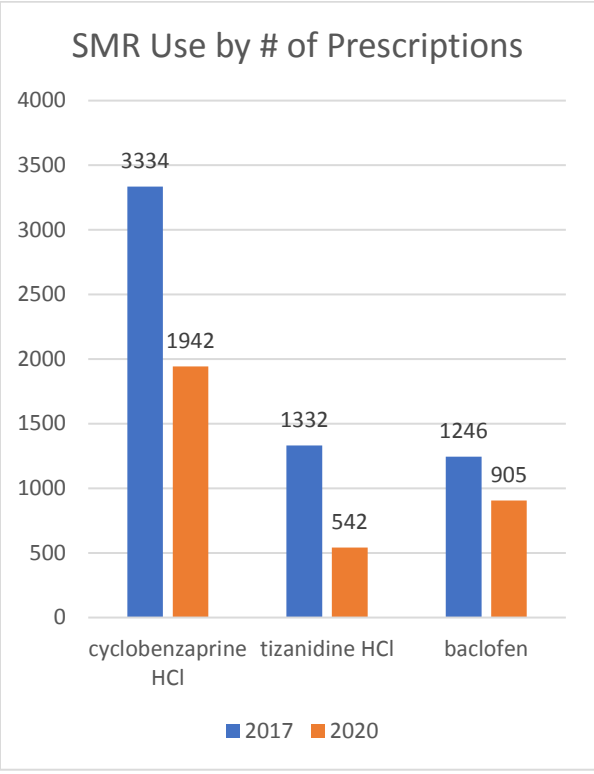
ND Medicaid Utilization (06/2019 – 06/2020)		
Label Name	**Rx Num**	**Total Reimb Amt**
Dojolvi	0	-

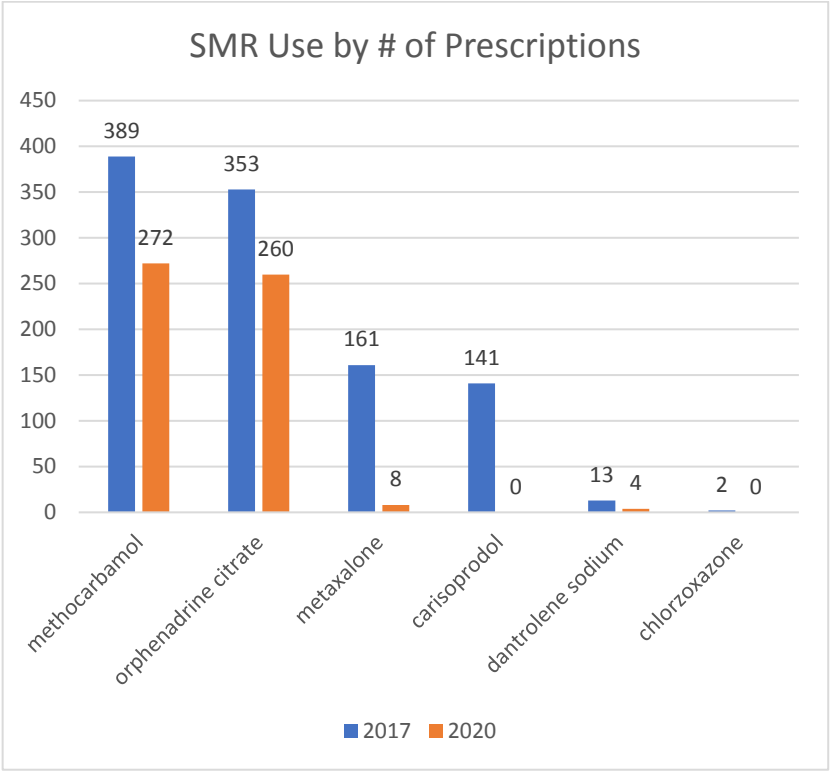
REFERENCES:

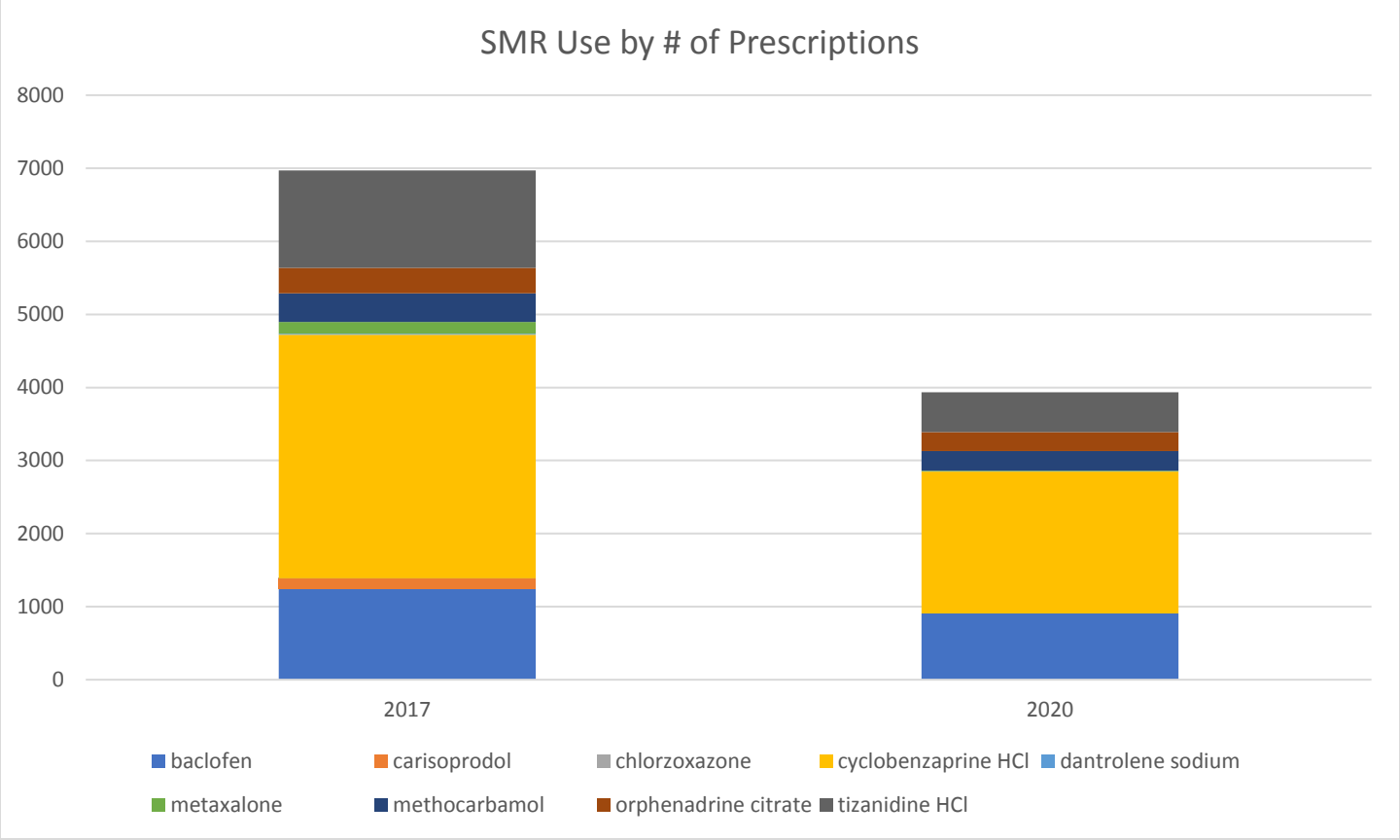
1. Facts & Comparisons eAnswers. Available at http://online.factsandcomparisons.com. Accessed on August 21. 2020.
2. UpToDate. Available at https://www.uptodate.com/contents/search. Accessed on August 21. 2020.
3. Dojolvi (triheptanoin) [prescribing information]. Novato, CA: Ultragenyx Pharmaceutical Inc; June 2020.

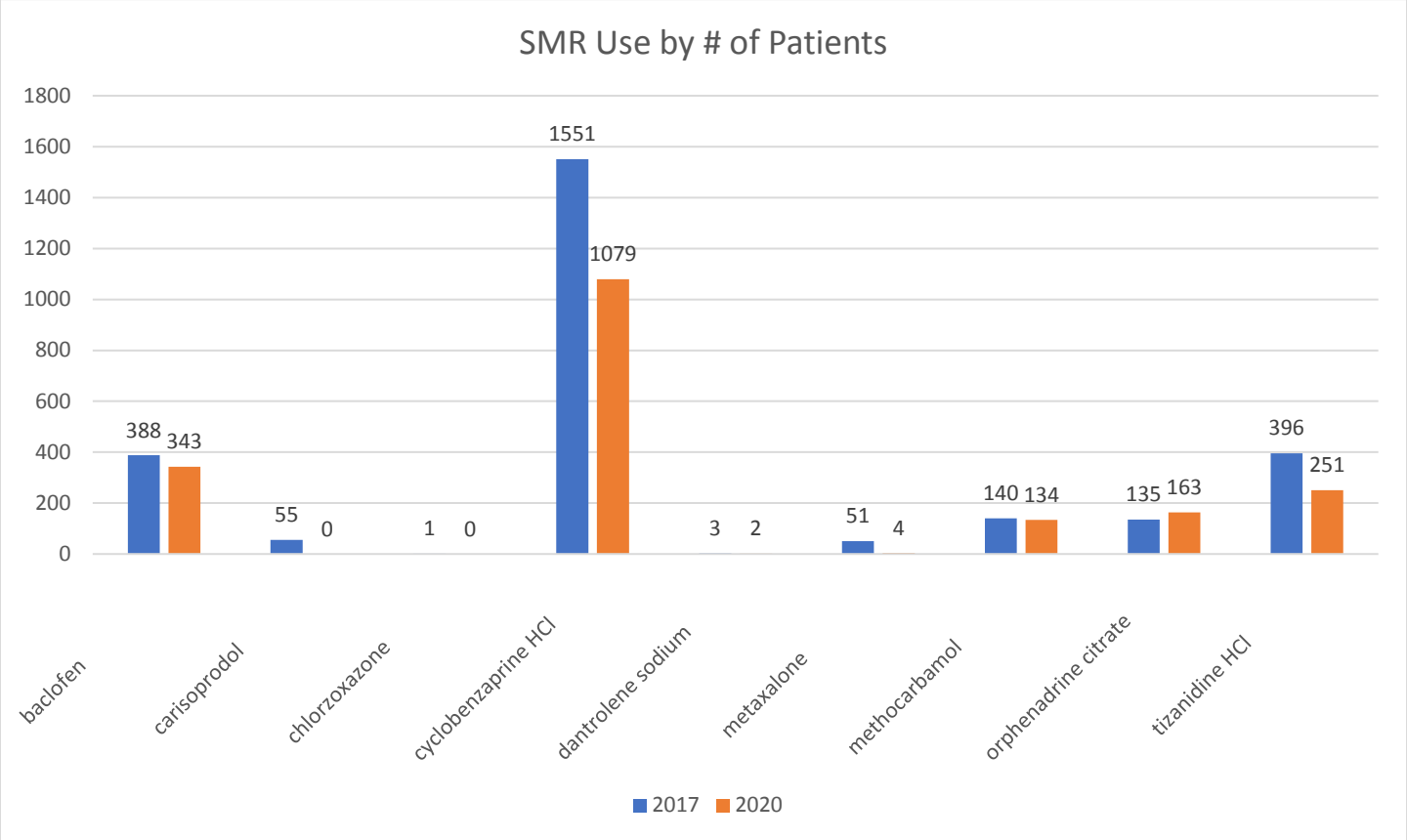
Skeletal Muscle Relaxant (SMR) Utilization

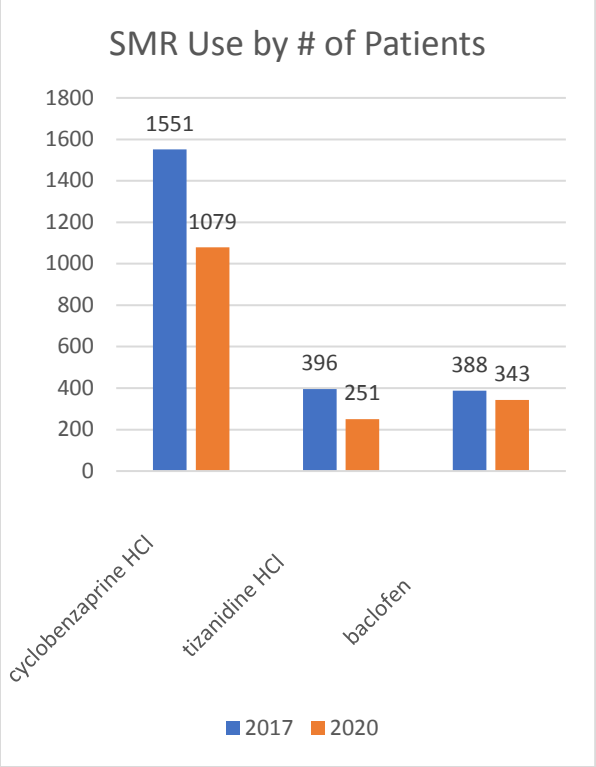


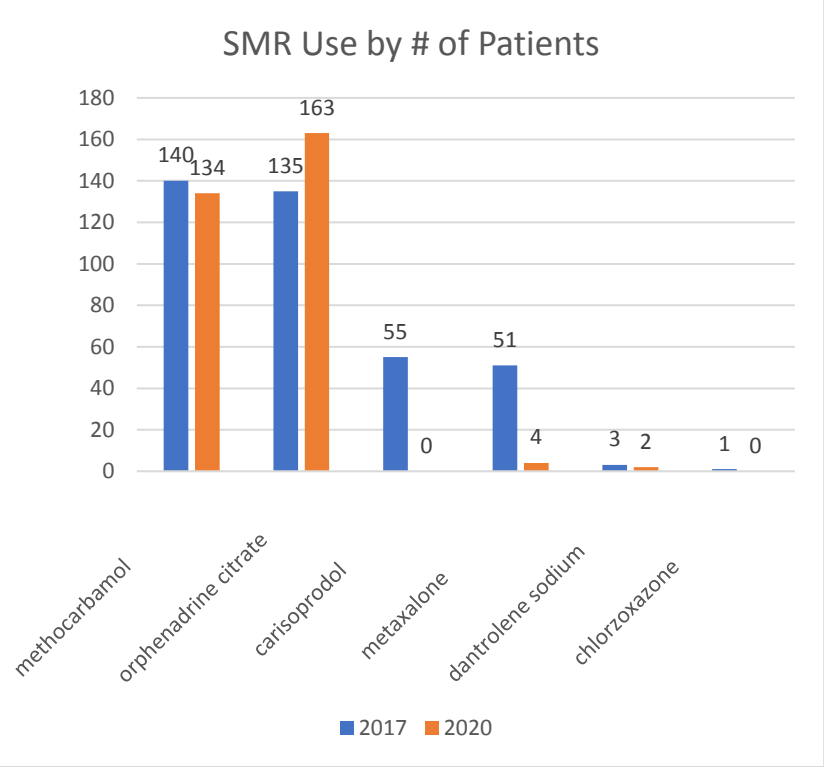


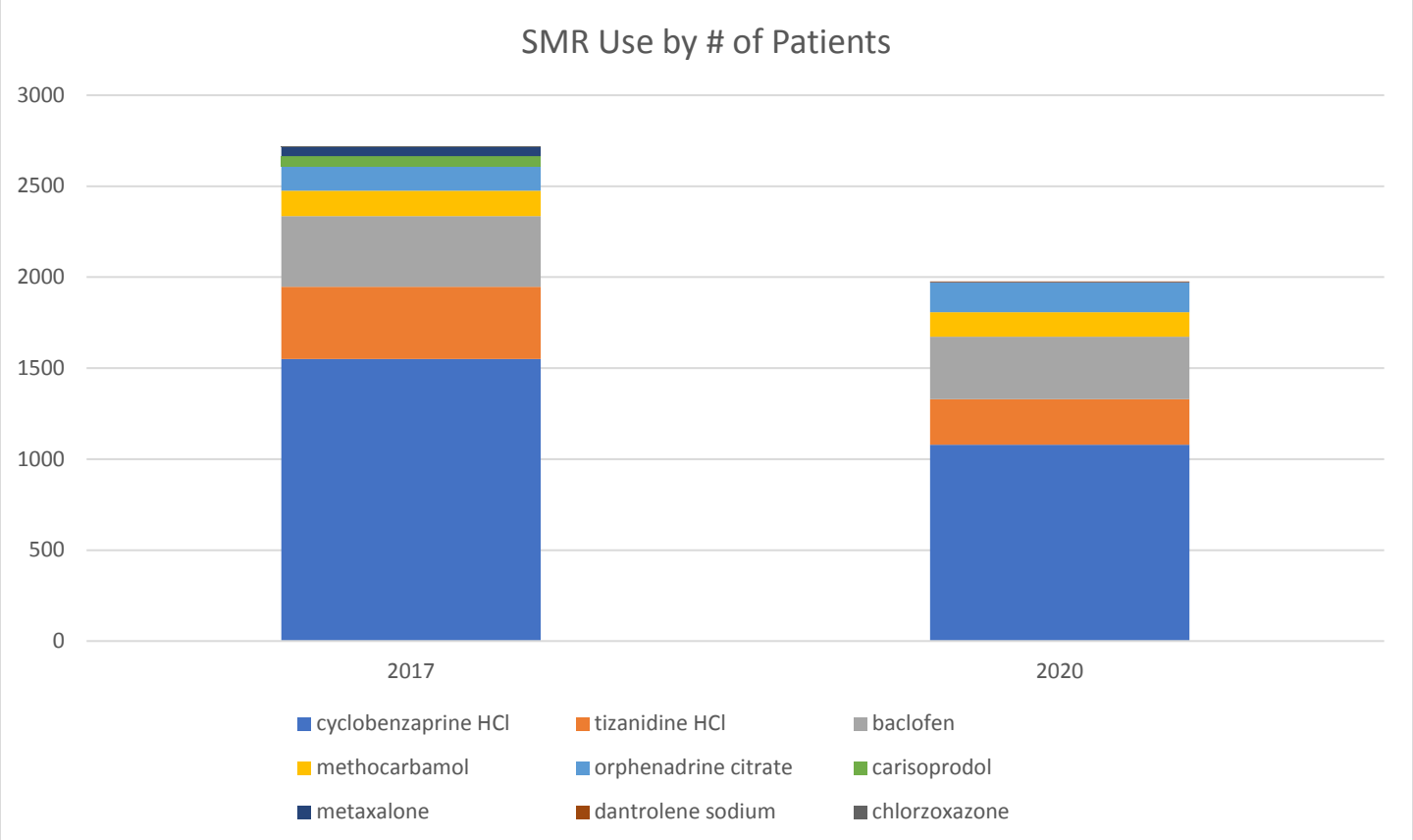


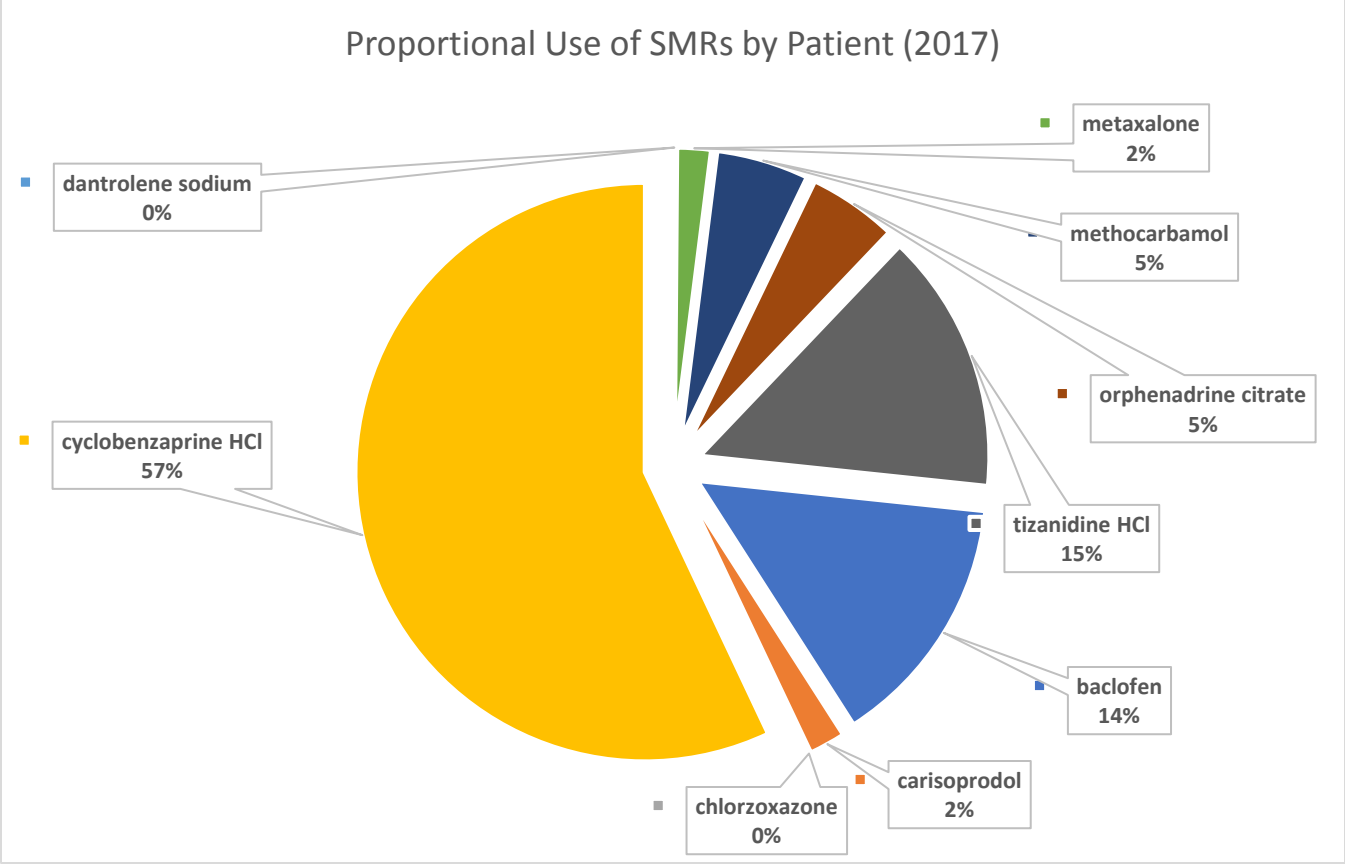

SMR Use by # of Prescriptions
8000
7000
6000
5000
4000
3000
2000
1000
0
2017
2020
baclofen
carisoprodol
chlorzoxazone
cyclobenzaprine HCl
dantrolene sodium
metaxalone
methocarbamol
orphenadrine citrate
tizanidine HCl

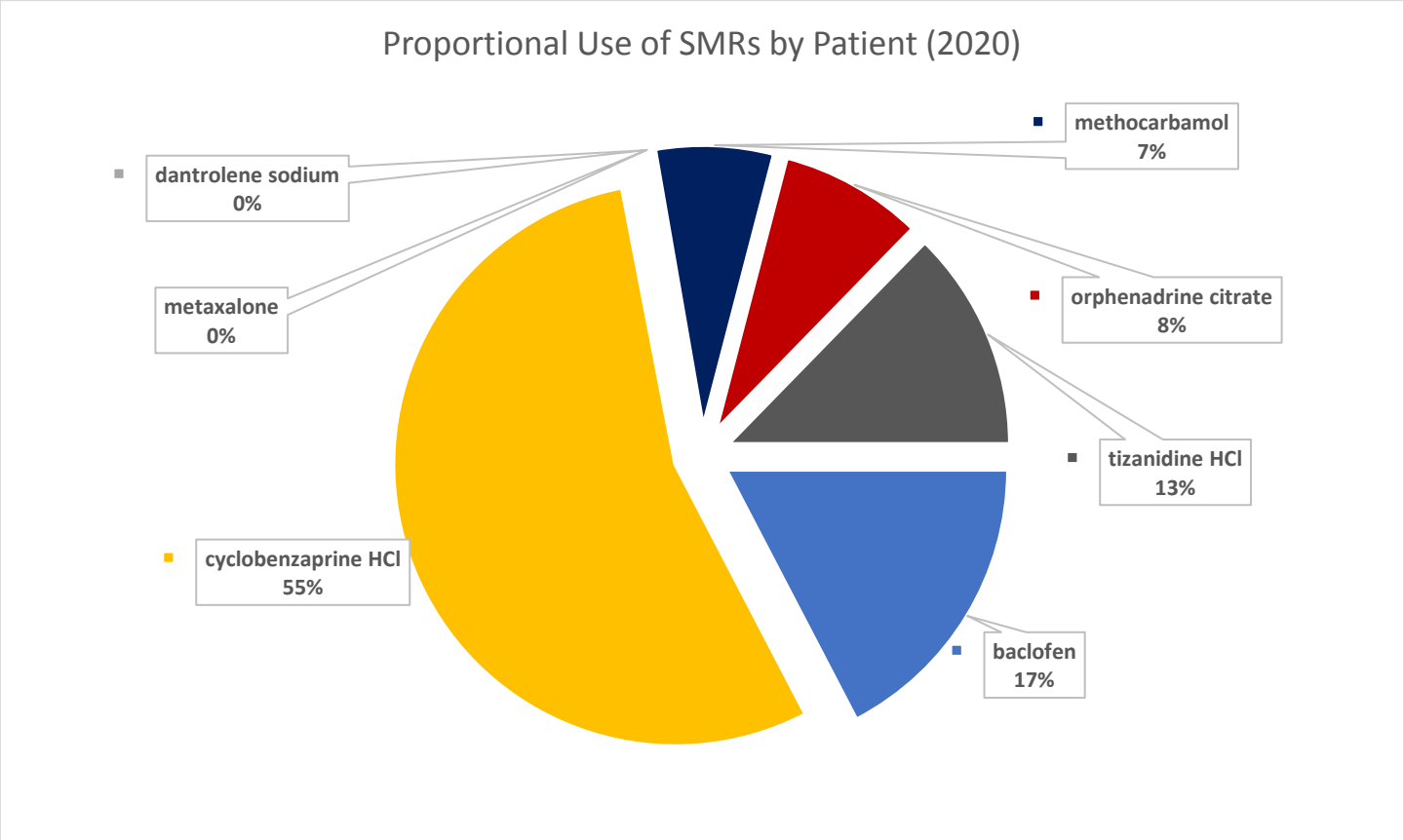

SMR Use by # of Patients
1800
1600
1400
1200
1000
800
600
400
200
0
388
343
55
0
1
0
1551
1079
3
2
51
4
140
134
135
163
396
251
baclofen
carisoprodol
chlorzoxazone
cyclobenzaprine HCl
dantrolene sodium
metaxalone
methocarbamol
orphenadrine citrate
tizanidine HCl
2017
2020


SMR Use by # of Patients
1800
1600
1400
1200
1000
800
600
400
200
0
1551
1079
396
251
388
343
cyclobenzaprine HCl
tizanidine HCl
baclofen
2017
2020

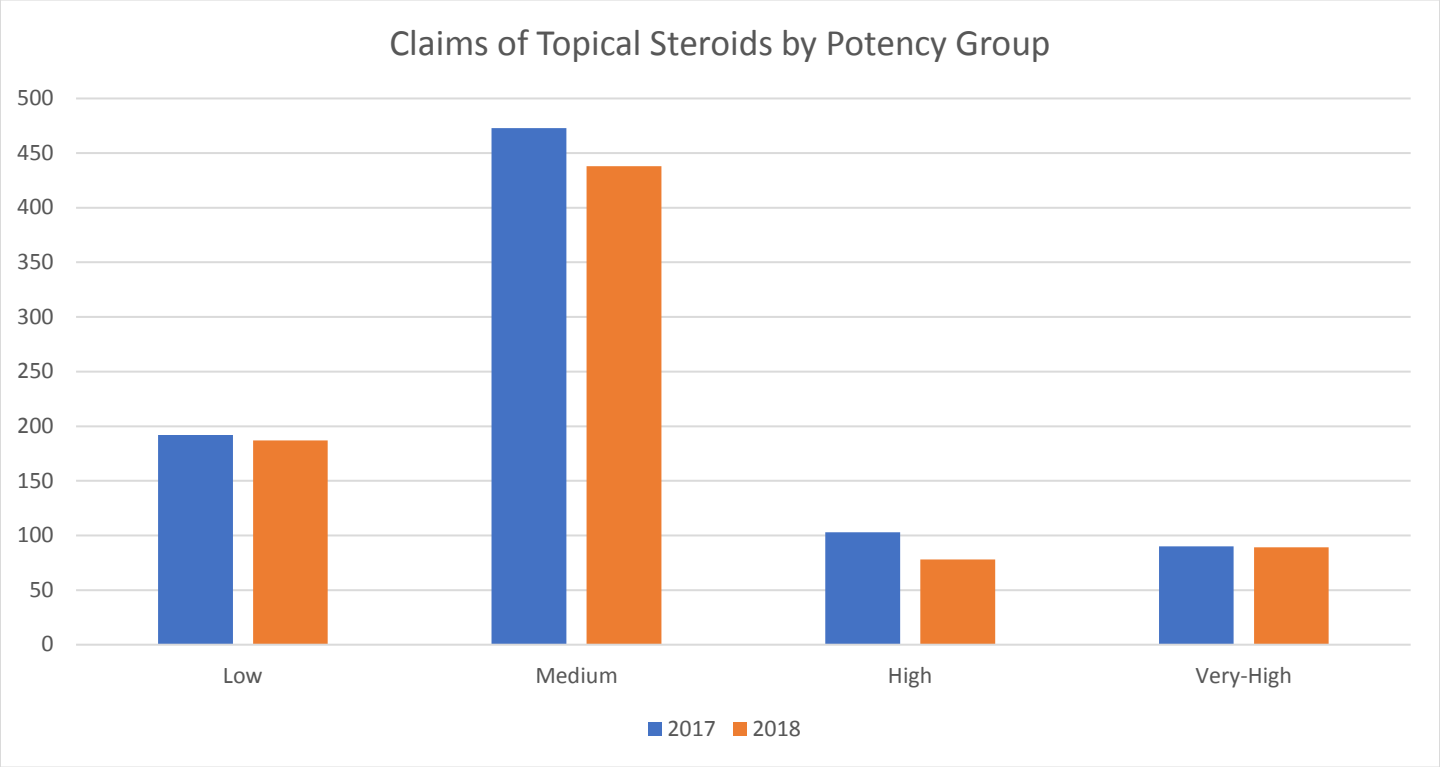

SMR Use by # of Patients
180
160
140
120
100
80
60
40
20
0
140
134
135
163
55
0
51
4
3
2
1
0
methocarbamol
orphenadrine citrate
carisoprodol
metaxalone
dantrolene sodium
chlorzoxazone
2017
2020

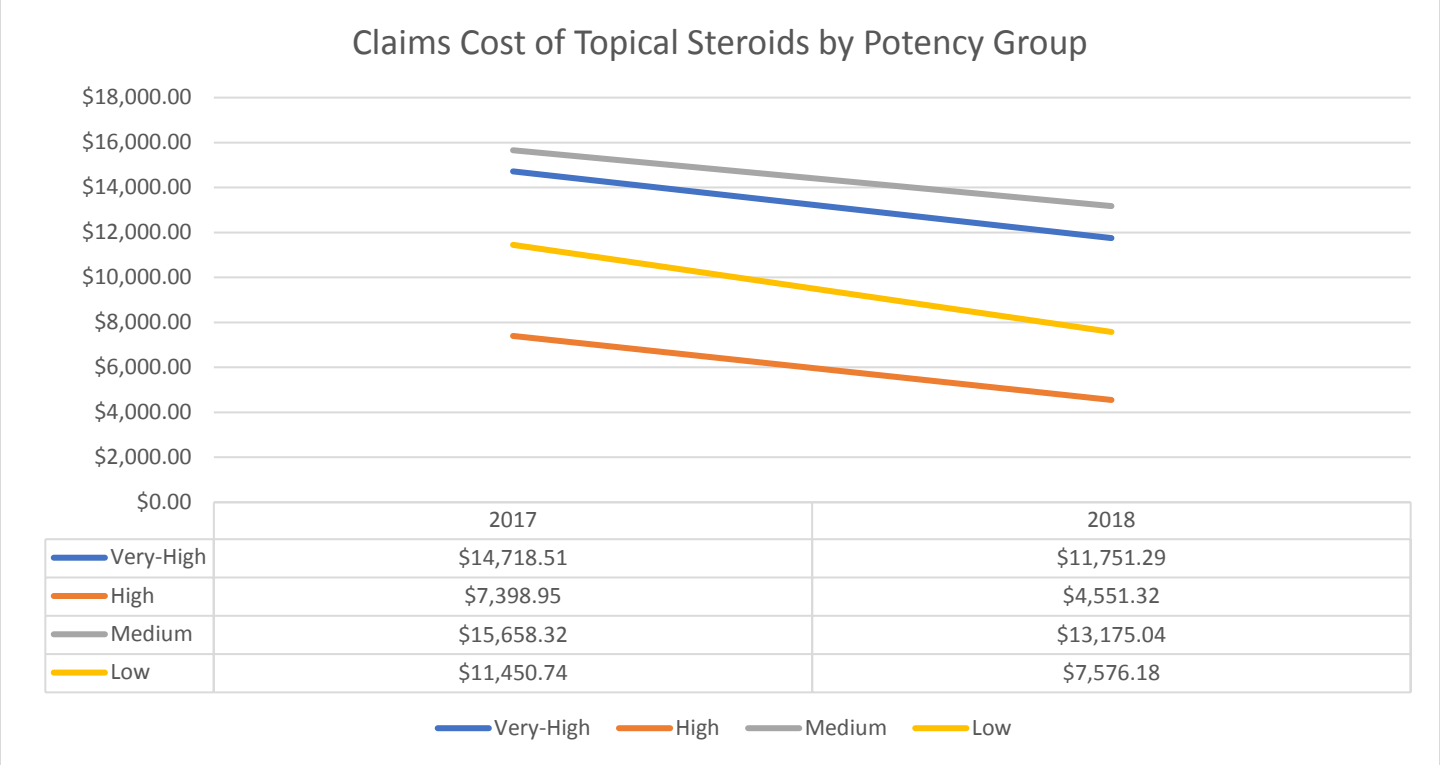

SMR Use by # of Patients
3000
2500
2000
1500
1000
500
0
2017
2020
cyclobenzaprine HCl
tizanidine HCl
baclofen
methocarbamol
orphenadrine citrate
carisoprodol
metaxalone
dantrolene sodium
chlorzoxazone


Proportional Use of SMRs by Patient (2017)
metaxalone 2%
dantrolene sodium 0%
methocarbamol 5%
orphenadrine citrate 5%
cyclobenzaprine HCl 57%
tizanidine HCl 15%
baclofen 14%
carisoprodol 2%
chlorzoxazone 0%

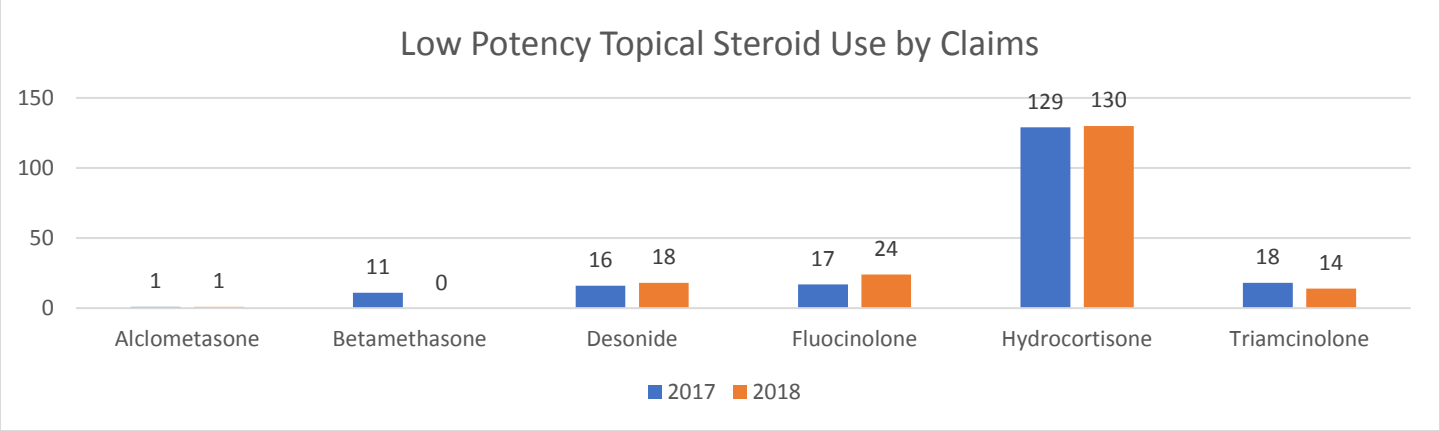

Proportional Use of SMRs by Patient (2020)
methocarbamol 7%
dantrolene sodium 0%
metaxalone 0%
orphenadrine citrate 8%
tizanidine HCl 13%
cyclobenzaprine HCl 55%
baclofen 17%

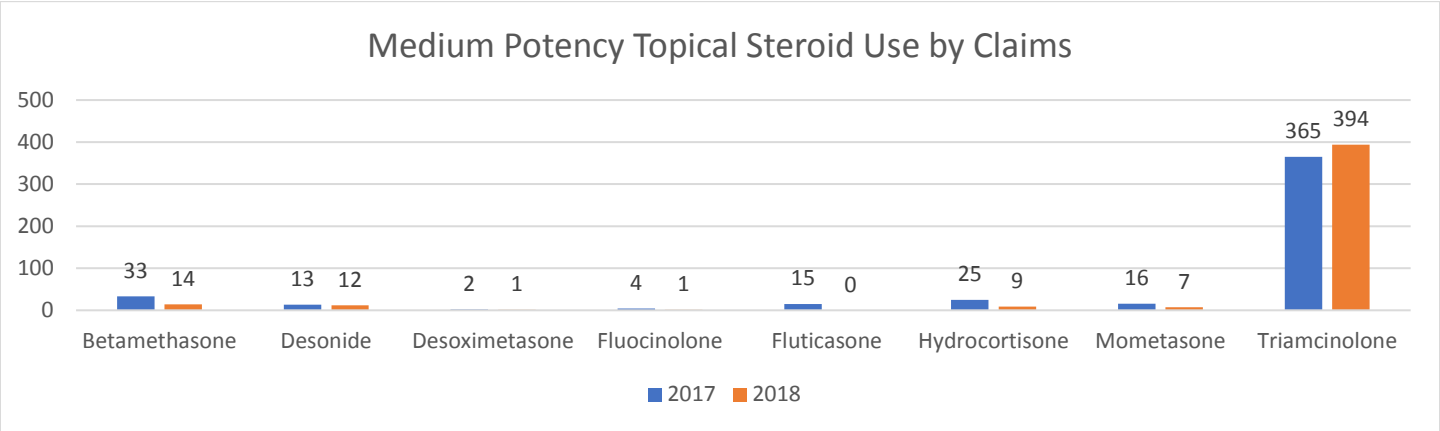
Topical Corticosteroid Utilization

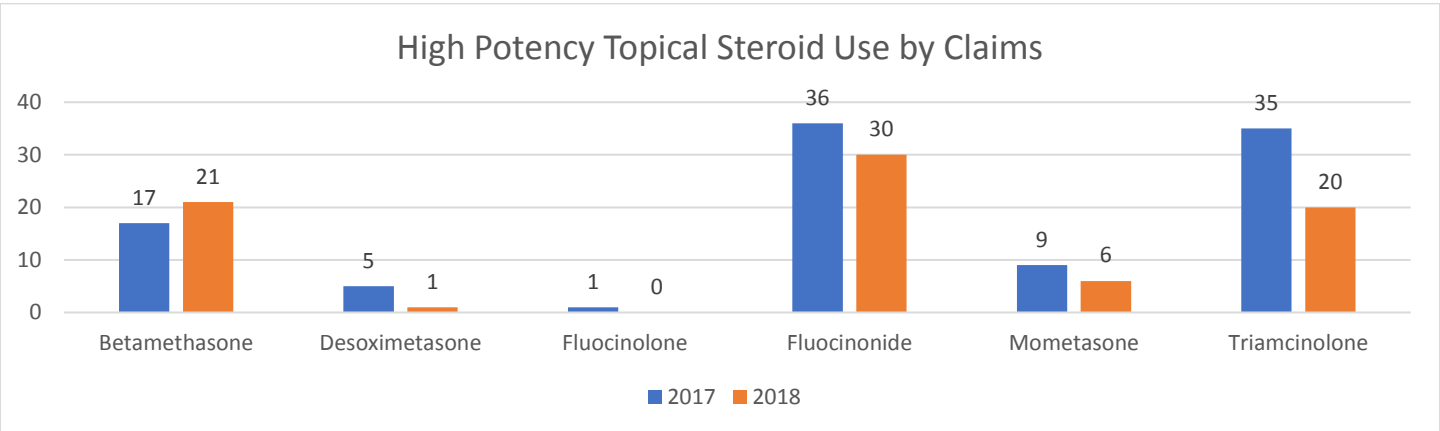


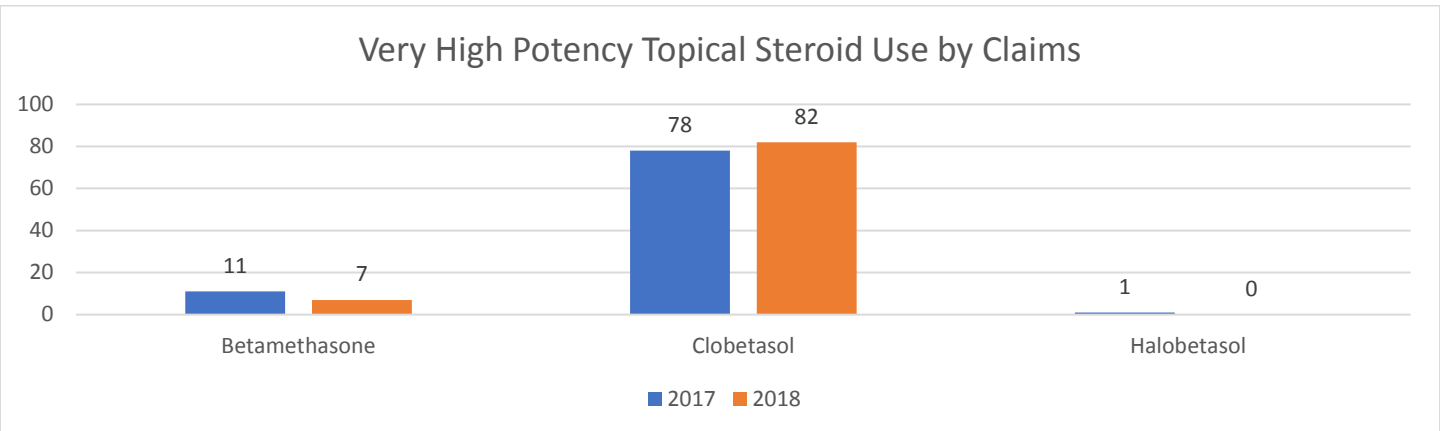


	2017	2018
Very-High	$14,718.51	$11,751.29
High	$7,398.95	$4,551.32
Medium	$15,658.32	$13,175.04
Low	$11,450.74	$7,576.18


Low Potency Topical Steroid Use by Claims
150
100
50
0
1 1
11 0
16 18
17 24
129 130
18 14
Alclometasone
Betamethasone
Desonide
Fluocinolone
Hydrocortisone
Triamcinolone
2017 2018


Medium Potency Topical Steroid Use by Claims
500
400
300
200
100
0
33 14
13 12
2 1
4 1
15 0
25 9
16 7
365 394
Betamethasone
Desonide
Desoximetasone
Fluocinolone
Fluticasone
Hydrocortisone
Mometasone
Triamcinolone
2017 2018


High Potency Topical Steroid Use by Claims
40
30
20
10
0
17 21
5 1
1 0
36 30
9 6
35 20
Betamethasone
Desoximetasone
Fluocinolone
Fluocinonide
Mometasone
Triamcinolone
2017 2018


Very High Potency Topical Steroid Use by Claims
100
80
60
40
20
0
11 7
78 82
1 0
Betamethasone
Clobetasol
Halobetasol
2017 2018

NORTH DAKOTA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
3RD QUARTER 2020

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

1. Lemborexant / Overuse _____ _____

Alert Message: The recommended dosage of Dayvigo (lemborexant) is 5 mg taken no more than once per night, immediately before going to bed, with at least 7 hours remaining before the planned time of awakening. The dose may be increased to the maximum recommended dose of 10 mg based on clinical response and tolerability.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Lemborexant		Hepatic Impairment
		Weak CYP3A4 Inhibitors

Max Dose: 10 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

2. Lemborexant 10 mg / Overuse – Hepatic Impairment _____ _____

Alert Message: The maximum recommended dose of Dayvigo (lemborexant) is 5 mg no more than once per night in patients with moderate hepatic impairment. In drug studies, lemborexant exposure (AUC and Cmax) and terminal half-life were increased in patients with moderate hepatic impairment (Child-Pugh B). Dosage adjustment is recommended in patients with moderate hepatic impairment. No dosage adjustment is recommended in patients with mild hepatic impairment (Child-Pugh A), but they may experience an increased risk of somnolence.

Drugs/Diseases

Util A	Util B	Util C (Include)
Lemborexant 10 mg		Hepatic Impairment

Max Dose: 5 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

3. Lemborexant / Cirrhosis _____ _____

Alert Message: Dayvigo (lemborexant) is not recommended in patients with severe hepatic impairment. In drug studies, lemborexant exposure (AUC and Cmax) and terminal half-life were increased in patients with moderate hepatic impairment (Child-Pugh B). Lemborexant has not been studied in patients with severe hepatic impairment.

Drugs/Diseases

Util A	Util B	Util C
Lemborexant	Cirrhosis	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

4. Lemborexant / Therapeutic Appropriateness _____ _____

Alert Message: Dayvigo (lemborexant) use is contraindicated in patients with narcolepsy. Lemborexant is a central nervous system (CNS) depressant that can impair daytime wakefulness even when used as prescribed.

Drugs/Diseases

Util A	Util B	Util C (Include)
Lemborexant		Narcolepsy

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

5. Lemborexant / Sleep Paralysis & Hallucinations _____ _____

Alert Message: Sleep paralysis (an inability to move or speak for up to several minutes during sleep-wake transitions) and hypnagogic/hypnopompic hallucinations (including vivid and disturbing perceptions) can occur with the use of Dayvigo (lemborexant). Symptoms similar to mild cataplexy also can occur with lemborexant. Such symptoms can include periods of leg weakness lasting from seconds to a few minutes, can occur either at night or during the day, and may not be associated with an identified triggering event (e.g., laughter or surprise). Prescribers should explain the nature of these events to patients when prescribing lemborexant.

Drugs/Diseases

Util A	Util B	Util C
Lemborexant	Recurrent Sleep Paralysis	
	Hallucinations	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

6. Lemborexant / Complex Sleep Behaviors _____ _____

Alert Message: Complex sleep behaviors, including sleep-walking, sleep-driving, and engaging in other activities while not fully awake (e.g., preparing and eating food, making phone calls, having sex), have been reported to occur with the use of hypnotics such as Dayvigo (lemborexant). Discontinue lemborexant immediately if a patient experiences a complex sleep behavior.

Drugs/Diseases

Util A	Util B	Util C
Lemborexant	Sleep Walking	
	Other Parasomnia	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

7. Lemborexant / Suicidal Ideation & Depression _____ _____

Alert Message: Worsening of depression or suicidal thinking may occur in patients receiving Dayvigo (lemborexant). Prescribe the lowest number of tablets feasible to avoid intentional overdose. The emergence of any new behavioral sign or symptom of concern requires careful and immediate evaluation.

Drugs/Diseases

Util A	Util B	Util C
Lemborexant	Depression	
	Suicide Attempt	
	Suicidal Ideation	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

8. Lemborexant / Compromised Respiratory Function _____ _____

Alert Message: The effect of Dayvigo (lemborexant) on respiratory function should be considered if prescribed to patients with compromised respiratory function. Lemborexant has not been studied in patients with moderate to severe obstructive sleep apnea (OSA) or in patients with chronic obstructive pulmonary disease (COPD).

Drugs/Diseases

Util A	Util B	Util C
Lemborexant	COPD	
	OSA	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

9. Lemborexant / Moderate & Strong CYP3A4 Inhibitors _____ _____

Alert Message: The concurrent use of Dayvigo (lemborexant) with a moderate or strong CYP3A4 inhibitor should be avoided. Lemborexant is a CYP3A4 substrate, and concomitant use with these drugs has been shown to significantly increase the AUC and Cmax of lemborexant, increasing the risk of lemborexant-related adverse reactions.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

10. Lemborexant 10 mg / Weak CYP3A4 Inhibitors _____ _____

Alert Message: The maximum recommended dosage of Dayvigo (lemborexant) is 5 mg no more than once per night when coadministered with weak CYP3A inhibitors. Lemborexant is a CYP3A4 substrate, and physiologically-based pharmacokinetic (PBPK) modeling predicted that concomitant use of weak CYP3A inhibitors increased lemborexant exposure by less than 2-fold.

Drugs/Diseases

Util A	Util B	Util C
Lemborexant 10 mg	Chlorzoxazone	
	Cilostazol	
	Fosaprepitant	
	Ivacaftor	
	Lomitapide	
	Ranitidine	
	Ranolazine	
	Tacrolimus	
	Ticagrelor	

Max Dose: 5 mg/day

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionaLabeling/ucm093664.htm

11. Lemborexant / Moderate & Strong CYP3A4 Inducers _____ _____

Alert Message: The concurrent use of Dayvigo (lemborexant) with moderate or strong CYP3A4 inducers should be avoided. Lemborexant is a CYP3A4 substrate, and concomitant use with these inducers has been shown to decrease lemborexant exposure and may reduce lemborexant efficacy.

Drugs/Diseases

Util A	Util B		Util C
Lemborexant	Apalutamide	Bosentan	
	Carbamazepine	Efavirenz	
	Enzalutamide	Etravirine	
	Lumacaftor	Dexamethasone	
	Mitotane	Modafinil	
	Phenobarbital		
	Phenytoin		
	Primidone		
	Rifabutin		
	Rifampin		
	Rifapentine		

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionaLabeling/ucm093664.htm

12. Lemborexant / CYP2B6 Substrates _____ _____

Alert Message: The concurrent use of Dayvigo (lemborexant) with a CYP2B6 substrate may result in the reduced efficacy of the substrate. Lemborexant is CYP2B6 inducer, and concomitant use with a CYP2B6 substrate can lead to decreased substrate exposure. Monitor the patient for adequate CYP2B6 substrate clinical response. Increasing the dose of the substrate may be considered as needed.

Drugs/Diseases

Util A	Util B	Util C
Lemborexant	Bupropion	
	Cyclophosphamide	
	Efavirenz	
	Methadone	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Facts & Comparisons, 2020 Updates, Wolters Kluwer health.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.
Hedrich WD, Hassan HE, Wang H. Insights into CYP2B6-mediated Drug-drug Interactions. Acta Pharm Sin B. 2016;6(5):413–425. doi:10.1016/j.apsb.2016.07.016

13. Lemborexant / Therapeutic Appropriateness _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Lemborexant		

Age Range: 0 – 17 yoa

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

14. Lemborexant / Lactation _____ _____

Alert Message: There are no data on the presence of Dayvigo (lemborexant) in human milk, the effects on the breastfed infant, or the effects on milk production. Lemborexant and its metabolites are present in the milk of lactating rats. Infants exposed to lemborexant through breastmilk should be monitored for excessive sedation. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for lemborexant and any potential adverse effects on the breastfed infant from lemborexant or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Lemborexant	Lactation	

Age Range: 11 – 50 yoa
Gender: Female

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

15. Lemborexant / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no available data on Dayvigo (lemborexant) use in pregnant women to evaluate for drug-associated risks of major birth defects, miscarriage, or adverse maternal or fetal outcomes. There is a pregnancy exposure registry that monitors pregnancy outcomes in women who are exposed to lemborexant during pregnancy. Healthcare providers are encouraged to register patients in the DAYVIGO pregnancy registry.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Lemborexant	Pregnancy	Abortion
		Delivery
		Miscarriage

Age Range: 11 – 50 yoa
Gender: Female

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

16. **Bempedoic Acid / Overuse** _____ _____

Alert Message: Nexletol (bempedoic acid) may be over-utilized. The recommended dosage of bempedoic acid, in combination with maximally tolerated statin therapy, is 180 mg orally once daily.

Drugs/Diseases

Util A	Util B	Util C
Bempedoic Acid		

Max Dose: 180 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Nexletol Prescribing Information, Feb. 2020, Esperion Therapeutics, Inc.

17. Bempedoic Acid / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Nexletol (bempedoic acid) have not been established in pediatric patients.

Drugs/Diseases

Util A	Util B	Util C
Bempedoic Acid		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Nexletol Prescribing Information, Feb. 2020, Esperion Therapeutics, Inc.

18. Bempedoic Acid / Therapeutic Appropriateness _____ _____

Alert Message: Nexletol (bempedoic acid) inhibits renal tubular OAT2 and may increase blood uric acid levels. In clinical trials, 26% of bempedoic acid-treated patients with normal baseline uric acid values (versus 9.5% placebo) experienced hyperuricemia one or more times, and 3.5% of patients experienced clinically significant hyperuricemia reported as an adverse reaction (versus 1.1% placebo). Elevated blood uric acid may lead to the development of gout. Monitor patients for signs and symptoms of hyperuricemia, and initiate treatment with urate-lowering drugs as appropriate.

Drugs/Diseases

Util A	Util B	Util C
Bempedoic Acid		

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Nexletol Prescribing Information, Feb. 2020, Esperion Therapeutics, Inc.

19. Bempedoic Acid / Tendon Rupture _____ _____

Alert Message: Nexletol (bempedoic acid) is associated with an increased risk of tendon rupture or injury. In clinical trials, tendon rupture occurred in 0.5% of patients treated with bempedoic acid versus 0% of placebo-treated patients and involved the rotator cuff (the shoulder), biceps tendon, or Achilles tendon. Discontinue bempedoic acid immediately if the patient experiences rupture of a tendon. Consider discontinuing bempedoic acid if the patient experiences joint pain, swelling, or inflammation. Consider alternative therapy in patients with a history of tendon disorders or tendon rupture.

Drugs/Diseases

Util A	Util B	Util C
Bempedoic Acid		

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Nexletol Prescribing Information, Feb. 2020, Esperion Therapeutics, Inc.

20. Bempedoic Acid / Simvastatin 40 & 80 mg _____ _____

Alert Message: The concurrent use of Nexletol (bempedoic acid) with simvastatin causes an increase in simvastatin concentration and may increase the risk of simvastatin-related myopathy. Avoid concomitant use of bempedoic acid with simvastatin greater than 20 mg.

Drugs/Diseases

Util A	Util B	Util C
Bempedoic Acid	Simvastatin 40mg	
	Simvastatin 80mg	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Nexletol Prescribing Information, Feb. 2020, Esperion Therapeutics, Inc.

21. Bempedoic Acid / Pravastatin 80 mg _____ _____

Alert Message: The concurrent use of Nexletol (bempedoic acid) with pravastatin causes an increase in pravastatin concentration and may increase the risk of pravastatin-related myopathy. Avoid concomitant use of bempedoic acid with pravastatin greater than 40 mg.

Drugs/Diseases

Util A	Util B	Util C
Bempedoic Acid	Pravastatin 80 mg	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Nexletol Prescribing Information, Feb. 2020, Esperion Therapeutics, Inc.

22. Bempedoic Acid / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Nexletol (bempedoic acid) therapy should be discontinued when pregnancy is recognized unless the benefits of therapy outweigh the potential risks to the fetus. There are no available data on bempedoic acid use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Bempedoic acid decreases cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol; therefore, bempedoic acid may cause fetal harm when administered to pregnant women based on the mechanism of action.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Bempedoic Acid	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Nexletol Prescribing Information, Feb. 2020, Esperion Therapeutics, Inc.

23. Bempedoic Acid / Therapeutic Appropriateness _____ _____

Alert Message: There is no information regarding the presence of Nexletol (bempedoic acid) in human or animal milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production. Bempedoic acid decreases cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol and may cause harm to the breastfed infant. Because of the potential for serious adverse reactions in a breastfed infant, based on the mechanism of action, advise patients that breastfeeding is not recommended during treatment with bempedoic acid.

Drugs/Diseases

Util A	Util B	Util C
Bempedoic Acid	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Nexletol Prescribing Information, Feb. 2020, Esperion Therapeutics, Inc.

24. Bempedoic Acid / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Nexletol (bempedoic acid). Non-adherence to the prescribed dosing regimen may result in subtherapeutic effects, which may lead to decreased outcomes and additional healthcare costs.

Drugs/Diseases

Util A	Util B	Util C
Bempedoic Acid		

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med. 2005;353:487-97.
Kumbhani DJ, Steg PG, Cannon CP, et al., Adherence to Secondary Prevention Medications for Four-Year Outcomes in Outpatients with Atherosclerosis. Am J Med. 2013 Aug;126(8):693-700.
Simpson RJ, Mendys P. The Effects of Adherence and Persistence on Clinical Outcomes in Patients Treated with Statins: A Systematic Review. Jrnl Clin Lipidol. 2010 Nov-Dec;4(6):462-471.
Blackburn DF, Dobson RT, Blackburn JL, et al. Cardiovascular Morbidity Associated with Nonadherence to Statin Therapy. Pharmacotherapy 2005;25(8):1035-1043.
Lindgren P, Eriksson J, Buxton M, et al., The Economic Consequences of Non-Adherence to Lipid-Lowering Therapy: Results from the Anglo-Scandinavian Cardia Outcomes Trial. Int J Clin Pract. 2010 May 24.

25. Asenapine Transdermal / Overuse _____ _____

Alert Message: Secuado (asenapine) transdermal system may be over-utilized. The recommended maximum dosage of transdermal asenapine is 7.6 mg/24 hours. The safety of doses above 7.6 mg/24 hours has not been evaluated in clinical studies.

Drugs/Diseases

Util A	Util B	Util C
Asenapine Transdermal		

Max Dose: 7.6 mg patch per day

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Secuado Prescribing Information, Oct. 2019, Noven Therapeutics, LLC.

26. Asenapine Transdermal / Therapeutic Appropriateness _____ _____

Alert Message: Secuado (asenapine) transdermal system is contraindicated in patients with severe hepatic impairment (Child-Pugh C). In clinical studies, asenapine exposure was shown to be 7-fold higher in subjects with severe hepatic impairment compared to the exposure observed in subjects with normal hepatic function. No dosage adjustment for transdermal asenapine is required in patients with mild to moderate hepatic impairment (Child-Pugh A and B) because asenapine exposure is similar to that in subjects with normal hepatic function.

Drugs/Diseases

Util A	Util B	Util C
Asenapine Transdermal	Cirrhosis Hepatic Failure	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Secuado Prescribing Information, Oct. 2019, Noven Therapeutics, LLC.

27. Asenapine Transdermal / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Secuado (asenapine) transdermal system in pediatric patients have not been established.

Drugs/Diseases

Util A	Util B	Util C
Asenapine Transdermal		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Secuado Prescribing Information, Oct. 2019, Noven Therapeutics, LLC.

28. Asenapine Transdermal / Tardive Dyskinesia _____ _____

Alert Message: Tardive dyskinesia, a syndrome of potentially irreversible, involuntary, dyskinetic movements, may develop in patients treated with antipsychotic drugs, including Secuado (asenapine) transdermal system. The risk appears to be highest among the elderly, especially elderly women, but it is not possible to predict which patients are likely to develop the syndrome. If signs and symptoms of tardive dyskinesia appear in a patient on asenapine, drug discontinuation should be considered. However, some patients may require treatment with asenapine despite the presence of the syndrome.

Drugs/Diseases

Util A	Util B	Util C
Asenapine Transdermal	Tardive Dyskinesia	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Secuado Prescribing Information, Oct. 2019, Noven Therapeutics, LLC.

29. Asenapine Transdermal / Orthostatic Hypotension _____ _____

Alert Message: Atypical antipsychotics, including Secuado (asenapine) transdermal system, cause orthostatic hypotension and syncope. Generally, the risk is greatest during initial dose titration and when increasing the dose. Orthostatic vital signs should be monitored in patients who are vulnerable to hypotension (elderly patients, patients with dehydration, hypovolemia, concomitant treatment with antihypertensive medications), patients with known cardiovascular disease (history of myocardial infarction or ischemic heart disease, heart failure, or conduction abnormalities), and patients with cerebrovascular disease.

Drugs/Diseases

Util A	Util B	Util C
Asenapine Transdermal	Orthostatic Hypotension	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Secuado Prescribing Information, Oct. 2019, Noven Therapeutics, LLC.

30. Asenapine Transdermal / QT Prolongation _____ _____

Alert Message: Asenapine has been shown to prolong the QT/QTc interval. The use of Secuado (asenapine) transdermal system should be avoided in patients with a history of cardiac arrhythmias and in other conditions that may increase the risk of the occurrence of torsade de pointes. The use of asenapine transdermal should also be avoided in combination with drugs that increase the QT interval.

Drugs/Diseases

Util A	Util B	Util C
Asenapine Transdermal	Long QT Syndrome	
	Hypokalemia	
	Hypomagnesemia	
	Bradycardia	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Secuado Prescribing Information, Oct. 2019, Noven Therapeutics, LLC.

31. Asenapine Transdermal / Seizures _____ _____

Alert Message: As with other antipsychotic drugs, Secuado (asenapine) transdermal system should be used with caution in patients with a history of seizures or with conditions that potentially lower the seizure threshold. Conditions that lower the seizure threshold may be more prevalent in patients 65 years or older.

Drugs/Diseases

Util A	Util B	Util C
Asenapine Transdermal	Seizures	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Secuado Prescribing Information, Oct. 2019, Noven Therapeutics, LLC.

32. Asenapine Transdermal / Strong CYP1A2 Inhibitors _____ _____

Alert Message: The concurrent use of Secuado (asenapine) transdermal system with a strong CYP1A2 inhibitor may result in increases in the AUC and Cmax of asenapine. Asenapine is metabolized by CYP1A2. Dosage reduction for asenapine transdermal based on clinical response may be necessary.

Drugs/Diseases

Util A	Util B	Util C
Asenapine Transdermal	Fluvoxamine	
	Ciprofloxacin	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Secuado Prescribing Information, Oct. 2019, Noven Therapeutics, LLC.

33. Asenapine Transdermal / Drugs That Cause QT Prolongation _____ _____

Alert Message: The use of Secuado (asenapine) transdermal system should be avoided in combination with other drugs known to prolong the QTc interval, including Class 1A or Class 3 antiarrhythmics, antipsychotic medications, and antibiotics. Asenapine has been associated with increases in the QTc interval.

Drugs/Diseases

Util A	Util B				Util C
Asenapine Transdermal	Abiraterone	Efavirenz	Levofloxacin	Rilpivirine	
	Alfuzosin	Eliglustat	Lithium	Risperidone	
	Amiodarone	Encorafenib	Lofexidine	Ritonavir	
	Amitriptyline	Entrectinib	Loperamide	Romidepsin	
	Anagrelide	Eribulin	Maprotiline	Saquinavir	
	Aripiprazole	Erythromycin	Methadone	Sertraline	
	Arsenic Trioxide	Escitalopram	Metoclopramide	Siponimod	
	Atazanavir	Ezogabine	Midostaurin	Solifenacin	
	Atomoxetine	Famotidine	Mifepristone	Sotalol	
	Azithromycin	Felbamate	Mirabegron	Sunitinib	
	Bedaquiline	Fingolimod	Mirtazapine	Tacrolimus	
	Bortezomib	Flecainide	Moexipril	Tamoxifen	
	Bendamustine	Fluconazole	Moxifloxacin	Telavancin	
	Bosutinib	Fluoxetine	Nelfinavir	Tetrabenazine	
	Buprenorphine	Fluvoxamine	Nilotinib	Thioridazine	
	Ceritinib	Foscarnet	Nortriptyline	Tizanidine	
	Chloroquine	Galantamine	Ofloxacin	Tolterodine	
	Chlorpromazine	Ganciclovir	Ondansetron	Toremifene	
	Cilostazol	Gemifloxacin	Osimertinib	Tramadol	
	Ciprofloxacin	Gilteritinib	Oxaliplatin	Trazodone	
	Citalopram	Glasdegib	Paliperidone	Trimipramine	
	Clarithromycin	Granisetron	Panobinostat	Valbenazine	
	Clomipramine	Haloperidol	Paroxetine	Vandetanib	
	Clozapine	Hydroxychloroquine	Pasireotide	Vemurafenib	
	Crizotinib	Hydroxyzine	Pazopanib	Venlafaxine	
	Dabrafenib	Ibutilide	Pentamidine	Voriconazole	
	Dasatinib	Iloperidone	Pimavanserin		
	Desipramine	Imipramine	Pimozide		
	Deutetrabenazine	Indapamide	Pitolisant		
	Diphenhydramine	Indinavir	Posaconazole		
	Disopyramide	Ivabradine	Procainamide		
	Dofetilide	Itraconazole	Promethazine		
	Dolasetron	Ivosidenib	Propafenone		
	Droperidol	Ketoconazole	Quetiapine		
	Doxepin	Lapatinib	Quinidine		
	Dronedarone	Lefamulin	Quinine		
	Droperidol	Lenvatinib	Ranolazine		

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Secuado Prescribing Information, Oct. 2019, Noven Therapeutics, LLC.

34. Asenapine Transdermal / Paroxetine _____ _____

Alert Message: The concurrent use of Secuado (asenapine) transdermal system with paroxetine may enhance the inhibitory effects of paroxetine on its own metabolism by CYP2D6. Concomitant use of these agents may cause increases in paroxetine AUC and Cmax. Reduce the paroxetine dose by half when paroxetine is used in combination with asenapine.

Drugs/Diseases

Util A	Util B	Util C
Asenapine Transdermal	Paroxetine	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Secuado Prescribing Information, Oct. 2019, Noven Therapeutics, LLC.

35. Asenapine Transdermal / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Secuado (asenapine) transdermal system. Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effects, which may lead to decreased patient outcomes and additional medical costs.

Drugs/Diseases

Util A	Util B	Util C
Asenapine Transdermal		

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005;353:487-97.
Stephenson JJ, Tuncelli O, Gu T, et al., Adherence to Oral Second-Generation Antipsychotic Medications in Patients with Schizophrenia and Bipolar Disorder: Physicians' Perceptions of Adherence vs. Pharmacy Claims. Int J Clin Pract, June 2012, 66, 6, 565-573.
Theida P, et.al., An Economic Review of Compliance with Medication Therapy in the Treatment of Schizophrenia, Psychiatric Services, 2003;54:508-516.
Berger A, Edelsbery J, Sanders KN, et al., Medication Adherence and Utilization in Patients with Schizophrenia or Bipolar Disorder Receiving Aripiprazole, Quetiapine, or Ziprasidone at Hospital Discharge: A Retrospective Cohort Study. BMC Psychiatry 2012,12:99.

36. Ubrogepant / Overuse _____ _____

Alert Message: Ubrelvy (ubrogepant) may be over-utilized. The recommended dose of ubrogepant is 50 mg or 100 mg orally with or without food. If needed, a second dose may be taken at least 2 hours after the initial dose. The maximum dose of ubrogepant in a 24-hour period is 200 mg. The safety of treating more than 8 migraines in a 30-day period has not been established.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Ubrogepant		Cirrhosis
		CKD 4
		CKD 5

Max Dose: 200 mg/day

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

37. Ubrogepant / Overuse _____ _____

Alert Message: Ubrelvy (ubrogepant) may be over-utilized. The recommended initial dose of ubrogepant in patients with severe hepatic impairment (Child-Pugh C) or severe renal impairment (CLcr 15-29 mL/min) is 50 mg. If needed, a second dose may be taken at least 2 hours after the initial dose. The maximum dose of ubrogepant in a 24-hour period is 100 mg. The safety of treating more than 8 migraines in a 30-day period has not been established.

Drugs/Diseases

Util A	Util B	Util C (Include)
Ubrogepant		Cirrhosis
		CKD 4
		CKD 5

Max Dose: 100 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

38. Ubrogepant / ESRD _____ _____

Alert Message: The use of Ubrelvy (ubrogepant) should be avoided in patients with end-stage renal disease (CLcr < 15mL/min). Ubrogepant has not been studied in patients with ESRD, and no dosing recommendations can be made for this patient population.

Drugs/Diseases

Util A	Util B	Util C (Include)
Ubrogepant		ESRD

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

39. Ubrogepant / Therapeutic Appropriateness _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Ubrogepant		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

40. Ubrogepant / Strong CYP3A4 Inhibitors _____ _____

Alert Message: The co-administration of Ubrelvy (ubrogepant) with strong CYP3A4 inhibitors is contraindicated. Ubrogepant is a CYP3A4 substrate, and concurrent use with a strong inhibitor may lead to significant increases in ubrogepant exposure. In in vivo studies, the co-administration of ubrogepant with ketoconazole (a strong CYP3A4 inhibitor) resulted in a 9.7-fold and 5.3-fold increase in the AUCinf and Cmax of ubrogepant, respectively.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

41. Ubrogepant 100 mg / Moderate CYP3A4 Inhibitors _____ _____

Alert Message: When Ubrelvy (ubrogepant) is co-administered with a moderate CYP3A4 inhibitor, the initial dose of ubrogepant should be limited to 50 mg, and the use of a second dose within 24 hours should be avoided. In in vivo drug studies, the co-administration of ubrogepant (a CYP3A4 substrate) with the moderate CYP3A4 inhibitor, verapamil, resulted in an approximate 3.5-fold and 2.8-fold increase in the AUCinf and Cmax of ubrogepant, respectively.

Drugs/Diseases

Util A	Util B		Util C
Ubrogepant 100 mg	Aprepitant	Erythromycin	
	Ciprofloxacin	Fluconazole	
	Crizotinib	Fluvoxamine	
	Cyclosporine	Imatinib	
	Diltiazem	Verapamil	
	Dronedarone		

References:
IBM Micromedex DRUGDEX (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA 2020.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

42. Ubrogepant 100 mg / Weak CYP3A4 Inhibitors _____ _____

Alert Message: When Ubrelvy (ubrogepant) is co-administered with a weak CYP3A4 inhibitor the initial dose of ubrogepant should be limited to 50 mg and the second dose, if needed, should be limited to 50 mg also. No dedicated drug interaction study has been conducted with ubrogepant (a CYP3A4 substrate) and a weak CYP3A4 inhibitor, but the conservative prediction of the maximal potential increase in ubrogepant exposure with weak CYP3A4 inhibitors is not expected to be more than 2-fold.

Drugs/Diseases

Util A	Util B		Util C
Ubrogepant 100 mg	Amiodarone	Lapatinib	
	Chlorzoxazone	Lomitapide	
	Cilostazol	Ranitidine	
	Fosaprepitant	Ranolazine	
	Istradefylline	Tacrolimus	
	Ivacaftor	Ticagrelor	

References:
IBM Micromedex DRUGDEX (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA 2020.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

43. Ubrogepant / Strong CYP3A4 Inducers _____ _____

Alert Message: The concurrent use of Ubrelvy (ubrogepant) with strong CYP3A4 inducers should be avoided. Ubrogepant is a CYP3A4 substrate, and concurrent use with a strong CYP3A4 inducer may result in decreased ubrogepant exposure and loss of efficacy. In in vivo drug studies, the co-administration of ubrogepant with the strong CYP3A4 inducer, rifampin, resulted in an approximate 80% reduction in ubrogepant exposure.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

44. Ubrogepant 100 mg / BCRP and/or P-gp Only Inhibitors _____ _____

Alert Message: When Ubrelvy (ubrogepant) is co-administered with a BCRP and/or P-gp only inhibitor, the initial dose of ubrogepant should be limited to 50 mg and the second dose, if needed, should be limited to 50 mg also. No dedicated drug interaction study has been conducted with ubrogepant (a BCRP and P-gp substrate) and BCRP and P-gp efflux inhibitors, but an increase in ubrogepant exposure may result from co-administration of these drugs.

Drugs/Diseases

Util A	Util B	Util C
Ubrogepant 100 mg	Carvedilol	
	Eltrombopag	
	Quinidine	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

45. Ubrogepant / Lactation _____ _____

Alert Message: There are no data on the presence of Ubrelvy (ubrogepant) in human milk, the effects ubrogepant on the breastfed infant, or the effects of ubrogepant on milk production. In lactating rats, oral dosing with ubrogepant resulted in levels of ubrogepant in milk comparable to peak plasma concentrations. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ubrogepant and any potential adverse effects on the breastfed infant from ubrogepant or underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Ubrogepant	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

46. Ubrogepant / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no adequate data on the developmental risk associated with the use of Ubrelvy (ubrogepant) in pregnant women. In animal studies, adverse effects on embryofetal development were observed following administration of ubrogepant during pregnancy (increased embryofetal mortality in rabbits) or during pregnancy and lactation (decreased body weight in offspring in rats) at doses greater than those used clinically and which were associated with maternal toxicity.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Ubrogepant	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

47. Larotrectinib / Overutilization _____ _____

Alert Message: Vitrakvi (larotrectinib) may be over-utilized. The recommended dosage of larotrectinib in adult and pediatric patients with a body surface area (BSA) of at least 1.0 m2 is 100 mg orally twice daily, with or without food, until disease progression or until unacceptable toxicity. The recommended dosage in pediatric patients with a BSA area less than 1.0 m2 is 100 mg/m2 orally twice daily, with or without food, until disease progression or until unacceptable toxicity.

Drugs/Diseases

Util A	Util B	Util C
Larotrectinib		

Max Dose: 200 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Vitrakvi Prescribing Information, July 2019, Bayer HealthCare Pharmaceuticals Inc.

48. Larotrectinib / Strong CYP3A4 Inhibitors _____ _____

Alert Message: The concurrent use of Vitrakvi (larotrectinib), a CYP3A4 substrate, with strong CYP3A4 inhibitors should be avoided. If coadministration of a strong CYP3A4 inhibitor cannot be avoided, reduce the larotrectinib dose by 50%. After the inhibitor has been discontinued for 3 to 5 elimination half-lives, resume the larotrectinib dose taken prior to initiating the CYP3A4 inhibitor.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Vitrakvi Prescribing Information, July 2019, Bayer HealthCare Pharmaceuticals Inc.

49. Larotrectinib / Strong CYP3A4 Inducers _____ _____

Alert Message: The concurrent use of Vitrakvi (larotrectinib), a CYP3A4 substrate, with strong CYP3A4 inducers should be avoided. If coadministration of a strong CYP3A4 inducer cannot be avoided, the larotrectinib dose should be double. After the inducer has been discontinued for 3 to 5 elimination half-lives, resume the larotrectinib dose taken prior to initiating the CYP3A4 inducer.

Drugs/Diseases

Util A	Util B		Util C
Larotrectinib	Carbamazepine	Primidone	
	Enzalutamide	Rifabutin	
	Mitotane	Rifampin	
	Phenytoin	Rifapentine	
	Phenobarbital		

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Vitrakvi Prescribing Information, July 2019, Bayer HealthCare Pharmaceuticals Inc.

50. Larotrectinib / Sensitive CYP3A4 Substrates _____ _____

Alert Message: The concurrent use of Vitrakvi (larotrectinib), a CYP3A4 inhibitor, with sensitive CYP3A4 substrates should be avoided. If coadministration of a sensitive CYP3A4 substrate cannot be avoided, monitor the patient for substrate-related adverse reactions.

Drugs/Diseases

Util A	Util B					Util C
Larotrectinib	Avanafil	Eletriptan	Lurasidone	Simvastatin	Vardenafil	
	Budesonide	Eplerenone	Maraviroc	Sirolimus		
	Buspirone	Everolimus	Midazolam	Tacrolimus		
	Conivaptan	Felodipine	Naloxegol	Ticagrelor		
	Darifenacin	Ibrutinib	Nisoldipine	Tipranavir		
	Darunavir	Lomitapide	Quetiapine	Tolvaptan		
	Dronedarone	Lovastatin	Sildenafil	Triazolam		

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Vitrakvi Prescribing Information, July 2019, Bayer HealthCare Pharmaceuticals Inc.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionaLabeling/ucm093664.htm

51. Larotrectinib / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on literature reports in human subjects with congenital mutations leading to changes in TRK signaling, findings from animal studies, and its mechanism of action, Vitrakvi (larotrectinib) can cause fetal harm when administered to a pregnant woman. Larotrectinib resulted in malformations in rats and rabbits at maternal exposures that were approximately 11- and 0.7- times, respectively, those observed at the clinical dose of 100 mg twice daily. Advise women of the potential risk to a fetus. Advise females of reproductive potential to use an effective method of contraception during treatment and for 1 week after the final dose of larotrectinib.

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Drugs/Diseases

Util A	Util B	Util C (Negating)
Larotrectinib	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Vitrakvi Prescribing Information, July 2019, Bayer HealthCare Pharmaceuticals Inc.

52. Larotrectinib / Lactation _____ _____

Alert Message: There are no data on the presence of Vitrakvi (larotrectinib) or its metabolites in human milk and no data on its effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with larotrectinib and for 1 week after the final dose.

Drugs/Diseases

Util A	Util B	Util C
Larotrectinib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Vitrakvi Prescribing Information, July 2019, Bayer HealthCare Pharmaceuticals Inc.

53. Larotrectinib / Reproductive Potential _____ _____

Alert Message: Vitrakvi (larotrectinib) can cause fetal harm. The manufacturer advises the use of effective contraception during treatment with larotrectinib and for at least 1 week after the final dose.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Larotrectinib		Contraceptives

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Vitrakvi Prescribing Information, July 2019, Bayer HealthCare Pharmaceuticals Inc.

54. Larotrectinib / Reproductive Potential _____ _____

Alert Message: Advise males with female partners of reproductive potential to use effective contraception during treatment with Vitrakvi (larotrectinib) and for 1 week after the final dose.

Drugs/Diseases

Util A	Util B	Util C
Larotrectinib		

Gender: Male

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Vitrakvi Prescribing Information, July 2019, Bayer HealthCare Pharmaceuticals Inc.

55. Voxelotor / Overuse _____ _____

Alert Message: Oxbryta (voxelotor) may be over-utilized. The recommended maximum daily dose of voxelotor in adults and pediatric patients 12 years of age and older is 1500 mg once daily with or without food.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Voxelotor		Cirrhosis
		Strong or Moderate CYP3A4 Inducers
		Strong CYP3A4 Inhibitors & Fluconazole

Max Dose: 1500 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Oxbryta Prescribing Information, Nov. 2019, Global Blood Therapeutics, Inc.

56. Voxelotor / Overuse – Hepatic Impairment _____ _____

Alert Message: Oxbryta (voxelotor) may be over-utilized. The recommended dosage of voxelotor in patients with severe hepatic impairment (Child-Pugh C) is 1000 mg taken once daily with or without food. No dosage adjustment of voxelotor is required for patients with mild or moderate hepatic impairment.

Drugs/Diseases

Util A	Util B	Util C (Include)
Voxelotor		Cirrhosis

Max Dose: 1000 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Oxbryta Prescribing Information, Nov. 2019, Global Blood Therapeutics, Inc.

57. Voxelotor / Strong CYP3A4 Inhibitors & Fluconazole _____ _____

Alert Message: The co-administration of Oxbryta (voxelotor) with strong CYP3A4 inhibitors or fluconazole should be avoided due to the increased risk of voxelotor toxicity. If concurrent use is warranted, decrease the voxelotor dosage to 1000 mg once daily.

Drugs/Diseases

Util A	Util B	Util C (Include)	
Voxelotor		Cobicistat	Nelfinavir
		Clarithromycin	Nefazodone
		Fluconazole	Posaconazole
		Indinavir	Ritonavir
		Itraconazole	Saquinavir
		Ketoconazole	Voriconazole

Max Dose: 1000 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Oxbryta Prescribing Information, Nov. 2019, Global Blood Therapeutics, Inc.

58. Voxelotor / Moderate & Strong CYP3A4 Inducers _____ _____

Alert Message: The co-administration of Oxbryta (voxelotor) with moderate or strong CYP3A4 inducers should be avoided. Concurrent use of these agents with voxelotor, a CYP3A4 substrate, may result in decreased voxelotor plasma concentrations and loss of efficacy. If concurrent use is warranted, increase the voxelotor dosage to 2500 mg once daily.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Oxbryta Prescribing Information, Nov. 2019, Global Blood Therapeutics, Inc.

59. Voxelotor / Sensitive CYP3A4 Substrates w/ NTI _____ _____

Alert Message: The co-administration of Oxbryta (voxelotor) with sensitive CYP3A4 substrates with a narrow therapeutic index should be avoided. In vivo drug studies have shown that concurrent use of voxelotor, a weak CYP3A4 inhibitor, with midazolam resulted in increased midazolam exposure by 1.6-fold and the predicted increase in patients after multiple dosing is 2-fold. If concomitant use is unavoidable, consider a dose reduction of the sensitive CYP3A4 substrate(s).

Drugs/Diseases

Util A	Util B					Util C
Voxelotor	Avanafil	Eletriptan	Lurasidone	Simvastatin	Vardenafil	
	Budesonide	Eplerenone	Maraviroc	Sirolimus		
	Buspirone	Everolimus	Midazolam	Tacrolimus		
	Carbamazepine	Felodipine	Naloxegol	Ticagrelor		
	Darifenacin	Ibrutinib	Nisoldipine	Tipranavir		
	Darunavir	Lomitapide	Quetiapine	Tolvaptan		
	Dronedarone	Lovastatin	Sildenafil	Triazolam		

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Oxbryta Prescribing Information, Nov. 2019, Global Blood Therapeutics, Inc.
1398 / FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionaLabeling/ucm093664.htm

60. Voxelotor / Therapeutic Appropriateness _____ _____

Alert Message: The safety and efficacy of Oxbryta (voxelotor) in pediatric patients below the age of 12 years have not been established.

Drugs/Diseases

Util A	Util B	Util C
Voxelotor		

Age Range: 0 – 11 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Oxbryta Prescribing Information, Nov. 2019, Global Blood Therapeutics, Inc.

61. Voxelotor / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no available data on Oxbryta (voxelotor) use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Voxelotor should only be used during pregnancy if the benefit of the drug outweighs the potential risk.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Voxelotor	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Oxbryta Prescribing Information, Nov. 2019, Global Blood Therapeutics, Inc.

62. Voxelotor / Lactation _____ _____

Alert Message: There are no data on the presence of Oxbryta (voxelotor) in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in the breastfed child, including changes in the hematopoietic system, advise patients that breastfeeding is not recommended during treatment with voxelotor, and for at least 2 weeks after the last dose.

Drugs/Diseases

Util A	Util B	Util C
Voxelotor	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Oxbryta Prescribing Information, Nov. 2019, Global Blood Therapeutics, Inc.

63. Levamlodipine / Overuse _____ _____

Alert Message: Conjupri (levamlodipine) may be over-utilized. The recommended maximum daily adult dose is 5 mg once daily.

Drugs/Diseases

Util A	Util B	Util C
Levamlodipine		

Max Dose: 5 mg/day
Age Range: 18 – 999 yoa

References:
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.
Conjupri Prescribing Information, Dec. 2019, CSPC Ouyi Pharmaceutical Co., Ltd.

64. Levamlodipine / Therapeutic Appropriateness _____ _____

Alert Message: Conjupri (levamlodipine) may be over-utilized. The effective antihypertensive oral dose in pediatric patients 6 to 17 years of age is 2.5 mg once daily. Doses in excess of 2.5 mg daily have not been studied in pediatric patients.

Drugs/Diseases

Util A	Util B	Util C
Levamlodipine		

Age Range: 6 – 17 yoa
Max Dose: 2.5 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Conjupri Prescribing Information, Dec. 2019, CSPC Ouyi Pharmaceutical Co., Ltd.

65. Levamlodipine / Simvastatin _____ _____

Alert Message: The dose of simvastatin should be limited to 20 mg daily in patients co-administered Conjupri (levamlodipine). Levamlodipine is the pharmacologically active enantiomer of amlodipine. In a drug study, co-administration of amlodipine with simvastatin resulted in a 77% increase in exposure to simvastatin compared to simvastatin alone.

Drugs/Diseases

Util A	Util B	Util C
Levamlodipine	Simvastatin 40 & 80	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Conjupri Prescribing Information, Dec. 2019, CSPC Ouyi Pharmaceutical Co., Ltd.

66. Levamlodipine / Moderate & Strong CYP3A4 Inhibitors _____ _____

Alert Message: Co-administration of Conjupri (levamlodipine) with moderate or strong CYP3A inhibitors may result in increased systemic exposure to amlodipine and may require levamlodipine dose reduction. Monitor the patient for symptoms of hypotension and edema when amlodipine is co-administered with CYP3A inhibitors to determine the need for dose adjustment.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Conjupri Prescribing Information, Dec. 2019, CSPC Ouyi Pharmaceutical Co., Ltd.

67. Levamlodipine / Cyclosporine & Tacrolimus _____ _____

Alert Message: The concurrent use of Conjupri (levamlodipine) with cyclosporine or tacrolimus may increase the systemic exposure of the immunosuppressive agent. Frequent monitoring of trough blood levels of cyclosporine and tacrolimus is recommended and adjust the dose when appropriate.

Drugs/Diseases

Util A	Util B	Util C
Levamlodipine	Cyclosporine	
	Tacrolimus	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Conjupri Prescribing Information, Dec. 2019, CSPC Ouyi Pharmaceutical Co., Ltd.

68. Amifampridine / Overutilization _____ _____

Alert Message: Firdapse (amifampridine) may be over-utilized. The recommended maximum total daily dosage of amifampridine is 80 mg.

Drugs/Diseases

Util A	Util B	Util C
Amifampridine		

Max Dose: 80 mg/day

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Firdapse Prescribing Information, November 2018, Catalyst Pharmaceuticals.

69. Amifampridine / History of Seizures _____ _____

Alert Message: Firdapse (amifampridine) is contraindicated in patients with a history of seizures. Seizures have been observed in patients without a history of seizures taking amifampridine at the recommended doses, at various times after initiation of treatment, at an incidence of approximately 2%. Many of the patients were taking medications or had comorbid medical conditions that may have lowered the seizure threshold. Seizures may be dose-dependent. Consider discontinuation or dose-reduction of amifampridine in patients who have a seizure while on treatment.

Drugs/Diseases

Util A	Util B	Util C (Include)
Amifampridine		Seizures
		Convulsions

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Firdapse Prescribing Information, November 2018, Catalyst Pharmaceuticals.

70. Amifampridine / Cholinergic Drugs _____ _____

Alert Message: The concomitant use of Firdapse (amifampridine) and drugs with cholinergic effects (e.g., direct or indirect cholinesterase inhibitors) may increase the risk of adverse reactions due to additive cholinergic effects.

Drugs/Diseases

Util A	Util B	Util C
Amifampridine	Donepezil	
	Galantamine	
	Pyridostigmine	
	Rivastigmine	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Firdapse Prescribing Information, November 2018, Catalyst Pharmaceuticals.

71. Amifampridine / Therapeutic Appropriateness _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Amifampridine		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Firdapse Prescribing Information, November 2018, Catalyst Pharmaceuticals.

72. Amifampridine / Drugs that Lower Seizure Threshold _____ _____

Alert Message: The concomitant use of Firdapse (amifampridine) with drugs that lower seizure threshold may lead to an increased risk of seizures. The decision to administer amifampridine concomitantly with drugs that lower the seizure threshold should be carefully considered in light of the severity of the associated risks.

Drugs/Diseases

Util A	Util B		Util C
Amifampridine	1st Generation Antipsychotics	SNRIs	
	Aripiprazole	SSRIs	
	Asenapine	Steroids	
	Baclofen	Stimulants	
	Bupropion	Tacrolimus	
	Clozapine	TCAs	
	Diphenhydramine	Tramadol	
	Olanzapine	Ziprasidone	
	Paliperidone		
	Quetiapine		
	Quinolones		

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Firdapse Prescribing Information, November 2018, Catalyst Pharmaceuticals.

73. Amifampridine / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no data on the developmental risk associated with the use of Firdapse (amifampridine) in pregnant women. In animal studies, administration of amifampridine phosphate to rats during pregnancy and lactation resulted in developmental toxicity (increase in stillbirths and pup deaths, reduced pup weight, and delayed sexual development) at doses associated with maternal plasma drug levels lower than therapeutic drug levels.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Amifampridine	Pregnancy	Abortion
		Delivery
		Miscarriage

Age Range: 11 – 50 yoa
Gender: Female

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Firdapse Prescribing Information, November 2018, Catalyst Pharmaceuticals.

74. Amifampridine / Lactation _____ _____

Alert Message: There are no data on the presence of Firdapse (amifampridine) in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for amifampridine and any potential adverse effects on the breastfed infant from amifampridine or the underlying maternal condition. In lactating rats, amifampridine was excreted in milk and reached levels similar to those in maternal plasma.

Drugs/Diseases

Util A	Util B	Util C
Amifampridine	Lactation	

Age Range: 11 – 50 yoa
Gender: Female

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Firdapse Prescribing Information, November 2018, Catalyst Pharmaceuticals.

75. Amifampridine / Nonadherence _____ _____

Alert Message: Based on the refill history, your patient may be underutilizing Firdapse (amifampridine). Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs.

Drugs/Diseases

Util A	Util B	Util C
Amifampridine		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Marcum ZA, Sevick MA, Handler SM. Medication Nonadherence: A Diagnosable and Treatable Medical Condition. *JAMA*. 2013;309(20):2105–2106. doi:10.1001/jama.2013.4638.
Kleinsinger F. The Unmet Challenge of Medication Nonadherence. Perm J. 2018;22:18–033. doi:10.7812/TPP/18-033.

76. Lasmiditan / Overuse _____ _____

Alert Message: Reyvow (lasmiditan) may be over-utilized. The maximum dose of lasmiditan is 200 mg. The recommended dose of lasmiditan is 50 mg, 100 mg, or 200 mg taken orally, as needed. No more than one dose should be taken in a 24 hour period. A second dose of lasmiditan has not been shown to be effective for the same migraine attack. The safety of treating more than 4 migraine attacks in a 30-day period has not been established.

Drugs/Diseases

Util A	Util B	Util C
Lasmiditan		

Max Dose: 200 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Reyvow Prescribing Information, Oct. 2019, Eli Lilly and Company.

77. Lasmiditan / Therapeutic Appropriateness _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Lasmiditan		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Reyvow Prescribing Information, Oct. 2019, Eli Lilly and Company.

78. Lasmiditan / Therapeutic Appropriateness _____ _____

Alert Message: Reyvow (lasmiditan) has not been studied in patients with severe hepatic impairment (Child-Pugh C), and its use in these patients is not recommended.

Drugs/Diseases

Util A	Util B	Util C
Lasmiditan	Cirrhosis	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Reyvow Prescribing Information, Oct. 2019, Eli Lilly and Company.

79. Lasmiditan / CNS Depressants _____ _____

Alert Message: Reyvow (lasmiditan) can cause central nervous system (CNS) depression, including dizziness and sedation. Because of the potential for lasmiditan to cause sedation, other cognitive and/or neuropsychiatric adverse reactions, and driving impairment, lasmiditan should be used with caution if used in combination with alcohol or other CNS depressants.

Drugs/Diseases

Util A	Util B	Util C
Lasmiditan	Anticonvulsants	
	Antidepressants	
	Antihistamines	
	Antipsychotics	
	Barbiturates	
	Benzodiazepines	
	Cannabidiol	
	Muscle Relaxants	
	Narcotics	
	Sedative/Hypnotics	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Reyvow Prescribing Information, Oct. 2019, Eli Lilly and Company.

80. Lasmiditan / Serotonergic Agents _____ _____

Alert Message: Caution should be exercised when Reyvow (lasmiditan) is co-administered with drugs that increase serotonin (i.e., SSRIs, SNRIs, TCAs, and MAOIs) due to the increased risk for serotonin syndrome. In clinical trials, the use of lasmiditan (a 5-HT1F receptor agonist) has been associated with reactions consistent with serotonin syndrome. Lasmiditan should be discontinued if serotonin syndrome is suspected.

Drugs/Diseases

Util A	Util B	Util C
Lasmiditan	Buspirone	
	Bupropion	
	Fentanyl	
	Linezolid	
	MAOIs	
	Meperidine	
	SNRIs	
	SSRIs	
	TCA's	
	Trazodone	
	Tramadol	
	Triptans	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Reyvow Prescribing Information, Oct. 2019, Eli Lilly and Company.

81. Lasmiditan / P-gp and BCRP Substrates _____ _____

Alert Message: Concomitant use of Reyvow (lasmiditan) and drugs that are P-gp or BCRP substrates should be avoided. Lasmiditan has been shown to inhibit P-gp and BCRP transport in vitro. Concurrent use of lasmiditan with these substrates would be expected to decrease substrate exposure and efficacy.

Drugs/Diseases

Util A	Util B		Util C
Lasmiditan	Afatinib	Methotrexate	
	Apixaban	Morphine	
	Aliskiren	Nilotinib	
	Alpelisib	Quinidine	
	Ambrisentan	Paliperidone	
	Canagliflozin	Pazopanib	
	Colchicine	Pibrentasvir	
	Dabigatran	Prazosin	
	Digoxin	Ranolazine	
	Dolutegravir	Rivaroxaban	
	Edoxaban	Rosuvastatin	
	Empagliflozin	Saxagliptin	
	Erythromycin	Sirolimus	
	Everolimus	Sitagliptin	
	Fexofenadine	Sulfasalazine	
	Fluvastatin	Talazoparib	
	Gefitinib	Tenofovir	
	Glyburide	Topotecan	
	Imatinib	Verapamil	
	Indinavir		
	Lapatinib		
	Loperamide		
	Maraviroc		

References:

Reyvow Prescribing Information, Oct. 2019, Eli Lilly and Company.
Lee CA, O'Connor MA, Ritchie TK, et al., Breast Cancer Resistance Protein (ABCG2) in Clinical Pharmacokinetics and Drug Interactions: Practical Recommendations for Clinical Victim and Perpetrator Drug-Drug Interaction Study Design. Drug Metab Dispos. 2015 Apr;43(4):490-509. doi:10.1124/dmd.114.062174.

82. Lasmiditan / Heart Rate Lowering Drugs _____ _____

Alert Message: Caution should be exercised when Reyvow (lasmiditan) is co-administered with drugs that lower heart rate, due to the risk of decreased heart rate. In clinical trials, lasmiditan use was associated with a mean decrease in heart rate of 5 to 10 beats per minute (bpm).

Drugs/Diseases

Util A	Util B		Util C
Lasmiditan	Amiodarone	Flecainide	
	Beta Blockers	Galantamine	
	Brigatinib	Ivabradine	
	Carbamazepine	Lacosamide	
	CCBs	Lanreotide	
	Ceritinib	Lithium	
	Clonidine	Mexiletine	
	Crizotinib	Pasireotide	
	Digoxin	Procainamide	
	Disopyramide	Propafenone	
	Donepezil	Quinidine	
	Dronedarone	Rivastigmine	
	Fingolimod	Siponimod	
		Thalidomide	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Reyvow Prescribing Information, Oct. 2019, Eli Lilly and Company.

83. CDK 4/6 Inhibitors / ILD Symptoms and Interstitial Pneumonitis _____ _____

Alert Message: Severe, life-threatening, or fatal interstitial lung disease (ILD) and/or pneumonitis can occur in patients treated with CDK 4/6 inhibitors (abemaciclib, palbociclib, and ribociclib). Monitor patients for pulmonary symptoms indicative of ILD/pneumonitis. Symptoms may include hypoxia, cough, dyspnea, or interstitial infiltrates on radiologic exams. Dose interruption or dose reduction is recommended for patients who develop persistent or recurrent Grade 2 ILD/pneumonitis. Permanently discontinue the CDK 4/6 inhibitor in all patients with Grade 3 or 4 ILD or pneumonitis.

Drugs/Diseases

Util A	Util B	Util C
Abemaciclib	Acute Interstitial Pneumonitis	
Palbociclib	Cough	
Ribociclib	Dyspnea	
	Fever	
	Hypoxemia	

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
US Food & Drug Administration. FDA Drug Safety Communications. FDA Warns About Rare But Severe Lung Inflammation with Ibrance, Kisqali, and Verzenio for Breast Cancer. Safety Announcement. [09-13-2019]. Available at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-about-rare-severe-lung-inflammation-ibrance-kisqali-and-verzenio-breast-cancer.