North Dakota Medicaid
Drug Utilization Review Board
Meeting
March 3, 2021
Via Teleconference

North Dakota Medicaid
DUR Board Meeting Agenda

Click here to join the meeting

(Click on link)
Join by phone: 1 701-328-0950, Conference ID 786 389 645#
March 3, 2021
1:00 pm

1. Administrative items
    - DHS announcements

2. Old business
    - Review and approval of January 2021 meeting minutes
    - Budget update
    - Review top 25 drugs for Fourth quarter of 2020
    - Prior authorization/PDL update
    - Second review of Evrysdi (risdiplam)
    - Update to criteria for hereditary angioedema
    - Update to criteria irritable bowel syndrome

3. New business
    - Review of Enspryng (satralizumab-mwge)
    - Review of agents for the management of Sickle Cell disease
    - Review of agents for the treatment of Fabry disease
    - Review of Imcivree (setmelonotide)
    - Review of utilization data for select medication classes
    - Retrospective DUR criteria recommendations
    - Upcoming meeting date/agenda.
        - Next meeting is June 2, 2021
4. Adjourn

Please remember to silence all cellular phones during the meeting.

North Dakota Medicaid Drug Use Review (DUR) Board
Meeting Minutes
January 6, 2021

Members Present: Amy Werremeyer, Andrea Honeyman, Gabriela Balf, Joshua Askvig, Laura Schield, Mary Aaland, Michael Booth, Michael Quast, Tanya Schmidt

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

Announcements

Chair A. Honeyman called the meeting to order at 1:04 p.m. The Board was notified of the open Vice-Chair position on the Board and opened the floor for nominations. A. Honeyman nominated T. Schmidt and M. Booth seconded the nomination. T. Schmidt consented to accept the nomination. No other nominations were made. The chair called for a voice vote on the position and T. Schmidt was elected unanimously by all present Board members.

Old Business

Chair A. Honeyman asked for a motion to approve the minutes of the September 2020 meeting. T. Schmidt moved that the minutes be approved, and JA 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

B. Joyce presented budget updates and 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 3rd quarter of 2020.

PDL/PA Criteria Updates

A. Murphy shared with the Board all of changes made to the Preferred Drug List since the last version of the Preferred Drug List was posted. Notable changes included Byetta, Cosentyx, amd Repatha being added to the list of medications requiring prior authorization; removing prior authorization requirements for Toujeo Max Solostar 300 unit/mL and Tresiba 200 unit/mL when used at a dose between 100 and 200 units per day; and the removal of prior authorization requirements for coverage of Xeljanz. All PDL updates are listed in the handouts for the September 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.

Second Review of Agents for the Treatment of Diabetic Gastroparesis

A motion and second was made at the September 2020 DUR Board meeting to place agents for the treatment of diabetic gastroparesis 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.

Second Review of Ohriahnn (elagolix/estradiol/norethindrone)
A motion and second was made at the September 2020 DUR Board meeting to place Ohriahnn on prior authorization. The topic was brought up for a second review. Prior authorization criteria were presented to the Board by T. DeRuiter. J. Gianninoto from Abbvie presented information on Ohriahnn and Orilissa to the Board. Chair A. Honeyman called for a voice vote to approve the updated criteria, which passed with no audible dissent.

Second Review of Dojolvi (triheptanoin)
A motion and second was made at the September 2020 DUR Board meeting to place Dojolvi on prior authorization. The topic was brought up for a second review. Prior authorization criteria were presented to the Board by T. DeRuiter. T. Arnhart provided testimony on Dojolvi and made himself available to the Board for questions during public comments. Chair A. Honeyman called for a voice vote to approve the updated criteria, which passed with no audible dissent.

Update to Criteria for Nucala (mepolizumab) for Hypereosinophilic Syndrome & EGPA
T. DeRuiter presented proposed updates to the prior authorization criteria for Nucala to include criteria for diagnoses of hypereosinophilic syndrome and eosinophilic granulomatosis with polyangiitis (EGPA). There was no public comment. Chair A. Honeyman called for a voice vote to approve the updated criteria, which passed with no audible dissent.

Annual Review of Prior Authorization Forms and Criteria
The Board reviewed all forms and criteria utilized for all medications that are currently placed on prior authorization. Notable updates to the criteria were highlighted by A. Murphy, including the listing of non-solid dosage formulation criteria; changes to prior authorization requirements for select insulin products; updates to criteria for agents used for the treatment of hepatitis C; changes to prior authorization criteria for Eucrisa; changes in preferred and non-preferred agents for the treatment of eosinophilic asthma; and updates to prior authorization criteria for agents used in the treatment of Parkinson's. A motion was made by M. Quast to approve the reviewed forms and criteria, which was seconded by A. Werremeyer. Chair A. Honeyman then called for a voice vote for approval of the reviewed forms and criteria, which passed with no audible dissent.

New Business
Review of Evrysdi (risdiplam)
T. DeRuiter presented a review of Evrysdi (risdiplam) for the treatment of spinal muscular atrophy (SMA) to the Board. There was no public comment. A motion was made by A. Werremeyer to manage these medications through prior authorization. The motion was seconded by J. Askvig. Prior authorization criteria for these agents 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. M. Booth moved to approve the new criteria and T. Schmidt seconded the motion. The motion passed with no audible dissent.

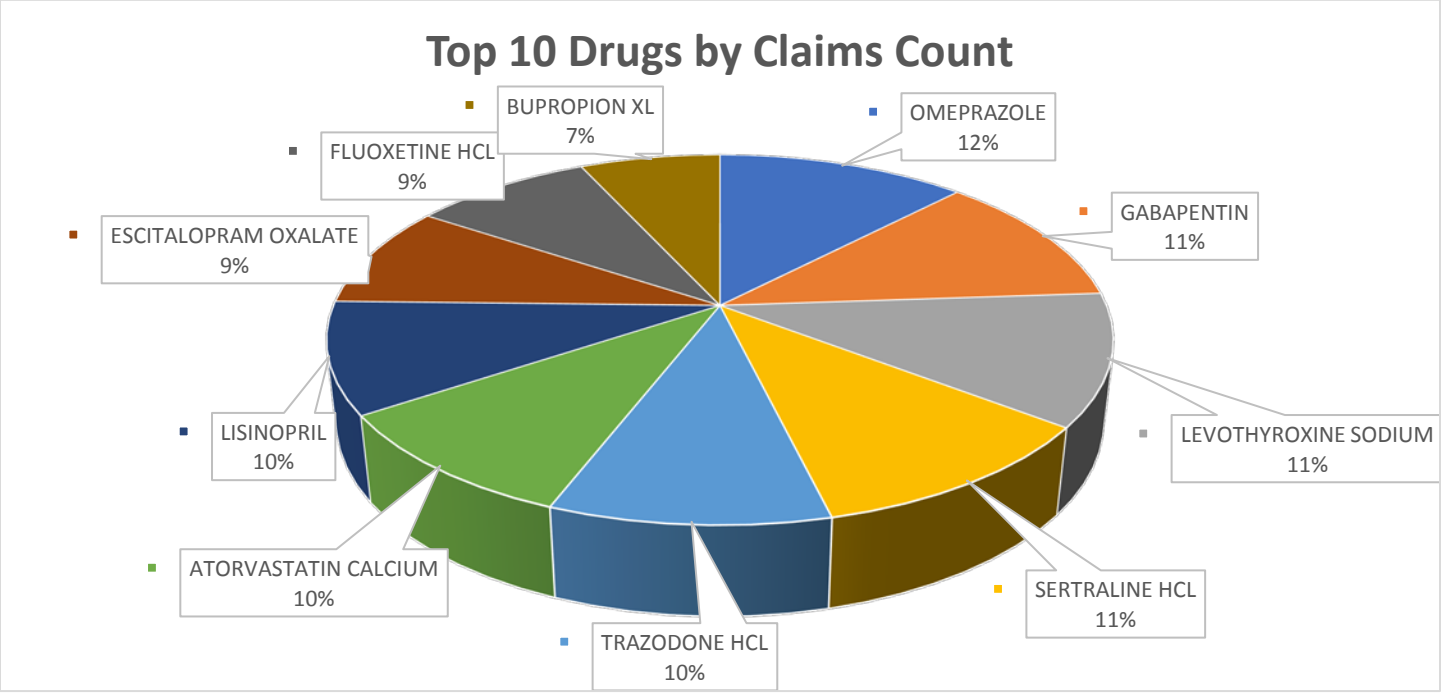
Adjournment and Upcoming Meeting Date

Chair A. Honeyman adjourned the meeting at 2:45 pm. The next DUR Board meeting will be held March 3, 2021 at 1:00 pm and will be held via teleconference.

Top 25 Drugs Based on Number of Claims from 10/01/2020 – 12/31/2020

Drug	Claims	Patients	Claims Cost	Cost Per Claim	% Total Claims
OMEPRAZOLE	5,060	2,278	$65,756.11	$13.00	2.14%
GABAPENTIN	4,819	1,843	$74,891.75	$15.54	2.04%
LEVOTHYROXINE SODIUM	4,748	1,751	$87,318.07	$18.39	2.01%
SERTRALINE HCL	4,461	2,254	$60,719.44	$13.61	1.89%
TRAZODONE HCL	4,024	1,826	$55,904.94	$13.89	1.70%
ATORVASTATIN CALCIUM	4,021	1,906	$57,584.64	$14.32	1.70%
LISINOPRIL	4,017	1,939	$50,783.31	$12.64	1.70%
ESCITALOPRAM OXALATE	3,691	1,870	$49,844.04	$13.50	1.56%
FLUOXETINE HCL	3,641	1,755	$49,777.05	$13.67	1.54%
BUPROPION XL	2,847	1,254	$49,393.07	$17.35	1.21%
HYDROCODONE-ACETAMINOPHEN	2,831	1,735	$44,792.64	$15.82	1.20%
METFORMIN HCL	2,812	1,337	$35,577.72	$12.65	1.19%
DULOXETINE HCL	2,798	1,167	$45,934.24	$16.42	1.19%
MONTELUKAST SODIUM	2,710	1,299	$39,017.15	$14.40	1.15%
PANTOPRAZOLE SODIUM	2,653	1,198	$37,099.67	$13.98	1.12%
VYVANSE	2,519	958	$618,206.03	$245.42	1.07%
LAMOTRIGINE	2,387	855	$33,226.32	$13.92	1.01%
PROAIR HFA	2,383	2,342	$169,883.83	$71.29	1.01%
BUPRENORPHINE-NALOXONE	2,383	487	$103,780.15	$43.55	1.01%
AMLODIPINE BESYLATE	2,341	1,175	$29,981.04	$12.81	0.99%
CLONIDINE HCL	2,316	1,002	$29,494.65	$12.74	0.98%
CYCLOBENZAPRINE HCL	2,310	1,311	$26,259.71	$11.37	0.98%
VENLAFAXINE HCL ER	2,275	892	$38,326.93	$16.85	0.96%
QUETIAPINE FUMARATE	2,241	837	$31,835.29	$14.21	0.95%
ARIPIPRAZOLE	2,237	968	$34,723.78	$15.52	0.95%

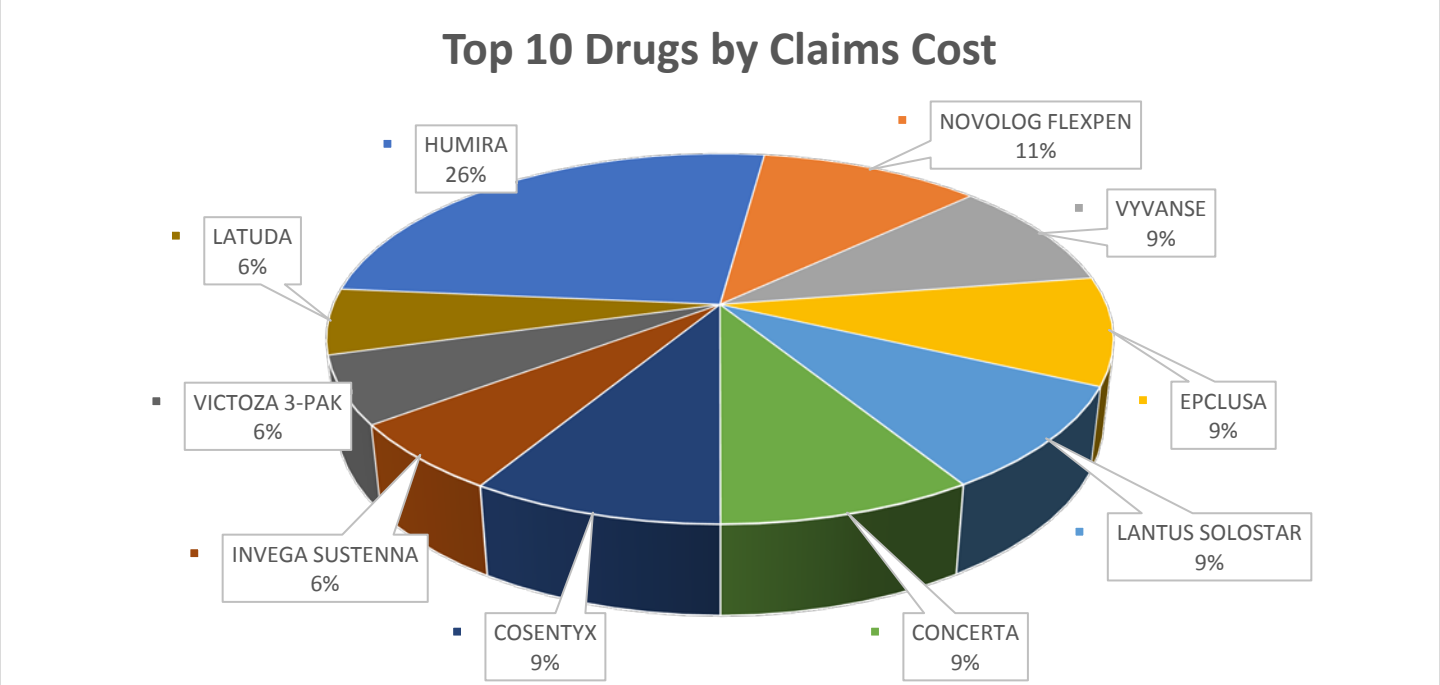
Total Claims From 10/01/2020 – 12/31/2020	**236,077**



Top 25 Drugs Based on Total Claims Cost from 10/01/2020 – 12/31/2020

Drug	Claims Cost	Claims	Patients	Cost Per Claim	% Total Cost
HUMIRA	$1,670,402.52	253	104	$6,602.38	6.85%
NOVOLOG FLEXPEN	$703,037.23	997	534	$1,316.55	2.88%
VYVANSE	$618,206.03	2,519	958	$645.31	2.54%
EPCLUSA	$608,645.00	25	12	$50,720.42	2.50%
LANTUS SOLOSTAR	$592,105.33	1,247	698	$848.29	2.43%
CONCERTA	$574,886.37	1,720	668	$860.61	2.36%
COSENTYX	$566,452.09	89	36	$6,364.63	2.32%
INVEGA SUSTENNA	$391,205.43	170	66	$5,927.36	1.61%
VICTOZA 3-PAK	$381,451.37	428	193	$1,976.43	1.57%
LATUDA	$371,350.46	475	195	$1,904.36	1.52%
JARDIANCE	$359,984.36	786	319	$1,128.48	1.48%
NORDITROPIN FLEXPRO	$357,004.40	90	37	$9,648.77	1.46%
ADVAIR DISKUS	$320,421.95	888	451	$710.47	1.31%
SYMBICORT	$312,687.04	940	506	$617.96	1.28%
STELARA	$301,334.64	14	11	$27,394.06	1.24%
LEVEMIR FLEXTOUCH	$292,777.35	544	287	$1,020.13	1.20%
TRIKAFTA	$286,903.08	12	4	$71,725.77	1.18%
ADDERALL XR	$250,368.93	1,450	604	$414.52	1.03%
SABRIL	$249,867.37	16	5	$49,973.47	1.03%
ENBREL SURECLICK	$233,521.39	43	19	$12,290.60	0.96%
ABILIFY MAINTENA	$223,611.47	108	39	$5,733.63	0.92%
STRATTERA	$223,116.56	554	264	$845.14	0.92%
ELIQUIS	$222,369.07	526	223	$997.17	0.91%
XIFAXAN	$220,291.73	98	47	$4,687.06	0.90%
BIKTARVY	$214,896.63	124	51	$4,213.66	0.88%

Total Claims Cost From 10/01/2020 – 12/31/2020	**$24,371,408.66**



Top 15 Therapeutic Classes Based on Number of Claims from 10/01/2020 – 12/31/2020

Therapeutic Class Description	Claims	Patients	Claims Cost	Cost/Claim	% Total Claims
ANTIDEPRESSANTS	30,384	10,903	$617,035.20	$20.31	12.87%
ANTICONVULSANTS, MISC	13,957	4,475	$974,027.28	$69.79	5.91%
ANTIPSYCHOTIC AGENTS	9,524	3,174	$1,709,155.53	$179.46	4.03%
PROTON-PUMP INHIBITORS	8,194	3,624	$149,092.29	$18.20	3.47%
OPIATE AGONISTS	7,384	3,552	$150,188.78	$20.34	3.13%
NSAIDS	6,883	3,937	$101,390.29	$14.73	2.92%
STATINS	6,643	3,116	$95,428.51	$14.37	2.81%
SEDATIVE/HYPNOTICS	6,556	3,033	$102,835.04	$15.69	2.78%
BETA BLOCKERS	5,922	2,696	$110,041.66	$18.58	2.51%
AMPHETAMINES	5,140	2,005	$912,402.16	$177.51	2.18%
ACE INHIBITORS	5,074	2,462	$70,886.74	$13.97	2.15%
THYROID AGENTS	5,057	1,824	$98,087.13	$19.40	2.14%
NON-AMPHETAMINE STIMULANTS	4,547	1,585	$839,620.59	$184.65	1.93%
BIGUANIDES	4,164	1,992	$55,144.61	$13.24	1.76%
INSULINS	3,723	1,281	$2,065,082.67	$554.68	1.58%

Top 15 Therapeutic Classes Based on Claims Cost from 10/01/2020 – 12/31/2020

Therapeutic Class Description	Claims Cost	Claims	Patients	Cost/Claim	% Total Cost
DMARDS	$2,314,008.68	452	175	$13,222.91	9.49%
INSULINS	$2,065,082.67	3,723	1,281	$1,612.09	8.47%
ANTIPSYCHOTIC AGENTS	$1,709,155.53	9,524	3,174	$538.49	7.01%
SKIN & MUCOUS MEMBRANE AGENTS, MISC	$1,147,460.24	517	307	$3,737.66	4.71%
INHALED CORTICOSTEROIDS	$979,665.50	3,438	1,892	$517.79	4.02%
ANTICONVULSANTS, MISC	$974,027.28	13,957	4,475	$217.66	4.00%
AMPHETAMINES	$912,402.16	5,140	2,005	$455.06	3.74%
NON-AMPHETAMINE STIMULANTS	$839,620.59	4,547	1,585	$529.73	3.45%
HCV ANTIVIRALS	$810,441.60	44	26	$31,170.83	3.33%
ANTINEOPLASTIC AGENTS	$809,794.57	531	207	$3,912.05	3.32%
ANTIRETROVIRALS	$764,897.45	599	204	$3,749.50	3.14%
INCRETIN MIMETICS	$737,535.81	1,030	446	$1,653.67	3.03%
ANTIDEPRESSANTS	$617,035.20	30,384	10,903	$56.59	2.53%
IMMUNOMODULATORY AGENTS MISC	$531,715.84	74	25	$21,268.63	2.18%
SGLT2 INHIBITORS	$462,845.35	1,015	416	$1,112.61	1.90%

PDL Update

ADDED TO PA	
Drug	**Class**
cycloserine	Antibiotic Resistance
Sirturo (bedaquline)	Antibiotic Resistance
Solosec (secnidazole)	Vaginal Anti-Infectives
ZOKINVY	3000
Impeklo	topical steroids
Qdolo	short acting opioids
Sutab	Bowel Prep agents
Eysuvis	ophthalmic anti-inflammatories
Oxlumo	3000
Sevenfact	Hemophilia
Orladeyo	HAE
Kesimpta	Multiple Sclerosis
Imcivree	3000
Alkindi Sprinkle	Oral Steroids
Semglee	Insulin
Armonair Digihaler	inhaled steroid
Xywav	narcolepsy
Bafiertam	Multiple Sclerosis
Breztri Aerosphere	COPD
Mycapssa	3000
AirDuo Digihaler	Steroid/LABA
Ortikos	Oral Steroids

REMOVED FROM PA	
Drug	**Class**
Sunosi	Narcolepsy

Evrysdi

General Prior Authorization Form

- **Initial Criteria:** *Approval Duration = 12 months*
  - The patient must have a diagnosis of spinal muscular atrophy (SMA), confirmed by genetic testing showing bi-allelic deletions or mutations in the SMN1 gene
  - The medication must be prescribed by or in consultation with a neurologist
  - The patient must be 2 years of age or older
  - The patient must not require invasive ventilation or tracheostomy
  - The patient must not be receiving/have received treatment a SMN2-targeting antisense oligonucleotide, SMN2 splicing modifier or gene therapy
  - The patient's weight and prescribed dose must be provided and within dosing recommendations per the manufacturer label
  - **For SMA Type 1**
    - The patient must have experienced signs or symptoms of SMA prior to the age of 3 months
    - The patient must have at least two survival motor neuron 2 (SMN2) gene copies, as confirmed by genetic testing
  - **For SMA Type 2 or 3:**
    - The provider must submit documentation of the patient's current motor function, as evidenced by scores from at least one of the following assessments (A and/or B):
      A. Motor Function Measure 32 (MFM32)
      B. Revised Upper Limb Module (RULM)

- **Renewal Criteria:** *Approval Duration = 12 months*
  - The patient must not require invasive ventilation or tracheostomy
  - The patient's weight and prescribed dose must be provided and within dosing recommendations per the manufacturer label
  - **For SMA Type 1**
    - The patient must have experienced and/or maintained clinical benefit since starting treatment with Evrysdi, as evidenced by medical documentation (e.g. chart notes) attached to the request (subject to clinical review)
  - **For SMA Type 2 or 3:**
    - The provider must submit documentation showing that the patient has experienced clinical benefit since starting treatment with Evrysdi, as evidenced by documentation of current MFM23 and/or RULM scores showing improvement or maintenance of baseline motor function.

PA REQUIRED
EVRYSDI (Risdiplam)

health information designs

Evrysdi
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 Medicaid

ND Medicaid requires that patients receiving a prescription for Evrysdi must meet the criteria listed in the preferred drug list (PDL). Please see the PDL at http://hidesigns.com/assets/files/ndmedicaid/NDPDL.pdf:

- Please complete this form in its entirety and provide any and all required documentation (if available)

Part I: TO BE COMPLETED BY PRESCRIBER/PRESCRIBER'S OFFICE

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:	**Diagnosis for this request:** □ SMA Type 1 □ SMA Type 2 □ SMA Type 3
Patient Weight	**Requested Dose**

Does the patient require invasive ventilation or tracheostomy?	□ YES □ NO
Has the patient previously received treatment a SMN2-targeting antisense oligonucleotide, SMN2 splicing modifier or gene therapy?	□ YES □ NO
SMA Type 1 ONLY: • Did the patient signs or symptoms of SMA prior to 3 months of age? • Does the patient have at least 2 (SMN2) gene copies, as confirmed by testing?	□ YES □ NO □ YES □ NO
SMA Type 2 or 3 ONLY: • Has the provider attached documentation of the patient's current motor function, as evaluated by MFM32 and/or RULM scores?	□ YES □ NO

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 #

Hereditary Angioedema

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 medication must be prescribed by or in consultation with an allergist, immunologist, or rheumatologist

Non-Preferred Agents Criteria:

- The request must meet the group criteria
- The patient must have a contraindication to or failed a trial of all preferred agents with the same indication for use (prophylaxis or acute treatment), as evidenced by paid claims or pharmacy print-outs
    - Required trial durations
        - Agents for acute attacks: a single trial
        - Agents for attack prophylaxis: 3 months

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
BERINERT (C1 Esterase Inhibitor)	FIRAZYR (icatibant)
CINRYZE (C1 Esterase Inhibitor)	KALBITOR (ecallantide)
HAEGARDA (C1 Esterase Inhibitor)	RUCONEST (C1 Esterase Inhibitor)
icatibant	
ORLADEYO (berotrlastat)	
TAKHZYRO (lanadelumab-FLYO)	

Irritable Bowel Syndrome - Diarrhea

General Prior Authorization Form

Group Criteria:

- **Non-Preferred Agents Criteria:**
    - Initial Criteria: Approval Duration = 3 months
        - The patient must have an FDA-approved indication for use (meets label recommendations for diagnosis, age, and duration of treatment).
        - The provider must submit medication 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 unique active ingredient, as evidenced by paid claims or pharmacy printouts.
    - Product Specific Criteria:
        - ***__alosetron__: The patient must be a female.
        - *** **dicyclomine** Oral Syrup: The patient must be unable to ingest solid dosage form as evidenced by swallow study documentation
    - Renewal Criteria: Approval Duration = 12 months
        - The patient must have experienced and maintained clinical benefit since starting treatment with requested product, as evidenced by medical documentation (e.g. chart notes) attached to the request (subject to clinical review)

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
dicyclomine Capsule	alosetron***
dicyclomine Tablet	dicyclomine oral syrup***
diphenoxylate/atropine	LOMOTIL (diphenoxylate/atropine)
loperamide	VIBERZI (eluxadoline)
LOTRONEX (alosetron)*** - Brand Preferred	XIFAXAN (rifaximin) 550 mg tablet

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 the following location:

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

Part I: TO BE COMPLETED BY PRESCRIBER/PRESCRIBER'S OFFICE

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 ENSPRYNG (satralizumab-mwge))

Indication: Treatment of neuromyelitis optica spectrum disorder in adults who are anti-aquaporin-4 (AQP4) antibody positive.

- **Neuromyelitis Optica Spectrum Disorders (NMOSD):**
  - inflammatory disorders of the central nervous system characterized by severe, immune-mediated demyelination and axonal damage predominantly targeting optic nerves and spinal cord.
  - Stepwise deterioration due recurrent attacks and accumulated disability
    - Acute attacks of bilateral or rapidly sequential optic neuritis (leading to severe visual loss) or transverse myelitis (often causing limb weakness, sensory loss, and bladder dysfunction)
      - Typically, relapsing course with attacks most often occuring over days, with variable degrees of recovery over weeks to months
  - Treatment:
    - Acute treatment for attacks: IV steroids and/or plasma exchange
    - Attack prevention: long-term immunotherapy.
      - Soliris (eculizumab) - IV
      - Uplizna (Inebilizumab) - IV
      - Enspryng (Satralizumab)

Mechanism of action: Antagonist of the interleukin-6 (IL-6) receptor, presumed to be via binding to soluble and membrane-bound IL-6 receptors

Clinical Trial Experience

- **Study 1**
  - **Patient demographics:**
    - EDSS Score of 0-6.5
    - Clinical evidence of relapse in the previous 12 months
    - Anti-AQP4 antibody positive and anti-AQP4 antibody negative patients
    - No recent other immunosuppressive therapy
  - **Results:**
    - The time to the first confirmed relapse was significantly increased in the treatment group vs placebo
      - 74% relapse risk reduction in anti-AQP4 antibody positive patients, no benefit in anti-AQP4 antibody negative patients
    - Sit without support for 5 seconds at 12 months
      - 41% able to sit independently (vs 0% expected)
    - Survival without permanent ventilation
      - 90% at 12 months (>15 months old)
      - 81% at 23 months (>28 months old)
      - In the normal population, 25% survive w/o ventilation beyond 14 months
- **Study 2**
  - **Patient demographics:**
    - EDSS Score of 0-6.5
    - Clinical evidence of at least 2 relapses in the previous 24 months, at least 1 of which occurred in past 12 months
    - Anti-AQP4 antibody positive and anti-AQP4 antibody negative patients
    - All patients receiving either oral steroids, mycophenolate, or azathioprine concurrently
  - **Results (at 12 months):**
    - The time to the first confirmed relapse was significantly increased in the treatment group vs placebo
      - 78% relapse risk reduction in anti-AQP4 antibody positive patients, no benefit in anti-AQP4 antibody negative patients

Contraindications:

- Hypersensitivity to satralizumab or any component of the formulation
- Active hepatitis B infection
- Active or untreated latent tuberculosis

Administration and Dosing:

- Adults:
  - **Loading Dose:** 120 mg subcutaneously once every 2 weeks for 3 doses (weeks 0, 2, and 4)
    - **If dose missed:** 120 mg subcutaneously as soon as possible (do not wait until next dose)
  - **Maintenance Dose:** 120 mg subcutaneously every 4 weeks
    - **If dose missed:**
      - <8 weeks since last dose: 120 mg subcutaneously as soon as possible, Reset dose schedule to every 4 weeks after missed dose administered
      - 8 to <12 weeks since last dose: 120 mg subcutaneously every 2 weeks for 2 doses (weeks 0 and 2), followed by 120 mg every 4 weeks.
      - ≥12 weeks since last dose: Re-do loading dose
  - **Dosage adjustment for toxicity causing neutropenia:** Interrupt therapy until neutrophil count >1,000/mm3
  - **Renal Impairment:**Has not been studied in patients with renal impairment
  - **Hepatic Impairment:**
    - ALT/AST >5 × ULN and any bilirubin elevation
      - Discontinue therapy. Reinitiation not recommended
    - ALT/AST >5 × ULN and not associated with bilirubin elevation
      - Interrupt therapy until ALT/AST return to normal range, then restart treatment

Warnings/Precautions:

- **Infection:** An increased risk of infection (sometimes serious or potentially fatal) has been observed with interleukin-6 (IL-6) receptor antagonist treatments. Enspryng is associated with an increased risk for cellulitis, nasopharyngitis, upper respiratory tract infections, and pharyngitis.
- **Hepatitis B reactivation:** Hepatitis B reactivation has occurred with immunosuppressant therapies
- **Tuberculosis:** Has occurred in patients treated with other IL-6 receptor antagonists. Evaluate for active/latent TB prior to initiating therapy. Do not administer to patients with an active TB infection or positive screening without history of appropriate treatment.
- **Immunizations:** Immunization with live-attenuated or live vaccines is not recommended during therapy.
- **Elevated liver enzymes:** Mild to moderate elevations in liver enzymes have occurred; monitor ALT/AST
- **Hematologic effects:** Decreased neutrophil counts and neutropenia may occur; monitor neutrophil counts

Adverse Effects

- **Common (>10%)**
  - **Dermatologic:** Skin rash
  - **Endocrine & metabolic:** Decreased serum fibrinogen, increased serum cholesterol, increased serum triglycerides, weight gain
  - **Gastrointestinal:** Nausea
  - **Hematologic & oncologic:** Decreased platelet count, disorder of hemostatic components of blood (reduction in C3 and C4 complement levels)
  - **Hepatic:** Increased serum alanine aminotransferase, increased serum aspartate aminotransferase
  - **Immunologic:** Antibody development
  - **Nervous system:** Fatigue
  - **Neuromuscular & skeletal:** Arthralgia, limb pain
  - **Respiratory:** Nasopharyngitis
- **Less Common (1-10%)**
  - **Dermatologic:** Cellulitis, pruritus
  - **Gastrointestinal:** Diarrhea
  - **Hematologic & oncologic:** Neutropenia
  - **Local:** Injection site reaction (including residual mass at injection site)
  - **Nervous system:** Depression, falling

Drug interactions

- No formal drug-drug interaction studies have been performed with Enspryng

Cost

Drug	Strength	Package Size	WAC Pkg Price	WAC Price Per Dose	Cost Per Loading Dose	Cost Per Year on Maintenance Dose
Enspryng	120 mg/1 mL	1 mL	$14,615.39	$14,615.39	$43,846.17	$190,000.07

CURRENT UTILIZATION

ND Medicaid Utilization (12/2019 – 12/2020)		
Label Name	**Rx Num**	**Total Reimb Amt**
Enspryng	0	-

REFERENCES:

1. Facts & Comparisons eAnswers. Available at http://online.factsandcomparisons.com. Accessed on February 11. 2021.
2. UpToDate. Available at https://www.uptodate.com/contents/search. Accessed on February 11. 2021.
3. Enspryng (satralizumab) [prescribing information]. South San Francisco, CA: Genentech Inc; August 2020.

REVIEW OF AGENTS FOR THE TREATMENT OF SICKLE CELL DISEASE

Sickle Cell Disease

- Sickle cell disease is a group of disorders affecting hemoglobin, which distorts red blood cells (RBCs) into a sickle, or crescent, shape
- **Clinical Presentation**
    - Vaso-occlusive phenomena and hemolysis are the clinical hallmarks of sickle cell disease (SCD)
        - Vaso-occlusion results in recurrent painful episodes and a variety of serious organ system complications that can lead to life-long disabilities and even death
            - Stroke
            - Renal infarction
            - Bone infarction
            - Myocardial infarction
            - Priapism
            - Venous thromboembolism
        - Hemolysis of RBCs causes chronic anemia and pigment gallstones
- Treatment/Management
    - There are multiple components to the management of SCD, including the prevention and treatment of the complications of SCD, as well as the potential cure for this illness:
        - Prevention and treatment of complications:
            - Infection prevention
            - Reduce vaso-occlusive events
                - Disease-modifying agents
                    - Hydroxyurea (Siklos, Droxia) – administered PO
                    - Voxelotor (Oxbryta) – administered PO
                    - Crizanlizumab (Adakveo) – administered IV
                - Blood transfusions
        - Cure: only through hematopoietic stem cell transplantation.

Hydroxyurea (Droxia and Siklos) and voxelotor Oxbryta

Indications

Hydroxyurea (Droxia and Siklos)	**Oxbryta**
Management of sickle cell anemia (to reduce the frequency of painful crises and to reduce the need for blood transfusions in patients with recurrent moderate to severe painful crises).	Treatment of sickle cell disease in adults and pediatric patients ≥12 years of age

Boxed Warning

Hydroxyurea (Droxia and Siklos)	**Oxbryta**
Bone marrow suppression Hydroxyurea may cause severe myelosuppression. Monitor blood counts at baseline and throughout treatment. Interrupt treatment and reduce dose as necessary **Secondary malignancy** Hydroxyurea is carcinogenic. Advise sun protection and monitor patients for malignancies	None

Mechanism of Action

Hydroxyurea (Droxia and Siklos)	Oxbryta
Antimetabolite that inhibits ribonucleoside diphosphate reductase. In sickle cell anemia, hydroxyurea increases (RBC) hemoglobin F levels, RBC water content, deformability of sickled cells, and alters adhesion of RBCs to endothelium.	HbS polymerization inhibitor that reversibly binds to Hb and stabilizes the oxygenated Hb state • Through the increased Hb affinity for oxygen, causes dose-dependent inhibition of HbS polymerization, and may inhibit RBC sickling, improve RBC deformability, and reduce whole blood viscosity o May also extend RBC half-life and reduce anemia and hemolysis

Dosing

	Hydroxyurea (Droxia and Siklos)	Oxbryta
Adult Dosing	**Initial**: 15 mg/kg (Droxia), 20 mg/kg/day (Siklos) **Maximum**: 35 mg/kg/day Dose should be adjusted for toxicity based on blood cell counts	1.5 g once daily May be administered with or without hydroxyurea
Pediatric Dosing	**≥2 years of age (Siklos only):** same as adult	**≥12 years of age:** same as adults
Renal/Hepatic Impairment	**Renal Impairment**: CrCl <60 mL/minute, reduce dose to 50% of initial **Hepatic Impairment:** No adjustments	**Renal Impairment**: no dose adjustments **Hepatic Impairment:** Reduce dose to 1 gram in severe impairment

Contraindications

Hydroxyurea (Droxia and Siklos)	Oxbryta
Hypersensitivity to hydroxyurea or any other component of its formulation.	Serious hypersensitivity (eg, generalized rash, urticaria, mild shortness of breath, mild facial swelling, eosinophilia) to any component of the formulation.

Warnings/Precautions

Hydroxyurea (Droxia and Siklos)	Oxbryta
Bone marrow suppression Correct severe anemia prior to initiating treatment. Do not initiate therapy if bone marrow function is markedly reduced. **Secondary malignancy** Hydroxyurea is carcinogenic **Cutaneous vasculitic toxicity** Vasculitic ulcerations and gangrene have been reported **Pulmonary toxicity** Interstitial lung disease, including pulmonary fibrosis, lung infiltration, pneumonitis, and alveolitis/allergic alveolitis (some cases fatal). D/C if pulmonary toxicity occurs and manage appropriately. **Macrocytosis** Self-limiting macrocytosis may be seen early in treatment. Prophylactic folic acid supplementation is recommended **Radiation therapy recipients** Patients with a history of radiation therapy are at risk for exacerbation of post irradiation erythema and myelosuppression. **Immunizations** Avoid use of live vaccines during hydroxyurea therapy	**Laboratory test interference** May interfere with high-performance liquid chromatography measurement of Hb subtypes (HbA, HbS, and HbF)

Adverse Effects

Hydroxyurea (Droxia and Siklos)	Oxbryta
Common (>10%): • Dermatologic: Eczema • Hematologic & oncologic: Macrocytosis, neutropenia • Infection: Infection, bacterial infection **Less Common (1-10%)** • CNS: Headache, severe nervous system disease • Dermatologic: Leg ulcer, dermatological reaction, dermal ulcer • Endocrine & metabolic: Vitamin D deficiency, weight gain • GI: Acute mucocutaneous toxicity, constipation, nausea • Hematologic & oncologic: Thrombocytopenia, anemia • Infection: Viral infection • Respiratory: Asthma • Miscellaneous: Fever	**Common (>10%):** • CNS: Headache, fatigue • Dermatologic: Skin rash • GI: Diarrhea, abdominal pain, nausea • Miscellaneous: Fever **Less Common (1-10%)** • Cardiovascular: Pulmonary embolism • Hypersensitivity: Hypersensitivity reaction

Drug Interactions

Hydroxyurea (Droxia and Siklos)	Oxbryta
No metabolic/transport effects, so interactions are with other immunosuppressive drugs, or those that may worsen ADRs of hydroxyurea	Substrate of CYP2B6 (minor), CYP2C19 (minor), CYP2C9 (minor), CYP3A4 (minor), and is a weak inhibitor of CYP3A4 • Consider therapy modification in CYP3A4 inducers or CYP substrates with a narrow therapeutic index

Cost

Drug	Strength	Package Size	WAC Pkg Price	Cost per dose*	Cost per Month*	Cost per Year*
Siklos	100 mg	60	$300.00	$65.00 - $115.00	$1,950.00 - $3,450.00	$23,725.00 - $41,975.00
Siklos	1,000 mg	30	$1,500.00			
Oxbryta	500 mg	90	$10,417.00	$347.23	$10,417.00	$126,740.17
Droxia	200 mg	60	$45.41	$136.23 - $275.64	$4,086.90 - $8,269.20	$49,723.95 - $100,608.60
Droxia	300 mg	60	$48.59			
Droxia	400 mg	60	$45.41			
*=based on a weight of 65 kg and using the most cost effective combination of strengths to achieve recommended dose						

Current Utilization

ND Medicaid Utilization (12/2019 – 12/2020)		
Label Name	**Rx Num**	**Total Reimb Amt**
Siklos	0	N/A
Oxbryta	0	N/A
Droxia	1	$31.34

REFERENCES:

1. Facts & Comparisons eAnswers. Available at http://online.factsandcomparisons.com. Accessed on February 11. 2021.
2. UpToDate. Available at https://www.uptodate.com/contents/search. Accessed on February 11. 2021.
3. Oxbryta (voxelotor) [prescribing information]. South San Francisco, CA: Global Blood Therapeutics Inc; November 2019.
4. Siklos (hydroxyurea) [prescribing information]. Rosemont, PA: Medunik USA Inc; May 2019.
5. Droxia (hydroxyurea) [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company; December 2020.

REVIEW OF AGENTS FOR THE TREATMENT OF FABRY DISEASE

Spinal muscular atrophy (SMA):

- Genetic, X-linked, disease caused by pathogenic variants in the alpha-galactosidase A (alpha-Gal A) gene, resulting in a deficiency of the lysosomal hydrolase alpha-galactosidase A
    - Causes a buildup of glycolipids within cells such as globotriaosylceramide (Gb3), which is thought to have cytotoxic, proinflammatory, and profibrotic effects
    - 3 majoy phenotypic "types"

Type	Presentation	alpha-Gal A Activity	Symptomology
Classic	Most severe phenotype, most common in males	<1% of normal mean	Severe neuropathic or limb pain Telangiectasias and angiokeratomas GI symptoms Corneal opacities Kidney disease
Heterozygous	Range from asymptomatic to as severe as classic disease	Large range	May have any or all classic symptoms
Atypical	Typically, has later onset and less severe disease	2-30% of normal mean	Usually disease symptoms dominate a particular organ system

- **Symptoms**
    - Spectrum of clinical manifestations, ranging from severe to asymptomatic. {potential symptoms include the following:
        - Severe neuropathic or limb pain
        - Telangiectasias and angiokeratomas
        - Abdominal pain, recurrent nausea and vomiting, and either diarrhea or constipation
        - Corneal opacities
        - Proteinuria, isosthenuria, polyuria, and polydipsia or otherwise unexplained renal insufficiency
        - Cardiac effects
            - Left ventricular hypertrophy (LVH), myocardial fibrosis, heart failure, coronary artery disease, aortic and mitral valve abnormalities, and conduction abnormalities
        - Cerebrovascular effects
            - TIA, ischemic strokes, blindness

- **Treatment of Fabry Disease:**
    - Treatment primarily focuses upon replacing the missing or deficient alpha-Gal A with enzyme replacement therapy (ERT) as well as treating the various symptoms and disease complications
        - ERT with the agent Fabrazyme (agalsidase beta), which is given IV
        - A pharmacologic chaperone (Galafold) can now be used instead of ERT in patients with amenable genetic variants (present in 35 to 50 percent of patients)
    - **Candidates for ERT or Galafold (if appropriate)**
        - All classically affected males, regardless of whether or not clinical manifestations are present
        - Female carriers and atypically affected males, if clinical manifestations (eg, kidney, cardiovascular, neurologic) are present
        - Other patients such as those with ESRD may be candidates for ERT, depending on their symptoms

GALAFOLD (migalastat)

- **Indication**: Treatment of adults with a confirmed diagnosis of Fabry disease and an amenable galactosidase alpha gene (GLA) variant based on in vitro assay data
- **Mechanism of action:** reversibly binds to the active site of the alpha-galactosidase A (alpha-Gal A) protein (encoded by the galactosidase alpha gene, GLA), which is deficient in Fabry disease.
    - Binding to the active site stabilizes alpha-Gal A allowing trafficking from the endoplasmic reticulum into the site of action, the lysosome.
- **Contraindications:** None per label
- **Administration and Dosing:**
    - Adults:
        - 123 mg once every other day (do not administer on 2 consecutive days)
    - Pediatric:
        - Safety and efficacy have not been established
    - Renal/Hepatic Impairment
        - Use not recommended if eGFR <30 mL/minute/1.73 m2
        - Has not been studied in patients with hepatic impairment
- **Warnings/Precautions:**
    - Select patients with confirmed Fabry disease for migalastat treatment if an amenable galactosidase alpha (GLA) variant is present
        - Consultation with a clinical geneticist is strongly recommended in cases where clinical significance of the amenable GLA variant is uncertain or may be benign
- **Adverse Effects**
    - **Common (>10%)**
        - **CNS:** Headache (35%)
        - **Gastrointestinal:** Nausea (12%)
        - **Genitourinary:** Urinary tract infection (15%)
        - **Respiratory:** Nasopharyngitis (18%)
        - **Miscellaneous:** Fever (12%)
    - **Less Common (1-10%)**
        - **Gastrointestinal:** Abdominal pain (9%), diarrhea (9%)
        - **Neuromuscular & skeletal:** Back pain (9%)
        - **Respiratory:** Cough (9%), epistaxis (9%)
- **Drug interactions**
    - There are no known significant interactions

Cost

Drug	Strength	Package Size	WAC Pkg Price	Cost per dose	Cost per Month	Cost per Year
Galafold	123 mg	14	$25,080.00	$1,791.43	$26,871.43	$326,935.70

Current Utilization

ND Medicaid Utilization (12/2019 – 12/2020)		
Label Name	**Rx Num**	**Total Reimb Amt**
Galafold	0	-

REFERENCES:

1. Facts & Comparisons eAnswers. Available at http://online.factsandcomparisons.com. Accessed on February 11. 2021.
2. UpToDate. Available at https://www.uptodate.com/contents/search. Accessed on February 11. 2021.
3. Galafold (migalastat) [prescribing information]. Philadelphia, PA: Amicus Therapeutics US, LLC; February 2021.

REVIEW OF IMCIVREE (setmelanotide)

Indication:

- For chronic weight management in adult and pediatric patients ≥6 years of age with obesity due to proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency confirmed by genetic testing demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance.
    - **Not for treatment of patients with**
        - Obesity due to suspected POMC, PCSK1, or LEPR deficiency with POMC, PCSK1, or LEPR variants classified as benign or likely benign
        - Other types of obesity not related to POMC, PCSK1, or LEPR deficiency, including obesity associated with other genetic syndromes and general (polygenic) obesity.

Mechanism of action:

- Analog of endogenous melanocortin peptide alpha-melanocyte stimulating hormone, and primarily acts as a melanocortin 4 (MC4) receptor agonist
    - MC4 receptors in the brain are involved in regulation of hunger, satiety, and energy expenditure
    - In patients with obesity due to POMC, PCSK1, or LEPR deficiency associated with insufficient activation of the MC4 receptor, Imcivree may reestablish MC4 receptor pathway activity to reduce hunger and promote weight loss through decreased caloric intake and increased energy expenditure

Contraindications: None per label

Administration and Dosing: Weight loss target in clinical trials was 1 to 2 kg/week and dosages were adjusted no more frequently than every 2 weeks

- **≥12 Years of Age:**
    - Initial Dosing: 2 mg subcutaneously once daily for 2 weeks
    - Dosage Adjustment/Maintenance:
        - If 2 mg dose is tolerated, increase to 3 mg dose
        - If 2 or 3 mg dose is not tolerated, reduce dose by 1 mg /day
- **6-<12 Years of Age:**
    - Initial Dosing: 1 mg subcutaneously once daily for 2 weeks
    - Dosage Adjustment/Maintenance:
        - If 1 mg dose is tolerated, increase by 1 mg per day up to max of 3 mg per day
        - If 1 mg dose is not tolerated, reduce to 0.5 mg/day
        - If 2 or 3 mg dose is not tolerated, reduce dose by 1 mg /day
- **Renal/Hepatic Impairment**
    - Use not recommended if eGFR <60 mL/minute/1.73 m2
    - Has not been studied in patients with hepatic impairment

Warnings/Precautions:

- Sexual adverse reactions (eg, spontaneous penile erection, priapism, labial hypersensitivity) may occur
- New or worsened depression or suicidal ideation may occur; patients with a history of severe depression were not included in clinical trials
- Increased skin pigmentation and darkening of preexisting nevi may occur

Adverse Effects

- **Common (>10%)**
    - **Dermatologic:** Alopecia, skin hyperpigmentation, skin rash, xeroderma
    - **Gastrointestinal:** Abdominal pain, constipation, diarrhea, nausea, vomiting, xerostomia
    - **Genitourinary:** Spontaneous erections
    - **Immunologic:** Antibody development
    - **Local:** Injection site reaction
    - **Nervous system:** Chills, depression, dizziness, fatigue, headache, insomnia, vertigo
    - **Neuromuscular & skeletal:** Arthralgia, asthenia, back pain, limb pain, muscle spasm
    - **Respiratory:** Flu-like symptoms, upper respiratory tract infection

Pregnancy:

- **Pregnancy:**
  - Adverse events were not observed in animal reproduction studies; however, moderate weight gain is required for positive fetal outcomes during pregnancy, therefore, medications for weight loss therapy are not recommended during pregnancy

Drug Interactions:

- There are no known significant drug interactions

Cost

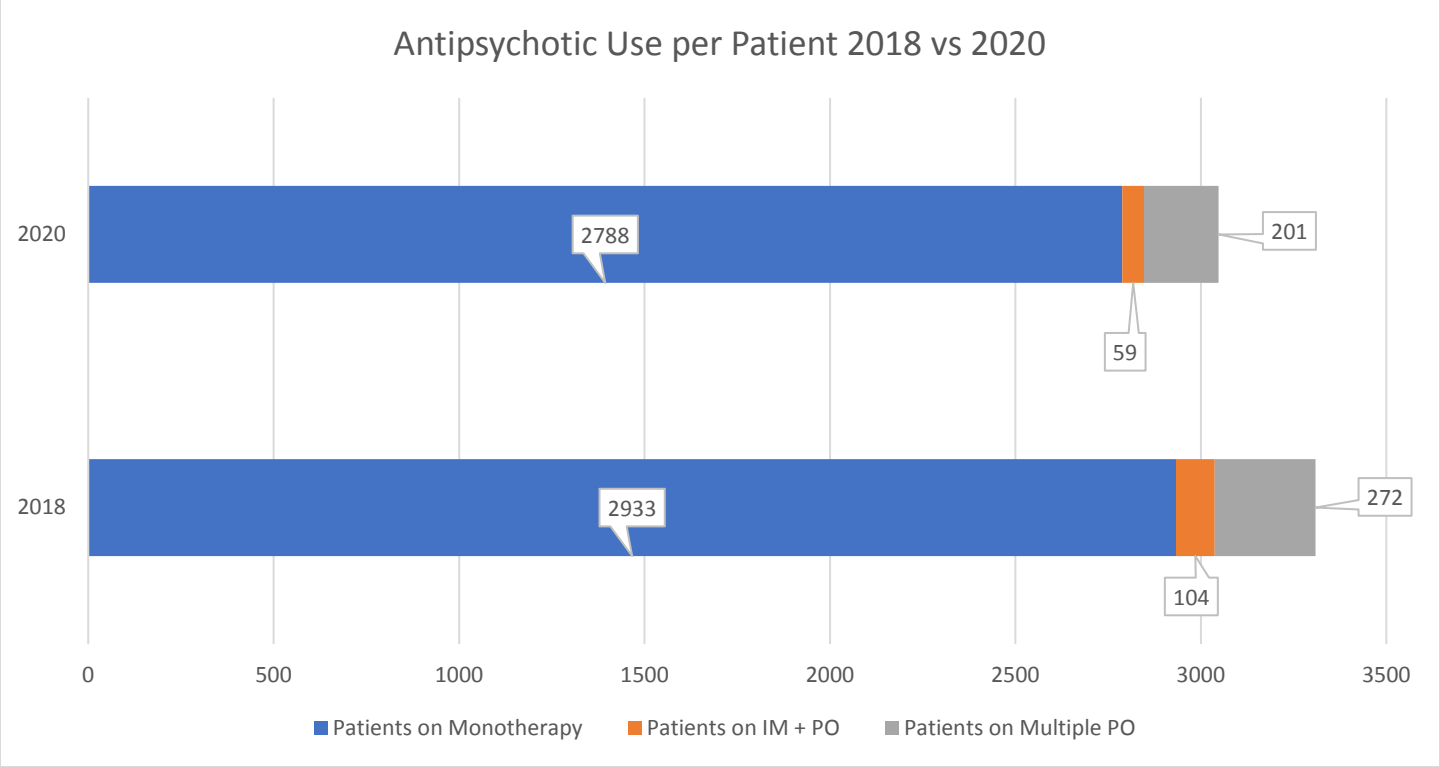
Drug	Strength	Package Size	WAC Pkg Price	Cost per dose	Cost per Month	Cost per Year
Imcivree	10 mg/mL	1 mL	$3,300.00	$165 - $990	$4,950 - $29,700	$60,225 - $361,350

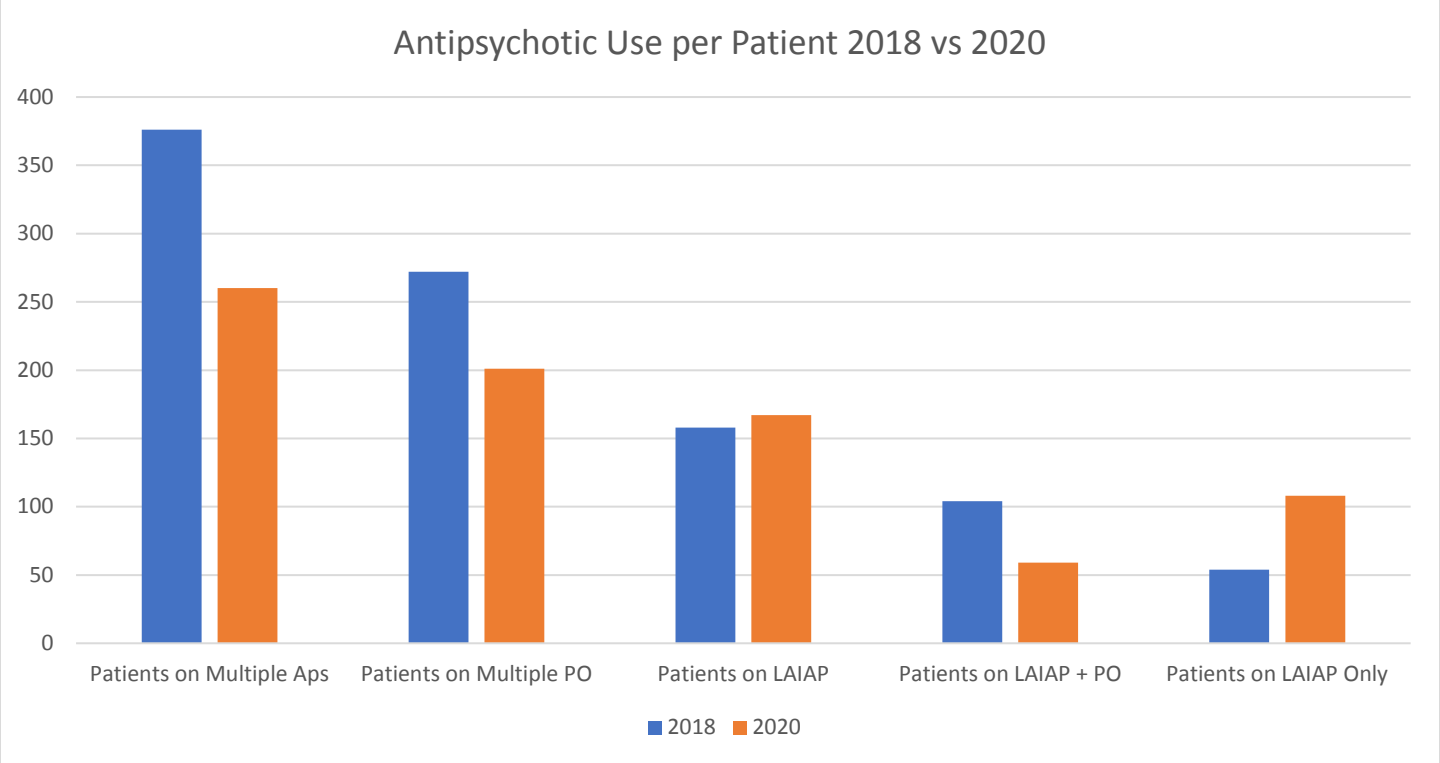
Current Utilization

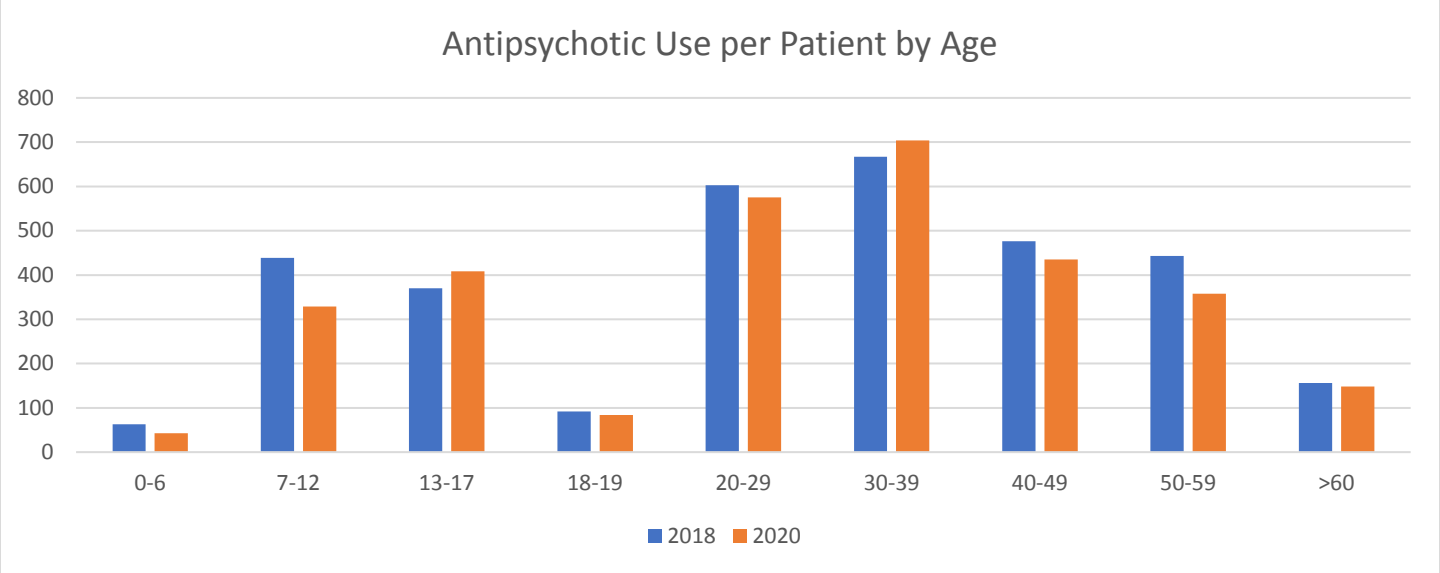
ND Medicaid Utilization (12/2019 – 12/2020)		
Label Name	**Rx Num**	**Total Reimb Amt**
Imcivree	0	-

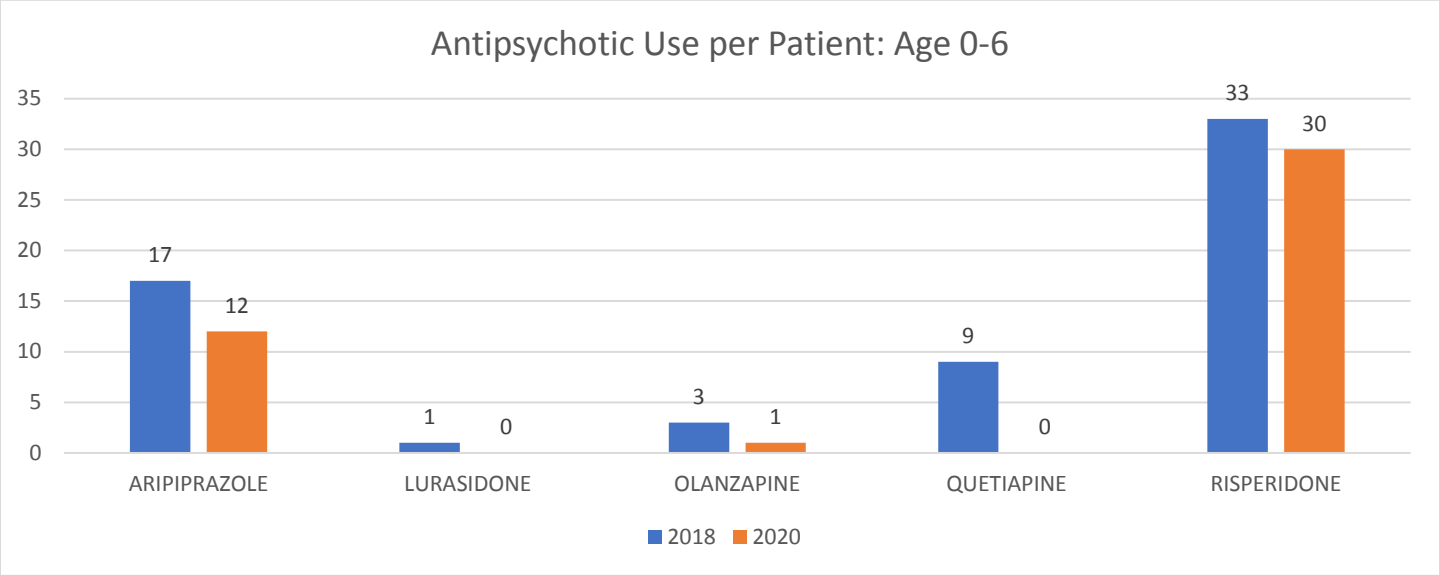
REFERENCES:

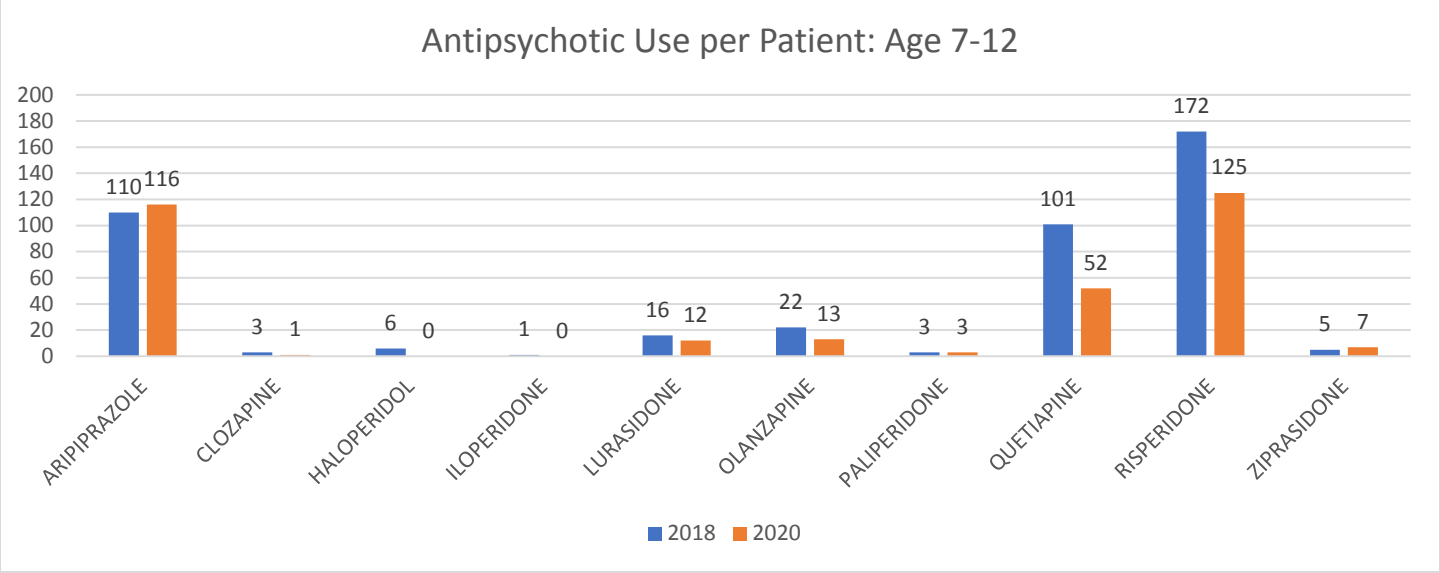
1. Facts & Comparisons eAnswers. Available at http://online.factsandcomparisons.com. Accessed on February 10, 2021.
2. UpToDate. Available at https://www.uptodate.com/contents/search. Accessed on February 10. 2021.
3. Imcivree (setmelanotide) [prescribing information]. Boston, MA; Rhythm Pharmaceuticals Inc; November 2020.

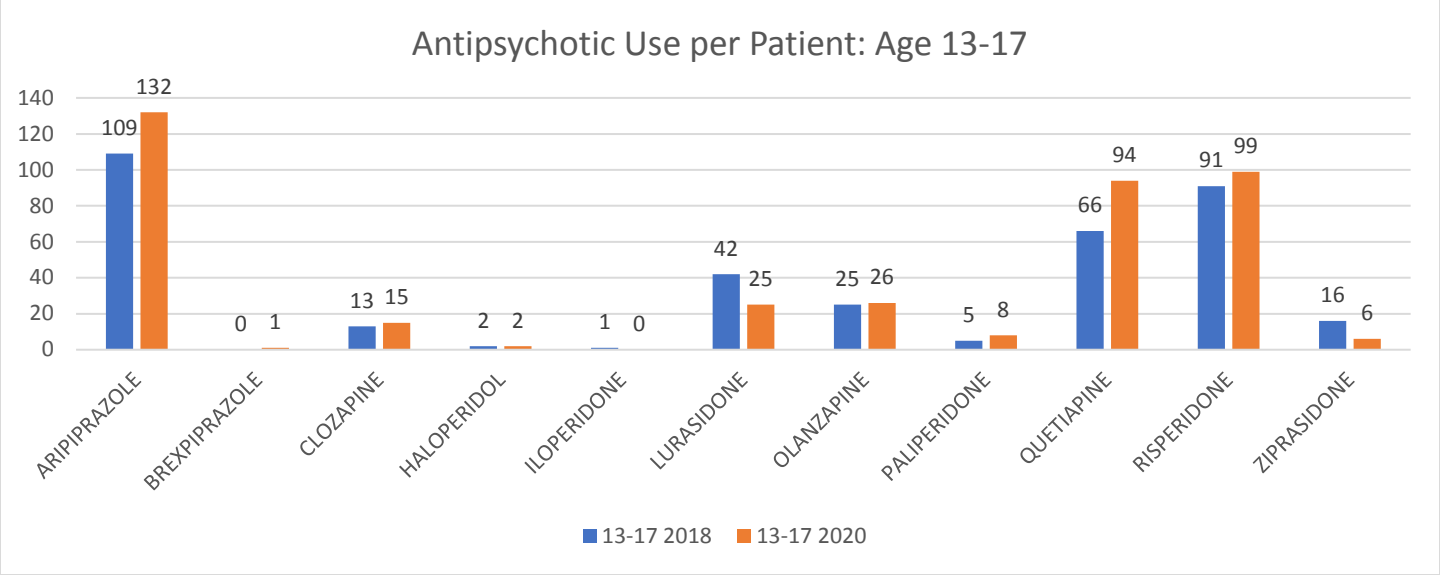

Antipsychotic Use per Patient 2018 vs 2020
2020
2018
2788
59
201
2933
104
272
0
500
1000
1500
2000
2500
3000
3500
Patients on Monotherapy
Patients on IM + PO
Patients on Multiple PO

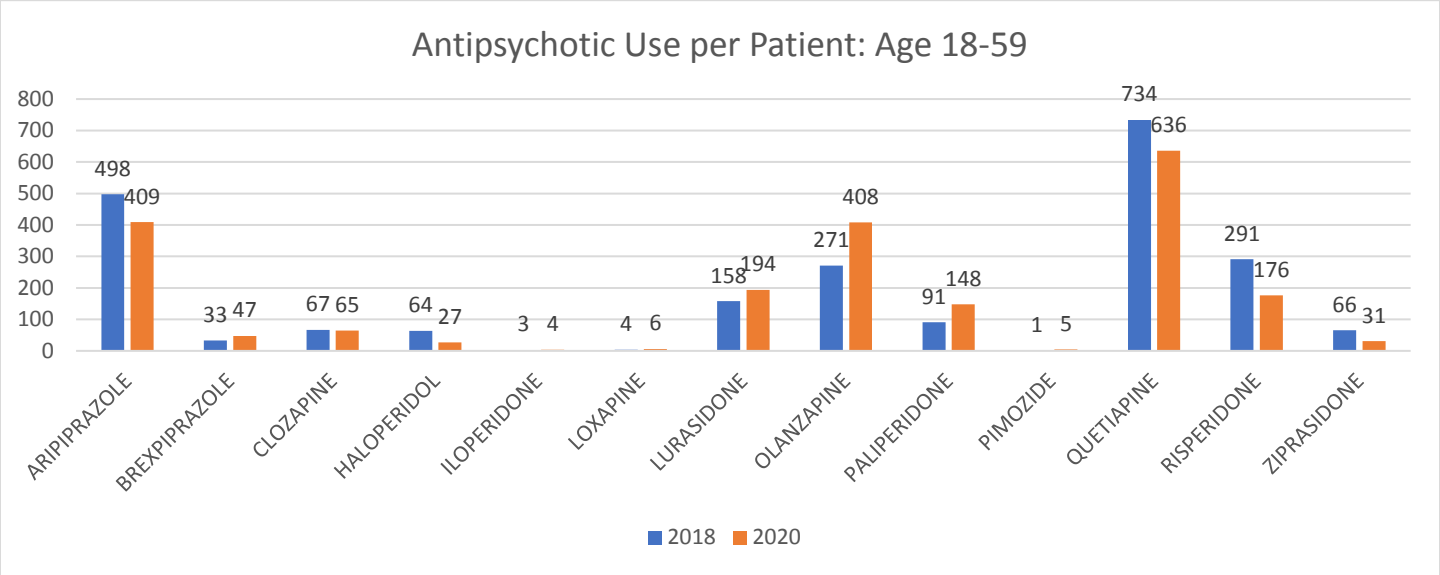

Antipsychotic Use per Patient 2018 vs 2020
400
350
300
250
200
150
100
50
0
Patients on Multiple Aps
Patients on Multiple PO
Patients on LAIAP
Patients on LAIAP + PO
Patients on LAIAP Only
2018
2020

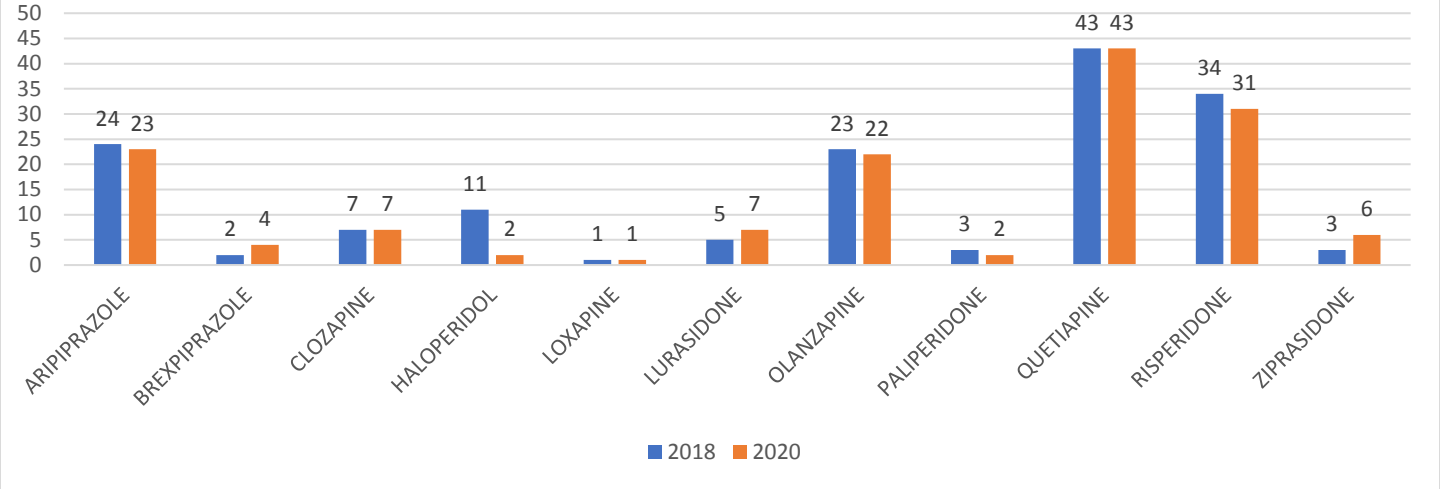

Antipsychotic Use per Patient by Age
800
700
600
500
400
300
200
100
0
0-6
7-12
13-17
18-19
20-29
30-39
40-49
50-59
>60
2018
2020

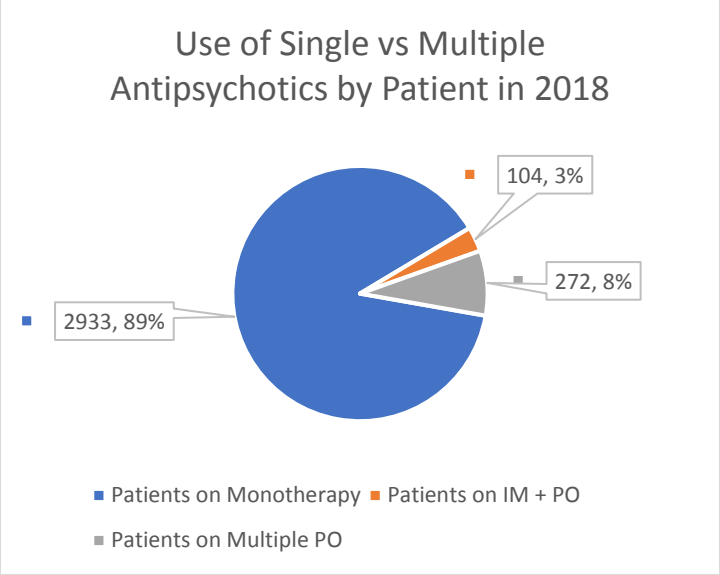

Antipsychotic Use per Patient: Age 0-6
35
30
25
20
15
10
5
0
17
12
1
0
3
1
9
0
33
30
ARIPIPRAZOLE
LURASIDONE
OLANZAPINE
QUETIAPINE
RISPERIDONE
2018
2020

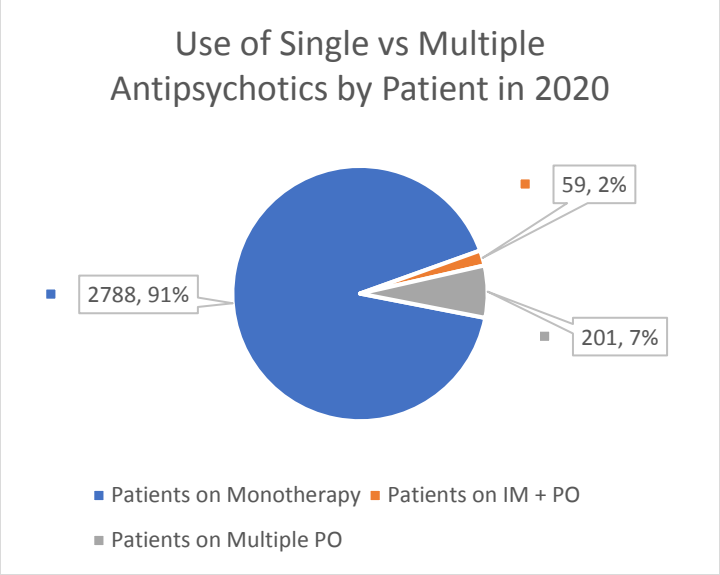

Antipsychotic Use per Patient: Age 7-12
200
180
160
140
120
100
80
60
40
20
0
110
116
3
1
6
0
1
0
16
12
22
13
3
3
101
52
172
125
5
7
ARIPIPRAZOLE
CLOZAPINE
HALOPERIDOL
ILOPERIDONE
LURASIDONE
OLANZAPINE
PALIPERIDONE
QUETIAPINE
RISPERIDONE
ZIPRASIDONE
2018
2020


Antipsychotic Use per Patient: Age 13-17
140
120
100
80
60
40
20
0
109 132
0 1
13 15
2 2
1 0
42 25
25 26
5 8
66 94
91 99
16 6
ARIPIPRAZOLE
BREXPIPRAZOLE
CLOZAPINE
HALOPERIDOL
ILOPERIDONE
LURASIDONE
OLANZAPINE
PALIPERIDONE
QUETIAPINE
RISPERIDONE
ZIPRASIDONE
13-17 2018
13-17 2020


Antipsychotic Use per Patient: Age 18-59
800
700
600
500
400
300
200
100
0
498 409
33 47
67 65
64 27
3 4
4 6
158 194
271 408
91 148
1 5
734 636
291 176
66 31
ARIPIPRAZOLE
BREXPIPRAZOLE
CLOZAPINE
HALOPERIDOL
ILOPERIDONE
LOXAPINE
LURASIDONE
OLANZAPINE
PALIPERIDONE
PIMOZIDE
QUETIAPINE
RISPERIDONE
ZIPRASIDONE
2018
2020


Antipsychotic Use per Patient: Age 60+
50
45
40
35
30
25
20
15
10
5
0
24 23
2 4
7 7
11 2
1 1
5 7
23 22
3 2
43 43
34 31
3 6
ARIPIPRAZOLE
BREXPIPRAZOLE
CLOZAPINE
HALOPERIDOL
LOXAPINE
LURASIDONE
OLANZAPINE
PALIPERIDONE
QUETIAPINE
RISPERIDONE
ZIPRASIDONE
2018
2020





Number of Patients on Each Antipsychotic by Drug and Age: 2018										
Age	**0-6**	**7-12**	**13-17**	**18-19**	**20-29**	**30-39**	**40-49**	**50-59**	**>60**	**TOTALS**
ARIPIPRAZOLE IM	0	0	1	3	17	16	5	7	3	52
ARIPIPRAZOLE PO	17	110	108	17	109	141	92	91	21	706
BREXPIPRAZOLE PO	0	0	0	0	8	15	7	3	2	35
CLOZAPINE PO	0	3	13	7	29	16	6	9	7	90
HALOPERIDOL IM	0	0	1	1	3	3	4	7	5	24
HALOPERIDOL PO	0	6	1	2	9	16	7	12	6	59
ILOPERIDONE PO	0	1	1	0	1	1	1	0	0	5
LOXAPINE PO	0	0	0	0	0	2	1	1	1	5
LURASIDONE PO	1	16	42	6	53	46	33	20	5	222
OLANZAPINE IM	0	0	0	0	4	0	0	0	0	4
OLANZAPINE PO	3	22	25	12	74	69	57	55	23	340
PALIPERIDONE IM	0	0	0	3	16	17	8	7	2	53
PALIPERIDONE PO	0	3	5	2	13	8	9	8	1	49
PIMOZIDE PO	0	0	0	0	0	0	1	0	0	1
QUETIAPINE PO	9	101	66	14	154	234	183	149	43	953
RISPERIDONE IM	0	0	1	1	12	6	2	0	2	24
RISPERIDONE PO	33	172	90	21	87	57	43	62	32	597
ZIPRASIDONE IM	0	1	0	0	0	0	0	0	0	1
ZIPRASIDONE PO	0	4	16	3	14	20	17	12	3	89

Number of Patients on Each Antipsychotic by Drug and Age: 2020										
Age	**0-6**	**7-12**	**13-17**	**18-19**	**20-29**	**30-39**	**40-49**	**50-59**	**>60**	**TOTALS**
ARIPIPRAZOLE IM	0	0	0	1	13	15	12	6	3	50
ARIPIPRAZOLE PO	12	116	132	11	99	114	78	60	20	642
BREXPIPRAZOLE PO	0	0	1	1	12	17	10	7	4	52
CLOZAPINE PO	0	1	15	7	26	19	7	6	7	88
HALOPERIDOL IM	0	0	0	0	2	3	2	2	0	9
HALOPERIDOL PO	0	0	2	0	7	7	1	3	2	22
ILOPERIDONE PO	0	0	0	0	2	1	1	0	0	4
LOXAPINE PO	0	0	0	0	5	0	0	1	1	7
LURASIDONE PO	0	12	25	6	83	56	30	19	7	238
OLANZAPINE IM	0	0	0	0	0	0	2	0	0	2
OLANZAPINE PO	1	13	26	15	167	96	72	56	22	468
PALIPERIDONE IM	0	0	0	2	42	35	9	7	1	96
PALIPERIDONE PO	0	3	8	2	30	13	3	5	1	65
PIMOZIDE PO	0	0	0	0	4	0	1	0	0	5
QUETIAPINE PO	0	52	94	16	81	252	158	129	43	825
RISPERIDONE IM	0	0	0	0	2	5	2	1	0	10
RISPERIDONE PO	30	125	99	19	0	57	42	48	31	451
ZIPRASIDONE IM	0	0	0	0	0	0	0	0	0	0
ZIPRASIDONE PO	0	7	6	4	0	14	5	8	6	50

NORTH DAKOTA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
1ST QUARTER 2021

Criteria Recommendations ***Approved Rejected***

1. Encorafenib / Overuse _____ _____

Alert Message: Braftovi (encorafenib) may be over-utilized. The recommended maximum dose of encorafenib is 450 mg (6 - 75 mg capsules) orally taken once daily in combination with binimetinib until disease progression or unacceptable toxicity.

Drugs/Diseases

Util A	Util B	Util C
Encorafenib		

Max Dose: 450 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Braftovi Prescribing Information, April 2020, Array BioPharma.

2. Encorafenib / Therapeutic Appropriateness - Pediatric _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Encorafenib		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Braftovi Prescribing Information, May 2019, Array BioPharma.

3. Encorafenib / Therapeutic Appropriateness _____ _____

Alert Message: A review of the patient's drug profile does not reveal a prescription for binimetinib. Braftovi (encorafenib) is approved to be used in combination with binimetinib. If binimetinib is temporarily interrupted or permanently discontinued, reduce the dose of encorafenib as recommended in the official prescribing information.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Encorafenib		Binimetinib

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Braftovi Prescribing Information, May 2019, Array BioPharma.

4. Encorafenib / Hemorrhage _____ _____

Alert Message: Hemorrhage can occur when Braftovi (encorafenib) is administered in combination with binimetinib. The most frequent hemorrhagic events were gastrointestinal, including rectal hemorrhage (4.2%), hematochezia (3.1%), and hemorrhoidal hemorrhage (1%). Withhold, reduce dose, or permanently discontinue encorafenib based on the severity of the adverse reaction.

Drugs/Diseases

Util A	Util B	Util C
Encorafenib	Hemorrhage	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Braftovi Prescribing Information, May 2019, Array BioPharma.

5. Encorafenib / Uveitis _____ _____

Alert Message: Uveitis, including iritis and iridocyclitis, has been reported in patients treated with Braftovi (encorafenib) in combination with binimetinib. Assess the patient for visual symptoms at each visit. Perform an ophthalmologic evaluation at regular intervals and for new or worsening visual disturbances, and to follow new or persistent ophthalmologic findings. Withhold, reduce dose, or permanently discontinue encorafenib based on the severity of the adverse reaction.

Drugs/Diseases

Util A	Util B	Util C
Encorafenib	Uveitis	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Braftovi Prescribing Information, May 2019, Array BioPharma.

6. Encorafenib / QT Prolongation _____ _____

Alert Message: Braftovi (encorafenib) is associated with dose-dependent QTc interval prolongation in some patients. Monitor patients who already have or who are at significant risk of developing QTc prolongation, including patients with known long QT syndromes, clinically significant bradyarrhythmias, severe or uncontrolled heart failure, and those taking other medicinal products associated with QT prolongation. Correct hypokalemia and hypomagnesemia prior to and during encorafenib administration. Withhold, reduce dose, or permanently discontinue for QTc > 500 ms.

Drugs/Diseases

Util A	Util B	Util C
Encorafenib	QT Prolongation	
	Heart Failure	
	Bradyarrhythmias	
	Hypokalemia	
	Hypomagnesemia	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Braftovi Prescribing Information, May 2019, Array BioPharma.

7. Encorafenib / Moderate & Strong CYP3A4 Inhibitors _____ _____

Alert Message: The concomitant administration of Braftovi (encorafenib) with a strong or moderate CYP3A4 inhibitor increased encorafenib plasma concentrations and may increase encorafenib adverse reactions. Avoid co-administration of encorafenib with strong or moderate CYP3A4 inhibitors, including grapefruit juice. If co-administration of strong or moderate CYP3A4 inhibitors cannot be avoided, modify the encorafenib dose as recommended in the official prescribing information.

Drugs/Diseases

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

References:

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

8. Encorafenib / Moderate & Strong CYP3A4 Inducers _____ _____

Alert Message: Concomitant administration of Braftovi (encorafenib) with a strong or moderate CYP3A4 inducer may decrease encorafenib plasma concentrations and may decrease encorafenib efficacy. Avoid concomitant administration of strong or moderate CYP3A4 inducers with encorafenib.

Drugs/Diseases

Util A	Util B	Util C
Encorafenib	Apalutamide	
	Bosentan	
	Carbamazepine	
	Efavirenz	
	Enzalutamide	
	Etravirine	
	Mitotane	
	Phenobarbital	
	Phenytoin	
	Primidone	
	Rifabutin	
	Rifampin	
	Rifapentine	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Braftovi Prescribing Information, May 2019, Array BioPharma.

9. Encorafenib / Sensitive CYP3A4 Substrates _____ _____

Alert Message: The coadministration of Braftovi (encorafenib) with CYP3A4 substrates may result in increased toxicity or decreased efficacy of these agents. In in vivo studies, encorafenib was shown to be a time-dependent CYP3A4 inhibitor and also a CYP3A4 inducer.

Drugs/Diseases

Util A	Util B			Util C
Encorafenib	Acalabrutinib	Felodipine	Quetiapine	
	Aprepitant	Ibrutinib	Simvastatin	
	Avanafil	Indinavir	Sirolimus	
	Bosutinib	Isavuconazonium	Tacrolimus	
	Budesonide	Ivacaftor	Ticagrelor	
	Buspirone	Lomitapide	Tolvaptan	
	Cobimetinib	Lovastatin	Triazolam	
	Darifenacin	Lurasidone	Venetoclax	
	Darunavir	Maraviroc		
	Dasatinib	Midazolam		
	Eletriptan	Midostaurin		
	Eplerenone	Nisoldipine		

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Braftovi Prescribing Information, May 2019, Array BioPharma.

10. Encorafenib / Hormonal Contraceptives _____ _____

Alert Message: The coadministration of Braftovi (encorafenib) with hormonal contraceptives (CYP3A4 substrates) can result in decreased hormone concentrations and loss of hormonal contraceptive efficacy. Avoid coadministration of hormonal contraceptives with encorafenib. Counsel patients to use a non-hormonal method of contraception during treatment with encorafenib and for 2 weeks after the final dose.

Drugs/Diseases

Util A	Util B	Util C
Encorafenib	Hormonal Contraceptives	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Braftovi Prescribing Information, May 2019, Array BioPharma.

11. Encorafenib / Drugs that Cause QT Prolongation _____ _____

Alert Message: Braftovi (encorafenib) use is associated with dose-dependent QTc interval prolongation in some patients. Avoid the coadministration of encorafenib with medicinal products with a known potential to prolong the QT/QTc interval.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Braftovi Prescribing Information, May 2019, Array BioPharma.

12. Encorafenib / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on its mechanism of action, Braftovi (encorafenib) can cause fetal harm when administered to a pregnant patient. Encorafenib produced embryo-fetal developmental changes in rats and rabbits and was an abortifacient in rabbits at doses greater than or equal to those resulting in exposures approximately 26 (in the rat) and 178 (in the rabbit) times the human exposure at the recommended dose of 450 mg, with no clear findings at lower doses. Advise patients of the potential risk to a fetus.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Braftovi Prescribing Information, May 2019, Array BioPharma.

13. Encorafenib / Lactation _____ _____

Alert Message: There are no data on the presence of Braftovi (encorafenib) or its metabolites in human milk or the effects of encorafenib on the breastfed infant, or milk production. Because of the potential for serious adverse reactions from encorafenib in breastfed infants, advise patients not to breastfeed during treatment with encorafenib and for 2 weeks after the final dose.

Drugs/Diseases

Util A	Util B	Util C
Encorafenib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Braftovi Prescribing Information, May 2019, Array BioPharma.

14. Encorafenib / Therapeutic Appropriateness _____ _____

Alert Message: Advise patients of reproductive potential to use an effective, non-hormonal method of contraception since Braftovi (encorafenib) can render hormonal contraceptives ineffective, during treatment and for 2 weeks after the final dose of encorafenib. Based on its mechanism of action, encorafenib can cause fetal harm when administered to a pregnant patient.

Drugs/Diseases

Util A	Util B	Util C
Encorafenib		

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Braftovi Prescribing Information, May 2019, Array BioPharma.

15. Encorafenib / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Braftovi (encorafenib). 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
Encorafenib		

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med. 2005;353:487-97.
Ruddy K, Mayer E, Partridge A. Patient Adherence and Persistence With Oral Anticancer Treatment. CA Cancer J Clin 2009;59:56-66.
Barillet M, Prevost V, Joly F, Clarisse B. Oral Antineoplastic Agents: How do We Care About Adherence?. Br J Clin Pharmacol. 2015;80(6):1289–1302. doi:10.1111/bcp.12734
Greer JA, Amoyal N, Nisotel L, et al. Systemic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist. 2016;21:354-376.

16. Rimegepant / Overuse _____ _____

Alert Message: Nurtec ODT (rimegepant) may be over-utilized. The recommended maximum dose of rimegepant is 75 mg in a 24-hour period. The safety of treating more than 15 migraines in a 30-day period has not been established.

Drugs/Diseases

Util A	Util B	Util C
Rimegepant		

Max Dose: 75 mg/day

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Nurtec ODT Prescribing Information, Feb. 2020, Biohaven Pharmaceuticals Inc.

17. Rimegepant / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Nurtec ODT (rimegepant) in pediatric patients have not been established.

Drugs/Diseases

Util A	Util B	Util C
Rimegepant		

Age Range: 0 – 17 yoa

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Nurtec ODT Prescribing Information, Feb. 2020, Biohaven Pharmaceuticals Inc.

18. Rimegepant / Therapeutic Appropriateness _____ _____

Alert Message: Avoid the use of Nurtec ODT (rimegepant) in patients with severe hepatic impairment. In clinical studies, plasma concentrations of rimegepant were significantly higher in subjects with severe (Child-Pugh C) hepatic impairment. No dosage adjustment rimegepant is required in patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment.

Drugs/Diseases

Util A	Util B	Util C
Rimegepant	Cirrhosis	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Nurtec ODT Prescribing Information, Feb. 2020, Biohaven Pharmaceuticals Inc.

19. Rimegepant / ESRD _____ _____

Alert Message: Avoid the use of Nurtec ODT (rimegepant) in patients with end-stage renal disease (CLcr < 15 mL/min). Rimegepant has not been studied in patients with end-stage renal disease and patients on dialysis. No dosage adjustment of rimegepant is required in patients with mild, moderate, or severe renal impairment.

Drugs/Diseases

Util A	Util B	Util C
Rimegepant	ESRD	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Nurtec ODT Prescribing Information, Feb. 2020, Biohaven Pharmaceuticals Inc.

20. Rimegepant / Strong CYP3A4 Inhibitors _____ _____

Alert Message: Avoid the concomitant administration of Nurtec ODT (rimegepant) with strong inhibitors of CYP3A4. The co-administration of rimegepant, a CYP3A4 substrate, with strong inhibitors of CYP3A4 may result in a significant increase in rimegepant exposure.

Drugs/Diseases

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

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Nurtec ODT Prescribing Information, Feb. 2020, Biohaven Pharmaceuticals Inc.

21. Rimegepant / Moderate CYP3A4 Inhibitors _____ _____

Alert Message: Concomitant administration of Nurtec ODT (rimegepant) with moderate inhibitors of CYP3A4 may result in increased exposure of rimegepant. Avoid another dose of rimegepant within 48 hours when it is concomitantly administered with moderate inhibitors of CYP3A4.

Drugs/Diseases

Util A	Util B		Util C
Rimegepant	Atazanavir	Dronedarone	
	Aprepitant	Erythromycin	
	Ciprofloxacin	Fluconazole	
	Crizotinib	Fluvoxamine	
	Cyclosporine	Fosamprenavir	
	Diltiazem	Verapamil	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.

Nurtec ODT Prescribing Information, Feb. 2020, Biohaven Pharmaceuticals Inc.

22. Rimegepant / Moderate & Strong CYP3A4 Inducers _____ _____

Alert Message: The concurrent use of Nurtec ODT (rimegepant) with strong or moderate CYP3A4 inducers should be avoided. Rimegepant is a CYP3A4 substrate, and concurrent use with a strong or moderate CYP3A4 inducer may result in decreased rimegepant exposure and loss of rimegepant efficacy.

Drugs/Diseases

Util A	Util B		Util C
Rimegepant	Apalutamide	Phenobarbital	
	Bosentan	Phenytoin	
	Carbamazepine	Primidone	
	Efavirenz	Rifabutin	
	Enzalutamide	Rifampin	
	Etravirine	Rifapentine	
	Mitotane		

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.

Nurtec ODT Prescribing Information, Feb. 2020, Biohaven Pharmaceuticals Inc.

23. Rimegepant / P-gp & BCRP Transport Inhibitors _____ _____

Alert Message: Nurtec ODT (rimegepant) is a substrate of P-gp and BCRP efflux transporters. Concomitant administration of rimegepant with inhibitors of P-gp or BCRP may result in a significant increase in rimegepant exposure. Avoid concurrent use of rimegepant with inhibitors of P-gp or BCRP.

Drugs/Diseases

Util A	Util B					Util C
Rimegepant	Acalabrutinib	Etravirine	Leflunomide	Ranolazine	Teriflunomide	
	Amiodarone	Flibanserin	Lomitapide	Regorafenib	Tolvaptan	
	Brigatinib	Fostamatinib	Mefloquine	Ritonavir	Velpatasvir	
	Cabozantinib	Glecaprevir	Mifepristone	Rolapitant	Vemurafenib	
	Carvedilol	Grazoprevir	Nelfinavir	Safinamide	Venetoclax	
	Clarithromycin	Ibrutinib	Neratinib	Sapropterin	Verapamil	
	Cobicistat	Isavuconazonium	Osimertinib	Saquinavir	Voxilaprevir	
	Cyclosporine	Istradefylline	Paritaprevir	Sarecycline		
	Daclatasvir	Itraconazole	Pibrentasvir	Sirolimus		
	Darolutamide	Ivacaftor	Ponatinib	Sorafenib		
	Ketoconazole	Lapatinib	Posaconazole	Sulfasalazine		
	Eltrombopag	Lasmiditan	Propafenone	Tafamidis		
	Erythromycin	Ledipasvir	Quinidine	Tedizolid		

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.

Nurtec ODT Prescribing Information, Feb. 2020, Biohaven Pharmaceuticals Inc.

24. Rimegepant / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no adequate data on the developmental risk associated with the use of Nurtec ODT (rimegepant) in pregnant patients. In animal studies, oral administration of rimegepant during organogenesis resulted in adverse effects on development in rats (decreased fetal body weight and increased incidence of fetal variations) at exposures greater than those used clinically, and which were associated with maternal toxicity.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Nurtec ODT Prescribing Information, Feb. 2020, Biohaven Pharmaceuticals Inc.

25. Rimegepant / Lactation _____ _____

Alert Message: There are no data on the presence of Nurtec ODT (rimegepant) in human milk, the effects of rimegepant on the breastfed infant, or the effects of rimegepant on milk production. There are no animal data on the excretion of rimegepant in milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for rimegepant and any potential adverse effects on the breastfed infant from rimegepant or from the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Rimegepant	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Nurtec ODT Prescribing Information, Feb. 2020, Biohaven Pharmaceuticals Inc.

26. Ibrutinib / Overutilization MCL & MZL _____ _____

Alert Message: Imbruvica (ibrutinib) may be over-utilized. The recommended dosage of ibrutinib for mantle cell lymphoma (MCL) and marginal zone lymphoma (MZL) is 560 mg orally once daily until disease progression or unacceptable toxicity.

Drugs/Diseases

Util A	Util B	Util C (Include)
Ibrutinib		Mantle Cell Lymphoma
		Marginal Zone Lymphoma

Max Dose: 560 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Imbruvica Prescribing Information, April 2020, Pharmacyclics.

27. Ibrutinib / Overutilization CLL/SLL & WM _____ _____

Alert Message: Imbruvica (ibrutinib) may be over-utilized. The recommended dosage of ibrutinib for chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) and Waldenstrom's macroglobulinemia (WM) as a single agent, in combination with rituximab for WM, or in combination with bendamustine and rituximab or with obinutuzumab for CLL/SLL is 420 mg once daily until disease progression or unacceptable toxicity.

Drugs/Diseases

Util A	Util B	Util C (Include)
Ibrutinib		Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Waldenstrom's Macroglobulinemia

Max Dose: 420 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Imbruvica Prescribing Information, April 2020, Pharmacyclics.

28. Ibrutinib / Overutilization cGVHD _____ _____

Alert Message: Imbruvica (ibrutinib) may be over-utilized. The recommended dosage of ibrutinib for chronic graft versus host disease (cGVHD) is 420 mg once daily until disease cGVHD progression, recurrence of underlying malignancy, or unacceptable toxicity.

Drugs/Diseases

Util A	Util B	Util C (Include)
Ibrutinib		Chronic Graft versus Host Disease

Max Dose: 420 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Imbruvica Prescribing Information, April 2020, Pharmacyclics.

29. Ibrutinib / Overutilization – Mild Hepatic Impairment _____ _____

Alert Message: Imbruvica (ibrutinib) may be over-utilized. The recommended dosage of ibrutinib for patients with mild hepatic impairment (Child-Pugh class A) is 140 mg daily. The recommended dosage of ibrutinib for patients with moderate hepatic impairment (Child-Pugh class B) is 70 mg daily.

Drugs/Diseases

Util A	Util B	Util C (Include)
Ibrutinib		Hepatic Impairment

Max Dose: 140 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Imbruvica Prescribing Information, April 2020, Pharmacyclics.

30. Ibrutinib / Overutilization – Severe Hepatic Impairment _____ _____

Alert Message: Imbruvica (ibrutinib) use should be avoided in patients with severe hepatic impairment (Child-Pugh class C). In clinical studies, the AUC of ibrutinib increased 2.7-fold in subjects with mild hepatic impairment (Child-Pugh class A), 8.2-fold in subjects with moderate hepatic impairment (Child-Pugh class B), and 9.8-fold in subjects with severe hepatic impairment (Child-Pugh class C) relative to subjects with normal liver function.

Drugs/Diseases

Util A	Util B	Util C (Include)
Ibrutinib		Cirrhosis
		Hepatic Failure

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Imbruvica Prescribing Information, April 2020, Pharmacyclics.

31. Ibrutinib / Strong CYP3A4 Inducers _____ _____

Alert Message: The concurrent use of Imbruvica (ibrutinib), a CYP3A4 substrate, with strong CYP3A4 inducers should be avoided. The coadministration of ibrutinib with a strong CYP3A4 inducer may decrease ibrutinib concentrations, and therefore its efficacy.

Drugs/Diseases

Util A	Util B		Util C
Ibrutinib	Apalutamide	Phenytoin	
	Carbamazepine	Phenobarbital	
	Enzalutamide	Primidone	
	Mitotane	Rifampin	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Imbruvica Prescribing Information, April 2020, Pharmacyclics.

32. Ibrutinib / Strong CYP3A4 Inhibitors _____ _____

Alert Message: The coadministration of Imbruvica (ibrutinib), a CYP3A4 substrate, with a strong CYP3A inhibitor may result in increased ibrutinib plasma concentrations. Increased ibrutinib concentrations may increase the risk of ibrutinib-related toxicity. Refer to the official prescribing information for the recommended ibrutinib dose modifications when used concomitantly with posaconazole or voriconazole. Avoid concomitant use of ibrutinib with other strong CYP3A inhibitors. If a strong CYP3A4 inhibitor will be used short-term (such as anti-infectives for seven days or less), interrupt ibrutinib therapy.

Drugs/Diseases

Util A	Util B		Util C
Ibrutinib 280 mg	Clarithromycin	Nelfinavir	
Ibrutinib 420 mg	Cobicistat	Posaconazole	
Ibrutinib 560 mg	Indinavir	Ritonavir	
	Itraconazole	Saquinavir	
	Ketoconazole	Voriconazole	
	Nefazodone		

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Imbruvica Prescribing Information, April 2020, Pharmacyclics.

33. Ibrutinib / Moderate CYP3A4 Inhibitors _____ _____

Alert Message: The coadministration of Imbruvica (ibrutinib), a CYP3A4 substrate, with a moderate CYP3A inhibitor may increase ibrutinib plasma concentrations. Increased ibrutinib concentrations may increase the risk of ibrutinib-related toxicity. Refer to the official prescribing information for the recommended ibrutinib dose modifications when used concomitantly with moderate CYP3A inhibitors. Interrupt ibrutinib if these inhibitors will be used short-term (such as anti-infectives for seven days or less).

Drugs/Diseases

Util A	Util B		Util C
Ibrutinib 420 & 560 mg	Atazanavir	Dronedarone	
	Aprepitant	Erythromycin	
	Ciprofloxacin	Fluconazole	
	Crizotinib	Fluvoxamine	
	Cyclosporine	Imatinib	
	Diltiazem	Verapamil	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Imbruvica Prescribing Information, April 2020, Pharmacyclics.

34. Ibrutinib / Therapeutic Appropriateness _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Ibrutinib		

Age Range: 0- 17 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Imbruvica Prescribing Information, April 2020, Pharmacyclics.

35. Ibrutinib / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Imbruvica (ibrutinib), a kinase inhibitor, can cause fetal harm based on findings from animal studies. There are no available data on ibrutinib use in pregnant patients to inform a drug-associated risk of major birth defects and miscarriage. If ibrutinib is used during pregnancy or if the patient becomes pregnant while taking ibrutinib, the patient should be apprised of the potential hazard to the fetus.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Imbruvica Prescribing Information, April 2020, Pharmacyclics.

36. Ibrutinib / Lactation _____ _____

Alert Message: There is no information regarding the presence of Imbruvica (ibrutinib) or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production. The development and health benefits of breastfeeding should be considered along with the mother's clinical need for ibrutinib and any potential adverse effects on the breastfed child from ibrutinib or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Ibrutinib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Imbruvica Prescribing Information, April 2020, Pharmacyclics.

37. Ibrutinib / Reproductive Potential - Female _____ _____

Alert Message: Advise patients of reproductive potential to avoid pregnancy while taking Imbruvica (ibrutinib) and for up to 1 month after ending treatment. If the drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be informed of the potential hazard to a fetus.

Drugs/Diseases

Util A	Util B	Util C
Ibrutinib		

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.

38. Ibrutinib / Reproductive Potential - Male _____ _____

Alert Message: Advise males with partners of reproductive potential to avoid fathering a child while receiving Imbruvica (ibrutinib), and for 1 month following the last dose of ibrutinib.

Drugs/Diseases

Util A	Util B	Util C
Ibrutinib		

Gender: Male

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Imbruvica Prescribing Information, April 2020, Pharmacyclics.

39. Ibrutinib / Hemorrhage _____ _____

Alert Message: Fatal bleeding events have occurred in patients treated with Imbruvica (ibrutinib). Major hemorrhage (≥ Grade 3, serious, or any central nervous system events; e.g., intracranial hemorrhage [including subdural hematoma], gastrointestinal bleeding, hematuria, and post-procedural hemorrhage) have occurred in 4% of patients, with fatalities occurring in 0.4% of 2,838 patients exposed to ibrutinib in 27 clinical trials. Bleeding events of any grade, including bruising and petechiae, occurred in 39% of patients treated with ibrutinib. Monitor patients for signs and symptoms of bleeding.

Drugs/Diseases

Util A	Util B	Util C
Ibrutinib	Intracranial Hemorrhage	
	Gastrointestinal Bleeding	
	Hematuria	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Imbruvica Prescribing Information, April 2020, Pharmacyclics.

40. Ibrutinib / Hemorrhage _____ _____

Alert Message: Fatal bleeding events have occurred in patients treated with Imbruvica (ibrutinib). Use of either anticoagulant or antiplatelet agents concomitantly with ibrutinib increases the risk of major hemorrhage. In ibrutinib clinical trials, 3.1% of patients taking ibrutinib without antiplatelet or anticoagulant therapy experienced major hemorrhage. Consider the risks and benefits of anticoagulant or antiplatelet therapy when co-administered with ibrutinib. Monitor for signs and symptoms of bleeding.

Drugs/Diseases

Util A	Util B	Util C
Ibrutinib	Anticoagulants	
	Antiplatelets	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Imbruvica Prescribing Information, April 2020, Pharmacyclics.

41. Ibrutinib / Serious Infections _____ _____

Alert Message: Fatal and non-fatal infections (including bacterial, viral, or fungal) have occurred with Imbruvica (ibrutinib) therapy. Grade 3 or greater infections occurred in 24% of 1,124 patients exposed to ibrutinib in clinical trials. Cases of progressive multifocal leukoencephalopathy (PML) and Pneumocystis jirovecii pneumonia (PJP) have occurred in patients treated with ibrutinib. Consider prophylaxis according to the standard of care in patients who are at increased risk for opportunistic infections. Monitor and evaluate patients for fever and infections and treat appropriately.

Drugs/Diseases

Util A	Util B	Util C
Ibrutinib	Serious Infections	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Imbruvica Prescribing Information, April 2020, Pharmacyclics.

42. Ibrutinib / Arrhythmia _____ _____

Alert Message: Fatal and serious cardiac arrhythmias have occurred with Imbruvica (ibrutinib) therapy. Grade 3 or greater ventricular tachyarrhythmias and Grade 3 or greater atrial fibrillation and atrial flutter occurred in patients exposed to ibrutinib in clinical trials. These events have occurred particularly in patients with cardiac risk factors, hypertension, acute infections, and a previous history of cardiac arrhythmias. Periodically monitor patients clinically for cardiac arrhythmias. Manage cardiac arrhythmias appropriately, and if it persists, consider the risks and benefits of ibrutinib treatment and follow dose modification guidelines.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Ibrutinib	Arrhythmias	Antiarrhythmic Agents

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Imbruvica Prescribing Information, April 2020, Pharmacyclics.

43. Ibrutinib / Hypertension _____ _____

Alert Message: Hypertension has been reported with Imbruvica (ibrutinib) therapy. Hypertension of any grade occurred in 12% of 1,124 patients treated with ibrutinib in clinical trials. Grade 3 or greater hypertension occurred in 5% of patients with a median time to onset of 5.9 months (range, 0.03 to 24 months). Monitor blood pressure in patients treated with ibrutinib and initiate or adjust antihypertensive medication throughout ibrutinib treatment as appropriate.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Ibrutinib	Hypertension	Antihypertensive Agents

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Imbruvica Prescribing Information, April 2020, Pharmacyclics.

44. Ibrutinib / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Imbruvica (ibrutinib). 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
Encorafenib		

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med. 2005;353:487-97.
Barillet M, Prevost V, Joly F, Clarisse B. Oral Antineoplastic Agents: How do We Care About Adherence?. Br J Clin Pharmacol. 2015;80(6):1289–1302. doi:10.1111/bcp.12734
Greer JA, Amoyal N, Nisotel L, et al. Systemic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist. 2016;21:354-376.

45. Cenobamate / Overuse _____ _____
Alert Message: Xcopri (cenobamate) may be over-utilized. The recommended maximum daily dose of cenobamate is 400 mg once daily.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Cenobamate		Hepatic Impairment

Max Dose: 400 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.

46. Cenobamate / Overuse _____ _____
Alert Message: Xcopri (cenobamate) should be used with caution in patients with mild to moderate hepatic impairment. For patients with mild to moderate (5-9 points on Child-Pugh assessment) hepatic impairment, the maximum recommended dosage is 200 mg once daily. The use of cenobamate is not recommended in patients with severe hepatic impairment.

Drugs/Diseases

Util A	Util B	Util C (Include)
Cenobamate		Hepatic Impairment

Max Dose: 200 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.

47. Cenobamate / Short QT Syndrome _____ _____
Alert Message: Xcopri (cenobamate) use is contraindicated in patients with familial short QT syndrome. In a placebo-controlled study of the QT interval, a higher percentage of subjects who took cenobamate (31% at 200 mg and 66% at 500 mg) had a QT shortening of greater than 20 msec compared to placebo (6-17%).

Drugs/Diseases

Util A	Util B	Util C (Include)
Cenobamate		Ventricular Fibrillation
		Ventricular Tachycardia

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.
Rudic B, Schimpf R, Borggrefe M. Short QT Syndrome - Review of Diagnosis and Treatment. Arrhythm Electrophysiol *Rev*. 2014;3(2):76-79. doi:10.15420/aer.2014.3.2.76

48. Cenobamate / Therapeutic Appropriateness _____ _____
Alert Message: The safety and effectiveness of Xcopri (cenobamate) in pediatric patients have not been established.

Drugs/Diseases

Util A	Util B	Util C
Cenobamate		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.

49. Cenobamate / DRESS _____ _____

Alert Message: Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) has been reported in patients taking Xcopri (cenobamate). DRESS has occurred, including one fatality, when cenobamate was titrated rapidly (weekly or faster titration). If such signs or symptoms are present, the patient should be evaluated immediately. Cenobamate should be discontinued immediately and not restarted if an alternative etiology for the signs or symptoms cannot be established.

Drugs/Diseases

Util A	Util B	Util C
Cenobamate	Fever	
	Generalized Skin Eruption Due to Drugs	
	Lymphadenopathy	
	Facial Swelling	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.

50. Cenobamate / Phenytoin _____ _____

Alert Message: The concurrent use of Xcopri (cenobamate) with phenytoin may result in as much as a 2-fold increase in phenytoin plasma concentrations. The official prescribing information recommends that the phenytoin dosage be gradually decreased by up to 50% as cenobamate is being titrated.

Drugs/Diseases

Util A	Util B	Util C
Cenobamate	Phenytoin	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.

51. Cenobamate / Phenobarbital _____ _____

Alert Message: The concurrent use of Xcopri (cenobamate) with phenobarbital may result in elevated phenobarbital plasma concentrations and an increased risk of phenobarbital-related adverse effects. Consider a reduction in the dosage of phenobarbital, as clinically appropriate, when used concomitantly with cenobamate.

Drugs/Diseases

Util A	Util B	Util C
Cenobamate	Phenobarbital	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.

52. Cenobamate / Clobazam _____ _____

Alert Message: The concurrent use of Xcopri (cenobamate) with clobazam may result in elevated clobazam plasma concentrations and an increased risk of clobazam-related adverse effects. Consider a reduction in the dosage of clobazam, as clinically appropriate, when used concomitantly with cenobamate.

Drugs/Diseases

Util A	Util B	Util C
Cenobamate	Clobazam	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.

53. Cenobamate / Lamotrigine _____ _____

Alert Message: The concurrent use of Xcopri (cenobamate) with lamotrigine may result in decreased plasma concentrations of lamotrigine and decreased efficacy. Increase the dose of lamotrigine as needed, when used concomitantly with cenobamate.

Drugs/Diseases

Util A	Util B	Util C
Cenobamate	Lamotrigine	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.

54. Cenobamate / Carbamazepine _____ _____

Alert Message: The concurrent use of Xcopri (cenobamate) with carbamazepine may result in decreased plasma concentrations of carbamazepine and decreased efficacy. Increase the dose of carbamazepine as needed, when used concomitantly with cenobamate.

Drugs/Diseases

Util A	Util B	Util C
Cenobamate	Carbamazepine	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.

55. Cenobamate / CYP2B6 or CYP3A4 Substrates _____ _____

Alert Message: The concurrent use of Xcopri (cenobamate) with a CYP2B6 or CYP3A4 substrate may result in decreased plasma concentrations of substrate and decreased substrate efficacy. Increase the dose of the CYP2B6 or CYP3A4 substrate as needed, when used concomitantly with cenobamate.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.

56. Cenobamate / CYP2C19 Substrates _____ _____

Alert Message: The concurrent use of Xcopri (cenobamate) with a CYP2C19 substrate may result in increased substrate plasma concentrations and risk of CYP2C19 substrate-related adverse reactions. If clinically appropriate, consider a reduction in dosage of the CYP2C19 substrate when used concomitantly with cenobamate.

Drugs/Diseases

Util A	Util B	Util C
Cenobamate	Carisoprodol	
	Cilostazol	
	Citalopram	
	Diazepam	
	Lansoprazole	
	Omeprazole	
	Voriconazole	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.

57. Cenobamate / Oral Hormonal Contraceptives _____ _____

Alert Message: The coadministration of Xcopri (cenobamate) with oral hormonal contraceptives (CYP3A4 substrates) can result in decreased hormone concentrations and loss of hormonal contraceptive efficacy. Counsel patients to use additional or alternative non-hormonal methods of contraception while taking cenobamate.

Drugs/Diseases

Util A	Util B	Util C
Cenobamate	Oral Hormonal Contraceptives	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.

58. Cenobamate / CNS Depressants _____ _____

Alert Message: The coadministration of Xcopri (cenobamate) with CNS depressants may increase the risk of neurological adverse reactions, including sedation and somnolence. Educate the patient to the risk of excessive CNS depression when these medications are coadministered.

Drugs/Diseases

Util A	Util B	Util C
Cenobamate	CNS Depressants	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.

59. Cenobamate / Drugs That Shorten Q Interval _____ _____

Alert Message: Xcopri (cenobamate) can shorten the QT interval; therefore, caution should be used when administering cenobamate with drugs that shorten the QT interval, as a synergistic effect on the QT interval could occur. Cenobamate use is contraindicated in patients with familial short QT syndrome.

Drugs/Diseases

Util A	Util B	Util C
Cenobamate	Isavuconazonium	
	Rufinamide	
	Mexiletine	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.

60. Cenobamate / Non-adherence _____ _____

Alert Message: Based on the refill history, your patient may be underutilizing Xcopri (cenobamate). 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
Cenobamate		

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Faught E, Duh MS, Weiner JR, et al. Nonadherence to Antiepileptic Drugs and Increased Mortality, Findings from the RANSOM Study. Neurology 2008;71(20): 1572-1578.
Faught RE, Weiner JR, Guerin A, et al. Impact of Nonadherence to Antiepileptic Drugs on Health Care Utilization and Costs: Findings from the RANSOM Study. Epilepsia 2009;50(3):501-509.
Hodges JC, Treadwell J, Malphrus AD, et al., Identification and Prevention of Antiepileptic Drug Noncompliance: The Collaborative Use of State-Supplied Pharmaceutical Data. ISRN Pediatr. 2014 Feb 19:1-8.
Viswanathan M, Golin CE, Jones DC, et al., Interventions to Improve Adherence to Self-administered Medications for Chronic Disease in the\United States: A Systemic Review. Ann Intern Med. 2012:157:785-792.

61. Cenobamate / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no adequate data on the developmental risk associated with the use of Xcopri (cenobamate) in pregnant patients. In animal studies, administration of cenobamate during pregnancy or throughout pregnancy and lactation resulted in adverse effects on development (increased embryofetal mortality, decreased fetal and offspring body weights, neurobehavioral and reproductive impairment in offspring) at clinically relevant drug exposures. Encourage patients who are taking cenobamate during pregnancy to enroll in the North American Antiepileptic Drug (NAAED) Pregnancy Registry.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.

62. Cenobamate / Lactation _____ _____

Alert Message: There are no data available on the presence of Xcopri (cenobamate) in human milk, the effects on the breastfed infant, or the effects of the drug on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for cenobamate and any potential adverse effects on the breastfed infant from cenobamate or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Cenobamate	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.

63. Cenobamate / End-Stage Renal Disease _____ _____

Alert Message: The use of Xcopri (cenobamate) is not recommended in patients with end-stage renal disease undergoing dialysis. The effect of hemodialysis on cenobamate pharmacokinetics has not been studied.

Drugs/Diseases

Util A	Util B	Util C (Include)
Cenobamate		End-Stage Renal Disease
		Hemodialysis

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.

64. Cenobamate / Mild to Severe Renal Impairment _____ _____

Alert Message: Xcopri (cenobamate) should be used with caution and dosage reduction considered in patients with mild to moderate (CLcr 30 to less than 90 mL/min) and severe (CLcr less than 30 mL/min) renal impairment. In pharmacokinetic studies, cenobamate plasma AUC was 1.4 fold to 1.5 fold higher in subjects with mild (CLcr 60 to less than 90 mL/min) and moderate (CLcr 30 to less than 60 mL/min) following a single oral 200 mg dose of cenobamate compared to healthy controls.

Drugs/Diseases

Util A	Util B	Util C (Include)
Cenobamate		CKD Stage 2, 3, 4, & 5.

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Xcopri Prescribing Information, August 2020, SK Life Science. Inc.

65. Budesonide/Glycopyrrolate/Formoterol / Overutilization _____ _____

Alert Message: The manufacturer's recommended maximum daily dose of Breztri Aerosphere (budesonide/glycopyrrolate/formoterol) is two inhalations twice daily. Excessive use of a formoterol-containing agent or use in conjunction with other medications containing a beta-2-agonist can result in clinically significant cardiovascular effects and may be fatal.

Drugs/Diseases

Util A	Util B	Util C
Budesonide/Glycopyrrolate/Formoterol		

Max Dose: 4 inhalations/day

References:
Breztri Aerosphere Prescribing Information, July 2020, AstraZeneca.
Clinical Pharmacology, 2020 Elsevier/Gold Standard.

66. Budesonide/Glycopyrrolate/Formoterol / Therapeutic Appropriateness _____ _____

Alert Message: The safety and efficacy of Breztri Aerosphere (budesonide/glycopyrrolate/formoterol) in patients with asthma have not been established. Budesonide/glycopyrrolate/formoterol is not indicated for the treatment of asthma.

Drugs/Diseases

Util A	Util B	Util C (Include)
Budesonide/Glycopyrrolate/Formoterol		Asthma

References:
Breztri Aerosphere Prescribing Information, July 2020, AstraZeneca.
Clinical Pharmacology, 2020 Elsevier/Gold Standard.

67. Budesonide/Glycopyrrolate/Formoterol / Therapeutic Appropriateness _____ _____

Alert Message: Breztri Aerosphere (budesonide/glycopyrrolate/formoterol) is not indicated for use in children. The safety and effectiveness of budesonide/glycopyrrolate/formoterol have not been established in children.

Drugs/Diseases

Util A	Util B	Util C
Budesonide/Glycopyrrolate /Formoterol		

Age Range: 0 – 17 yoa

References:
Breztri Aerosphere Prescribing Information, July 2020, AstraZeneca.
Clinical Pharmacology, 2020 Elsevier/Gold Standard.

68. Budesonide/Glycopyrrolate/Formoterol / Cardiovascular, Diabetes, Convulsive Disorders, & Thyrotoxicosis _____ _____

Alert Message: Breztri Aerosphere (budesonide/glycopyrrolate/formoterol) should be used with caution in patients with cardiovascular or convulsive disorders, thyrotoxicosis, or sensitivity to sympathomimetic drugs. The formoterol component is a sympathomimetic amine and can exacerbate these conditions.

Drugs/Diseases

Util A	Util B	Util C
Budesonide/Glycopyrrolate/Formoterol	Hypertension	
	Arrhythmias	
	Heart Failure	
	Diabetes	
	Seizures	
	Epilepsy	
	Thyrotoxicosis	

References:
Breztri Aerosphere Prescribing Information, July 2020, AstraZeneca.
Clinical Pharmacology, 2020 Elsevier/Gold Standard.

69. Budesonide/Glycopyrrolate/Formoterol / Adrenergic Drugs _____ _____

Alert Message: Caution should be exercised when Breztri Aerosphere (budesonide/glycopyrrolate/formoterol) is prescribed concurrently with other adrenergic sympathomimetic agents, administered by any route, because the sympathetic effects of the formoterol component of the combination product may be potentiated.

Drugs/Diseases

Util A	Util B		Util C
Budesonide/Glycopyrrolate/Formoterol	Amphetamine	Methylphenidate	
	Benzphetamine	Naphazoline	
	Dextroamphetamine	Oxymetazoline	
	Diethylpropion	Phenylephrine	
	Ephedrine	Phendimetrazine	
	Epinephrine	Phentermine	
	Lisdexamfetamine	Pseudoephedrine	
	Methamphetamine	Tetrahydrozoline	

References:
Breztri Aerosphere Prescribing Information, July 2020, AstraZeneca.
Clinical Pharmacology, 2020 Elsevier/Gold Standard.

70. Budesonide/Glycopyrrolate/Formoterol / Xanthine Derivatives & Steroids _____ _____

Alert Message: Caution should be exercised when Breztri Aerosphere (budesonide/glycopyrrolate/formoterol) is prescribed concurrently with xanthine derivatives or steroids because concomitant administration may potentiate the hypokalemic effect of the formoterol component of the combination agent.

Drugs/Diseases

Util A	Util B		Util C
Budesonide/Glycopyrrolate/Formoterol	Aminophylline	Dexamethasone	
	Dyphylline	Hydrocortisone	
	Theophylline	Methylprednisolone	
	Betamethasone	Prednisolone	
	Budesonide	Prednisone	
	Cortisone		

References:
Breztri Aerosphere Prescribing Information, July 2020, AstraZeneca.
Clinical Pharmacology, 2020 Elsevier/Gold Standard.

71. Budesonide/Glycopyrrolate/Formoterol / Non-Potassium Sparing Diuretics _____ _____

Alert Message: Caution should be exercised when Breztri Aerosphere (budesonide/glycopyrrolate/formoterol), a beta2-agonist containing combo product, is prescribed concurrently with non-potassium-sparing diuretics. The hypokalemia and/or ECG changes that may result from the administration of non-potassium sparing diuretics (such as loop or thiazide diuretics) can be acutely worsened by beta2-agonists, especially when the recommended dose of the beta2-agonist is exceeded.

Drugs/Diseases

Util A	Util B		Util C
Budesonide/Glycopyrrolate/Formoterol	Bumetanide	Indapamide	
	Furosemide	Metolazone	
	Chlorothiazide	Torsemide	
	Chlorthalidone		
	HCTZ		

References:
Breztri Aerosphere Prescribing Information, July 2020, AstraZeneca.
Clinical Pharmacology, 2020 Elsevier/Gold Standard.

72. Budesonide/Glycopyrrolate/Formoterol / Nonselective Beta Blockers _____ _____

Alert Message: Concurrent use of a beta-adrenergic blocker with Breztri Aerosphere (budesonide/glycopyrrolate/formoterol), a beta2-agonist containing combo product, may diminish the pulmonary effect of the beta-agonist component, formoterol. Beta-blockers not only block the therapeutic effects of beta2-agonists but may produce severe bronchospasm in patients with COPD. If concomitant therapy cannot be avoided, consider a cardioselective beta-blocker, but administer with caution.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Budesonide/Glycopyrrolate/Formoterol	Carvedilol	Acebutolol
	Labetalol	Atenolol
	Nadolol	Betaxolol
	Pindolol	Bisoprolol
	Propranolol	Metoprolol
	Sotalol	Nebivolol
	Timolol	

References:
Breztri Aerosphere Prescribing Information, July 2020, AstraZeneca.
Clinical Pharmacology, 2020 Elsevier/Gold Standard.

73. Budesonide/Glycopyrrolate/Formoterol / QT Prolonging Meds _____ _____

Alert Message: Breztri Aerosphere (budesonide/glycopyrrolate/formoterol) should be administered with extreme caution to patients being treated with MAOIs, TCAs, or other drugs known to prolong the QTc interval because the action of the adrenergic agonist, formoterol, on the cardiovascular system may be potentiated by these agents.

Drugs/Diseases

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

References:

Breztri Aerosphere Prescribing Information, July 2020, AstraZeneca.
Clinical Pharmacology, 2020 Elsevier/Gold Standard.

74. Budesonide/Glycopyrrolate/Formoterol / Anticholinergics _____ _____

Alert Message: The concurrent use of Breztri Aerosphere (budesonide/glycopyrrolate/formoterol) with anticholinergic agents should be avoided. The glycopyrrolate component of the combo product is an anticholinergic agent, and concomitant use with other anticholinergics may lead to an increase in anticholinergic adverse effects.

Drugs/Diseases

Util A	Util B		Util C
Budesonide/Glycopyrrolate/Formoterol	Benztropine	Oxybutynin	
	Darifenacin	Propantheline	
	Dicyclomine	Scopolamine	
	Fesoterodine	Solifenacin	
	Flavoxate	Tolterodine	
	Glycopyrrolate	Trihexyphenidyl	
	Hyoscyamine	Trospium	
	Methscopolamine		
	Orphenadrine		

References:
Breztri Aerosphere Prescribing Information, July 2020, AstraZeneca.
Clinical Pharmacology, 2020 Elsevier/Gold Standard.

75. Budesonide/Glycopyrrolate/Formoterol / Other LABAs _____ _____

Alert Message: Breztri Aerosphere (budesonide/glycopyrrolate/formoterol) should not be used in conjunction with other medications containing a LABA, as an overdose may result. Clinically significant cardiovascular effects and fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs.

Drugs/Diseases

Util A	Util B	Util C
Budesonide/Glycopyrrolate/Formoterol	Arformoterol	
	Formoterol	
	Indacaterol	
	Olodaterol	
	Salmeterol	
	Vilanterol	

References:
Breztri Aerosphere Prescribing Information, July 2020, AstraZeneca.
Clinical Pharmacology, 2020 Elsevier/Gold Standard.

76. Budesonide/Glycopyrrolate/Formoterol / Strong CYP3A4 Inhibitors _____ _____

Alert Message: Caution should be exercised when co-administering Breztri Aerosphere (budesonide/glycopyrrolate/formoterol) with long-term ketoconazole or other known strong CYP3A4 inhibitors. The budesonide component of the combination inhalation product is a CYP3A4 substrate, and the concurrent use with a strong CYP3A4 inhibitor can result in increased budesonide plasma concentrations and risk of budesonide-related adverse effects.

Drugs/Diseases

Util A	Util B		Util C
Budesonide/Glycopyrrolate/Formoterol	Clarithromycin	Nelfinavir	
	Cobicistat	Posaconazole	
	Indinavir	Ritonavir	
	Itraconazole	Saquinavir	
	Ketoconazole	Voriconazole	
	Nefazodone		

References:
Breztri Aerosphere Prescribing Information, July 2020, AstraZeneca.
Clinical Pharmacology, 2020 Elsevier/Gold Standard.

77. Budesonide/Glycopyrrolate/Formoterol / Narrow Angle Glaucoma _____ _____

Alert Message: Breztri Aerosphere (budesonide/glycopyrrolate/formoterol) should be used with caution in patients with narrow-angle glaucoma. Glaucoma, increased intraocular pressure, and cataracts have been reported in patients with COPD following the long-term administration of ICS or with the use of inhaled anticholinergics. Prescribers and patients should be alert for signs and symptoms of acute narrow-angle glaucoma. Instruct patients to consult a physician immediately should any signs or symptoms develop. Consider referral to an ophthalmologist in patients who develop ocular symptoms.

Drugs/Diseases

Util A	Util B	Util C
Budesonide/Glycopyrrolate/Formoterol	Narrow Angle Glaucoma	

References:

Breztri Aerosphere Prescribing Information, July 2020, AstraZeneca.
Clinical Pharmacology, 2020 Elsevier/Gold Standard.

78. Budesonide/Glycopyrrolate/Formoterol / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Breztri Aerosphere (budesonide/glycopyrrolate/formoterol). Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effects, which may lead to decreased outcomes and additional healthcare costs.

Drugs/Diseases

Util A	Util B	Util C
Budesonide/Glycopyrrolate/Formoterol		

References:

van Boven JF, Chavannes NH, van der Molen T, et al. Clinical and Economic Impact of Non-adherence in COPD: A Systematic Review. Respir Med. 2015 Jan;108(1):103-113.
Restrepo RD, Alvarez MT, Wittnebel LD, et al., Medication Adherence Issues in Patients Treated for COPD. International Journal of COPD. 2008;3(3):371-384.
Simoni-Wastila L, Wei Y, Qian J, et al., Association of Chronic Obstructive Pulmonary Disease Maintenance Medication Adherence With All-Cause Hospitalization and Spending in a Medicare Population. Am Jrnl Geriatr Pharmacother. 2012 Jun;10(3):201-210.
Lareau SC, Yawn BP. Improving Adherence with Inhaler Therapy in COPD. International Journal COPD. 2010 Nov 24;5:401-406.

79. Fluticasone-Umeclidinium-Vilanterol / Overutilization (Asthma) _____ _____

Alert Message: The manufacturer's recommended dose of Trelegy Ellipta (fluticasone/umeclidinium/vilanterol) for the maintenance treatment of asthma is 1 inhalation (200 mcg fluticasone/62.5mcg umeclidinium/25mcg vilanterol) once daily by orally inhaled route only. Clinically significant cardiovascular effects and fatalities have been reported in association with excessive use of inhaled sympathomimetic-containing drugs.

Drugs/Diseases

Util A	Util B	Util C (Include)
Fluticasone/Umeclidinium/Vilanterol		Asthma

Max Dose: 200mcg fluticasone/62.5 mcg umeclidinium/25mcg vilanterol per day

References:

Trelegy Ellipta Prescribing Information, September 2020, GlaxoSmithKline.
Clinical Pharmacology, 2020 Elsevier/Gold Standard.

Criteria Recommendations *Approved* *Rejected*

80. Osilodrostat / Overuse _____ _____

Alert Message: Isturisa (osilodrostat) may be over-utilized. The recommended maximum dose of osilodrostat is 30 mg twice daily. The maintenance dosage varied between 2 mg and 7 mg twice daily in clinical trials.

Drugs/Diseases

Util A	Util B	Util C
Osilodrostat		

Max Dose: 60 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Isturisa Prescribing Information, March 2020, Recordati Rate Diseases, Inc.

81. Osilodrostat / Therapeutic Appropriateness _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Osilodrostat		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Isturisa Prescribing Information, March 2020, Recordati Rate Diseases, Inc.

82. Osilodrostat / QT Prolongation _____ _____

Alert Message: Isturisa (osilodrostat) is associated with a dose-dependent QT interval prolongation (maximum mean estimated QTcF increase of up to 5.3 ms at 30 mg), which may cause cardiac arrhythmias. Use osilodrostat with caution in patients with risk factors for QT prolongation, (such as congenital long QT syndrome, congestive heart failure, bradyarrhythmias, uncorrected electrolyte abnormalities, and concomitant medications known to prolong the QT interval) and consider more frequent ECG monitoring.

Drugs/Diseases

Util A	Util B	Util C
Osilodrostat	QT Prolongation	
	Heart Failure	
	Bradyarrythmias	
	Hypomagnesemia	
	Hypokalemia	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Isturisa Prescribing Information, March 2020, Recordati Rate Diseases, Inc.

83. Osilodrostat / Strong CYP3A4 Inhibitor _____ _____

Alert Message: Concomitant use of Isturisa (osilodrostat) with a strong CYP3A4 inhibitor (e.g., itraconazole, clarithromycin) may cause an increase in osilodrostat concentrations and may increase the risk of osilodrostat-related adverse reactions. Reduce the dose of osilodrostat by half with concomitant use of a strong CYP3A4 inhibitor.

Drugs/Diseases

Util A	Util B		Util C
Osilodrostat	Clarithromycin	Nelfinavir	
	Cobicistat	Posaconazole	
	Indinavir	Ritonavir	
	Itraconazole	saquinavir	
	Ketoconazole	Voriconazole	
	Nefazodone		

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Isturisa Prescribing Information, March 2020, Recordati Rate Diseases, 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

84. Osilodrostat / Strong CYP3A4 and CYP2B6 Inducers _____ _____

Alert Message: Concomitant use of Isturisa (osilodrostat) with strong CYP3A4 and/or CYP2B6 inducers (e.g., carbamazepine, rifampin, phenobarbital) may cause a decrease in osilodrostat concentration and may reduce the efficacy of osilodrostat. During concomitant use of osilodrostat with strong CYP3A4 and CYP2B6 inducers, monitor cortisol concentration and patient's signs and symptoms. An increase in osilodrostat dosage may be needed.

Drugs/Diseases

Util A	Util B	Util C
Osilodrostat	Apalutamide	
	Carbamazepine	
	Enzalutamide	
	Mitotane	
	Phenobarbital	
	Phenytoin	
	Primidone	
	Rifampin	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Isturisa Prescribing Information, March 2020, Recordati Rate Diseases, 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

85. Osilodrostat / CYP1A2 and CYP2C19 Substrates _____ _____

Alert Message: Isturisa (osilodrostat) should be used with caution when coadministered with CYP1A2 and CYP2C19 substrates with a narrow therapeutic index, such as theophylline, tizanidine, and omeprazole. In drug studies, osilodrostat has shown inhibition potential of CYP1A2 and CYP2C19 isozymes.

Drugs/Diseases

Util A	Util B	Util C
Osilodrostat	Alosetron	
	Duloxetine	
	Omeprazole	
	Ramelteon	
	Tasimelteon	
	Tizanidine	
	Theophylline	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Isturisa Prescribing Information, March 2020, Recordati Rate Diseases, 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

86. Osilodrostat / Therapeutic Appropriateness _____ _____

Alert Message: There are no available data on the presence of Isturisa (osilodrostat) in human or animal milk, the effects on the breastfed infant, or the effects on milk production. Because of the potential for serious adverse reactions (such as adrenal insufficiency) in the breastfed infant, advise patients that breastfeeding is not recommended during treatment with osilodrostat and for one week after the final dose.

Drugs/Diseases

Util A	Util B	Util C
Osilodrostat	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Isturisa Prescribing Information, March 2020, Recordati Rate Diseases, Inc.

87. Osilodrostat / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Isturisa (osilodrostat). 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
Osilodrostat		

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005;353:487-97.
Brown MT, Bussell J, Supmarna D, et al. Medication Adherence: Truth and Consequences. Am J Med Sci. 2016 Apr;351(4):387-399.
Iuga AO, McGuire MJ. Adherence and Health Care Costs. Risk Manag Healthc Policy. 2014 Feb 20;7:35-44.

88. Osilodrostat / QT prolongation _____ _____

Alert Message: Isturisa (osilodrostat) is associated with a dose-dependent QT interval prolongation (maximum mean estimated QTcF increase of up to 5.3 ms at 30 mg), which may cause cardiac arrhythmias. Use osilodrostat with caution in patients with risk factors for QT prolongation, (such as congenital long QT syndrome, congestive heart failure, bradyarrhythmias, uncorrected electrolyte abnormalities, and concomitant medications known to prolong the QT interval) and consider more frequent ECG monitoring.

Drugs/Diseases

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

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Isturisa Prescribing Information, March 2020, Recordati Rate Diseases, Inc.