North Dakota Medicaid
Drug Utilization Review Board
Meeting
September 1st, 2021
Conference Room 210/212

North Dakota Medicaid
DUR Board Meeting Agenda
Conference Room 210/212
North Dakota State Capitol

Click here to join the meeting

(Click on link)

Join by phone: 1 701-328-0950, Conference ID 496 023 327#

September 1, 2021

1:00 pm

1. Administrative items
    - DHS announcements

2. Old business
    - Review and approval of June 2021 meeting minutes
    - Budget update
    - Review top 25 drugs for second quarter of 2021
    - Prior authorization/PDL update
    - Second review of agents for the treatment of heart failure
    - Update to agents for nasal polyps criteria
    - Update to agents for chronic idiopathic urticaria
    - Update to agents for the treatment of uterine fibroids criteria
    - Update to Empaveli criteria
    - Update to Sedative/Hypnotics - Hetlioz criteria

3. New business
    - Review of non-stimulant agents for the treatment of ADHD
    - Review of drug utilization trends for select medication classes
    - Retrospective DUR profile review update
    - Retrospective DUR criteria recommendations
    - Upcoming meeting date/agenda.
        - Next meeting is December 1, 2021
4. Adjourn

Please remember to silence all cellular phones during the meeting.

North Dakota Medicaid Drug Use Review (DUR) Board
Meeting Minutes
June 2, 2021

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

Medicaid Pharmacy Department: Alexi Murphy, Brendan Joyce

Old Business

Chair A. Honeyman called the meeting to order at 1:07 p.m. Chair A. Honeyman asked for a motion to approve the minutes of the March 3, 2021 meeting. M. Quast moved that the minutes be approved, and J. Askvig 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

A. Murphy presented budget updates and the quarterly review of the top 25 drugs based on total cost of claims, the top 25 drugs based on the total number of claims, and the top drug classes based on claims and cost for the 2nd quarter of 2021. Newly added to the top drug/drug class lists was a column showing the difference from the previous quarter, as requested by the Board. A. Murphy presented data to the Board that was reflective of the changes in the number of patients enrolled in ND Medicaid from January 2020 to March 2021, as well as per member spend, which indicated increased costs to the Medicaid program over the past year have been due to the increased number of enrollees during this time. A Murphy also presented utilization data of select medication classes to the Board to illustrate drug utilization trends during this time. Drug classes presented included Antipsychotics, beta agonists, non-steroidal anti-inflammatory drugs, and antidepressants.

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 the addition of multiple combination agents to the "Kit" PA criteria, as well as adding newly approved agents such as Filphilia, Udenyca, Gemtasa, Epclusa 200-50 mg to already existing PA category criteria. All PDL updates are listed in the handouts for the Junea 2021 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 Management of Sickle Cell Anemia

A motion and second was made at the March 2021 DUR Board meeting to place agents for the management of sickle cell anemia on prior authorization. The topic was brought up for a second review. Prior authorization criteria were presented to the Board by T. DeRuiter. During public comment, C. Henderson from Global Blood Therapeutics, Inc. made herself available to the Board for any questions they had. Chair A. Honeyman called for a voice vote to approve the updated criteria, which passed with no audible dissent.

Second Review of Agents for the Treatment of Fabry Disease

A motion and second was made at the March 2021 DUR Board meeting to place agents for the treatment of Fabry disease 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 Imcivree (setmelonotide)
A motion and second was made at the March 2021 DUR Board meeting to place Imcivree (setmelonotide) 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 Bowel Prep Agents
A motion and second was made at a prior DUR Board meeting to place bowel prep agents 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.

Update to the Prior Authorization Criteria for Evrysdi (risdiplam)
At the March 2021 DUR Board meeting, Evrysdi criteria was approved by the Board and the Medicaid Pharmacy Department informed the Board that the criteria would be updated at the following meeting after further discussion with specialists and experts in the treatment of SMA. T. DeRuiter presented the proposed updates to the prior authorization criteria for Evrysdi (risdiplam). The proposed updates included more clearly specifying requirements for confirmation of the patient's diagnosis, requiring the medication be prescribed by or in consultation with a neuromuscular neurologist or neuromuscular physiatrist, clarifying requirements surrounding ventilation/intubation, specifying what medications the patient cannot previously have been treated with, expanding the acceptable baseline motor function tests, requiring neuromuscular clinical information, and consolidating the criteria to apply to all SMA types. J. Whalen from Genentech presented on Evrysdi to the Board and made himself available for questions. A. Murphy proposed that the Board amend the criteria to specify that only patients who have received prior treatment with Zolgensma be excluded from coverage, allowing for coverage for those who had been treated with Spinraza. M. Aaland spoke to concerns they had with allowing coverage for Evrysdi due to concerns with its cost and available trial data. J. Askvig made a motion to amend the criteria to specify that only patients who have received/are receiving Zolgensma should not meet criteria for coverage. A. Werremeyer seconded the motion. Chair A. Honeyman called for a voice vote to approve the amendment, and all but one member voted in the affirmative, with M. Aaland voting against the amendment. A. Werremeyer made a motion to approve the amended criteria, and J. Askvig seconded the motion. Chair A. Honeyman called for a voice vote to approve the updated criteria, which passed with no audible dissent.

Update to the Prior Authorization Criteria for Medications that Cost >$3,000
T. DeRuiter presented proposed updates to the prior authorization criteria for medications that cost >$3,000. The proposed updates included the addition of criteria that requires documentation to confirm serum marker or pathogenic gene variants amenable to treatment, if applicable. There was no public comment. L. Schield made a motion to adopt the updated criteria and P. Woodrow seconded the motion. Chair A. Honeyman called for a voice vote to approve the updated criteria, which passed with no audible dissent.

Update to the Prior Authorization Criteria for Hepatitis C Treatment Agents
T. DeRuiter presented proposed updates to the prior authorization criteria for agents used to treat hepatitis C. The proposed updates included criteria that eliminated additional drug and alcohol testing for patients with a history of drug or alcohol abuse, lowering the medication adherence timeframe to 90 days, and adding medication-specific criteria for select agents in specified scenarios. P. Woodrow inquired as to who covers incarcerated patients, and A. Murphy clarified they are covered by the department of corrections. P. Woodrow made a motion to approve the updated criteria and L. Schield seconded the motion. Chair A. Honeyman called for a voice vote to approve the updated criteria, which passed with no audible dissent.

New Business

Review of Agents Used in the Treatment of Heart Failure

T. DeRuiter presented a review of agents used in the treatment of heart failure to the Board. There was no public comment. A motion was made by L. Schield to manage these medications through prior authorization. The motion was seconded by A. Werremeyer. Prior authorization criteria for these agents will be presented, reviewed, and voted on by the Board at the next meeting.

Utilization Review of Select Medication Classes

A. Murphy presented utilization data to the board regarding the use of opioid analgesics vs. NSAIDs by family medicine practitioners. T. DeRuiter presented data on the utilization of montelukast, comparing utilization by dose per age, comparing utilization before and after new requirements were implemented that required the appropriate, FDA-approved dose of the medication is being used for the patient's age. The data indicated a significant decrease in the number of patient's receiving the incorrect dose of montelukast since the requirements were implemented (7% of patients vs 0.2% of patients after the change). T. DeRuiter also presented utilization data of CGRP inhibitors and migraine abortive therapies over time. The data indicated that there was a sharp decline in triptan claims in January 2020, however triptan claims have been increasing over time to approach December 2019 levels despite utilization of CGRP inhibitors increasing over time. T. DeRuiter also presented data on the utilization of Xifaxan with and without lactulose, comparing utilization before and after new requirements were implemented that require a PA for Xifaxan for diagnoses other than hepatic encephalopathy, and required concomitant use of lactulose for a diagnosis of hepatic encephalopathy. The data indicated an overall decrease in Xifaxan over this period of time.

Retrospective Drug Utilization Review (RDUR) Criteria Recommendations

T. DeRuiter reviewed the RDUR criteria that were selected for review of each month of the last quarter. Presented data included number of profiles reviewed, number of cases identified for intervention, and the number of letters sent, as well as an overview of what RDUR interventions were identified as most prevalent for each monthly cycle.

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. A. Werremeyer moved to approve the new criteria and M. Quast seconded the motion. Chair A. Honeyman called for a voice vote to approve the new criteria, which passed with seven members voting to approve and one voting against approval.

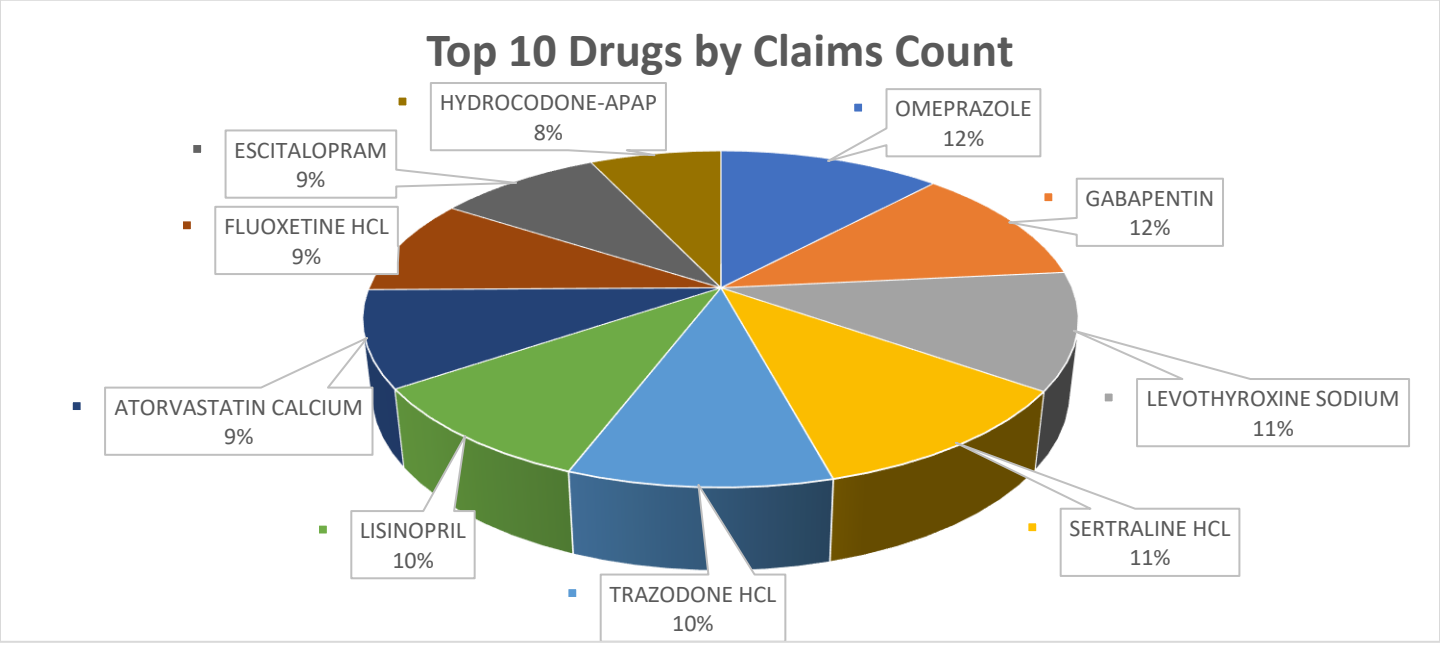
Adjournment and Upcoming Meeting Date

Chair A. Honeyman adjourned the meeting at 3:20 pm. The next DUR Board meeting will be held September 1, 2021 at 1:00 pm at the state capitol building.

Top 25 Drugs Based on Number of Claims from 04/01/2021 – 06/30/2021

Drug	Claims	Patients	Claims Cost	Cost / Claim	% Total Claims	Dif.
OMEPRAZOLE	4,890	2,384	63,339.20	$12.95	1.94%	NC
GABAPENTIN	4,656	1,929	69,416.58	$14.91	1.84%	NC
SERTRALINE HCL	4,368	2,297	59,576.91	$13.64	1.73%	↑1
LEVOTHYROXINE SODIUM	4,319	1,821	80,418.96	$18.62	1.71%	↓1
TRAZODONE HCL	3,964	1,879	54,451.82	$13.74	1.57%	NC
LISINOPRIL	3,810	2,037	48,744.55	$12.79	1.51%	NC
ATORVASTATIN CALCIUM	3,731	1,933	52,835.04	$14.16	1.48%	NC
ESCITALOPRAM OXALATE	3,683	1,994	49,470.02	$13.43	1.46%	↑1
FLUOXETINE HCL	3,671	1,900	50,729.89	$13.82	1.45%	↓1
HYDROCODONE-APAP	3,099	1,941	46,776.00	$15.09	1.23%	NC
BUPROPION XL	2,814	1,373	49,468.63	$17.58	1.11%	NC
PANTOPRAZOLE SODIUM	2,800	1,321	37,557.27	$13.41	1.11%	↑2
METFORMIN HCL	2,676	1,383	34,857.75	$13.03	1.06%	NC
DULOXETINE HCL	2,640	1,247	41,610.39	$15.76	1.05%	↓2
MONTELUKAST SODIUM	2,597	1,410	36,487.53	$14.05	1.03%	↑1
VYVANSE	2,469	1,007	638,134.01	$258.46	0.98%	↓1
LAMOTRIGINE	2,354	912	32,917.18	$13.98	0.93%	↑5
CYCLOBENZAPRINE HCL	2,342	1,434	27,091.45	$11.57	0.93%	↓1
BUPRENORPHINE-NALOXONE	2,324	520	106,133.46	$45.67	0.92%	↓1
PROAIR HFA	2,315	2,295	170,233.73	$73.54	0.92%	NC
CLONIDINE HCL	2,264	1,043	28,590.37	$12.63	0.90%	↓2
AMLODIPINE BESYLATE	2,258	1,221	28,188.30	$12.48	0.89%	↑2
AMOXICILLIN	2,230	2,044	30,562.77	$13.71	0.88%	↑6
PREDNISONE	2,198	1,693	27,572.69	$12.54	0.87%	↑8
CLONAZEPAM	2,185	944	29,755.05	$13.62	0.87%	NC

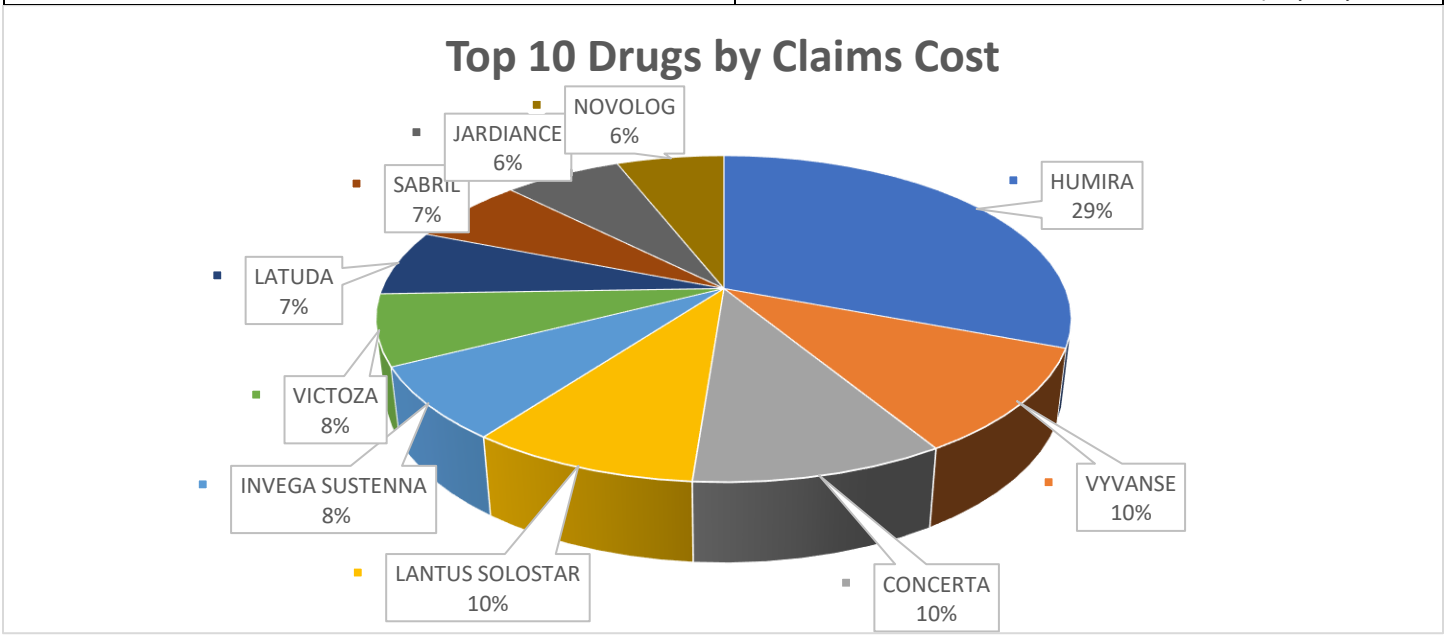
Total Claims	**252,543**



Top 25 Drugs Based on Total Claims Cost from 04/01/2021 – 06/30/2021

Drug	Claims Cost	Claims	Patients	Cost /Claim	% Total Cost	Dif.
HUMIRA PEN	1,757,824.41	255	104	$6,893.43	6.32%	NC
VYVANSE	638,134.01	2,469	1,007	$258.46	2.29%	NC
CONCERTA	611,454.44	1,775	749	$344.48	2.20%	NC
LANTUS SOLOSTAR	598,676.01	1,255	736	$477.03	2.15%	NC
INVEGA SUSTENNA	462,519.05	195	78	$2,371.89	1.66%	↑1
VICTOZA 3-PAK	461,745.23	508	249	$908.95	1.66%	↑1
LATUDA	407,868.70	506	199	$806.06	1.47%	↑2
SABRIL	400,037.01	18	6	$22,224.28	1.44%	↑13
JARDIANCE	391,268.20	822	359	$476.00	1.41%	↑3
NOVOLOG FLEXPEN	381,826.86	538	333	$709.72	1.37%	↓5
STELARA	350,392.50	15	12	$23,359.50	1.26%	↓1
NORDITROPIN FLEXPRO	344,594.05	84	39	$4,102.31	1.24%	↓4
ADVAIR DISKUS	326,917.72	888	487	$368.15	1.17%	↑2
SYMBICORT	310,825.76	929	524	$334.58	1.12%	NC
TRIKAFTA	310,440.15	13	5	$23,880.01	1.12%	↑1
TALTZ AUTOINJECTOR	305,205.26	41	18	$7,444.03	1.10%	↑4
LEVEMIR FLEXTOUCH	300,775.57	552	305	$544.88	1.08%	NC
COSENTYX PEN (2 PENS)	299,359.48	46	18	$6,507.81	1.08%	↓7
ADDERALL XR	294,795.33	1,699	696	$173.51	1.06%	NC
XIFAXAN	266,911.18	109	53	$2,448.73	0.96%	↑5
GILENYA	265,935.82	32	13	$8,310.49	0.96%	↑8
ELIQUIS	262,755.46	606	268	$433.59	0.94%	↑2
BIKTARVY	260,719.72	138	64	$1,889.27	0.94%	↓5
ENBREL SURECLICK	250,295.69	43	20	$5,820.83	0.90%	↓11
STRATTERA	243,006.74	605	290	$401.66	0.87%	↓2

Total Claims Cost	**$27,832,755.31**



Top 15 Therapeutic Classes Based on Number of Claims from 04/01/2021 – 06/30/2021

Therapeutic Class Description	Claims	Patients	Claims Cost	Cost/Claim	% Total Claims	Dif.
ANTIDEPRESSANTS	29,465	11,497	$611,617.88	$20.76	11.67%	NC
ANTICONVULSANTS, MISC	13,623	4,631	$1,138,926.72	$83.60	5.39%	NC
ANTIPSYCHOTIC AGENTS	8,985	3,361	$2,008,140.17	$223.50	3.56%	NC
PROTON-PUMP INHIBITORS	8,125	3,856	$150,753.39	$18.55	3.22%	NC
OPIATE AGONISTS	7,469	3,789	$129,782.43	$17.38	2.96%	NC
SEDATIVE/HYPNOTICS	6,685	3,279	$144,632.27	$21.64	2.65%	NC
NSAIDs	6,560	4,112	$96,182.39	$14.66	2.60%	NC
STATINS	6,257	3,234	$89,593.82	$14.32	2.48%	NC
BETA BLOCKERS	5,684	2,851	$104,988.87	$18.47	2.25%	NC
AMPHETAMINES	5,395	2,184	$976,236.20	$180.95	2.14%	NC
ACE INHIBITORS	4,824	2,578	$68,343.20	$14.17	1.91%	↑1
NON-AMPHETAMINE STIMULANTS	4,729	1,755	$908,366.16	$192.08	1.87%	↓1
THYROID AGENTS	4,614	1,898	$90,751.47	$19.67	1.83%	NC
BIGUANIDES	4,128	2,157	$56,177.31	$13.61	1.63%	NC
PENICILLIN ANTIBIOTICS	4,101	3,618	$64,616.96	$15.76	1.62%	↑2

Top 15 Therapeutic Classes Based on Claims Cost from 04/01/2021 – 06/30/2021

Therapeutic Class Description	Claims Cost	Claims	Patients	Cost/Claim	% Total Cost	Dif.
DMARDS	$2,810,667.35	503	193	$5,587.81	10.10%	NC
ANTIPSYCHOTIC AGENTS	$2,008,140.17	8,985	3,361	$223.50	7.22%	NC
INSULINS	$1,892,628.00	3,716	1,362	$509.32	6.80%	NC
SKIN & MUCOUS MEMBRANE AGENTS, MISC.	$1,505,887.29	610	382	$2,468.67	5.41%	NC
ANTICONVULSANTS, MISCELLANEOUS	$1,138,926.72	13,623	4,631	$83.60	4.09%	↑1
AMPHETAMINES	$976,236.20	5,395	2,184	$180.95	3.51%	↑2
INHALED CORTICOSTEROIDS	$955,172.15	3,278	1,896	$291.39	3.43%	NC
ANTINEOPLASTIC AGENTS	$954,285.77	584	227	$1,634.05	3.43%	↑2
NON-AMPHETAMINE STIMULANTS	$908,366.16	4,729	1,755	$192.08	3.26%	NC
ANTIRETROVIRALS	$861,557.58	686	243	$1,255.91	3.10%	↓5
INCRETIN MIMETICS	$786,657.60	1,019	478	$771.99	2.83%	NC
ANTIDEPRESSANTS	$611,617.88	29,465	11,497	$20.76	2.20%	NC
IMMUNOMODULATORY AGENTS	$610,429.45	82	33	$7,444.26	2.19%	NC
SGLT2 INHIBITORS	$525,953.41	1,103	487	$476.84	1.89%	NC
ANTIMUSCARINICS/ANTISPASMODICS	$408,588.39	1,803	901	$226.62	1.47%	NC

PDL Update

Drug Name	PA status	Class
Ingrezza 60mg	PA	Tardive Dyskinesia
Koselugo	PA	Over 3000
Exservan	PA	Non-Solid Dosage Forms
Clobetex	PA	Kit
Empaveli	PA	Over 3000
Doxycycline ER 80mg	PA	Acne
Atelvia	PA	Osteoporosis
Varubi	PA	Chemo Induced Nausea and Vomiting
Tetracycline	remove PA	Acne
Fluorouracil topical solution	remove PA	Actinic Keratosis
Enstilar foam	remove PA	Antipsoriatics - Topical
Sorilux foam	remove PA	Antipsoriatics - Topical
Testopel	remove PA	Androgens
teriparatide	remove PA	Osteoporosis
Peg 3350 - Electrolyte 420 G (Nulytely/Gavilte-N)	remove PA	Bowel Prep agents
Clenpiq	remove PA	Bowel Prep agents
Relistor vial and syringe	remove PA	Constipation

Heart Failure

Electronic Diagnosis Verification

- Corlanor, Entresto, and Verquvo require an FDA-approved indication for use.

Product Specific Criteria:

- **Verquvo:**
  - The member must meet FDA-approved age for use.
  - The member must have left ventricular ejection fraction (LVEF) < 45%
  - Documentation of a recent hospitalization or need for IV diuretics (within the past 6 months) must be submitted with request
  - The member is receiving concurrent Entresto, a beta-blocker, a SGLT-2 Inhibitor, and a mineralocorticoid receptor antagonist.
- **Corlanor:**
  - The member must meet FDA-approved age for use.
  - The member must have a resting HR ≥ 70 beats per minute on maximally tolerated or target beta blocker dose in sinus rhythm

AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
ACE (angiotensin-converting enzyme) inhibitors - *all oral agents preferred*	
ARBs (angiotensin receptor blockers) - *all oral agents preferred*	
Beta blockers - *all oral agents preferred*	
CORLANOR (ivabradine)	
ENTRESTO (sacubitril/valsartan)	
eplerenone	
FARXIGA (dapagliflozin)	
spironolactone	
VERQUVO (vericiguat) PA***	

Nasal polyps

General Prior Authorization Form

Category Criteria (Initial): *Approval Duration = 3 months*

- The member must meet label recommendations for indication and age.
- Must be prescribed by, or in consult with, an ear/nose/throat specialist or allergist/immunologist.
- The member must have had a 12-week trial of intranasal or oral corticosteroid
- The member must have bilateral polyps confirmed by sinus CT, sinus MRI, or nasal endoscopy
- The member must have documentation of at least two of the following symptoms:
  - Nasal blockade/obstruction/congestion or nasal discharge (anterior/posterior nasal drip)
  - Facial pain/pressure
  - Reduction or loss of smell

Category Criteria (Renewal): *Approval Duration = 12 months*

- The prescriber must provide documentation showing that the member has achieved a significant reduction in nasal polyp size and symptoms since treatment initiation
- The member must be receiving intranasal steroids

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
DUPIXENT (dupilumab)	
XOLAIR (omalizumab)	

Chronic Idiopathic urticaria

General Prior Authorization Form

Category Criteria (Initial): *Approval Duration = 3 months*

- The member must meet label recommendations for indication and age.
- Must be prescribed by, or in consult with, an allergist/immunologist.
- The member must have had a 30-day trial of a type 1 (H1) antihistamine at maximally tolerated dose either non-sedating (e.g. cetirizine, fexofenadine, loratadine, desloratadine, or levocetirizine) or sedating (e.g. diphenhydramine, chlorpheniramine, cyproheptadine) in addition to one of the following:
  - Leukotriene receptor antagonist (e.g. Montelukast, zafirlukast, zileuton)
  - Histamine H2-receptor (e.g. ranitidine, famotidine, nizatidine, cimetidine)

Category Criteria (Renewal): *Approval Duration = 12 months*

- The prescriber must provide documentation showing that the member has achieved a clinical benefit since treatment initiation.

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
XOLAIR (omalizumab)	

Uterine Fibroids Criteria

Electronic Diagnosis Verification

- The patient must have an FDA approved indication

Electronic Age Verification

- The patient must be 18 years of age or older

Prior Authorization Form

General Prior Authorization Form

Category Criteria:

- **Initial Criteria:** *Approval Duration = 12 months*
  - The patient must have an FDA-approved indication for use (meets label recommendations for diagnosis and age)
  - The patient must not be pregnant
  - The provider must attest that the patient does not have any contraindications to treatment with the requested product
- The patient must have failed the following trials (A and B), as evidenced by paid claims or pharmacy printouts:
  - A. A 3-menstual cycle trial of mefenamic acid or meclofenamate, celecoxib, ibuprofen 1800mg/day or equivalent high dose NSAID
  - B. A 3-menstual cycle trial of an oral estrogen-progestin or progestin contraceptives
- **Renewal Criteria:** *Approval Duration = 12 months*
  - The patient must not have received ≥24 months of the requested product, as evidenced by paid claims or pharmacy printouts
  - The provider must attest that the patient does not have any contraindications to treatment with the requested product
  - The patient must have experienced and maintained clinical benefit since starting treatment with the 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)
ORIAHNN (Elagolix, Estradiol, and Norethindrone acetate)	
MYFEMBREE (Relugolix, Estradiol, and Norethindrone acetate)	

Empaveli (pegcetacoplan)

General Prior Authorization Form

Initial Criteria: *Approval Duration = 6 months*

- The patient must be 18 years of age or older
- Must be prescribed by or in consultation with a hematologist, oncologist, or immunology specialist
- Must have a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH) laboratory confirmed by one of the following:
    a. flow cytometry
    b. LDH level of 1.5 times the upper limit of normal
    c. bone marrow aspirate and biopsy
- Must have documented full course of meningococcal, pneumococcal, and Hib vaccines or a test for antibodies against encapsulated bacteria at least 2 weeks before starting treatment
- One of the following criteria must be met (A or B):
    A. Patient is transfusion dependent (Hb ≤ 7 g/dL or Hb ≤ 9 g/dL and member is experiencing symptoms of anemia)
    B. Patient has symptoms of thromboembolic complications (abdominal pain, shortness of breath, chest pain, end-organ damage)

Renewal Criteria: *Approval Duration = 12 months*

- The patient must have experienced an improvement, such as decreased fatigue, decrease in transfusions, increase in Hb levels, or normalization of LDH levels.

AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
EMPAVELI (pegcetacoplan)	

health information designs

Empaveli

Prior Authorization Form

Fax Completed Form to:

855-207-0250

For questions regarding this

Prior Authorization Vendor for ND

ND Medicaid requires that patients receiving a prescription for Empaveli (pegcetacoplan) to meet specific clinical criteria for coverage. Criteria for coverage for Empaveli 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:** □ PAROXYSMAL NOCTURNAL HEMOGLOBINURIA (PNH) □ OTHER:

Qualifications for coverage:	
Does the patient have transfusion dependent anemia and is currently experiencing symptoms of anemia?	□ YES □ NO
Does the patient have symptoms of thromboembolic complications (abdominal pain, shortness of breath, chest pain, end-organ damage)?	□ YES □ NO
Has the patient received a full course of meningococcal, pneumococcal, and Hib vaccines OR a test for antibodies against encapsulated bacteria, at least 2 weeks before starting treatment?	□ YES □ NO

Please confirm that all the following is attached to the request, along with any other relevant documentation:

□ Documentation of lab results confirming a diagnosis of PNH (i.e. flow cytometry, LDH level of 1.5 times the upper limit of normal, or bone marrow aspirate and biopsy).

□ (Renewal ONLY): Documentation supporting that the patient has experienced and/or maintained a clinical benefit since starting treatment with Empaveli, as evidenced by medical documentation (e.g. reduced fatigue, decrease in transfusions, increase in Hb levels, or normalization of LDH).

□ *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 #

Non-24 Hour Sleep-Wake Disorder

Group Criteria:

- **Initial Criteria:** *Approval Duration = 6 months*
  - The member must meet criteria as outlined in prescribing information (PI) including recommendations for diagnosis and age.
  - The prescriber is a specialist, or the prescriber has consulted with a specialist in sleep disorders
  - The member must have had a 30-day trial of Rozerem (ramelteon), as evidenced by paid claims or pharmacy printouts.
  - Documentation must be attached to confirm one of the following:
    - Member must be unable to perceive light in either eye
    - Sighted members must confirm diagnosis by self-reported sleep diaries or actigraphy for at least 14 days demonstrating a gradual daily drift (typically later) in rest-activity patterns not better explained by sleep hygiene, substance or medication use, or other neurological or mental disorders.
- **Renewal Criteria**: *Approval Duration = 12 months*
  - The member must have experienced and maintained clinical benefit since starting treatment with the requested medication, as evidenced by medical documentation (e.g. chart notes) attached to the request (subject to clinical review).

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
ROZEREM (ramelteon) – *Brand Preferred*	HETLIOZ (tasimelteon)
	ramelteon

REVIEW OF NON-STIMULANT ADHD PRODUCTS

Attention-deficit hyperactivity disorder is usually treated with cognitive behavioral therapy (CBT), stimulants, and/or nonstimulants. Nonstimulants are not typically used first-line; for use of nonstimulant medication is suggested in patients who are intolerant of or lacked a response to stimulants. Nonstimulants may be used as monotherapy or as adjunctive with concurrent stimulant therapy.

General Dosing and FDA Indications

Drug Name	Mechanism of Action	Dosing	Indication
Clonidine (off-label)	Alpha2-Adrenergic Agonist	**≤45 kg:** 0.05mg/day; sequentially increase to 4 times daily **>45 kg:** 0.1mg/day; sequentially increase to 4 times daily	ADHD, Hypertension (adults)
Clonidine ER	Alpha2-Adrenergic Agonist	0.1mg – 0.2mg twice daily after titration	ADHD monotherapy or as adjunctive therapy
Guanfacine (off-label)	Alpha2-Adrenergic Agonist	**≤45 kg:** 0.5mg/day; may titrate up to 4 times daily **>45 kg:** 1mg/day; may titrate up to 4 times daily	ADHD, Hypertension (adults)
Guanfacine ER	Alpha2-Adrenergic Agonist	**Weight based:** 1mg once daily up to 7mg per day	ADHD
viloxazine	SNRI	**6-11 years old:** 100mg – 400mg per day **≥12 and ≤17 years old:** 200mg – 400mg per day	ADHD
Atomoxetine	SNRI	<u>Adults</u> **Target dose:** ~80mg per day **Dose adjustments based on CYP2D6 poor metabolizer:** Initiate at 40mg/day and increase to 80mg/day if symptoms fail to improve after 4 weeks at initial dose <u>Children 6-17</u> **>70 kg:** Dosed as adults **≤70 kg:** Target dose: 1.2mg/kg/day **Dose adjustments based on CYP2D6 poor metabolizer:** Initiate at 0.5mg/kg/day and increase to 1.2mg/kg/day if symptoms fail to improve after 4 weeks at initial dose	ADHD

Approval Status and Special Designations

Drug Name	Special Designation	Approval Status
Clonidine (off-label)	Children ≥6 years of age and adolescents	Approved 09/03/1974
Kapvay (clonidine ER) **Clonidine ER**	Children ≥6 years of age and adolescents	Approved 09/03/1974
Guanfacine (off-label)	Children ≥6 years of age and adolescents	Approved 10/27/1986
Intuniv (guanfacine ER) **Guanfacine ER**	Children ≥6 years of age and adolescents	Approved 10/27/1986
Qelbree (viloxazine)	Children ≥6 years of age and adolescents	Approved 04/02/2021
Strattera (atomoxetine) **Atomoxetine**	Children 6 years of age and adolescents; **adults**	Approved 11/26/2002

Place in Therapy/Guidelines

Childhood ADHD

Preschool-aged children: age 4 years to the sixth birthday

- First line: parent training in behavior management (PTBM) and/or behavioral classroom interventions. PTBM evidence is strong in the preschool aged population.
- Should these non-pharmacologic measures not work, methylphenidate may be trialed. Other stimulant and nonstimulant medications in children < 6 years of age has not been adequately studied.

Elementary and middle school–aged children: age 6 years to the 12th birthday

- First line: FDA approved medication for ADHD (methylphenidate or amphetamine stimulants) in conjunction with behavioral and classroom interventions.
- The evidence is strongest for stimulant medications in this age group, however, there is sufficient data for atomoxetine, extended-release guanfacine, and extended-release clonidine. (Strength of evidence follows in that order)
- Nonstimulants are suggested in patients who are intolerant of or lacked a response to stimulants; an adequate stimulant trial of at least 6 weeks is suggested prior to initiating nonstimulants.

Adolescents: age 12 years to the 18th birthday

- First line: FDA approved medication for ADHD (methylphenidate or amphetamine stimulants).
- Behavioral interventions and school accommodations are encouraged.
- Nonstimulants are suggested in patients who are intolerant of or lacked a response to stimulants; an adequate stimulant trial of at least 6 weeks is suggested prior to initiating nonstimulants.

Adult ADHD

- First line: typically medications (methylphenidate or amphetamine stimulants).
- Amphetamine products are typically recommended first before methylphenidate or non-stimulant products.
- Alternative, nonpharmacologic treatment options include cognitive behavioral therapy (CBT), although there have been no trials evaluating their comparative efficacy to pharmacotherapy.
- Nonstimulants (Strattera or atomoxetine) are suggested in patients who are intolerant of or lacked a response to stimulants; an adequate stimulant trial of at least 6 weeks is suggested prior to initiating nonstimulants.

Wolraich ML, Hagan JF Jr, Allan C, et al. Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents [published correction appears in Pediatrics. 2020 Mar;145(3):]. Pediatrics. 2019;144(4):e20192528. doi:10.1542/peds.2019-2528

Therapeutically Important Adverse Effects/Advantages

Clonidine, Clonidine ER:

- Withdrawal: Abrupt discontinuation may result in symptoms of withdrawal (eg. agitation, headache, tachycardia, nausea, tightness in chest, anxiety, tremor, rebound hypertension)
- Decreased BP and HR
- Clonidine may be an optimal selection for patients with tics or Tourette syndrome comorbidity
- Typically utilized in patients who have not had an adequate response to stimulants or atomoxetine

Guanfacine, Guanfacine ER, Intuniv (guanfacine ER):

- Rebound hypertension and increases in heart rate, in some cases leading to hypertensive encephalopathy, has been reported with abrupt discontinuation of therapy
- Decreased BP and HR
- May be an optimal selection for patients with tics or Tourette syndrome comorbidity or if stimulant diversion or misuse is a concern
- Typically utilized in patients who have not had an adequate response to stimulants or atomoxetine

Qelbree (viloxazine):

- BBW: Suicidal thoughts and behaviors
- Do not administer Qelbree during therapy with or within 2 weeks of discontinuing an MAOI
- Can be opened and sprinkled over applesauce or other soft foods, unlike atomoxetine
- May be more appropriate if there are concerns about illicit drug abuse

Strattera (atomoxetine), atomoxetine:

- BBW: Increased risk of suicidal ideation in children and adolescents
- Do not administer Strattera/atomoxetine during therapy with or within 2 weeks of discontinuing an MAOI
- Increased HR and BP
- Indicated for adult use also
- May be more appropriate if there are concerns about illicit drug abuse

Cost

Drug	Strength	Package Size	WAC Pkg Price	Cost Per Day*	Cost Per Month*	Cost Per Year*
Clonidine	0.1mg – 0.3mg	30 - 1,000 tablets	$2 - 77	$0.06	$1.80	$21.60
Clonidine ER	0.1mg	60 tablets	$19.80-199.80	$1.32	$39.60	$475.20
Kapvay (clonidine ER)	0.1mg	60 tablets	$484.80	$32.32	$969.60	$11,635.20
Guanfacine	1 mg – 2mg	30 – 100 tablets	$14.50 - 112	$0.14 – 0.58	$4.20 – 17.40	$50.40 – 208.80
Guanfacine ER	1mg, 2mg, 3mg, 4mg	100 tablets	$41.90-349	$0.42 – 0.84	$12.60 – 25.14	$151.20 – 301.68
Intuniv (guanfacine ER)	1mg, 2mg, 3mg, 4mg	100 tablets	$971	$9.71 – 19.42	$291.30 – 582.60	$3,495.60 – 6,991.20
Strattera (atomoxetine)	10mg, 18mg, 25mg, 40mg, 60mg, 80mg (target dose), 100mg	30 tablets	$395.40 – 463.50	$15.45 (target dose)	$463.50 (target dose)	$5,562 (target dose)
Atomoxetine	10mg, 18mg, 25mg, 40mg, 60mg, 80mg (target dose), 100mg	30 tablets	$54.90 - 208.35	$2.37 (target dose)	$70.80 (target dose)	$849.60 (target dose)
Qelbree (viloxazine)	100mg, 150mg, 200mg	30 tablets	$298.98	$9.97 – 19.93	$299.10 - 597.96	$3,589.20 -7,175.52

*Based on lowest per unit WAC cost

Current Utilization

ND Medicaid Utilization (07/01/20 – 06/30/21)		
Label Name	**Rx Number**	**Total Reimbursement Amt**
Clonidine (IR and ER)	9809	$222,636.37
Guanfacine (IR and ER)	8243	$186,533.76
Qelbree (viloxazine)	0	0
Strattera (atomoxetine)	1790	$723,324.47
atomoxetine	2914	$780,968.84

Qelbree Clinical Trials:

The efficacy of Qelbree in the treatment of ADHD in pediatric patients 6 to 17 years of age was evaluated in three short-term, randomized, placebo-controlled monotherapy trials (Studies 1, 2, and 3):

Study 1 (NCT03247530) was a multicenter, randomized, double-blind, three-arm placebo-controlled, parallel group monotherapy trial in patients 6 to 11 years of age with ADHD.

- Total duration of treatment was 6 weeks, including a 1-week titration period (starting at 100 mg once daily) and 5-week maintenance phase. Patients were randomized to receive 100 mg, 200 mg, or placebo, given once daily as a single dose.
- The primary endpoint was the change from baseline to the end of study on the total score on the ADHD Rating Scale (ADHD-RS-5 The Clinical Global Impression-Improvement (CGI-I) score at the end of the study was a secondary endpoint.
- A total of 477 patients were randomized in Study 1; 399 completed the study, and 78 discontinued.
- The change from baseline (reduction) in ADHD-RS-5 total score was statistically significantly greater in patients treated with Qelbree 100 mg or with Qelbree 200 mg than in patients on placebo. Compared with patients on placebo, a statistically significantly greater reduction (improvement) in CGI-I score at the end of the study was observed both in patients treated with Qelbree 100 mg and in patients treated with Qelbree 200 mg.

Study 2 (NCT03247543) was a multicenter, randomized, double-blind, three-arm, placebo-controlled, parallel-group monotherapy trial in patients 6 to 11 years of age with ADHD.

- Total duration of treatment was 8 weeks, including a 3-week titration period (starting at 100 mg once daily), and a 5-week maintenance phase. Patients were randomized to receive Qelbree 200 mg, Qelbree 400 mg, or placebo, given once daily as a single dose.
- The primary endpoint was the change from baseline to the end of study on the total score on the ADHD Rating Scale (ADHD-RS-5). The Clinical Global Impression-Improvement (CGI-I) score at the end of the study was a secondary endpoint.
- A total of 313 patients were randomized in Study 2; 251 completed the study, and 62 discontinued.
- The change from baseline (reduction) in ADHD-RS-5 total score was statistically significantly greater in patients treated with Qelbree 200 mg or with Qelbree 400 mg than in patients on placebo. Compared with patients on placebo, a statistically significantly greater reduction (improvement) in CGI-I score at the end of the study was observed both in patients treated with Qelbree 200 mg and in patients treated with Qelbree 400 mg.

Study 3 (NCT03247517) was a multicenter, randomized, double-blind, three-arm, placebo-controlled, parallel-group monotherapy trial in patients 12 to 17 years of age with ADHD.

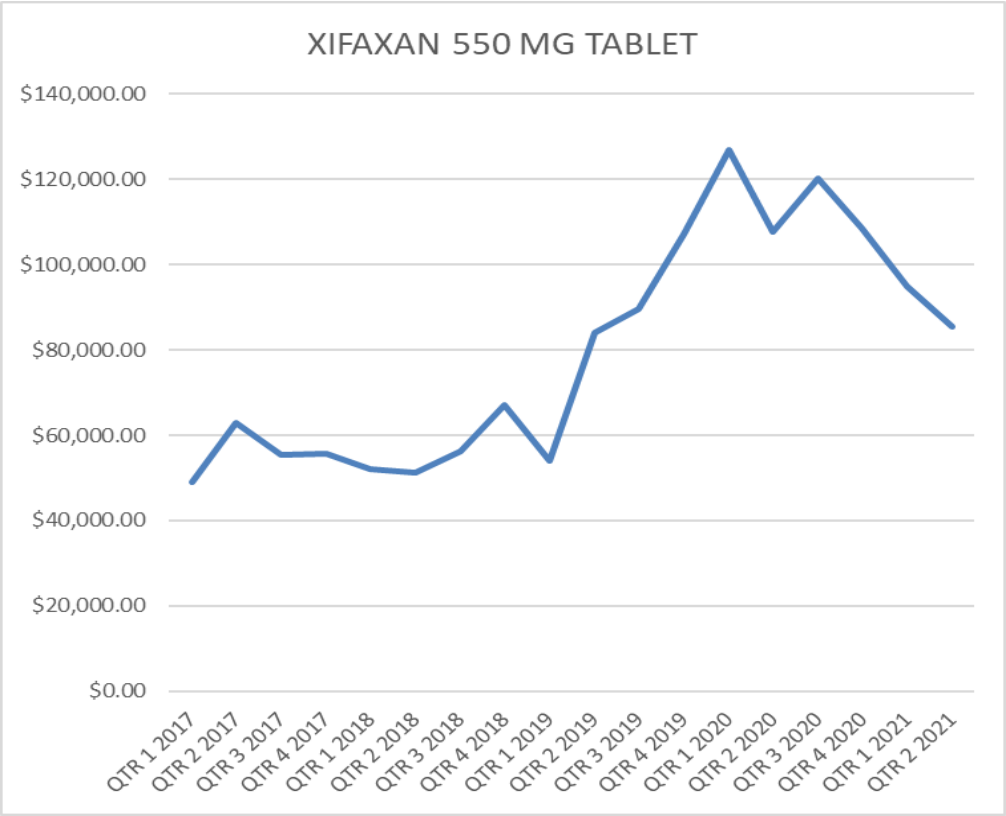
- Total duration of treatment was 6 weeks, including 1-week titration period (starting at 200mg once daily) and a 5-week maintenance phase. Patients were randomized to receive Qelbree 200 mg, Qelbree 400 mg, or placebo, given once daily as a single dose.
- The primary endpoint was the change from baseline to the end of study on the total score on the ADHD Rating Scale (ADHD-RS-5). The Clinical Global Impression-Improvement (CGI-I) score at the end of the study was a secondary endpoint.
- A total of 310 patients were randomized in Study 3; 266 completed and 44 discontinued.
- The change from baseline (reduction) in ADHD-RS-5 total score was statistically significantly greater in patients treated with Qelbree 200 mg or with Qelbree 400 mg than in patients on placebo. Compared with patients on placebo, a statistically significantly greater reduction (improvement) in CGI-I score at the end of the study was observed both in patients treated with Qelbree 200 mg and in patients treated with Qelbree 400 mg.

References

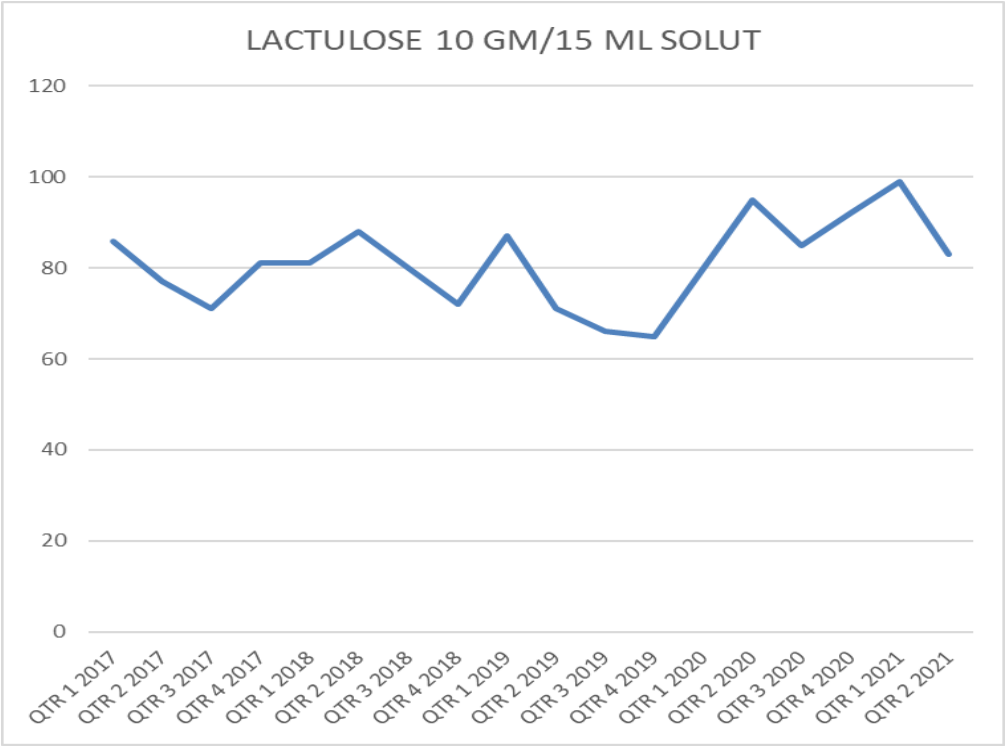
1. Wolraich ML, Hagan JF Jr, Allan C, et al. Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents [published correction appears in Pediatrics. 2020 Mar;145(3):]. Pediatrics. 2019;144(4):e20192528. doi:10.1542/peds.2019-2528
2. Facts & Comparisons eAnswers. Available at http://online.factsandcomparisons.com. Accessed on July 12. 2021.
3. Kapvay (clonidine) [prescribing information]. Dublin 9, Ireland: Concordia Pharmaceuticals; February 2020.
4. Qelbree (viloxazine) [prescribing information]. Rockville, MD: Supernus Pharmaceuticals Inc; April 2021.
5. Intuniv (guanfacine) [prescribing information]. Lexington, MA: Takeda Pharmaceuticals America, Inc; August 2020.
6. Strattera (atomoxetine) [prescribing information]. Indianapolis, IN: Lilly USA LLC; February 2020.

Claims before and after Xifaxan Step Care was initiated

- **Xifaxan reimbursement has decreased from Qtr 1 2020 by approximately $40,000 per quarter**

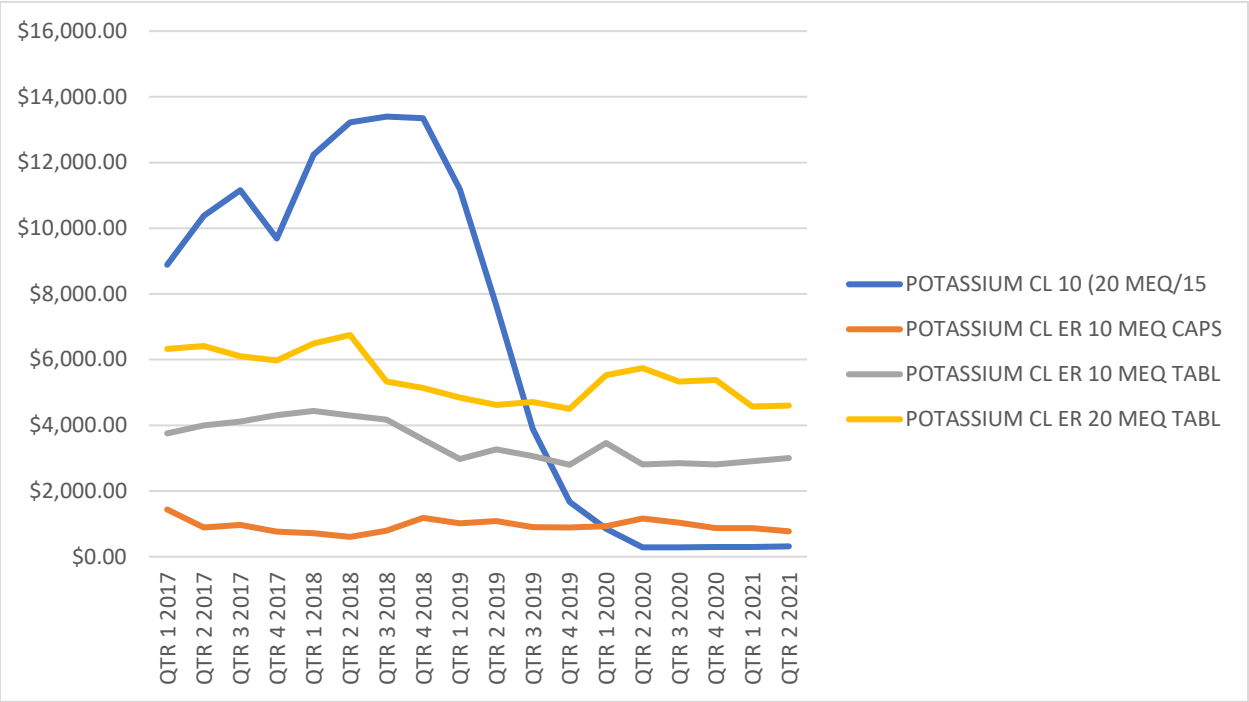


- **At the same time, the number of members receiving Lactulose has increased since Qtr1 2020**

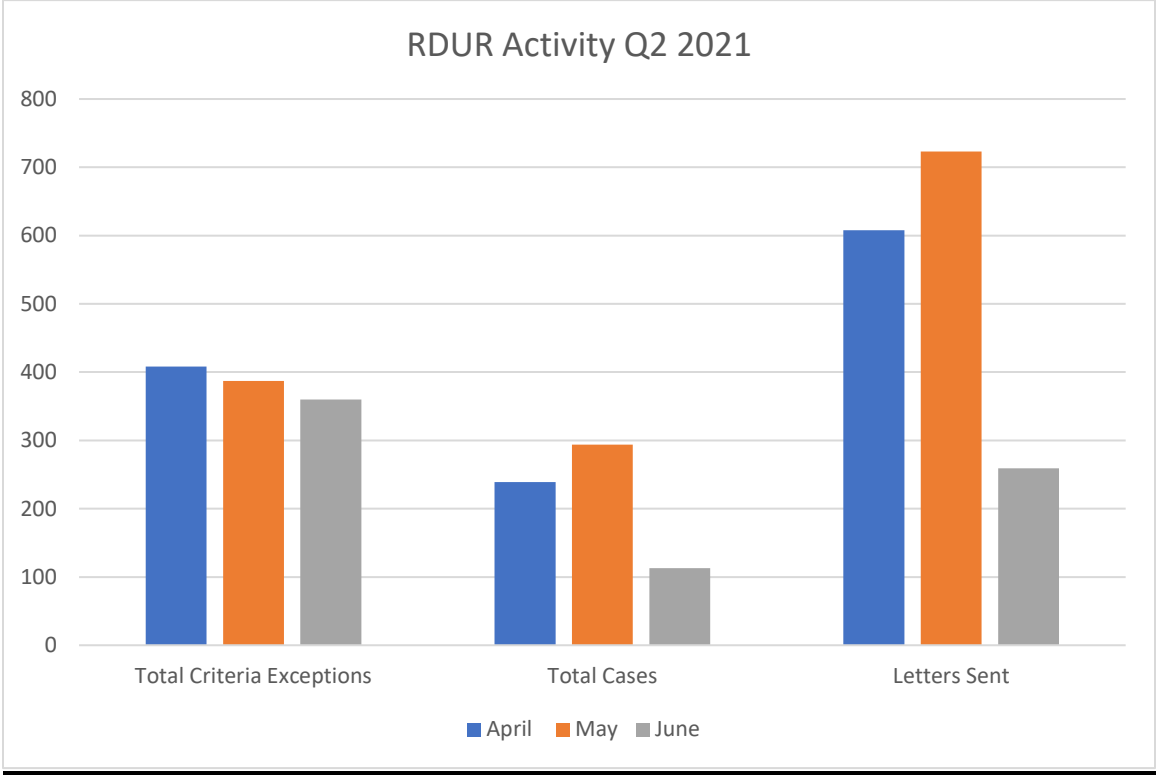


Effect of Potassium utilization management initiated

- **Liquid potassium – swallowing difficulty verification and quantity limits implemented**



RDUR Activity Overview: Q2 2021



April Cases by Type of Criteria

Criteria Description	# of Cases	% of Cases
STIMULANT + HTN	106	44.35%
DIURETIC + HYPERURICEMIA	24	10.04%
ANTIPSYCHOTICS + PARKINSON'S	9	3.77%
HEPATIC IMPAIRMENT	1	0.42%
NSAIDS + CV DISEASE/RENAL TOXICITY	60	25.10%
ANTIDEPRESSANT	5	2.09%
ARIPIPRAZOLE AND HYPOTENSION	23	9.62%
TRIPTAN CONTRAINDICATIONS	8	3.35%
QT PROLONGATION	3	1.26%

May Cases by Type of Criteria

Criteria Description	# of Cases	% of Cases
CLONIDINE SIDE EFFECTS	58	18.83%
CARBAMAZEPINE INTERACTIONS	1	0.32%
BARBITURATE TOXICITY	2	0.65%
DRUG INDUCED RESP/CNS DEPRESSION	42	13.64%
TRICYCLIC ANTIDEPRESSANT INTERACTIONS	11	3.57%
BARBITURATE DOSING	1	0.32%
NSAID INTERACTION	122	39.61%
SSRI INTERACTIONS	2	0.65%
LITHUM TOXICITY	14	4.55%
HEPATIC IMPAIRMENT	2	0.65%
ZIPRASIDONE + ANTIHYPERTENSIVE INTERACTION	16	5.19%
HYPOGLYCEMIA + B-BLOCKERS	19	6.17%
NSAIDS + BP/RENAL FAILURE	5	1.62%
METHOTREXATE + PPI INTERACTION	13	4.22%

June Cases by Type of Criteria

Criteria Description	# of Cases	% of Cases
HYPERKALEMIA	9	7.89%
BENZODIAZEPINE INTERACTIONS/TOXICITY	14	12.28%
SALICYLATE CONCENTRATIONS	1	0.88%
POTASSIUM -SPARING DIURETIC INTERACTIONS	11	9.65%
B-BLOCKERS + PVD	1	0.88%
DUPLICATE SEDATIVE/HYPNOTIC THERAPY	2	1.75%
MYOPATHY/RHABDOMYOLYSIS	12	10.53%
DROSPIRENONE INTERACTIONS	1	0.88%
NSAID INTERACTIONS	32	28.07%
SALICYLATE INTERACTIONS	1	0.88%
OMEPRAZOLE INTERACTIONS	4	3.51%
SSRIS + TRIPTANS	12	10.53%
SEIZURE THRESHOLD	12	10.53%
RISPERDAL CONSTA + ORAL SUPPLEMENTATION	2	1.75%

NORTH DAKOTA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
3RD QUARTER 2021

Criteria Recommendations ***Approved Rejected***

1. Rosuvastatin/Ezetimibe / Overuse _____ _____
Alert Message: Roszet (rosuvastatin/ezetimibe) may be over-utilized. The recommended daily dose of rosuvastatin/ezetimibe is 40 mg/10 mg once daily.

Drugs/Diseases

Util A	Util B	Util C
Rosuvastatin/Ezetimibe		

Max Dose: 40 mg/10 mg once daily

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Roszet Prescribing Information, March 2021, Althera Pharmaceuticals, LLC.

2. Rosuvastatin/Ezetimibe / Therapeutic Appropriateness _____ _____
Alert Message: The safety and effectiveness of Roszet (rosuvastatin/ezetimibe) have not been established in pediatric patients.

Drugs/Diseases

Util A	Util B	Util C
Rosuvastatin/Ezetimibe		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Roszet Prescribing Information, March 2021, Althera Pharmaceuticals, LLC.

3. Rosuvastatin/Ezetimibe / Therapeutic Appropriateness _____ _____
Alert Message: Roszet (rosuvastatin/ezetimibe) is contraindicated in patients with decompensated cirrhosis or active liver disease.

Drugs/Diseases

Util A	Util B	Util C
Rosuvastatin/Ezetimibe	Cirrhosis	
	Liver Disease	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Roszet Prescribing Information, March 2021, Althera Pharmaceuticals, LLC.

4. Rosuvastatin/Ezetimibe / Warfarin _____ _____

Alert Message: The concurrent use of Roszet (rosuvastatin/ezetimibe) with warfarin may result in significantly increased INR in patients receiving warfarin. In patients taking warfarin, obtain an INR before starting rosuvastatin/ezetimibe and frequently enough after initiation, dose titration, or discontinuation to ensure that no significant alteration in INR occurs. Once the INR is stable, monitor INR at regularly recommended intervals.

Drugs/Diseases

Util A	Util B	Util C
Rosuvastatin/Ezetimibe	Warfarin	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Roszet Prescribing Information, March 2021, Althera Pharmaceuticals, LLC.

5. Rosuvastatin/Ezetimibe / Bile Acid Sequestrants _____ _____

Alert Message: The concurrent use of Roszet (rosuvastatin/ezetimibe) with bile acid sequestrants may result in decreased mean exposure of ezetimibe. In patients taking a bile acid sequestrant, administer rosuvastatin/ezetimibe at least 2 hours before or at least 4 hours after the bile acid sequestrant.

Drugs/Diseases

Util A	Util B	Util C
Rosuvastatin/Ezetimibe	Cholestyramine	
Colesevelam		
Colestipol		

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Roszet Prescribing Information, March 2021, Althera Pharmaceuticals, LLC.

6. Rosuvastatin/Ezetimibe / Antacids _____ _____

Alert Message: The concurrent use of Roszet (rosuvastatin/ezetimibe) with aluminum and magnesium hydroxide combination antacid may result in decreased mean exposure of rosuvastatin (50%) and total ezetimibe (4%). In patients taking an antacid, administer rosuvastatin/ezetimibe at least 2 hours after the antacid.

Drugs/Diseases

Util A	Util B	Util C
Rosuvastatin/Ezetimibe	Al/Mg Antacids	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Roszet Prescribing Information, March 2021, Althera Pharmaceuticals, LLC.

7. Rosuvastatin/Ezetimibe / Cyclosporine _____ _____

Alert Message: The concurrent use of Roszet (rosuvastatin/ezetimibe) with cyclosporine should be avoided, as concurrent use may increase the risk of myopathy and rhabdomyolysis. Both rosuvastatin and ezetimibe have been shown to cause myopathy and rhabdomyolysis. Concomitant use of cyclosporine with rosuvastatin has been shown to increase rosuvastatin exposure approximately 7-fold. The coadministration of cyclosporine with ezetimibe has been shown to increase exposure to both ezetimibe and cyclosporine.

Drugs/Diseases

Util A	Util B	Util C
Rosuvastatin/Ezetimibe	Cyclosporine	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Roszet Prescribing Information, March 2021, Althera Pharmaceuticals, LLC.

8. Rosuvastatin/Ezetimibe / Gemfibrozil _____ _____

Alert Message: The concurrent use of Roszet (rosuvastatin/ezetimibe) with gemfibrozil should be avoided, as concurrent use may increase the risk of myopathy and rhabdomyolysis. Rosuvastatin, ezetimibe, and gemfibrozil have been shown to cause myopathy and rhabdomyolysis. Concomitant use of gemfibrozil with rosuvastatin has been shown to significantly increase rosuvastatin exposure.

Drugs/Diseases

Util A	Util B	Util C
Rosuvastatin/Ezetimibe	Gemfibrozil	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Roszet Prescribing Information, March 2021, Althera Pharmaceuticals, LLC.

9. Rosuvastatin/Ezetimibe / Viekira Pak _____ _____

Alert Message: The dose of Roszet (rosuvastatin/ezetimibe) should not exceed 10 mg of rosuvastatin per day when co-administered with Viekira Pak (ombitasvir/paritaprevir/ritonavir/dasabuvir). Rosuvastatin is a BCRP, OATP1B1, and OATP1B3 substrate. The components of the antiviral combination product inhibit BCRP-, OATP1B1-, and OAT1B3-mediated transport. Concurrent use of these agents may result in increased rosuvastatin plasma concentrations and risk of rosuvastatin-related adverse effects (e.g., myopathy and rhabdomyolysis).

Drugs/Diseases

Util A	Util B	Util C
Rosuvastatin/Ezetimibe	Ombitasvir/paritaprevir/ritonavir/dasabuvir	

Max Dose: 10 mg/day

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Roszet Prescribing Information, March 2021, Althera Pharmaceuticals, LLC.

10. Rosuvastatin/Ezetimibe / Elbasvir/Grazoprevir _____ _____

Alert Message: The dose of Roszet (rosuvastatin/ezetimibe) should not exceed 10 mg of rosuvastatin once daily when co-administered with Zepatier (elbasvir/grazoprevir). Both elbasvir and grazoprevir are BCRP inhibitors, and concurrent use with rosuvastatin, a BCRP substrate, can result in elevated rosuvastatin plasma concentrations increasing the risk of rosuvastatin-associated adverse reactions (e.g., myopathy and rhabdomyolysis).

Drugs/Diseases

Util A	Util B	Util C
Rosuvastatin/Ezetimibe	Elbasvir/Grazoprevir	

Max Dose: 10 mg/day

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Roszet Prescribing Information, March 2021, Althera Pharmaceuticals, LLC.

11. Rosuvastatin/Ezetimibe / Sofosbuvir/Velpatasvir _____ _____

Alert Message: The dose of Roszet (rosuvastatin/ezetimibe) should not exceed 10 mg of rosuvastatin once daily when co-administered with Epclusa (sofosbuvir/velpatasvir). The velpatasvir component of the combination antiviral product is a BCRP and OATP1B1 transport inhibitor, and concurrent use with rosuvastatin, a BCRP and OATP1B1 substrate, can result in elevated rosuvastatin plasma concentrations increasing the risk of rosuvastatin-associated adverse reactions (e.g., myopathy and rhabdomyolysis).

Drugs/Diseases

Util A	Util B	Util C
Rosuvastatin/Ezetimibe	Sofosbuvir/Velpatasvir	

Max Dose: 10 mg/day

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Roszet Prescribing Information, March 2021, Althera Pharmaceuticals, LLC.

12. Rosuvastatin/Ezetimibe / Glecaprevir/Pibrentasvir _____ _____

Alert Message: The dose of Roszet (rosuvastatin/ezetimibe) should not exceed 10 mg of rosuvastatin per day when co-administered with Mavyret (glecaprevir/pibrentasvir). Rosuvastatin is a BCRP, OATP1B1, and OATP1B3 substrate. The components of the antiviral combination product inhibit BCRP-, OATP1B1-, and OAT1B3-mediated transport. Concurrent use of these agents may result in increased rosuvastatin plasma concentrations and risk of rosuvastatin-related adverse effects (e.g., myopathy and rhabdomyolysis).

Drugs/Diseases

Util A	Util B	Util C
Rosuvastatin/Ezetimibe	Glecaprevir/Pibrentasvir	

Max Dose: 10 mg/day

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Roszet Prescribing Information, March 2021, Althera Pharmaceuticals, LLC.

13. Rosuvastatin/Ezetimibe / Lopinavir/Ritonavir _____ _____

Alert Message: The dose of Roszet (rosuvastatin/ezetimibe) should not exceed 10 mg once daily when co-administered with lopinavir/ritonavir. Lopinavir is a OATP1B1 transport inhibitor, and concurrent use with rosuvastatin, an OATP1B1 substrate, may elevate rosuvastatin plasma concentrations and increase the risk of rosuvastatin-related adverse reactions (e.g., myopathy and rhabdomyolysis).

Drugs/Diseases

Util A	Util B	Util C
Rosuvastatin/Ezetimibe	Lopinavir/ritonavir	

Max Dose: 10 mg/day

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Roszet Prescribing Information, March 2021, Althera Pharmaceuticals, LLC.

14. Rosuvastatin/Ezetimibe / Atazanavir / Ritonavir _____ _____

Alert Message: The dose of Roszet (rosuvastatin/ezetimibe) should not exceed 10 mg once daily when co-administered ritonavir-boosted atazanavir. Atazanavir is an OATP1B1 transport inhibitor, and concurrent use with rosuvastatin, an OATP1B1 substrate, may elevate rosuvastatin plasma concentrations and increase the risk of rosuvastatin-related adverse reactions (e.g., myopathy and rhabdomyolysis).

Drugs/Diseases

Util A	Util B	Util C (Include)
Rosuvastatin/Ezetimibe	Atazanavir	Ritonavir

Max Dose: 10 mg/day

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Roszet Prescribing Information, March 2021, Althera Pharmaceuticals, LLC.

15. Rosuvastatin/Ezetimibe / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Discontinue Roszet (rosuvastatin/ezetimibe) when pregnancy is recognized. Alternatively, consider the ongoing therapeutic needs of the individual patient. The rosuvastatin component of the combination product decreases the synthesis of cholesterol and possibly other biologically active substances derived from cholesterol; therefore, the rosuvastatin-containing product may cause fetal harm when administered to pregnant patients based on the mechanism of action.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Rosuvastatin/Ezetimibe	Pregnancy	Abortion Delivery Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Roszet Prescribing Information, March 2021, Althera Pharmaceuticals, LLC.

16. Rosuvastatin/Ezetimibe / Lactation _____ _____

Alert Message: Because of the potential for serious adverse reactions in a breastfed infant, based on the mechanism of action, advise patients that breastfeeding is not recommended during treatment with Roszet (rosuvastatin/ezetimibe). Limited data from case reports in published literature indicate that rosuvastatin is present in human milk. There is no information about the presence of ezetimibe in human milk. Ezetimibe is present in rat milk.

Drugs/Diseases

Util A	Util B	Util C
Rosuvastatin/Ezetimibe	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Roszet Prescribing Information, March 2021, Althera Pharmaceuticals, LLC.

17. Capmatinib / Overuse _____ _____

Alert Message: Tabrecta (capmatinib) may be over-utilized. The recommended dosage of capmatinib is 400 mg orally twice daily with or without food.

Drugs/Diseases

Util A	Util B	Util C
Capmatinib		

Max Dose: 800 mg/day

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tabrecta Prescribing Information, May 2020, Novartis Pharmaceuticals Corporation.

18. Capmatinib / Therapeutic Appropriateness _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Capmatinib		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tabrecta Prescribing Information, May 2020, Novartis Pharmaceuticals Corporation.

19. Capmatinib / Interstitial Lung Disease _____ _____

Alert Message: Tabrecta (capmatinib) can cause interstitial lung disease (ILD)/pneumonitis. Monitor the patient for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (e.g., dyspnea, cough, and fever). Immediately withhold capmatinib in patients with suspected ILD/pneumonitis and permanently discontinue capmatinib if no other potential causes of ILD/pneumonitis are identified.

Drugs/Diseases

Util A	Util B	Util C
Capmatinib	Cough	
	Dyspnea	
	Fever	
	Interstitial Pneumonia	

References:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tabrecta Prescribing Information, May 2020, Novartis Pharmaceuticals Corporation.

20. Capmatinib / Hepatotoxicity _____ _____

Alert Message: Hepatotoxicity has occurred in patients treated with Tabrecta (capmatinib). Monitor liver function tests (including ALT, AST, and total bilirubin) prior to the start of capmatinib, every 2 weeks during the first 3 months of treatment, then once a month or as clinically indicated, with more frequent testing in patients who develop increased transaminases or bilirubin. Based on the severity of the adverse reaction, withhold, dose reduce, or permanently discontinue capmatinib.

Drugs/Diseases

Util A	Util B	Util C
Capmatinib	Liver Function Test	
	Unspecified Jaundice	

References:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tabrecta Prescribing Information, May 2020, Novartis Pharmaceuticals Corporation.

21. Capmatinib / Strong & Moderate CYP3A4 Inducers _____ _____

Alert Message: Avoid coadministration of Tabrecta (capmatinib) with strong and moderate CYP3A inducers. Capmatinib is a CYP3A substrate, and coadministration with a strong CYP3A inducer has been shown to decrease capmatinib exposure. Coadministration of capmatinib with a moderate CYP3A inducer may also decrease capmatinib exposure. Decreases in capmatinib exposure may decrease capmatinib anti-tumor activity.

Drugs/Diseases

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

References:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tabrecta Prescribing Information, May 2020, Novartis Pharmaceuticals Corporation.

22. Capmatinib / Strong CYP3A Inhibitors _____ _____

Alert Message: Tabrecta (capmatinib) is a CYP3A substrate. Coadministration of capmatinib with a strong CYP3A inhibitor has been shown to increase capmatinib exposure, which may increase the incidence and severity of capmatinib-related adverse reactions. Closely monitor patients for adverse reactions during coadministration of capmatinib with strong CYP3A inhibitors.

Drugs/Diseases

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

References:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tabrecta Prescribing Information, May 2020, Novartis Pharmaceuticals Corporation.

23. Capmatinib / CYP1A2 Substrates _____ _____

Alert Message: Coadministration of Tabrecta (capmatinib) with a CYP1A2 substrate has been shown to increase the exposure of the CYP1A2 substrate. Concurrent use of capmatinib with a CYP1A2 substrate may increase the risk of substrate-related adverse reactions. If coadministration is unavoidable between capmatinib and CYP1A2 substrates where minimal concentration changes may lead to serious adverse reactions, decrease the CYP1A2 substrate dosage in accordance with the approved prescribing information.

Drugs/Diseases

Util A	Util B	Util C
Capmatinib	Alosetron	
	Anagrelide	
	Clozapine	
	Duloxetine	
	Mexiletine	
	Ramelteon	
	Tasimelteon	
	Tizanidine	

References:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tabrecta Prescribing Information, May 2020, Novartis Pharmaceuticals Corporation.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors, and Inducers. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionaLabeling/ucm093664.htm

24. Capmatinib / P-gp Substrates & BCRP Substrates _____ _____

Alert Message: In drug studies, the coadministration of Tabrecta (capmatinib) with P-gp or BCRP substrates resulted in increased exposure of the P-gp substrate and BCRP substrate. The concurrent use of capmatinib with drugs that are P-gp or BCRP substrates may increase the adverse reactions of these substrates. If coadministration is unavoidable between capmatinib and P-gp or BCRP substrates where minimal concentration changes may lead to serious adverse reactions, decrease the P-gp or BCRP substrate dosage in accordance with the approved prescribing information.

Drugs/Diseases

Util A	Util B		Util C
Capmatinib	Alpelisib	Rimegepant	
	Atorvastatin	Rosuvastatin	
	Digoxin	Sulfasalazine	
	Fexofenadine	Talazoparib	
	Glecaprevir	Tenofovir	
	Glyburide	Topotecan	
	Loperamide	Ubrogepant	
	Ombitasvir/Paritaprevir/RTV		
	Ombitasvir/Paritaprevir/Dasabuvir/RTV		
	Quinidine		
	Pazopanib		

References:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tabrecta Prescribing Information, May 2020, Novartis Pharmaceuticals Corporation.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors, and Inducers. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionaLabeling/ucm093664.htm

25. Capmatinib / MATE1 and MATE2 Substrates _____ _____

Alert Message: In in vivo studies, Tabrecta (capmatinib) inhibits MATE1 and MATE2K transport. The coadministration of capmatinib may increase the exposure of MATE1 and MATE2K substrates, which may increase the adverse reactions of these substrates. If coadministration is unavoidable between capmatinib and MATE1 or MATE2K substrates where minimal concentration changes may lead to serious adverse reactions, decrease the MATE1 or MATE2K substrate dosage in accordance with the approved prescribing information.

Drugs/Diseases

Util A	Util B	Util C
Capmatinib	Metformin	

References:

Tabrecta Prescribing Information, May 2021, Novartis Pharmaceuticals Corporation.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors, and Inducers. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionaLabeling/ucm093664.htm

26. Capmatinib / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on findings from animal studies and its mechanism of action, Tabrecta (capmatinib) can cause fetal harm when administered to a pregnant patient. Oral administration of capmatinib to pregnant rats and rabbits during the period of organogenesis resulted in malformations at exposures less than the human exposure based on area under the curve (AUC) at the 400 mg twice daily clinical dose. Advise pregnant patients of the potential risk to a fetus.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tabrecta Prescribing Information, May 2020, Novartis Pharmaceuticals Corporation.

27. Capmatinib / Lactation _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Capmatinib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tabrecta Prescribing Information, May 2020, Novartis Pharmaceuticals Corporation.

28. Capmatinib / Therapeutic Appropriateness _____ _____

Alert Message: Advise patients of reproductive potential to use effective contraception during treatment with Tabrecta (capmatinib) and for 1 week after the last dose.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Capmatinib		Contraceptives

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tabrecta Prescribing Information, May 2020, Novartis Pharmaceuticals Corporation.

29. Capmatinib / Therapeutic Appropriateness _____ _____
Alert Message: Advise males with partners of reproductive potential to use effective contraception during treatment with Tabrecta (capmatinib) and for 1 week after the last dose.

Drugs/Diseases
Util A Util B Util C
Capmatinib

Gender: Male

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tabrecta Prescribing Information, May 2020, Novartis Pharmaceuticals Corporation.

30. Capmatinib / Non-adherence _____ _____
Alert Message: Based on refill history, your patient may be under-utilizing Tabrecta (capmatinib). 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
Capmatinib

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.

31. Vibegron / Overuse _____ _____
Alert Message: Gemtesa (vibegron) may be over-utilized. The recommended dosage of vibegron is one 75 mg tablet orally, once daily with or without food. Swallow vibegron whole with a glass of water.

Drugs/Diseases
Util A Util B Util C
Vibegron

Max Dose: 75 mg/day

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gemtesa Prescribing Information, Dec. 2020, Urovant Sciences, Inc.

32. Vibegron / Therapeutic Appropriateness _____ _____
Alert Message: The safety and effectiveness of Gemtesa (vibegron) in pediatric patients have not been established.

Drugs/Diseases

Util A	Util B	Util C
Vibegron		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gemtesa Prescribing Information, Dec. 2020, Urovant Sciences, Inc.

33. Vibegron / Therapeutic Appropriateness _____ _____
Alert Message: Urinary retention has been reported in patients taking Gemtesa (vibegron). The risk of urinary retention may be increased in patients with bladder outlet obstruction and also in patients taking muscarinic antagonist medications for the treatment of OAB. Monitor patients for signs and symptoms of urinary retention, particularly in patients with bladder outlet obstruction and patients taking muscarinic antagonist medications for the treatment of OAB. Discontinue vibegron in patients who develop urinary retention.

Drugs/Diseases

Util A	Util B	Util C (Include)
Vibegron		Urinary Retention

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gemtesa Prescribing Information, Dec. 2020, Urovant Sciences, Inc.

34. Vibegron / Digoxin _____ _____
Alert Message: Concomitant use of Gemtesa (vibegron) increases digoxin maximal concentrations (Cmax) and systemic exposure as assessed by area under the concentration-time curve (AUC). Serum digoxin concentrations should be monitored before initiating and during therapy with vibegron and used for titration of the digoxin dose to obtain the desired clinical effect. Continue monitoring digoxin concentrations upon discontinuation of vibegron and adjust digoxin dose as needed.

Drugs/Diseases

Util A	Util B	Util C
Vibegron	Digoxin	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gemtesa Prescribing Information, Dec. 2020, Urovant Sciences, Inc.

35. Vibegron / CKD Stage 5 _____ _____
Alert Message: Gemtesa (vibegron) has not been studied in patients with eGFR < 15mL/min/1.73m2 (with or without hemodialysis) and is not recommended in these patients.

Drugs/Diseases

Util A	Util B	Util C (Include)
Vibegron		CKD Stage 5

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gemtesa Prescribing Information, Dec. 2020, Urovant Sciences, Inc.

36. Vibegron / Severe Hepatic Impairment _____ _____
Alert Message: Gemtesa (vibegron) has not been studied in patients with severe hepatic impairment (Child-Pugh C) and is not recommended in this patient population.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gemtesa Prescribing Information, Dec. 2020, Urovant Sciences, Inc.

37. Vibegron / Lactation _____ _____
Alert Message: There are no data on the presence of Gemtesa (vibegron) in human milk, the effects of the drug on the breastfed infant, or the effects on milk production. When a single oral dose of radiolabeled vibegron was administered to postnatal nursing rats, radioactivity was observed in milk. When a drug is present in animal milk, it is likely that the drug will be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for vibegron and any potential adverse effects on the breastfed infant from vibegron or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Vibegron	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gemtesa Prescribing Information, Dec. 2020, Urovant Sciences, Inc.

38. Pralsetinib / Overuse _____ _____

Alert Message: Gavreto (pralsetinib) may be over-utilized. The recommended maintenance dose of pralsetinib is 400 mg orally once daily on an empty stomach (no food intake for at least 2 hours before and at least 1 hour after taking pralsetinib.

Drugs/Diseases

Util A	Util B	Util C
Pralsetinib		

Max Dose: 400 mg/day

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gavreto Prescribing Information, April 2021, Genentech.

39. Pralsetinib / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Gavreto (pralsetinib) for the treatment of RET fusion-positive NSCLC have not been established in pediatric patients.

Drugs/Diseases

Util A	Util B	Util C (Include)
Pralsetinib		Malignant Neoplasm of Bronchus and Lung

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gavreto Prescribing Information, April 2021, Genentech.

40. Pralsetinib / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Gavreto (pralsetinib) for the treatment of with RET-mutant MTC or RET-fusion thyroid cancer have not been established in pediatric patients younger than 12 years of age.

Drugs/Diseases

Util A	Util B	Util C (Include)
Pralsetinib		Malignant Neoplasm of Thyroid

Age Range: 0 – 11 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gavreto Prescribing Information, April 2021, Genentech.

41. Pralsetinib / Interstitial Lung Disease _____ _____

Alert Message: Severe, life-threatening, and fatal interstitial lung disease (ILD)/pneumonitis can occur in patients treated with Gavreto (pralsetinib). Monitor the patient for pulmonary symptoms indicative of ILD/pneumonitis. Withhold pralsetinib and promptly investigate for ILD in any patient who presents with acute or worsening of respiratory symptoms that may be indicative of ILD (e.g., dyspnea, cough, and fever). Withhold, reduce dose, or permanently discontinue pralsetinib based on the severity of confirmed ILD.

Drugs/Diseases

Util A	Util B	Util C
Pralsetinib	Cough	
	Dyspnea	
	Fever	
	Interstitial Pneumonia	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gavreto Prescribing Information, April 2021, Genentech.

42. Pralsetinib / Hypertension _____ _____

12ert Message: Do not initiate Gavreto (pralsetinib) in patients with uncontrolled hypertension. In clinical studies, hypertension occurred in 29% of patients, including Grade 3 hypertension in 14% of patients. Optimize blood pressure prior to initiating pralsetinib. Monitor blood pressure after 1 week, at least monthly thereafter, and as clinically indicated during pralsetinib therapy. Initiate or adjust anti-hypertensive therapy an appropriate. Withhold, reduce dose, or permanently discontinue pralsetinib based on the severity.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Pralsetinib	Hypertension	Antihypertensive Medication

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gavreto Prescribing Information, April 2021, Genentech.

43. Pralsetinib / Hepatotoxicity _____ _____

Alert Message: In clinical studies, serious hepatic adverse reactions occurred in 2.1% of patients treated for Gavreto (pralsetinib). Increased AST occurred in 69% of patients, including Grade 3 or 4 in 5.4% and increased ALT occurred in 46% of patients, including Grade 3 or 4 in 6%. Monitor AST and ALT prior to initiating pralsetinib, every 2 weeks during the first 3 months, then monthly thereafter and as clinically indicated. Withhold, reduce dose, or permanently discontinue pralsetinib based on severity.

Drugs/Diseases

Util A	Util B	Util C
Pralsetinib	Liver Function Test	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gavreto Prescribing Information, April 2021, Genentech.

44. Pralsetinib / Hemorrhage _____ _____

Alert Message: Serious, including fatal, hemorrhagic events can occur with Gavreto (pralsetinib). In clinical studies, Grade ≥ 3 hemorrhagic events occurred in 2.5% of patients treated with pralsetinib including one patient with a fatal hemorrhagic event. Permanently discontinue pralsetinib in patients with severe or life-threatening hemorrhage.

Drugs/Diseases

Util A	Util B	Util C
Pralsetinib	Hemorrhage	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gavreto Prescribing Information, April 2021, Genentech.

45. Pralsetinib / Therapeutic Appropriateness _____ _____

Alert Message: Gavreto (pralsetinib) is a kinase inhibitor that can inhibit the vascular endothelial growth factor (VEGF) signaling pathway, therefore, pralsetinib has the potential to adversely affect wound healing. Withhold pralsetinib for at least 5 days prior to elective surgery. Do not administer pralsetinib for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of pralsetinib after resolution of wound healing complications has not been established.

Drugs/Diseases

Util A	Util B	Util C
Pralsetinib		

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gavreto Prescribing Information, April 2021, Genentech.

46. Pralsetinib / Certain Strong CYP3A Inhibitors _____ _____

Alert Message: Avoid coadministration of Gavreto (pralsetinib) with strong CYP3A inhibitors. Coadministration of pralsetinib with a strong CYP3A inhibitor increases pralsetinib exposure, which may increase the incidence and severity of adverse reactions of pralsetinib.

Drugs/Diseases

Util A	Util B	Util C
Pralsetinib	Nefazodone	
	Voriconazole	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gavreto Prescribing Information, April 2021, Genentech.

47. Pralsetinib / Strong Combined CYP3A Inhibitors/P-gp Inhibitors _____ _____

Alert Message: Avoid coadministration of Gavreto (pralsetinib) with drugs that are known combined P-gp and strong CYP3A inhibitors. If coadministration with a combined P-gp and strong CYP3A inhibitor cannot be avoided, a pralsetinib dose reduction is recommended. If taking pralsetinib 400 mg or 300 mg once daily, reduce to 200 mg once daily. If taking 200 mg once daily, reduce to 100 mg once daily. After the inhibitor has been discontinued for 3 to 5 elimination half-lives, resume pralsetinib at the dose taken prior to initiating the combined P-gp and strong CYP3A inhibitor.

Drugs/Diseases

Util A	Util B		Util C
Pralsetinib	Clarithromycin	Mifepristone	
	Cobicistat	Nelfinavir	
	Indinavir	Posaconazole	
	Itraconazole	Ritonavir	
	Ketoconazole	Saquinavir	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gavreto Prescribing Information, April 2021, Genentech.

48. Pralsetinib / Strong CYP3A Inducers _____ _____

Alert Message: Avoid coadministration of Gavreto (pralsetinib) with strong CYP3A inducers. Coadministration of pralsetinib with a strong CYP3A inducer decreases pralsetinib exposure, which may decrease the efficacy of pralsetinib. If coadministration cannot be avoided, increase the starting dose of pralsetinib to double the current pralsetinib dosage starting on Day 7 of coadministration of pralsetinib with the strong CYP3A inducer. After the inducer has been discontinued for at least 14 days, resume pralsetinib at the dose taken prior to initiating the strong CYP3A inducer.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gavreto Prescribing Information, April 2021, Genentech.

49. Pralsetinib / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on findings from animal studies and its mechanism of action, Gavreto (pralsetinib) can cause fetal harm when administered to a pregnant patient. Oral administration of pralsetinib to pregnant rats during the period of organogenesis resulted in malformations and embryolethality at maternal exposures below the human exposure at the clinical dose of 400 mg once daily. Advise pregnant patients of the potential risk to a fetus.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:Clinical Pharmacology, 2021 Elsevier/Gold Standard., Gavreto Prescribing Information, April 2021, Genentech.

50. Pralsetinib / Therapeutic Appropriateness _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Pralsetinib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gavreto Prescribing Information, April 2021, Genentech.

51. Pralsetinib / Therapeutic Appropriateness _____ _____

Alert Message: Advise patients of reproductive potential to use effective non-hormonal contraception during treatment with Gavreto (pralsetinib) and for 2 weeks after the final pralsetinib dose. Pralsetinib can cause fetal harm when administered to a pregnant patient.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Pralsetinib		Contraceptives

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gavreto Prescribing Information, April 2021, Genentech.

52. Pralsetinib / Therapeutic Appropriateness _____ _____

Alert Message: Advise males with partners of reproductive potential to use effective contraception during treatment with Gavreto (pralsetinib) and for 1 week after the last dose.

Drugs/Diseases

Util A	Util B	Util C
Pralsetinib		

Gender: Male

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Gavreto Prescribing Information, April 2021, Genentech.

53. Pralsetinib / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Gavreto (pralsetinib). 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
Pralsetinib		

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.

54. Brigatinib / Overuse _____ _____

Alert Message: Alunbrig (brigatinib) may be over-utilized. The recommended dosage of brigatinib is 90 mg orally once daily for the first 7 days, then increase the dose to 180 mg orally once daily.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Brigatinib		Moderate CYP3A Inducers
		Cirrhosis
		Hepatic Failure
		CKD Stage 4 & 5
		ESRD

Max Dose: 180 mg/day

References:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

55. Brigatinib / Therapeutic Appropriateness _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Brigatinib		

Age Range: 0 – 17 yoa

References:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

56. Brigatinib / Interstitial Lung Disease _____ _____

Alert Message: Severe, life-threatening, and fatal pulmonary adverse reactions consistent with interstitial lung disease (ILD)/pneumonitis have occurred with Alunbrig (brigatinib). Monitor patient for new or worsening respiratory symptoms, particularly during the first week of initiating brigatinib. Withhold brigatinib in any patient with new or worsening respiratory symptoms, and promptly evaluate for ILD/pneumonitis or other causes of respiratory symptoms. For Grade 1 or 2 ILD/pneumonitis, either resume brigatinib with dose reduction according to official prescribing information after recovery to baseline or permanently discontinue brigatinib. Permanently discontinue brigatinib for Grade 3 or 4 ILD/pneumonitis or recurrence of Grade 1 or 2 ILD/pneumonitis.

Drugs/Diseases

Util A	Util B	Util C
Brigatinib	Cough	
	Dyspnea	
	Fever	
	Interstitial Pneumonia	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

57. Brigatinib / Hypertension _____ _____

Alert Message: Alunbrig (brigatinib) can cause hypertension. Control blood pressure prior to treatment with brigatinib. Monitor blood pressure after 2 weeks and at least monthly thereafter during treatment with brigatinib. Withhold brigatinib for Grade 3 hypertension despite optimal antihypertensive therapy. Upon resolution or improvement to Grade 1, resume brigatinib at the same dose. Consider permanent discontinuation of treatment with brigatinib for Grade 4 hypertension or recurrence of Grade 3 hypertension.

Drugs/Diseases

Util A	Util B	Util C
Brigatinib	Hypertension	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

58. Brigatinib / Bradycardia _____ _____

Alert Message: Alunbrig (brigatinib) can cause bradycardia. For symptomatic bradycardia, withhold brigatinib and review concomitant medications for those known to cause bradycardia. If a concomitant medication known to cause bradycardia is identified and discontinued or dose adjusted, resume brigatinib at the same dose following resolution of symptomatic bradycardia; otherwise, reduce the dose of brigatinib following resolution of symptomatic bradycardia. Discontinue brigatinib for life-threatening bradycardia if no contributing concomitant medication is identified.

Drugs/Diseases

Util A	Util B	Util C
Brigatinib	Bradycardia	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

59. Brigatinib / Visual Disturbances _____ _____

Alert Message: Alunbrig (brigatinib) can cause visual disturbances (e.g., blurred vision, photophobia, diplopia, and reduced visual acuity). Advise patients to report any visual symptoms. Withhold brigatinib and obtain an ophthalmologic evaluation in patients with new or worsening visual symptoms of Grade 2 or greater severity. Upon recovery of Grade 2 or Grade 3 visual disturbances to Grade 1 severity or baseline, resume brigatinib at a reduced dose. Permanently discontinue treatment with brigatinib for Grade 4 visual disturbances.

Drugs/Diseases

Util A	Util B	Util C
Brigatinib	Blurred Vision	
	Diplopia	
	Photophobia	
	Photopsia	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

60. Brigatinib / Creatine Phosphokinase Elevation _____ _____

Alert Message: Alunbrig (brigatinib) can cause creatine phosphokinase elevation. Advise patients to report any unexplained muscle pain, tenderness, or weakness. Monitor the patient's CPK levels during brigatinib treatment. Withhold brigatinib for Grade 3 or 4 CPK elevation with Grade 2 or higher muscle pain or weakness. Upon resolution or recovery to Grade 1 CPK elevation or baseline, resume brigatinib at the same dose or a reduced dose as described in the official prescribing information.

Drugs/Diseases

Util A	Util B	Util C
Brigatinib	Myopathy	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

61. Brigatinib / Hyperglycemia _____ _____

Alert Message: Alunbrig (brigatinib) can cause new or worsening hyperglycemia. Assess fasting serum glucose prior to initiation of brigatinib and monitor periodically thereafter. Initiate or optimize antihyperglycemic medications as needed. If adequate hyperglycemic control cannot be achieved with optimal medical management, withhold brigatinib until adequate hyperglycemic control is achieved and consider reducing the dose of brigatinib as described in the official prescribing information or permanently discontinuing brigatinib.

Drugs/Diseases

Util A	Util B	Util C
Brigatinib	Hyperglycemia	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

62. Brigatinib / Strong CYP3A Inhibitors _____ _____

Alert Message: Coadministration of Alunbrig (brigatinib) with a strong CYP3A inhibitor may increase brigatinib plasma concentrations, which may increase the incidence of adverse reactions. Avoid coadministration of brigatinib with strong CYP3A inhibitors. If coadministration of a strong CYP3A inhibitor cannot be avoided, reduce the brigatinib once daily dose by approximately 50% (i.e., from 180 mg to 90 mg, or from 90 mg to 60 mg). After discontinuation of a strong CYP3A inhibitor, resume the brigatinib dose that was tolerated prior to initiating the CYP3A inhibitor.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

63. Brigatinib / Moderate CYP3A Inhibitors _____ _____

Alert Message: Coadministration of Alunbrig (brigatinib) with a moderate CYP3A inhibitor may increase brigatinib plasma concentrations, which may increase the incidence of adverse reactions. Avoid coadministration of brigatinib with moderate CYP3A inhibitors. If coadministration of a moderate CYP3A inhibitor cannot be avoided, reduce the brigatinib once daily dose by approximately 40% (i.e., from 180 mg to 120 mg, 120 mg to 90 mg, or from 90 mg to 60 mg). After discontinuation of a moderate CYP3A inhibitor, resume the brigatinib dose that was tolerated prior to initiating the CYP3A inhibitor.

Drugs/Diseases

Util A	Util B			Util C
Brigatinib	Atazanavir	Diltiazem	Verapamil	
	Aprepitant	Dronedarone		
	Cimetidine	Erythromycin		
	Ciprofloxacin	Fluconazole		
	Crizotinib	Fluvoxamine		
	Cyclosporine	Imatinib		

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

64. Brigatinib / Strong CYP3A Inducers _____ _____

Alert Message: Coadministration of Alunbrig (brigatinib) with a strong CYP3A inducer should be avoided as concomitant use can result in decreased brigatinib exposure which may result in decreased brigatinib efficacy. In clinical studies, the concurrent use of brigatinib with the strong CYP3A inducer rifampin resulted in a decrease in brigatinib Cmax by 60% and AUC0-inf by 80%.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

Criteria Recommendations ***Approved Rejected***

65. Brigatinib / Moderate CYP3A Inducers _____ _____

Alert Message: Coadministration of Alunbrig (brigatinib) with a moderate CYP3A inducer should be avoided as concomitant use can cause decreased brigatinib exposure resulting in decreased brigatinib efficacy. A moderate CYP3A inducer is predicted to decrease the AUC of brigatinib by approximately 50%. If coadministration cannot be avoided, increase the brigatinib once daily dose in 30 mg increments after 7 days of treatment with the current brigatinib dose as tolerated, up to a maximum of twice the brigatinib dose that was tolerated prior to initiating the moderate CYP3A inducer. After discontinuation of a moderate CYP3A inducer, resume the brigatinib dose that was tolerated prior to initiating the moderate CYP3A inducer.

Drugs/Diseases

Util A	Util B	Util C
Brigatinib	Bosentan	
	Butalbital	
	Efavirenz	
	Etravirine	
	Modafinil	
	Rifabutin	
	Rifapentine	

References:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

66. Brigatinib / Sensitive CYP3A Substrates _____ _____

Alert Message: Caution should be exercised when co-administrating Alunbrig (brigatinib) with sensitive CYP3A substrates. Coadministration of brigatinib with CYP3A substrates, including hormonal contraceptives, can result in decreased substrate concentrations and loss of efficacy of sensitive CYP3A substrates. In in vitro studies, brigatinib, at clinically relevant plasma concentrations, induced CYP3A via activation of the pregnane X receptor (PXR).

Drugs/Diseases

Util A	Util B	Util C
Brigatinib	Budesonide	
	Buspirone	
	Darifenacin	
	Ergotamine	
	Everolimus	
	Dihydroergotamine	
	Hormonal Contraceptives	
	Midazolam	
	Sildenafil	
	Sirolimus	
	Tacrolimus	
	Triazolam	

References:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

67. Brigatinib / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on its mechanism of action and findings in animals, Alunbrig (brigatinib) can cause fetal harm when administered to a pregnant patient. There are no clinical data on the use of brigatinib in pregnant patients. Administration of brigatinib to pregnant rats during the period of organogenesis resulted in dose-related skeletal anomalies at doses as low as 12.5 mg/kg/day as well as increased post-implantation loss, malformations, and decreased fetal body weight at doses of 25 mg/kg/day (approximately 1.26 times the human exposure at 180 mg once daily) or greater. Advise pregnant patients of the potential risk to a fetus.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

68. Brigatinib / Lactation _____ _____

Alert Message: There are no data regarding the secretion of Alunbrig (brigatinib) in human milk or its effects on the breastfed infant or milk production. Because of the potential for adverse reactions in breastfed infants, advise lactating women not to breastfeed during treatment with brigatinib and for 1 week following the final dose.

Drugs/Diseases

Util A	Util B	Util C
Brigatinib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

69. Brigatinib / Therapeutic Appropriateness _____ _____

Alert Message: Alunbrig (brigatinib) can cause fetal harm when administered to a pregnant patient. Advise patients of reproductive potential to use effective non-hormonal contraception during treatment with brigatinib and for at least 4 months after the final dose. Counsel patients to use a non-hormonal method of contraception since brigatinib can render some hormonal contraceptives ineffective.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Brigatinib		Contraceptives

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

Criteria Recommendations *Approved* *Rejected*

70. Brigatinib / Therapeutic Appropriateness _____ _____

Alert Message: Because of the potential for genotoxicity, advise males with partners of reproductive potential to use effective contraception during treatment with Alunbrig (brigatinib) and for at least 3 months after the final dose.

Drugs/Diseases

Util A	Util B	Util C
Brigatinib		

Gender: Male

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

71. Brigatinib / Overuse – Severe Hepatic Impairment _____ _____

Alert Message: Alunbrig (brigatinib) may be over-utilized. The recommended once daily dose of brigatinib should be reduced by approximately 40% (i.e., from 180 mg to 120 mg, 120 mg to 90 mg, or from 90 mg to 60 mg) for patients with severe hepatic impairment (Child-Pugh C). In drug studies, following a single dose of brigatinib 90 mg, unbound brigatinib systemic exposure (AUC0-INF) was 37% higher in subjects with severe hepatic impairment (Child-Pugh C) compared to subjects with normal hepatic function.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

72. Brigatinib / Overuse – Severe Renal Impairment _____ _____

Alert Message: Alunbrig (brigatinib) may be over-utilized. The recommended once daily dose of brigatinib should be reduced by approximately 50% without breaking tablets (i.e., from 180 mg to 90 mg, or from 90 mg to 60 mg) for patients with severe renal impairment (creatinine clearance (CLcr) 15 to 29 mL/min by Cockcroft-Gault). In drug studies, following a single dose of brigatinib 90 mg, unbound brigatinib systemic exposure (AUC0-INF) was 86% higher in subjects with severe renal impairment (creatinine clearance (CLcr) 15 to 29 mL/min) compared to subjects with normal renal function.

Drugs/Diseases

Util A	Util B	Util C (Include)
Brigatinib		CKD Stage 4
		CKD Stage 5
		ESRD

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

73. Brigatinib / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Alunbrig (brigatinib). 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
Brigatinib		

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487-497.
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.

74. Guselkumab / Infection _____ _____

Alert Message: Tremfya (guselkumab) may increase the risk of infection. In clinical trials, infections occurred in 23% of subjects in the guselkumab group versus 21% of subjects in the placebo group through 16 weeks of treatment. Treatment with guselkumab should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated. Instruct patients to seek medical help if signs or symptoms of clinically important chronic or acute infection occur.

Drugs/Diseases

Util A	Util B	Util C
Guselkumab	Infections	

References:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

75. Guselkumab / Therapeutic Appropriateness (0 – 17 yoa) _____ _____

Alert Message: The safety and effectiveness of Tremfya (guselkumab) in pediatric patients less than 18 years of age have not been established.

Drugs/Diseases

Util A	Util B	Util C
Guselkumab		

Age Range: 0 - 17 yoa

References:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

76. Guselkumab / Tuberculosis _____ _____

Alert Message: Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with Tremfya (guselkumab). Initiate treatment of latent TB prior to administering guselkumab. Monitor patients for signs and symptoms of active TB during and after guselkumab treatment. Do not administer guselkumab to patients with active TB infection.

Drugs/Diseases

Util A	Util B	Util C (Include)
Guselkumab		Tuberculosis

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

77. Guselkumab / Nonadherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Tremfya (guselkumab). Nonadherence 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
Guselkumab		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med. 2005; 353(5):487–497.
Soobraty A, Boughdady S, Selinger CP. Current Practice and Clinicians' Perception of Medication Non-adherence in Patients with Inflammatory Bowel Disease: A Survey of 98 Clinicians. World J Gastro Pharma Ther. 2017; 8(1):67-73.
McKay KA, Tremlett H, Patten SB, et al. Determinants of Non-Adherence to Disease-Modifying Therapies in Multiple Sclerosis: A Cross-Canada Prospective Study. Mult Scler. 2016;23(4):588-596.
Joplin S, van der Zwan R, Joshua F, Wong PK. Medication Adherence in Patients with Rheumatoid Arthritis: The Effect of Patient Education, Health Literacy, and Musculoskeletal Ultrasound. Biomed Res Int. 2015;2015:150658.

78. Guselkumab / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no available data on Tremfya (guselkumab) use in pregnant women to inform a drug-associated risk of adverse developmental outcomes. Human IgG antibodies are known to cross the placental barrier, therefore, guselkumab may be transmitted from the mother to the developing fetus.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

79. Guselkumab / Lactation _____ _____

Alert Message: There are no data on the presence of Tremfya (guselkumab) in human milk, the effects on the breastfed infant, or the effects on milk production. Maternal IgG is known to be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for guselkumab and any potential adverse effects on the breastfed infant from guselkumab or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Guselkumab	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.

80. Tacrolimus / Strong CYP3A4 Inducers _____ _____

Alert Message: The concomitant use of tacrolimus (a CYP3A4 substrate) with strong CYP3A4 inducers may increase the metabolism of tacrolimus, leading to lower whole blood trough concentrations and greater risk of rejection. Dose adjustment of tacrolimus may be necessary when administered concomitantly with CYP3A4 inducers. Closely monitor tacrolimus whole blood trough concentrations.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.