North Dakota Medicaid
Drug Utilization Review Board
Meeting
June 2, 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 903 925 001#
June 2, 2021
1:00 pm

1. Administrative items
    - DHS announcements

2. Old business
    - Review and approval of March 2021 meeting minutes
    - Budget update
    - Review top 25 drugs for first quarter of 2021
    - Prior authorization/PDL update
    - Second review of agents for the management of Sickle Cell disease
    - Second review of agents for the treatment of Fabry disease
    - Second review of Imcivree (setmelonotide)
    - Second review of bowel prep agents
    - Update to Evrysdi (risdiplam) criteria
    - Update to Medications that cost over $3000/month criteria
    - Update to Hepatitis C criteria

3. New business
    - Review of agents for the treatment of heart failure
    - 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 September 1, 2021
4. Adjourn

Please remember to silence all cellular phones during the meeting.

North Dakota Medicaid Drug Use Review (DUR) Board
Meeting Minutes
March 3, 2021

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

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

Old Business

Chair A. Honeyman called the meeting to order at 1:05 p.m. Chair A. Honeyman asked for a motion to approve the minutes of the January 6, 2021 meeting. J. Askvig moved that the minutes be approved, and T. Schmidt seconded the motion. The chair called for a voice vote to approve the minutes. The motion passed with no audible dissent.

Review Top 25 Drugs

B. Joyce 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 1st quarter of 2021. B. Joyce presented data to the Board that was reflective of actual end costs to ND Medicaid to better reflect potential areas of high cost to the program. M. Aaland inquired about the possibility of getting information that is reflective of the trends on where drugs/drug classes rank on the top 25 lists and T. DeRuiter stated he will attempt to do so at future meetings.

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 4 medications to the >$3,000 prior authorization criteria; the addition of cycloserine and Sirturo to the Antibiotic Resistance class on the PDL requiring prior authorization; and removing prior authorization requirements for Sunosi. All PDL updates are listed in the handouts for the March 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 Evrysdi

A motion and second was made at the January 2021 DUR Board meeting to place Evrysdi 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, M. Schroth from Cure SMA, J. Whalen from Genetech, and R. Richardson from Gillette Children's Hospital presented information to the Board and spoke in favor of adjusting the criteria as presented. During Board discussion, changes were proposed based on speaker testimony including correcting the age requirements, removing limitations on use in patients with tracheostomy, adding in a route for approval for patients that were diagnosed at newborn screening, and adjusting requirements around assessments used. M. Aaland made a motion to table the criteria for the next meeting, but the motion was not seconded. A. Werremeyer made a motion to correct the age requirements, removing limitations on use in patients with tracheostomy, and removing the testing requirements for SMA1. G. Balf seconded the motion. The Board requested that the criteria be brough back for

potential updates at the next meeting after consultation on further potential adjustments to the criteria. Chair A. Honeyman called for a voice vote to approve the amended criteria, which passed with no audible dissent.

Update to the Prior Authorization Criteria for Hereditary Angioedema

T. DeRuiter presented proposed updates to the prior authorization criteria for agents used to treat hereditary angioedema. The proposed updates included criteria that requires that the patient has an FDA-approved indication for use, that the medication be prescribed by or in consultation with a specialist, and that the patient has had a trial of the preferred agents to meet criteria for coverage for non-preferred agents. During public comment, J. Williamson from the U.S. Hereditary Angioedema Association presented information on HAE to the Board. J. Askvig made a motion to adopt the updated criteria and T. Schmidt 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 Irritable Bowel Syndrome

T. DeRuiter presented proposed updates to the prior authorization criteria for agents used to treat irritable bowel syndrome. The proposed updates included criteria for non-preferred agents that requires that the patient has an FDA-approved indication for use, confirmation that the provider has ruled out other etiologies for diarrhea, and that the patient has had a trial of each preferred agent. Renewal criteria requiring documentation of improvement while taking the medication was also added. A. Werremeyer made a motion to adopt the updated criteria and G. Balf 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 Enspryng (satralizumab)

T. DeRuiter presented a review of Enspryng (satralizumab) for the treatment of neuromyelitis optica spectrum disorder to the Board. During public comment, J. Whalen of Genetech presented information on Enspryng to the Board. A motion was made by A. Werremeyer to manage these medications through prior authorization. The motion was seconded by G. Balf. Prior authorization criteria for these agents will be presented, reviewed, and voted on by the Board at the next meeting.

Review of Agents for the Management of Sickle Cell Disease

T. DeRuiter presented a review of agents used in the management of sickle cell disease to the Board. J. Smutko of Global Blood Therapeutics presented information on Oxbryta to the Board. A motion was made by L. Schield to manage these medications through prior authorization. The motion was seconded by J. Askvig. Prior authorization criteria for these agents will be presented, reviewed, and voted on by the Board at the next meeting.

Review of Agents for the Treatment of Fabry Disease

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

Review of Imcivree (setmelonotide)
T. DeRuiter presented a review of Imcivree (setmelonotide) for the weight management in patients with POMC, PCSK1, or LEPR deficiencies to the Board. There was no public comment. A motion was made by T. Schmidt 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 Antipsychotic Agents
T. DeRuiter presented data on the utilization of antipsychotic agents in the Medicaid population, comparing utilization before and after new requirements have been implemented including requiring use for FDA-approved indications and ages to qualify for coverage. The data indicated an overall reduction in antipsychotic utilization, including a 31% reduction in patients receiving multiple antipsychotics concurrently with the overall reduction in antipsychotic utilization only decreasing by 5%.

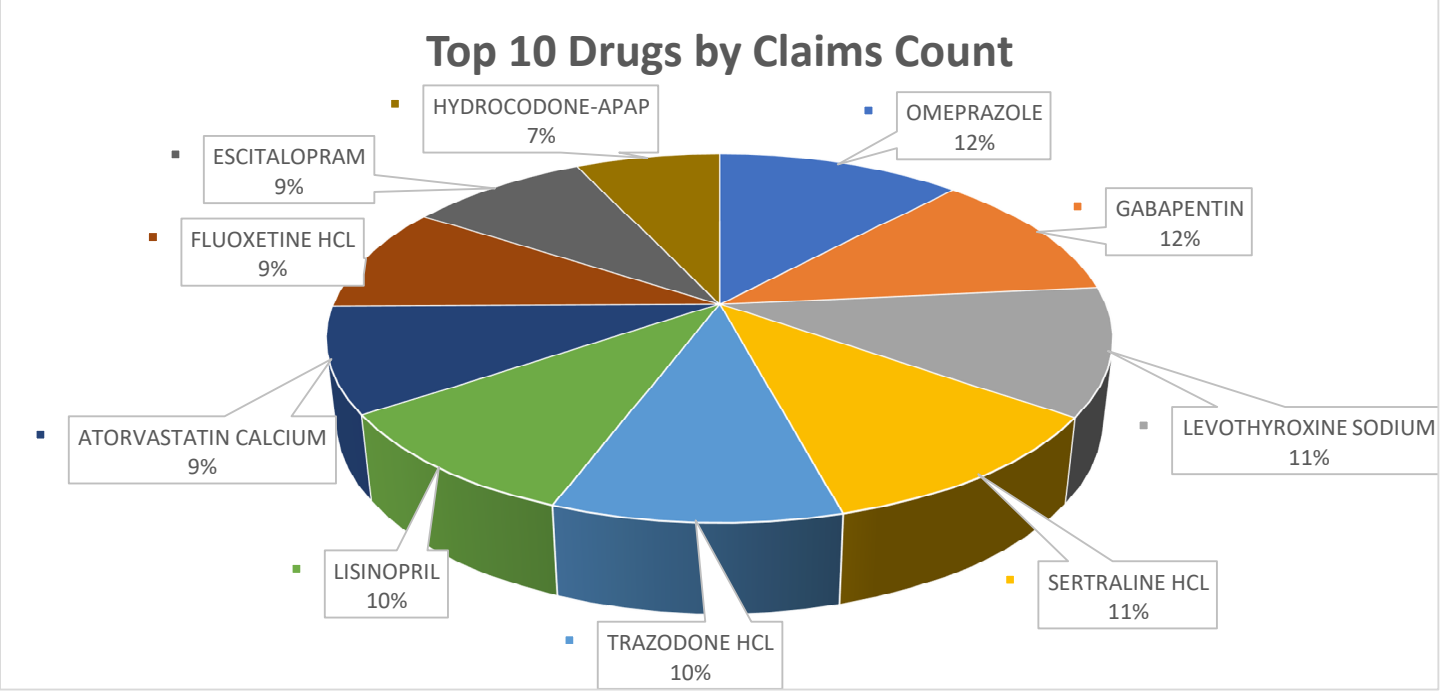
Retrospective Drug Utilization Review (RDUR) Criteria Recommendations
The recommended RDUR criteria enclosed in the packet were developed from product information provided by the manufacturers and are consistent with new indications, new drugs added, and new warnings. These proposed criteria will be added to the current set of criteria and will be used in future DUR cycles. MW moved to approve the new criteria and T. Schmidt 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 3:21 pm. The next DUR Board meeting will be held June 2, 2021 at 1:00 pm with location TBD.

Top 25 Drugs Based on Number of Claims from 01/01/2021 – 03/31/2021

Drug	Claims	Patients	Claims Cost	Cost / Claim	% Total Claims	Dif.
OMEPRAZOLE	4,819	2,376	$62,363.55	$12.94	1.94%	NC
GABAPENTIN	4,600	1,912	$70,947.09	$15.42	1.86%	NC
LEVOTHYROXINE SODIUM	4,503	1,794	$81,051.57	$18.00	1.82%	NC
SERTRALINE HCL	4,458	2,355	$60,944.53	$13.67	1.80%	NC
TRAZODONE HCL	4,027	1,951	$54,555.62	$13.55	1.62%	NC
LISINOPRIL	3,911	2,045	$49,479.64	$12.65	1.58%	↑1
ATORVASTATIN CALCIUM	3,716	1,964	$53,005.21	$14.26	1.50%	↓1
FLUOXETINE HCL	3,715	1,929	$50,876.84	$13.69	1.50%	↑1
ESCITALOPRAM OXALATE	3,548	1,941	$47,740.61	$13.46	1.43%	↓1
HYDROCODONE-APAP	2,847	1,768	$44,455.62	$15.61	1.15%	↑1
BUPROPION XL	2,794	1,358	$49,478.39	$17.71	1.13%	↓1
DULOXETINE HCL	2,709	1,237	$42,882.46	$15.83	1.09%	↑1
METFORMIN HCL	2,699	1,400	$34,188.73	$12.67	1.09%	↓1
PANTOPRAZOLE SODIUM	2,665	1,292	$35,531.51	$13.33	1.08%	↑1
VYVANSE	2,593	1,021	$647,038.26	$249.53	1.05%	↑1
MONTELUKAST SODIUM	2,526	1,328	$35,666.63	$14.12	1.02%	↓2
CYCLOBENZAPRINE HCL	2,447	1,433	$27,208.07	$11.12	0.99%	↑5
BUPRENORPHINE-NALOXONE	2,391	516	$100,170.00	$41.89	0.96%	↑1
CLONIDINE HCL	2,337	1,096	$29,468.82	$12.61	0.94%	↑2
PROAIR HFA	2,318	2,282	$167,755.57	$72.37	0.94%	↓2
ARIPIPRAZOLE	2,287	1,034	$34,818.73	$15.22	0.92%	↑4
LAMOTRIGINE	2,277	903	$31,897.13	$14.01	0.92%	↓5
VENLAFAXINE HCL ER	2,214	950	$37,140.68	$16.78	0.89%	NC
AMLODIPINE BESYLATE	2,195	1,219	$27,474.80	$12.52	0.89%	↓4
CLONAZEPAM	2,119	911	$28,830.27	$13.61	0.85%	↑1

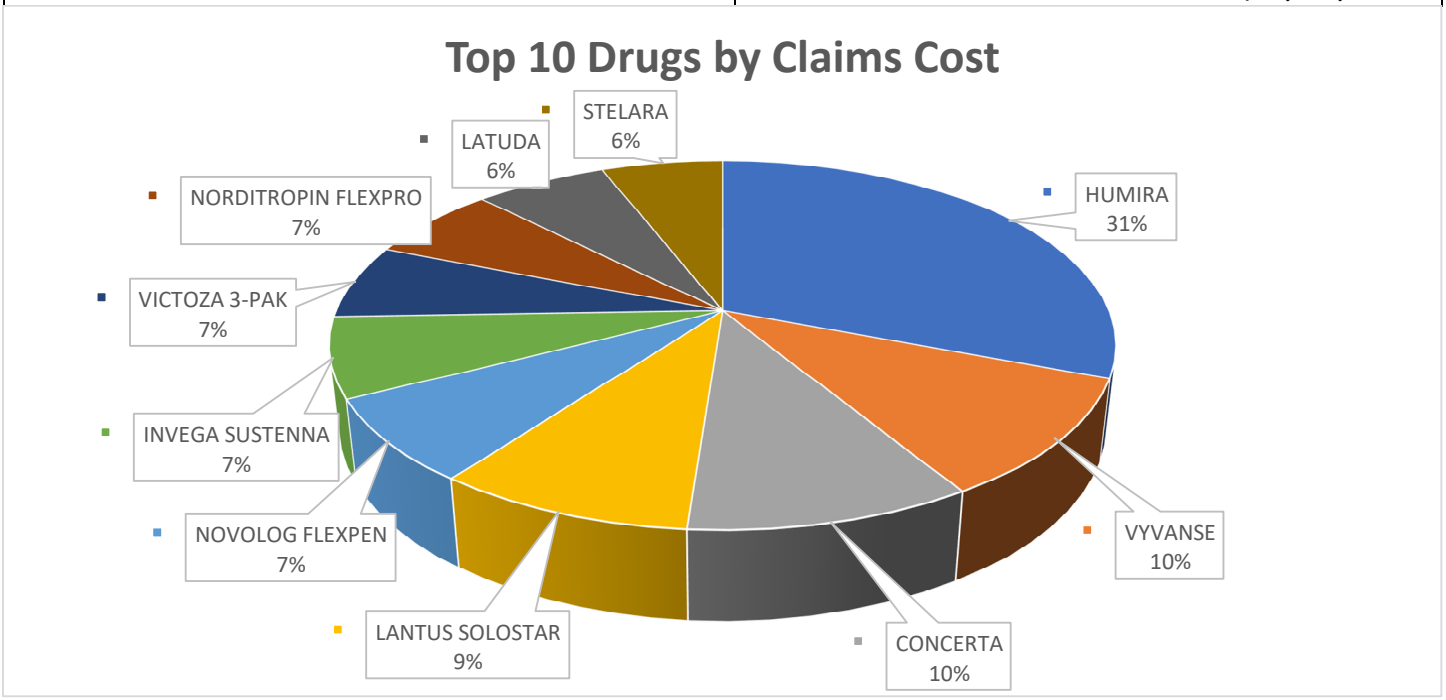
Total Claims	**247,852**



Top 25 Drugs Based on Total Claims Cost from 01/01/2021 – 03/31/2021

Drug	Claims Cost	Claims	Patients	Cost /Claim	% Total Cost	Dif.
HUMIRA	$1,895,499.03	264	126	$7,179.92	6.98%	NC
VYVANSE	$647,038.26	2,593	1,021	$249.53	2.38%	↑1
CONCERTA	$611,971.83	1,838	751	$332.96	2.25%	↑3
LANTUS SOLOSTAR	$553,906.58	1,199	721	$461.97	2.04%	↑1
NOVOLOG FLEXPEN	$447,707.81	674	417	$664.25	1.65%	↓3
INVEGA SUSTENNA	$431,579.55	183	74	$2,358.36	1.59%	↑2
VICTOZA 3-PAK	$402,805.93	448	221	$899.12	1.48%	↑2
NORDITROPIN FLEXPRO	$402,130.43	106	45	$3,793.68	1.48%	↑4
LATUDA	$400,813.34	499	197	$803.23	1.48%	↑1
STELARA	$367,336.02	16	11	$22,958.50	1.35%	↑5
COSENTYX	$364,510.36	61	32	$5,975.58	1.34%	↓4
JARDIANCE	$361,189.05	756	332	$477.76	1.33%	↓1
ENBREL	$350,693.02	64	28	$5,479.58	1.29%	↑7
SYMBICORT	$317,809.37	952	530	$333.83	1.17%	NC
ADVAIR DISKUS	$309,970.55	855	467	$362.54	1.14%	↓2
TRIKAFTA	$294,458.51	14	6	$21,032.75	1.08%	↑1
LEVEMIR FLEXTOUCH	$292,580.46	547	296	$534.88	1.08%	↓1
BIKTARVY	$281,933.60	159	69	$1,773.17	1.04%	↑7
ADDERALL XR	$269,513.58	1,564	646	$172.32	0.99%	↓1
TALTZ AUTOINJECTOR	$261,254.92	22	13	$11,875.22	0.96%	↑70
SABRIL	$245,192.64	12	6	$20,432.72	0.90%	↓2
STRATTERA	$232,284.87	574	282	$404.68	0.86%	NC
ABILIFY MAINTENA	$230,712.45	113	47	$2,041.70	0.85%	↓2
ELIQUIS	$223,744.11	518	242	$431.94	0.82%	↓1
XIFAXAN	$217,283.75	90	49	$2,414.26	0.80%	↓1

Total Claims Cost	**$27,152,365.52**



Top 15 Therapeutic Classes Based on Number of Claims from 01/01/2021 – 03/31/2021

Therapeutic Class Description	Claims	Patients	Claims Cost	Cost/Claim	% Total Claims	Dif.
ANTIDEPRESSANTS	29,827	11,538	$611,489.67	$20.50	12.03%	NC
ANTICONVULSANTS, MISC	13,517	4,665	$1,008,794.76	$74.63	5.45%	NC
ANTIPSYCHOTIC AGENTS	9,305	3,348	$1,912,545.54	$205.54	3.75%	NC
PROTON-PUMP INHIBITORS	7,935	3,820	$143,810.85	$18.12	3.20%	NC
OPIATE AGONISTS	6,967	3,553	$129,423.57	$18.58	2.81%	NC
SEDATIVE/HYPNOTICS	6,798	3,337	$125,847.76	$18.51	2.74%	↑2
NSAIDS	6,647	4,132	$98,217.99	$14.78	2.68%	↓1
STATINS	6,205	3,240	$89,263.14	$14.39	2.50%	↓1
BETA BLOCKERS	5,521	2,792	$104,088.32	$18.85	2.23%	NC
AMPHETAMINES	5,345	2,144	$959,416.06	$179.50	2.16%	NC
NON-AMPHETAMINE STIMULANTS	4,964	1,784	$925,295.19	$186.40	2.00%	↑2
ACE INHIBITORS	4,920	2,585	$71,227.89	$14.48	1.99%	↓1
THYROID AGENTS	4,786	1,870	$90,903.73	$18.99	1.93%	↓1
BIGUANIDES	4,057	2,118	$53,993.81	$13.31	1.64%	NC
BENZODIAZEPINES	3,617	1,801	$65,267.19	$18.04	1.46%	↑1

Top 15 Therapeutic Classes Based on Claims Cost from 01/01/2021 – 03/31/2021

Therapeutic Class Description	Claims Cost	Claims	Patients	Cost/Claim	% Total Cost	Dif.
DMARDS	$2,525,540.42	444	188	$5,688.15	9.30%	NC
ANTIPSYCHOTIC AGENTS	$1,912,545.54	9,305	3,348	$205.54	7.04%	↑1
INSULINS	$1,847,279.99	3,595	1,342	$513.85	6.80%	↓1
SKIN & MUCOUS MEMBRANE AGENTS, MISC	$1,469,372.24	532	337	$2,761.98	5.41%	NC
ANTIRETROVIRALS	$1,048,417.24	772	269	$1,358.05	3.86%	↑6
ANTICONVULSANTS, MISC	$1,008,794.76	13,517	4,665	$74.63	3.72%	NC
INHALED CORTICOSTEROIDS	$969,036.36	3,376	1,929	$287.04	3.57%	↓2
AMPHETAMINES	$959,416.06	5,345	2,144	$179.50	3.53%	↓1
NON-AMPHETAMINE STIMULANTS	$925,295.19	4,964	1,784	$186.40	3.41%	↓1
ANTINEOPLASTIC AGENTS	$865,554.67	582	230	$1,487.21	3.19%	NC
INCRETIN MIMETICS	$775,468.33	1,040	480	$745.64	2.86%	↑1
ANTIDEPRESSANTS	$611,489.67	29,827	11,538	$20.50	2.25%	↑1
IMMUNOMODULATORY AGENTS MISC	$564,259.33	79	34	$7,142.52	2.08%	↑1
SGLT2 INHIBITORS	$481,604.99	1,011	450	$476.36	1.77%	↑1
ANTIMUSCARINICS/ANTISPASMODICS	$412,972.10	1,827	894	$226.04	1.52%	↑1

PDL Update

ADDED TO PA	
Drug	**Class**
Fulphila	Hematopoietic, Colony Stimulating Factors
Udenyca	Hematopoietic, Colony Stimulating Factors
Epclusa 200-50mg	Hepatitis C
Hetlioz	Over 3000
Nulibry	Over 3000
Thyquidity	Preferred Dosage Forms
Gemtesa	Overactive Bladder
Klisyri	Actinic Keratosis
Lupkynis	Over 3000
Reltone	Preferred Dosage Forms
INAVIX (diclofenac/capsaicin)	Kit
NUVAKAAN KIT (lidocaine/prilocaine/silicone)	Kit
NUSURGEPAK (mupirocin/chlorhexidine/dimethacone)	Kit
Dojolvi	Doljovi
Gimoti	Gastroparesis
TRIVIX (Triamcinolone/dimethacone/silicone)	Kit
Wynzora	Antipsoriatics - Topical
Hemady	Oral Steroids
Tramadol 100mg	Opioid Analgesic - Short Acting
Ponvory	Multiple Sclerosis
Roszet	Lipid-Lowering Agents
Zegalogue	Glucose Rescue Medications
DERMALID (lidocaine/elastic bandage)	Kit

Sickle Cell Disease

General Prior Authorization Form

Initial Criteria *Approval Duration = 12 months*

Group Criteria:

- The patient must have an FDA-approved indication for use (meets label recommendations for diagnosis, age, and duration of treatment)
- The patient must have had a 30-day trial of a preferred agent at the maximum (35 mg/kg/day) or maximally tolerated dose, as evidenced by paid claims or pharmacy print-outs
- Prescribed by, or in consultation, with a hematologist, or other specialist with expertise in the diagnosis and management of sickle cell disease
- Patient has experienced at least one sickle cell-related vaso-occlusive crisis within past 12 months (documentation required)
- Baseline hemoglobin (Hb) ≤ 10.5 g/dL

Product Specific Criteria:

****Siklos:**

- Clinical justification must be provided explaining why the patient is unable to use the preferred agents (subject to clinical review).

Renewal Criteria *Approval Duration = 12 months*

- The patient must have experienced and/or 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) by one of the following:
    - Increase in hemoglobin (Hb) by ≥ 1 g/dL from baseline
    - Decrease in indirect bilirubin from baseline
    - Decrease in percent reticulocyte count from baseline
    - Patient has experienced a reduction in sickle cell-related vasoocculusive crisis

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
DROXIA (Hydroxyurea capsule)	SIKLOS (Hydroxyurea tablet)**
Hydroxyurea capsule	OXBRYTA (voxelotor)

Fabry Disease

General Prior Authorization Form

Initial Criteria: *Approval Duration = 6 months*

- The patient must have a diagnosis of Fabry disease
- The patient must be 18 years of age or older
- The patient must be assigned male at birth.
- Baseline value for plasma or urinary globotriosylceramide (GL-3) levels ≥ 5 ng/mcL or GL-3 inclusions ≥ 0.3 per kidney interstitial capillary (KIC) as measured in kidney biopsy
- The patient's diagnosis must be confirmed to be caused by a pathologic galactosidase alpha gene (GLA) variant that is amenable to treatment with Galafold interpreted from a clinical genetics professional, as evidenced by medical documentation attached to the request.
- The medication must not be used in conjunction with enzyme replacement therapy.
- The patient must not have significant renal impairment (eGFR <30 mL/minute/1.73 m2)

Renewal Criteria: *Approval Duration = 12 months*

- The patient must have a decreased GL-3 level or CL-3 inclusion per KIC level and experienced and maintained improvement in one of the following symptoms since starting treatment with requested product, as evidenced by medical documentation (e.g. chart notes) attached to the request (subject to clinical review):
    - Proteinuria
    - GFR
    - Left ventricular hypertrophy
    - Cardiac conduction or rhythm
    - Mitral or aortic insufficiency
    - Optic neuropathy
    - Neuropathic pain
    - Gastrointestinal symptoms

PA REQUIRED
GALAFOLD (Migalastat)

Imcivree

General Prior Authorization Form

Initial Criteria: *Approval Duration = 4 months*

- The patient must have a diagnosis of obesity (BMI > 30 kg/m2 for adults or > 95th percentile using growth chart assessments for pediatric patients), as confirmed by genetic testing attached to the request
- The patient's obesity must be due to one of the following variants interpreted as pathogenic, likely pathogenic, or of unknown significance:
    - proopiomelanocortin (POMC)
    - proprotein convertase subtilisin/kexin type 1 (PCSK1)
    - leptin receptor (LEPR) deficiency
- The patient must be 6 years of age or older
- The medication is prescribed by, or in consultation with, an endocrinologist or expert in rare genetic disorders of obesity
- The patient's weight and body mass index (BMI) must be provided within the last 60 days
- The patient must not have significant renal impairment (eGFR <60 mL/minute/1.73 m2)

Renewal Criteria: *Approval Duration = 12 months*

- The patient must have achieved or maintained a 5% weight reduction or 5% of BMI for patients < 18 years old, since starting treatment with Imcivree, as evidenced by medical documentation (e.g. chart notes) attached to the request.

PA REQUIRED
IMCIVREE (Setmelanotide)

Bowel Prep Agents

General Prior Authorization Form

Non-Preferred Agents Criteria: *Approval Duration = 1 month*

- The patient must have a diagnosis of an FDA-approved indication for use
- One of the following must be met (A or B):
    A. The patient must have failed a trial of each preferred agent within the past 2 years, as evidenced by paid claims or pharmacy printouts
    B. Clinical justification must be provided explaining why the patient is unable to use the preferred agents, with medical documentation (e.g. chart notes) documenting the reason(s) preferred agents cannot be used (subject to clinical review).

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
GAVILYTE-G	CLENPIQ
GOLYTELY 227.1-21.5	COLYTE
MOVIPREP	GOLYTELY 236-22.74G
OSMOPREP	GAVILYTE-C
PEG-3350 AND ELECTROLYTES 236-22.74G	GAVILYTE-N
	NULYTELY
	PEG 3350-ELECTROLYTE 240-22.72G
	PEG 3350-ELECTROLYTE 420 G
	PEG 3350/SOD SUL/NACL/KCL/ASB/C
	PLENVU
	SUPREP
	SUTAB
	TRILYTE

Medications that cost over $3000/month

General Prior Authorization Form

Group Criteria:

- **Initial Criteria:** *Approval Duration = 6 months*
  - The patient 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 the area of the patient's diagnosis
  - As applicable, documentation must be attached to confirm serum marker or pathogenic gene variants amenable to treatment
- **Renewal Criteria**: *Approval Duration = 12 months*
  - The provider 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).

PA REQUIRED
CYSTADROPS (cysteamine)
CYSTARAN (cysteamine)
ENSPRYNG (satralizumab)
GATTEX (teduglutide)
HETLIOZ (tasimelteon)
INCRELEX (mecasermin)
LUPKYNIS (voclosporin)
MYCAPSSA (octreotide)
NULIBRY (fosdenopterin)
OXERVATE (cenegermin-bkbj)
SAMSCA (tolvaptan)
SYPRINE (trientine)
ZOKINVY (lonafamib)

Evrysdi

Evrysdi Prior Authorization Form

- **Initial Criteria:** *Approval Duration = 12 months*
  - The patient must have a diagnosis of spinal muscular atrophy (SMA) with the following (as evidenced with submitted documentation):
    - Bi-allelic deletions or mutations of SMN1 as confirmed by genetic testing, reported as one of the following:
      - Homozygous deletions of exon 7
      - Compound heterozygous mutations
    - One of the following (A and/or B):
      A. Patient has number of SMN2 gene copies ≥ 1 but ≤ 4 as confirmed by genetic testing
      B. Patient is symptomatic (e.g. loss of reflexes, motor delay, motor weakness, abnormal EMG/neuromuscular ultrasound)
  - The medication must be prescribed by or in consultation with a neuromuscular neurologist or neuromuscular physiatrist
  - The patient must visit with a neuromuscular clinic once per year and clinic name, contact information, and date of last visit must be provided
  - The patient must be 2 months of age or older
  - The patient must not require continuous intubation > 3 weeks
  - The patient must not be receiving/have received treatment a SMN2-targeting antisense oligonucleotide, SMN2 splicing modifier or gene therapy (i.e. Spinraza and Zolgensma)
  - The patient's weight and prescribed dose must be provided and within dosing recommendations per the manufacturer label
  - The provider must submit documentation of the patient's current motor function, as evidenced by scores from at least two of the following assessments
    A. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorder (CHOP-INTEND)
    B. Hammersmith Infant Neurological Examination (HINE) Section 2 motor milestone score
    C. Hammersmith Functional Motor Scale Expanded (HFMSE)
    D. Motor Function Measure – 32 items (MFM-32)
    E. Revised Upper Limb Module (RULM)
    F. 6 minute walk test (6MWT)
    G. Forced Vital Capacity (FVC) via Pulmonary Function Test

- **Renewal Criteria:** *Approval Duration = 12 months*
  - The patient's weight and prescribed dose must be provided and within dosing recommendations per the manufacturer label
  - The patient must visit with a neuromuscular clinic once per year and clinic name, contact information, and date of last visit must be provided
  - The patient must not require continuous intubation > 3 weeks
    A. The provider must submit documentation showing that the patient has experienced clinical benefit since starting treatment with Evrysdi, as evidenced by documentation of current Forced Vital capacity (FVC and FEV1) via Pulmonary Function Test, CHOP-INTEND, HINE, HFMSE, MFM-32, 6MWT, or RULM scores showing maintenance of baseline motor function or significant slowed rate of decline (vs expected natural course of the disease).

PA REQUIRED
EVRYSDI (Risdiplam)

Hepatitis C Treatments

Electronic Step Care and Concurrent Medications

- A total of 28 days of ribavirin must be billed within the previous 14 days of an Epclusa (and its generic) claim if patient has decompensated cirrhosis (Child Pugh B or C).
    - Epclusa (and its generic) requires prior authorization and after prior authorization is approved, Epclusa (and its generic) will continue to reject for prior authorization unless ribavirin is billed first when it is recommended to be used concurrently.

Prior Authorization Criteria

Prior Authorization Form – Hepatitis C

Antivirals

Category Criteria: *Approval duration – based on label recommendations*

- The patient must have an FDA-approved indication for use (meets label recommendations for diagnosis and age).
- Chronic Hepatitis C must be documented by one of the following:
    - **Liver fibrosis F1 and below**: 2 positive HCV RNA levels at least 6 months apart.
    - **Liver fibrosis F2 and above**: 1 positive HCV RNA test within the last 12 months.
- The patient must be drug (drugs of abuse by injection) and alcohol free as documented by 2 drug and alcohol tests, dated at least 3 months apart, with the most current test completed within 30 days of the request date, in addition to meeting criteria below as applicable:
- **If the patient has a history of alcohol use disorder**, one of the following must be met (A or B)
    A. The provider must submit chart notes documenting that the patient has abstained from alcohol for the past year
    B. All of the following must be met:
        - The patient must be receiving treatment from an enrolled addiction medicine/chemical dependency treatment provider, and the provider/facility name must be provided with the request
        - Chart notes must be attached regarding assessment of patient's readiness for treatment including readiness for abstinence from alcohol use during and after treatment
- **If the patient has a history of using drugs of abuse by injection**, one of the following must be met (A or B)
    A. The provider must submit chart notes documenting that the patient has abstained from drugs of abuse for the past year
    B. All of the following must be met:
        - The patient must be receiving treatment from an enrolled addiction medicine/chemical dependency treatment (or buprenorphine waived) provider, and the provider/facility name must be provided with the request
        - Chart notes must be attached regarding assessment of readiness for treatment of the patient including readiness for abstinence from illicit drug use by injection during and after treatment
- The patient must not be receiving a known recreationally used high risk combination of drugs (e.g. "the holy trinity") for the past 6 months.
- Prescriber must be a hepatology, gastroenterology, or infectious disease specialist if the patient has any of the following:
    - Decompensated cirrhosis (Child's Pugh B or C)
    - Status post solid organ transplantation
    - Known or suspected hepatocellular carcinoma
    - Evidence/suspicion of acute liver injury while on HCV treatment
    - Prior hepatitis C treatment with a Direct Acting Antiviral Regimen
    - HIV or HBsAg positive
    - Current pregnancy or breastfeeding
- Prescriber must be, or in consult with, a hepatology, gastroenterology, or infectious disease specialist (including via Project ECHO) if the patient has any of the following:
    - Compensated cirrhosis (Child's Pugh A)
    - Prior hepatitis C treatment with a Direct Acting Antiviral Regimen

- Females using ribavirin must have a negative pregnancy test in the last 30 days and receive monthly pregnancy tests during treatment.
- Patient must have established compliant behavior including attending scheduled provider visits (defined as 1 or less no-shows) and filling all maintenance medications on time for the past 90 days, as evidenced by pharmacy claims history.
- Patient must be tested for hepatitis B, and if the test is positive, hepatitis B must either be treated or closely monitored if patient does not need treatment.
- Patient must not have life expectancy of less than 12 months due to non-liver related comorbid conditions.
- Patient and Prescriber attestation forms must be attached to request

Non-Preferred Agents Criteria:

- The patient must have had a trial of each preferred treatment options indicated for the patient's genotype, as evidenced by paid claims or pharmacy printouts.

Product Specific Criteria:

- Epclusa 200mg-50mg:
  - Patient must be 6 years old or older and weigh between 17 to 30 kg
- Harvoni:
  - 45mg-200mg strength: Patient must be 3 years old or older and weigh between 17 and 35kg
  - 33.75mg/150mg strength: Patient must be 3 years old or older and weigh less than 17 kg.
- Sovaldi 200mg:
  - Patient must be 3 years old or older and weigh between 17 to 35 kg
- Vosevi:
  - If the patient has experienced reinfection due to use of **drugs of abuse by injection**, all of the following (A, B AND C) must be met:
    A. The patient must submit an additional drug test dated 6 months prior to request date
    B. The patient must have received/be receiving treatment from an enrolled addiction medicine/chemical dependency treatment (or buprenorphine waived) provider, and the provider/facility name must be provided with the request.
    C. The patient must have risk assessment attached and must not be at high risk of relapse from illicit drug use by injection during and after treatment.
  - If the patient has prior treatment failure due to non-compliance, the patient must have established compliant behavior including attending scheduled provider visits (defined as 1 or less no-shows) and filling all maintenance medications on time for the past 180 days, as evidenced by pharmacy claims history.

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
HARVONI (ledipasvir/sofosbuvir) 45 mg/200mg tablet	EPCLUSA (sofosbuvir/velpatasvir)
MAVYRET (glecaprevir/pibrentasvir)***	HARVONI (ledipasvir/sofosbuvir) 90mg/400mg tablet
sofosbuvir/velpatasvir	HARVONI (ledipasvir/sofosbuvir) ORAL PALLET
SOVALDI (sofosbuvir) 200 MG TABLET	ledipasvir/sofosbuvir 90mg/400mg tablet
VOSEVI (sofosbuvir/velpatasvir/voxilaprevir)***	SOVALDI (sofosbuvir) 400MG TABLET
	SOVALDI (sofosbuvir) ORAL PALLET
	VIEKIRA PAK (dasabuvir/ombitasvir/paritaprevir/ritonavir)
	ZEPATIER (elbasvir/grazoprevir)

Ribavirin

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
ribavirin capsule	
ribavirin tablet	

health information designs

Hepatitis C Treatments Prior Authorization Form

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

Prior Authorization Vendor for ND

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

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

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

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name	Specialist involved in therapy		
Prescriber NPI	Telephone Number	Fax Number	
Address	City	State	Zip Code

Requested Drug and Dose:	**Duration requested:**	**Patient's liver fibrosis score:** □ F0-F1 □ F2-F4
Diagnosis: □ HCV □ OTHER:	**Genotype:**	**Patient's Child–Pugh Class:** □ A □ B □ C □ N/A

Please list any previous treatments the patient has failed for chronic HCV: □ N/A	Regimen:	Dates of treatment:	Response:

Has the patient remained drug (illicit use by injection) and alcohol free for the past 3 months?	□ YES □ NO
Does patient have a diagnosis of alcohol use disorder?	□ YES □ NO
Does patient have a history of illicit use of drugs by injection?	□ YES □ NO
Has patient completed or is currently in a treatment program from an enrolled addiction medicine/chemical dependency provider (or buprenorphine waived provider if history of IV drug use)? Approximate Dates of Treatment:	□ YES □ NO Attested by: □ PROVIDER □ PATIENT
Does the patient have Hepatitis B?	□ YES □ NO
If the patient has Hepatitis B, has it been treated or will it be closely monitored during treatment?	□ YES □ NO
Is the patient post-liver transplant?	□ YES □ NO
Does the patient's life expectancy greater than one year?	□ YES □ NO
Does patient attended scheduled visits with no more than 1 no-show and fill maintenance medications on time?	□ YES □ NO
Does patient have any contraindications to therapy with the requested agent?	□ YES □ NO
ONLY IF RIBAVIRIN IS BEING USED IN A PATIENT OF CHILD-BEARING POTENTIAL Has the patient had a negative pregnancy test in the last 30 days and will receive monthly pregnancy tests during treatment?	□ YES □ NO □ N/A

Please confirm that all of the following is attached to the request, along with any other documentation required, as stated in the PDL:

□ Baseline HCV RNA
□ ≥ 2 drug and alcohol tests dated at least 3 months apart
□ Chart notes addressing patient's alcohol and drug free status over the past year
□ Patient & Prescriber attestation forms
□ Documentation of patient's fibrosis score if available (e.g. APRI, Fibroscan, Fibrotest)

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 #

Hepatitis C Patient Consent Form

I, _____, have been counseled by my healthcare provider on the following:

- ☐ I am planning to live in North Dakota during the entire treatment period. I will complete the entire course of treatment, attend office visits, and have laboratory tests as ordered by my healthcare provider during the treatment period.
- ☐ I will notify my chosen pharmacy of a need to refill one week prior to running out of medication. I understand I must take my medication each day as directed for the entire course of treatment. If the medication does not work due to missed doses, I may not be approved for re-treatment.
- ☐ I understand to keep my liver healthy, I must not drink alcohol or use illicit injectable drugs prior to, during, or after my treatment. If indicated, I will participate in a treatment program to remain abstinent.
- ☐ I understand that after treatment, I can be re-infected with Hepatitis C. My provider has educated me on routes of Hepatitis C transmission, and I will avoid or modify high risk activities to avoid re-infection.
- ☐ I understand that medications that treat Hepatitis C may be harmful to unborn babies. I will use methods to avoid getting pregnant or another person pregnant during treatment and when advised by my provider or pharmacist, for at least 6 months after treatment is complete.

Patient Signature _____ **Date** __/__/____

Pharmacy or Prescriber Representative:

Signature _____**Date** __/__/____

By signature, the pharmacy or prescriber representative confirms the contract has been reviewed with the patient

Hepatitis C Prescriber Agreement Form

- ☐ I agree that I will counsel my patient on how, where, and when to obtain refills on their hepatitis C medications.
- ☐ I agree that I will have intermittent telephone check-ins with my patient, at minimum at 2 weeks and 6 weeks of treatment. I will assess continued adherence with medication, labs, and office visits, treatment tolerability, as well as medication changes that may affect treatment.
- ☐ I have reviewed my patient's medications for drug interactions that would make Hepatitis C medications less effective or cause other adverse effects.
- ☐ I have reviewed the treatment plan with my patient including medications, lab, vaccinations, and follow-up visits.
- ☐ I have assessed my patient's readiness for treatment and believe they are ready and willing to comply with the treatment plan. I have assessed social and psychological stability, substance use abstinence, compliance to follow up visits and medications, pregnancy status, and concurrent health risks.
- ☐ I understand that ND Medicaid tracks refill history and may contact me to provide additional information in the event of a dropped or late refill.
- ☐ I have a dedicated individual or team which may include pharmacy and nursing support to fulfill the elements of this form and have listed key members contact information below.

Name: _____Location: _____

Phone #: _____

Name: _____Location: _____

Phone #: _____

Pharmacy or Prescriber Representative:

Signature _____**Date** __/__/____

REVIEW OF AGENTS FOR MANAGEMENT OF HEART FAILURE WITH REDUCED EJECTION FRACTION

Heart Failure with Reduced Ejection Fraction Overview

- Heart failure (HF) is a common clinical syndrome in which symptoms result from a structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood
    - May be caused by disease of the myocardium, pericardium, endocardium, heart valves, vessels, or by metabolic disorders
        - HF due to left ventricular (LV) dysfunction is categorized according to LV ejection fraction (LVEF)
            - HF with reduced ejection fraction (HFrEF) is patients with LVEF ≤40%
            - HF with preserved ejection fraction (HFpEF) is patients with LVEF ≥50%
            - HF with mid-range ejection fraction (HFmrEF) is patients with LVEF 41-49%

Goals of Pharmacotherapy Treatment in HFrEF:

- Reduce morbidity (symptoms, QoL/functional status, and rate of hospitalization)
    - Can be achieved by diuretics, beta blockers, renin-angiotensin system (RAS) agents, dapagliflozin, hydralazine plus nitrate, digoxin, and mineralocorticoid receptor antagonists (MRA)
- Reduce mortality
    - Prolongation of patient survival has been documented with beta blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARB), angiotensin receptor-neprilysin inhibitor (ARNI), dapagliflozin (an SGLT2 inhibitor), hydralazine plus nitrate, and MRA.
- Several published guidelines for the treatment of HFrEF exist, however these guidelines make similar recommendations regarding the treatment of HFrEF and all recommend combination therapy with drugs proven to improve clinical outcomes in randomized trials:
    - **Initial pharmacologic therapy of HFrEF includes the following combination:**
        - Diuretic therapy (as needed to treat volume overload)
        - A renin-angiotensin system (RAS) targeted medication
            - Or hydralazine plus nitrate if RAS targeted medications cannot be used
        - A beta blocker
    - **Secondary pharmacologic agents:** used in selected patients with HFrEF
        - Mineralocorticoid receptor antagonist (MRAs)
        - Ivabradine
        - SGLT2 inhibitors (e.g. dapagliflozin)
        - Hydralazine plus nitrate
        - Digoxin

Overview of Agents Used in HFrEF

- **Renin-angiotensin system (RAS) targeted agents:** Block harmful effects of renin-angiotensin-aldosterone system activation and attenuates adverse cardiac and vascular remodeling.

	ACE Inhibitors	**ARBS**	**ARNI**
Agents Indicated for HF	Captopril Enalapril Fosinopril Lisinopril Quinapril Ramipril Trandolapril	Candesartan Valsartan Losartan	Entresto (sacubitril/valsartan)
Mechanism of Action	Prevents conversion of angiotensin I to angiotensin II	Blocks angiotensin II receptors	Blocks angiotensin II receptors + inhibits neprilysin
FDA-Approved Ages for Use	Adults	Adults	≥1 year old

Efficacy Evidence	Reduced mortality and hospitalizations	Reduced mortality and hospitalizations	Reduced mortality and hospitalizations vs ACE inhibitor alone
Contraindications	Prior HSR; use with aliskiren in patients with DM; prior angioedema w/ ACE; use with a neprilysin inhibitor	Prior HSR; use with aliskiren in patients with DM	Prior HSR; history of angioedema related to previous ACE inhibitor or ARB therapy; concomitant use or use within 36 hours of ACE inhibitors; use with aliskiren in patients with DM
Warnings/Precautions	Angioedema Hypotension Renal function loss Renal artery stenosis Cough Hyperkalemia Cholestatic jaundice Collagen vascular disease Aortic stenosis Ascites Aortic/Mitral stenosis Pregnancy	Angioedema Hypotension Renal function loss Renal artery stenosis Hyperkalemia Ascites Aortic/Mitral stenosis Pregnancy	Angioedema Hypotension Renal function loss Renal artery stenosis Hyperkalemia Aortic/Mitral stenosis Pregnancy
Dose Adjustments for Renal Impairment	Reduce dose, agent dependent	Use with caution	Reduce dose 50% in severe impairment
Dose Adjustments for Hepatic Impairment	None	Reduce dose in hepatic impairment (Losartan)	Lower dose in moderate impairment; avoid use in severe impairment

- **<u>Beta Blocker Agents:</u>**
  - **Agents Studied for HF**
    - Carvefilol, metoprolol succinate, and bisoprolol
  - **Mechanism of action**
    - Blocks beta1-adrenergic receptors (metoprolol and bisoprolol)
    - Blocks beta-adrenergic and alpha-adrenergic receptors
  - **Approved Ages for Use**
    - Adults
  - **Efficacy Evidence**
    - Reduced mortality and hospitalizations (NYHA functional class II to III)
  - **Contraindications**
    - HSR; decompensated cardiac failure; 2nd or 3rd degree AV block; severe bradycardia; cardiogenic shock; severe hepatic impairment; bronchial asthma or related bronchospastic conditions (carvedilol only)
  - **Warnings/Precautions**
    - Should not be withdrawn abruptly
    - Bradycardia
    - Hypotension
    - Use with caution in patients with
      - Angina, PVD, DM, bronchospastic disease, conduction abnormalities, pheochromocytoma, thyroid disease, myasthenia gravis, aortic/mitral stenosis
  - **Dose Adjustments for Renal Impairment**
    - Bisoprolol requires dose reduction in severe impairment
  - **Dose Adjustments for Hepatic Impairment**
    - Bisoprolol requires dose reduction in severe impairment

        - Carvedilol is contraindicated in severe impairment

- **Mineralocorticoid receptor antagonists (MRA):**
    - **Agents Studied for HF**
        - Spironolactone, eplerenone
    - **Mechanism of action**
        - Blocks the binding of aldosterone at mineralocorticoid receptors at the distal renal tubules, increasing NaCl and water excretion while conserving K
    - **Approved Ages for Use**
        - Adults
    - **Efficacy Evidence**
        - Reduced mortality, manage edema, and reduce and hospitalizations (NYHA functional class II to III)
    - **Contraindications**
        - Hyperkalemia; Addison disease; concomitant use with each other; CrCl 30 mL/min or less (eplerenone); concomitant administration of strong CYP3A4 inhibitors (eplerenone)
    - **Warnings/Precautions**
        - Tumorigenic (spironolactone): avoid unnecessary use
        - Hyperkalemia may occur
        - Fluid/electrolyte imbalance
        - Heart failure
        - Gout
        - Gynecomastia
        - Avoid use as triple therapy with ACE and ARB
    - **Dose Adjustments for Renal Impairment**
        - Requires dosing adjustments in moderate impairment and not recommended in severe (contraindicated for eplerenone).
    - **Dose Adjustments for Hepatic Impairment**
        - Eplerenone
            - No dosage adjustments
        - Spironolactone
            - Use with caution

- **Sodium-glucose cotransporter 2 (SGLT2) inhibitors:**
    - **Agents Studied for HF**
        - **FDA-approved indication:**
            - Separate indication: **Farxiga** (dapagliflozin)
                - To reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure with reduced ejection fraction (NYHA class II to IV)
            - Included in DM indication: **Invokana** (canagliflozin)
                - “risk reduction of major cardiovascular events (cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease”
        - **Off-label: Jardiance** (empagliflozin)
    - **Mechanism of action**
        - Inhibits sodium-glucose cotransporter 2 (SGLT2) in the proximal renal tubules, reducing reabsorption of filtered glucose and sodium. Exact mechanism unknown.
    - **Approved Ages for Use**
        - Adults
    - **Efficacy Evidence**
        - Reduced mortality and hospitalizations (NYHA functional class II to IV)
    - **Contraindications**
        - HSR; severe renal impairment (eGFR <30 mL/minute/1.73 m2), end-stage renal disease (dapagliflozin, empagliflozin only), or patients on dialysis

- **Warnings/Precautions**
  - Increased risk of volume depletion/AKI; necrotizing fasciitis; limb amputation; UTI; genital mycotic infection; hyperkalemia; and hypotension
- **Dose Adjustments for Renal Impairment**
  - Dose adjustments required, contraindicated in ESRD (or GFR<30 for dapagliflozin and empagliflozin)
- **Dose Adjustments for Hepatic Impairment**
  - Not recommended for severe (canagliflozin) or <30 mL/minute/1.73 m2 (others) and contraindicated in ESRD
  - Not studied in severe (dapagliflozin)

- **Hydralazine + nitrates:**
  - **Mechanism of action**
    - Causes direct vasodilation of arterioles (with little effect on veins) with decreased systemic resistance
  - **Approved Ages for Use**
    - Adults, off-label for pediatric patients
  - **Efficacy Evidence**
    - May reduce symptoms and mortality (NYHA functional class II to III)
  - **Contraindications**
    - Hydralazine
      - HSR; coronary artery disease; mitral valve rheumatic heart disease
    - Isosorbide dinitrate
      - HSR; concurrent use with PDE inhibitors or riociguat.
  - **Warnings/Precautions**
    - Hydralazine
      - Increased risk of drug-induced lupous like syndrome; hypotension; peripheral neuritis; MI; blood dyscrasias
    - Isosorbide dinitrate
      - Increased risk of increased ICP; hypotension.
      - May worsen hypertrophic cardiomyopathy
  - **Dose Adjustments for Renal Impairment**
    - Reduce dosing interval (hydralazine)
  - **Dose Adjustments for Hepatic Impairment**
    - No adjustments necessary

- **Corlanor (ivabradine)**
  - **Mechanism of action**
    - Selective and specific inhibition of the hyperpolarization-activated cyclic nucleotide-gated (HCN) channels (f-channels) within the sinoatrial (SA), leading to reduced heart rate.
  - **Approved Ages for Use**
    - ≥6 months
  - **Efficacy Evidence**
    - Reduced hospitalizations (NYHA functional class II to III)
  - **Contraindications**
    - Acute decompensated heart failure; Clinically significant hypotension; sick sinus syndrome, SA block, or 3rd-degree AV; clinically significant bradycardia; severe hepatic impairment; pacemaker dependence; concomitant use with strong CYP3A4 inhibitors
  - **Warnings/Precautions**
    - Increased risk of atrial fibrillation
    - Bradycardia, sinus arrest, and heart block may occur
    - Phosphenes may occur (visual function effects)
    - Effective contraception is recommended in women of reproductive potential (fetal harm may occur)
  - **Dose Adjustments for Renal Impairment**
    - No dose adjustments provided

- **Dose Adjustments for Hepatic Impairment**
  - Contraindicated in severe impairment

- **Digoxin**
  - **Mechanism of action**
    - Inhibition of the sodium/potassium ATPase pump in myocardial cells results in a transient increase of intracellular sodium, which in turn promotes calcium influx via the sodium-calcium exchange pump leading to increased contractility
  - **Approved Ages for Use**
    - All ages
  - **Efficacy Evidence**
    - Reduced hospitalizations (NYHA functional class III and IV)
  - **Contraindications**
    - HSR; ventricular fibrillation
  - **Warnings/Precautions**
    - Increases risk of prolonged PR interval; digoxin toxicity (anorexia, nausea, vomiting, visual changes and cardiac arrhythmias); arrhythmias
    - Use with caution in patients with history of ACS; myocarditis; electrolyte imbalances; and thyroid disease
  - **Dose Adjustments for Renal Impairment**
    - Requires renal dosing adjustments
  - **Dose Adjustments for Hepatic Impairment**
    - Bisoprolol requires dose reduction in severe impairment

- **Verquvo (vericiguat)**
  - **Indication**
    - To reduce the risk of cardiovascular death and heart failure hospitalization following a hospitalization for heart failure or need for outpatient IV diuretics, in adults with symptomatic chronic heart failure and ejection fraction <45%
  - **Mechanism of Action**
    - Enhances production of cGMP by directly stimulating soluble guanylate cyclase (sGC) and enhances sGC sensitivity to endogenous NO, increasing cGMP production
      - Increased levels of cGMP lead to smooth muscle relaxation and vasodilation.
  - **Approved Ages for Use**
    - Adults
  - **Efficacy Evidence**
    - Reduced mortality and hospitalizations (NYHA functional class II to IV)
  - **Contraindications**
    - Concomitant use of other soluble guanylate cyclase stimulators (eg, riociguat); pregnancy.
  - **Warnings/Precautions**
    - Has not been studied in patients concurrently using long-acting nitrates or PDE-5 inhibitors
    - Based on data from animal reproduction studies, in utero exposure to vericiguat may cause fetal harm
  - **Dose Adjustments for Renal Impairment**
    - No dose adjustments for eGFR ≥15 mL/minute/1.73 m2
      - eGFR <15 mL/minute/1.73 m2 has not been studied
  - **Dose Adjustments for Hepatic Impairment**
    - No dose adjustments for mild-moderate impairment (severe has not been studied)

Cost

Drug	Strength	Package Size	WAC Pkg Price	Cost per day*	Cost per Month*	Cost per Year*
Lisinopril	2.5-20 mg	30-5,000 tablets	$0.97-$215.20	$0.14	$4.20	$51.10
Valsartan	40-320 mg	30-500 tablets	$3.00-$258.38	$0.20	$6.00	$73.00
Entresto	24/26 mg 49/51 mg 97/103 mg	1-180 tablets	$7.71-$1,748.68	$15.42	$462.60	$5,628.30
Metoprolol Succinate	25-200 mg	10-1000 tablets	$6.00-$1,251.33	$0.05	$1.50	$18.25
Hydralazine	10-100 mg	100-1000 tablets	$2.95-$279.78	$0.06	$1.98	$22.08
Spironolactone	25-100 mg	30-1000 tablets	$5.76-$372.25	$0.06	$1.98	$22.08
Verquvo	2.5 mg 5 mg 10 mg	14-100 tablets	$272.02-$1,943.00	$38.86	$1,165.80	$14,183.90
Corlanor	5 mg 7.5 mg	60-180 tablets	$491.49-$1,288.59	$14.32	$429.60	$5,226.80
Digoxin	0.125-0.25 mg	100-1000 tablets	$59.25-$1,523.83	$0.59	$17.70	$215.35
**= based on lowest per unit WAC cost*						

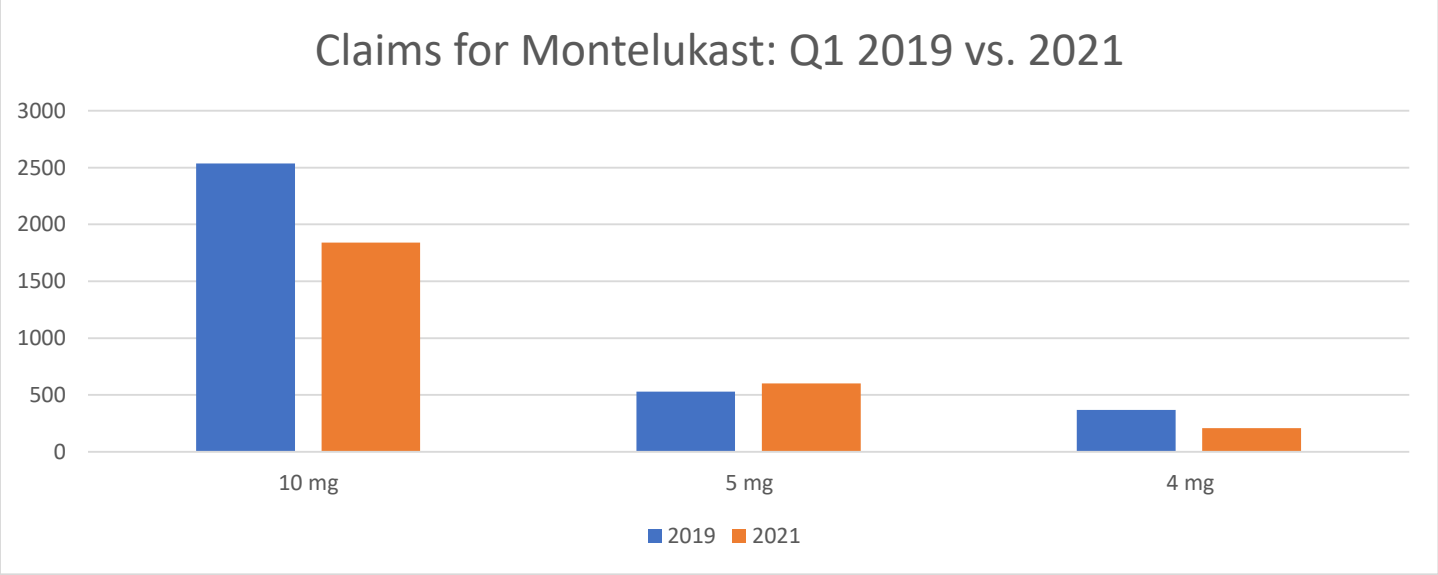
Current Utilization

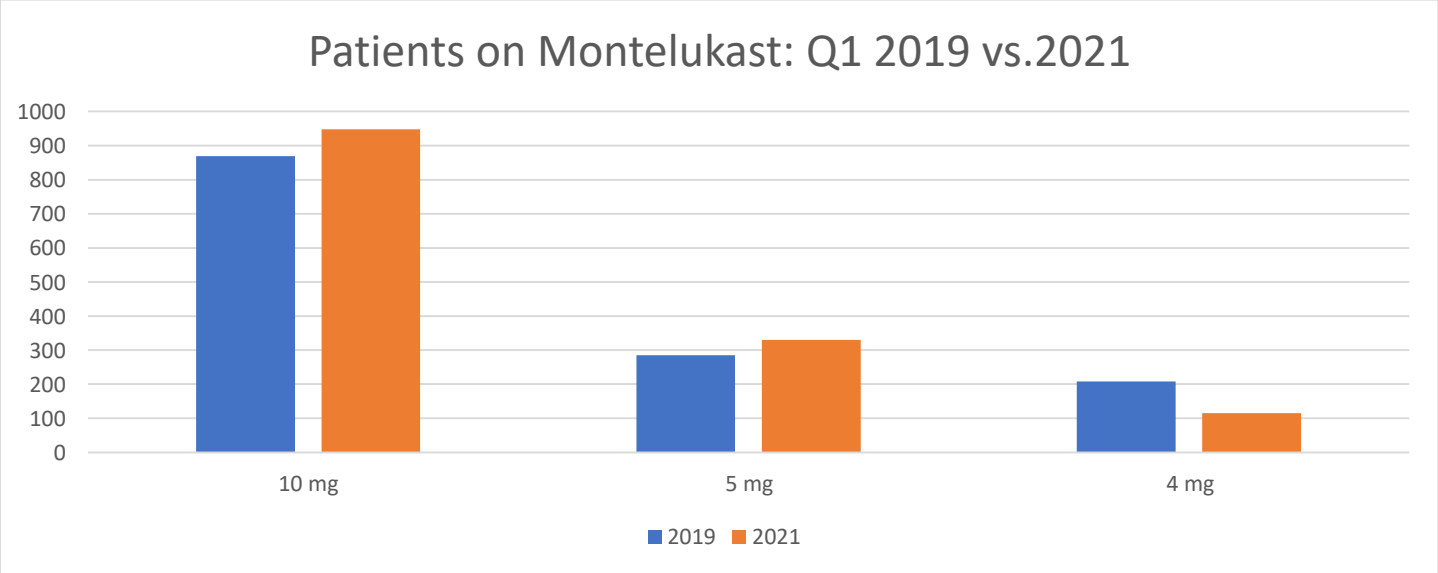
ND Medicaid Utilization (03/2020 – 02/2021)		
Label Name	**Rx Num**	**Total Reimb Amt**
bisoprolol fumarate	7	$126.65
bumetanide	433	$16,986.03
candesartan cilexetil	1	$55.73
captopril	26	$346.07
carvedilol	1517	$31,885.55
dapagliflozin propanediol	55	$28,103.94
digoxin	265	$5,138.62
enalapril maleate	126	$11,144.27
eplerenone	0	$0.00
fosinopril sodium	0	$0.00
hydralazine HCl	241	$3,596.25
ivabradine HCl	44	$19,737.63
lisinopril	2260	$45,270.13
losartan potassium	905	$19,527.57
metoprolol succinate	1499	$29,716.46
quinapril HCl	26	$501.59
ramipril	63	$853.67
Entresto	170	$86,023.84
spironolactone	1168	$17,756.98
telmisartan	50	$937.17
valsartan	22	$771.29
Verquvo	0	N/A

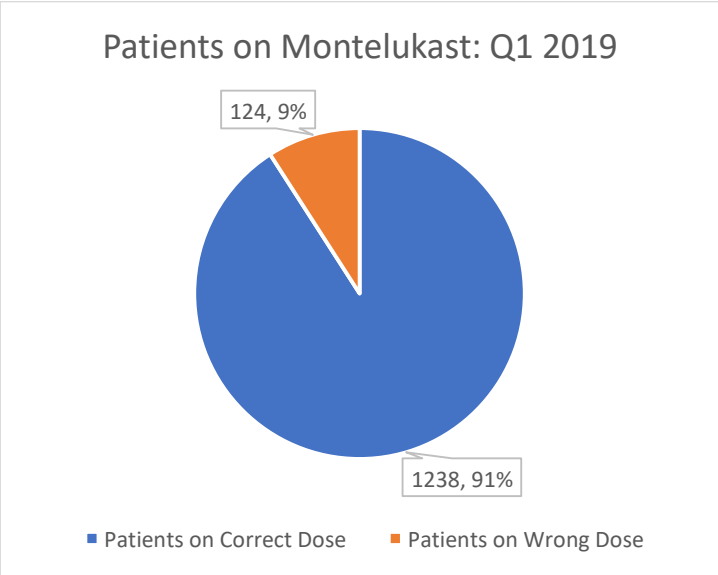
REFERENCES:

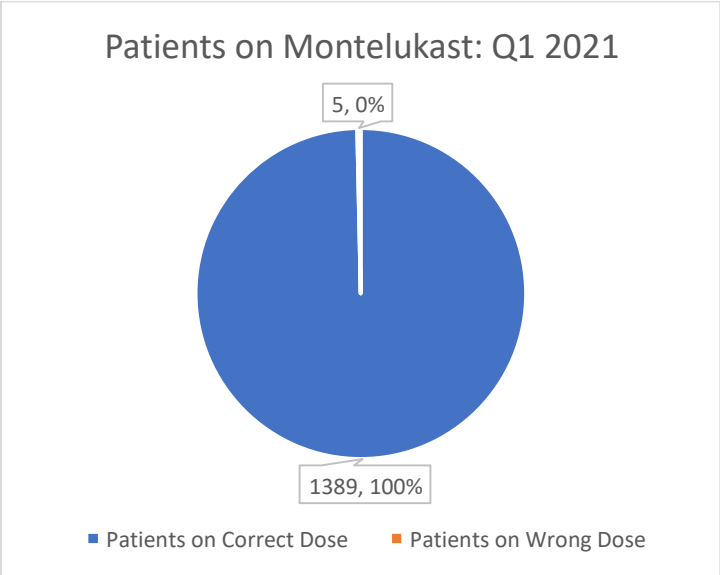
1. Facts & Comparisons eAnswers. Available at http://online.factsandcomparisons.com. Accessed on April 11. 2021.
2. UpToDate. Available at https://www.uptodate.com/contents/search. Accessed on April 11. 2021.
3. Cozaar (losartan) [prescribing information]. Whitehouse Station, NJ: Merck & Co Inc; October 2018.
4. Diovan (valsartan) [prescribing information]. East Hanover, NJ: Novartis; June 2019.
5. Atacand (candesartan) [prescribing information]. AstraZeneca; May 2018.
6. Mavik (trandolapril) [prescribing information]. North Chicago, IL: AbbVie; August 2017.
7. Altace (ramipril) [prescribing information]. New York, NY: Pfizer; June 2017.
8. Capoten (captopril) [prescribing information]. Spring Valley, NY: Par Pharmaceutical Companies Inc; August 2017.
9. Fosinopril sodium [prescribing information]. Weston, FL: Apotex; November 2013.
10. Zestril (lisinopril) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals; July 2017.
11. Vasotec oral (enalapril) [prescribing information]. Bridgewater, NJ: Valeant Pharmaceuticals; August 2018.
12. Aldactone (spironolactone) [prescribing information]. New York, NY: Pfizer Inc; February 2021.
13. Inspra (eplerenone) [prescribing information]. New York, NY: Pfizer; June 2020.

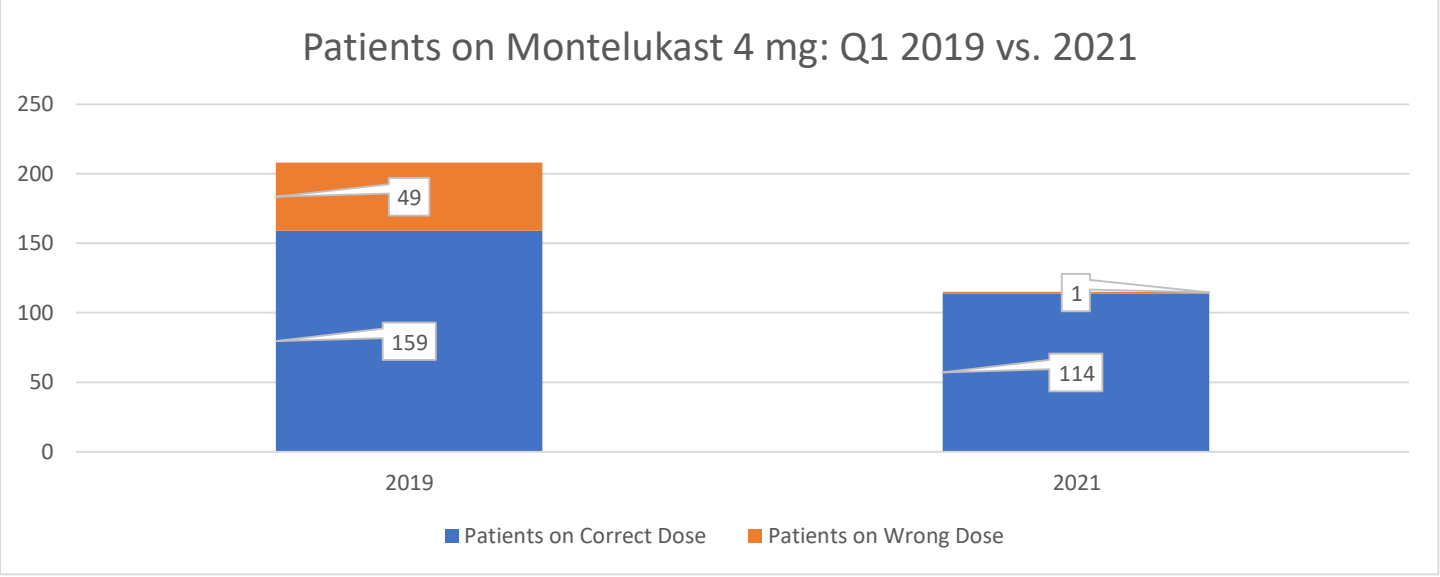
14. Accupril (quinapril) [prescribing information]. New York, NY: Pfizer; July 2017.
15. Bisoprolol fumarate (bisoprolol) [prescribing information]. Tampa, FL: TruPharma, LLC; February 2019.
16. Toprol XL (metoprolol succinate) [prescribing information]. Princeton, NJ: Aralez Pharmaceuticals; December 2016.
17. Coreg (carvedilol immediate release) [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; September 2017.
18. Coreg CR (carvedilol extended release) [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; November 2020.
19. Verquvo (vericiguat) [prescribing information]. Whitehouse Station, NJ: Merck Sharp and Dohme Corp; January 2021.
20. Corlanor (ivabradine) [prescribing information]. Thousand Oaks, CA: Amgen Inc; April 2019.
21. Invokana (canagliflozin) [prescribing information]. Titusville, NJ: Janssen Pharmaceuticals; January 2020.
22. Farxiga (dapagliflozin) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; January 2020.
23. Jardiance (empagliflozin) [prescribing information]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals Inc; January 2020.
24. Steglatro (ertugliflozin) [prescribing information]. Whitehouse Station, NJ: Merck Sharp & Dohme; January 2020.
25. Digoxin (digoxin) oral solution [prescribing information]. Largo, FL: VistaPharm, Inc; August 2019.
26. Hydralazine Hydrochloride tablets [prescribing information]. Hauppauge, NY; ScieGen Pharmaceuticals, Inc; February 2021.
27. Verquvo (vericiguat) [prescribing information]. Whitehouse Station, NJ: Merck Sharp and Dohme Corp; January 2021.

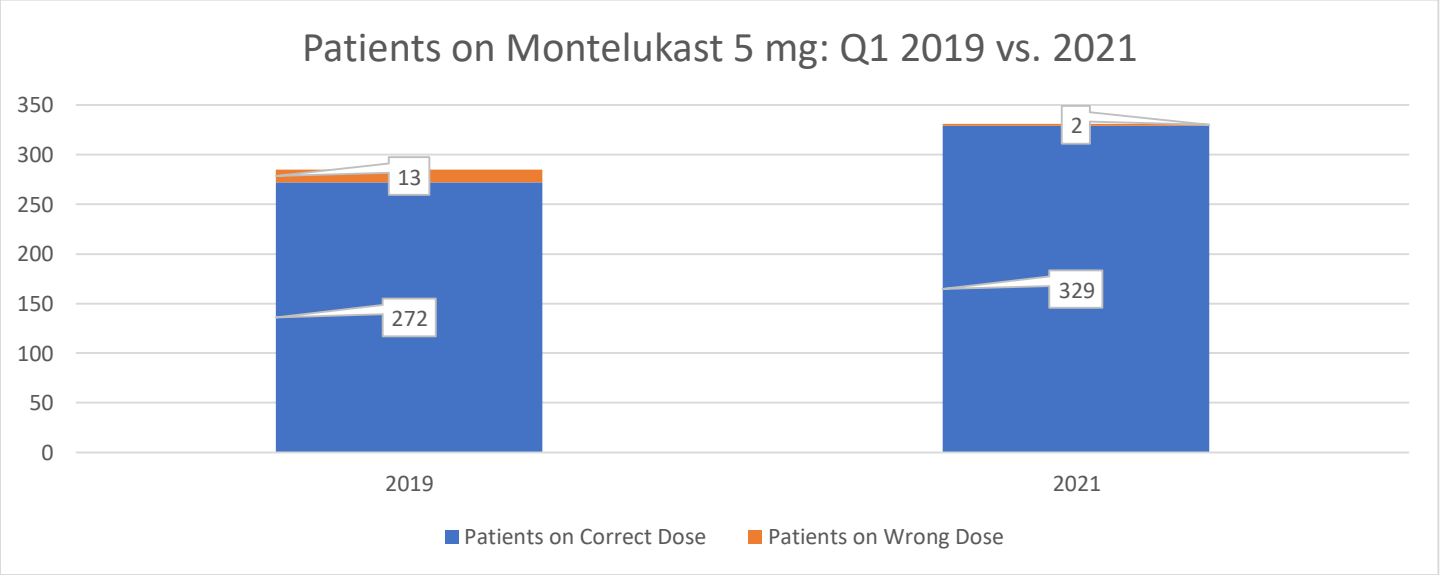

Claims for Montelukast: Q1 2019 vs. 2021
3000
2500
2000
1500
1000
500
0
10 mg
5 mg
4 mg
2019
2021

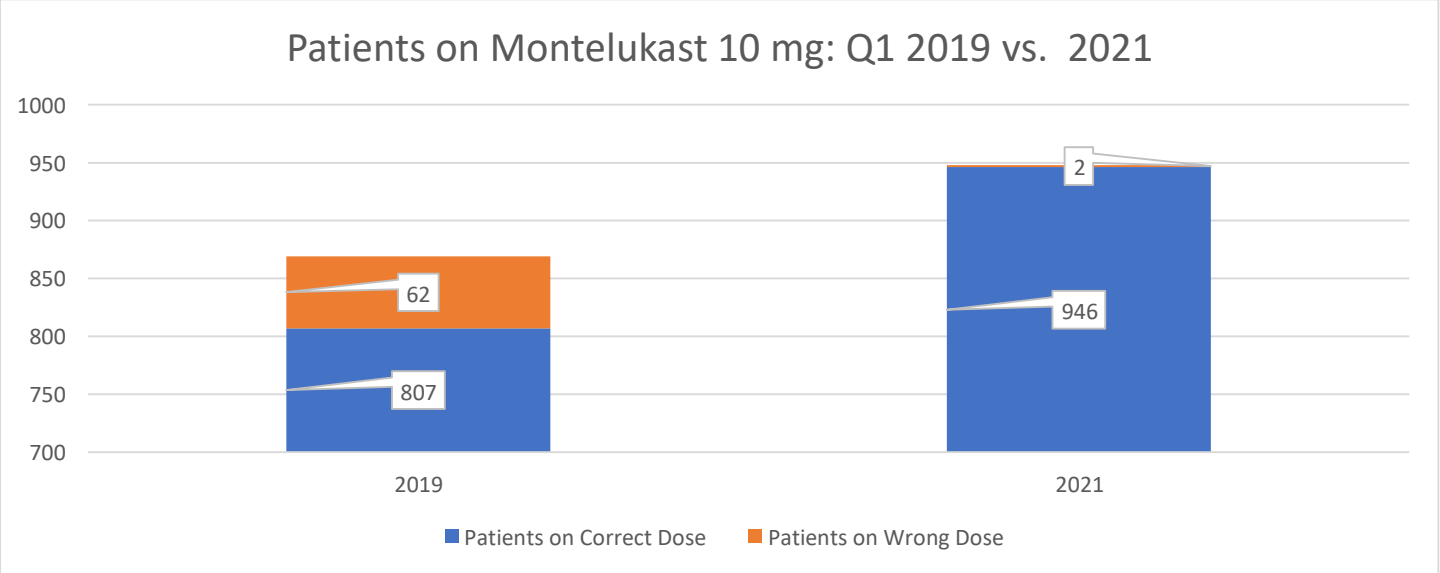

Patients on Montelukast: Q1 2019 vs.2021
1000
900
800
700
600
500
400
300
200
100
0
10 mg
5 mg
4 mg
2019
2021

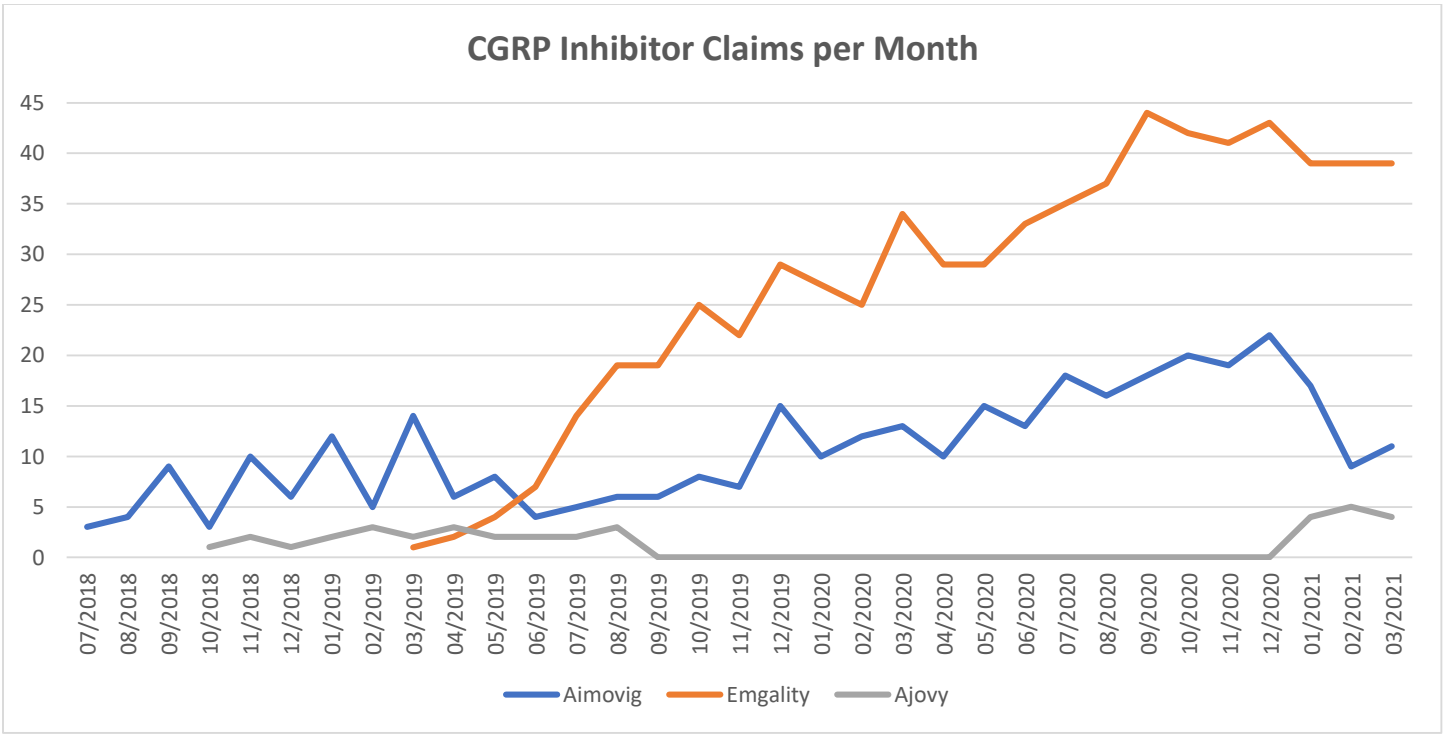

Patients on Montelukast: Q1 2019
124, 9%
1238, 91%
Patients on Correct Dose
Patients on Wrong Dose

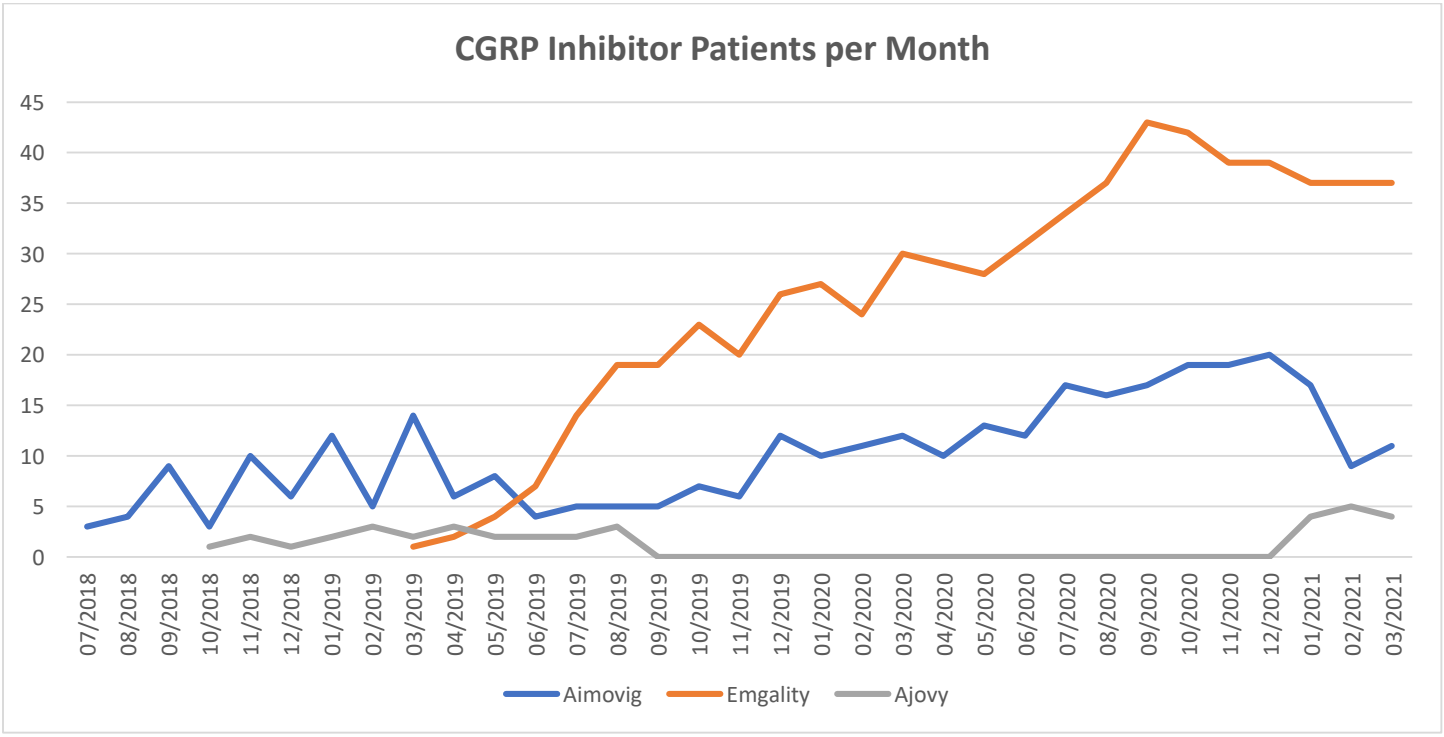

Patients on Montelukast: Q1 2021
5, 0%
1389, 100%
Patients on Correct Dose
Patients on Wrong Dose

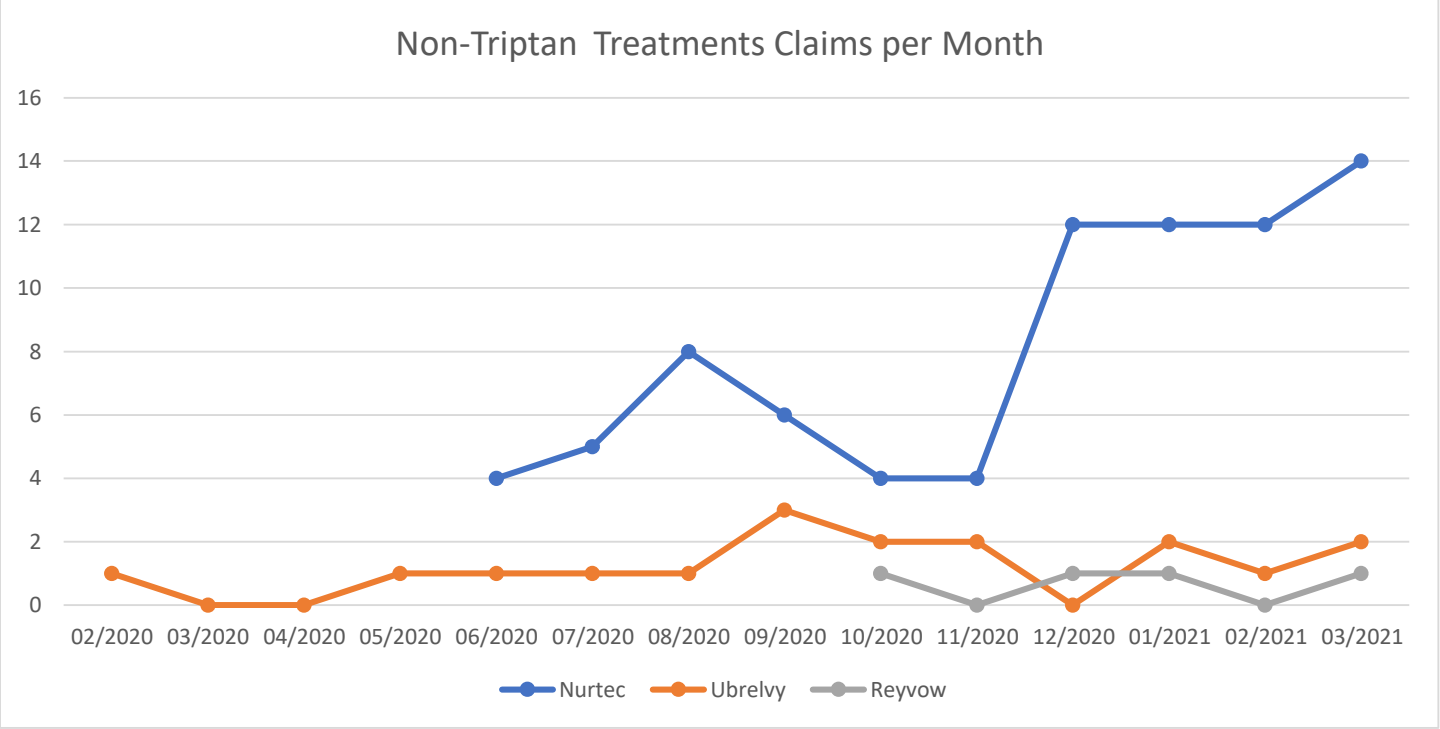

Patients on Montelukast 4 mg: Q1 2019 vs. 2021
250
200
150
100
50
0
49
159
1
114
2019
2021
Patients on Correct Dose
Patients on Wrong Dose

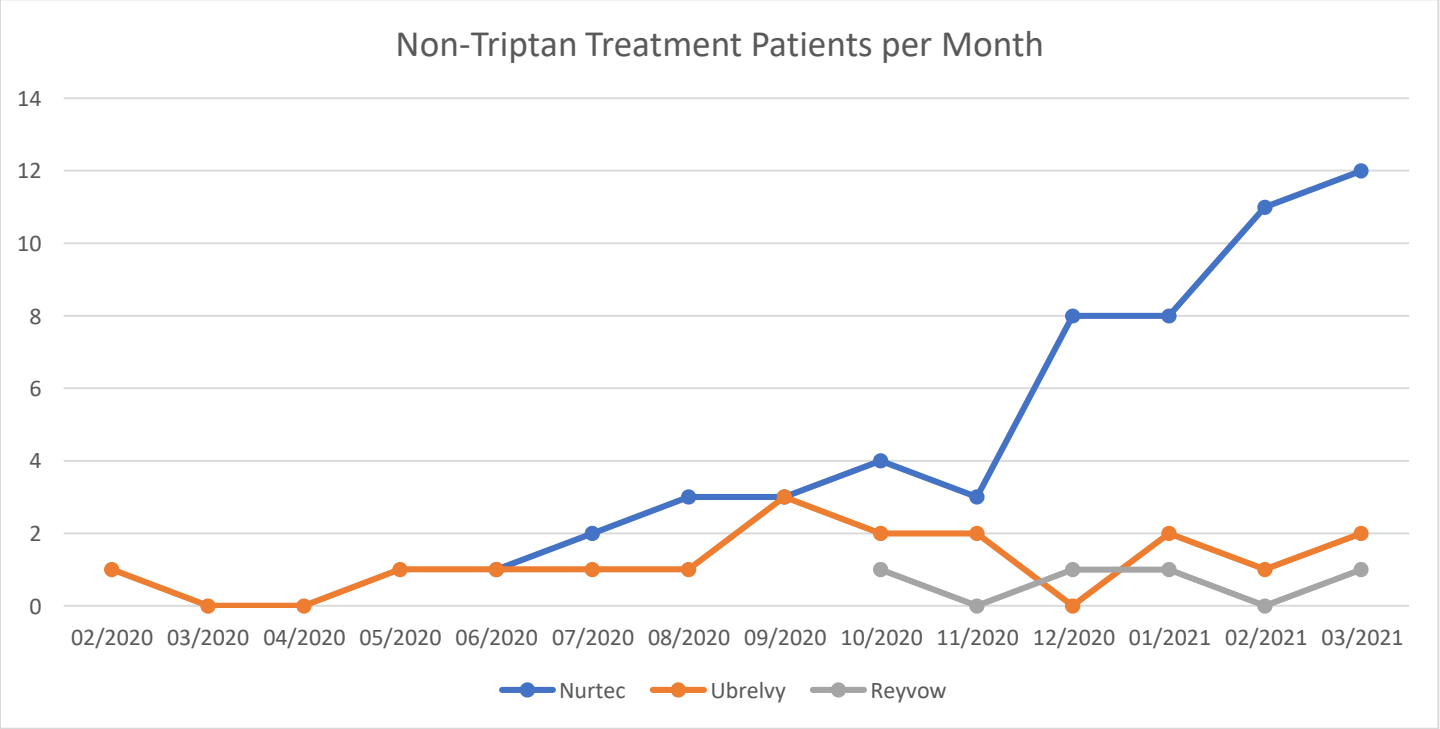

Patients on Montelukast 5 mg: Q1 2019 vs. 2021
350
300
250
200
150
100
50
0
13
272
2
329
2019
2021
Patients on Correct Dose
Patients on Wrong Dose

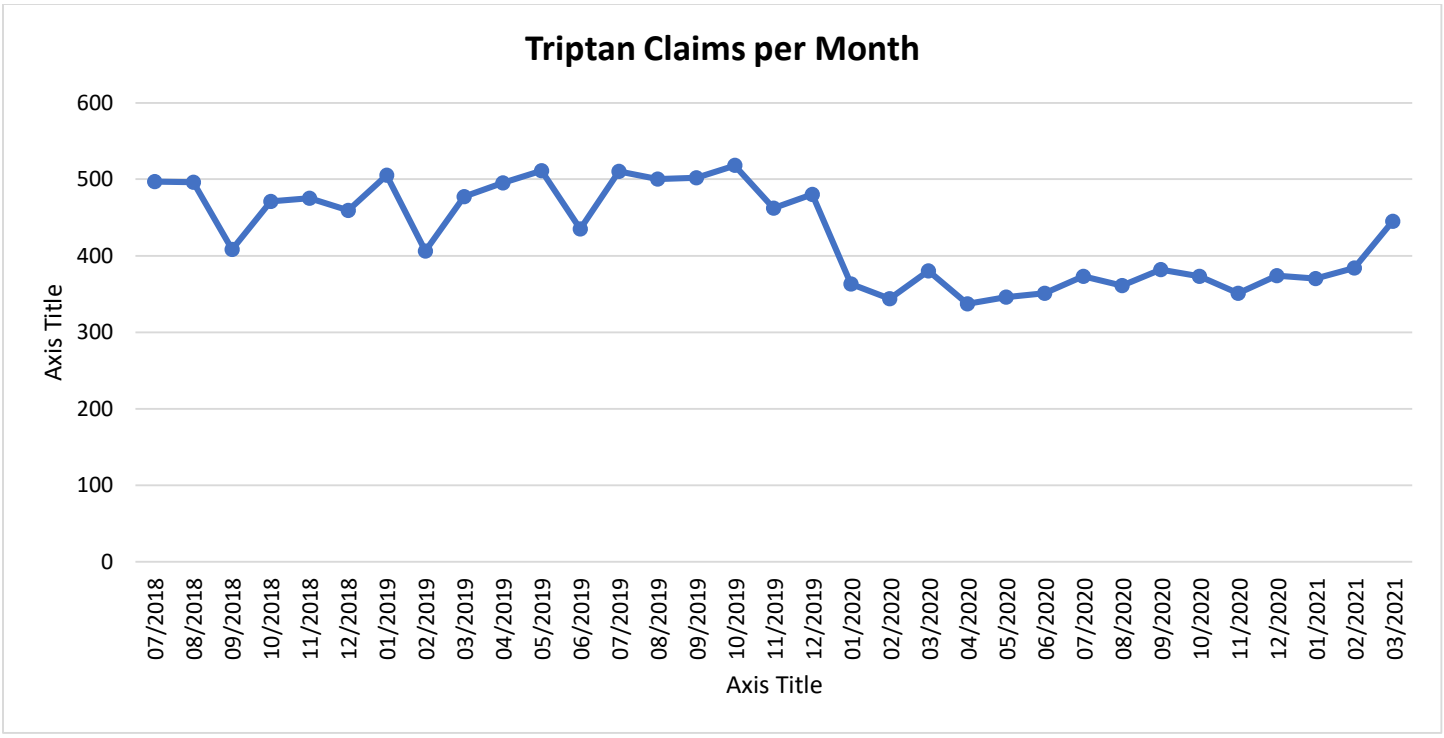

Patients on Montelukast 10 mg: Q1 2019 vs. 2021
1000
950
900
850
800
750
700
62
807
2
946
2019
2021
Patients on Correct Dose
Patients on Wrong Dose

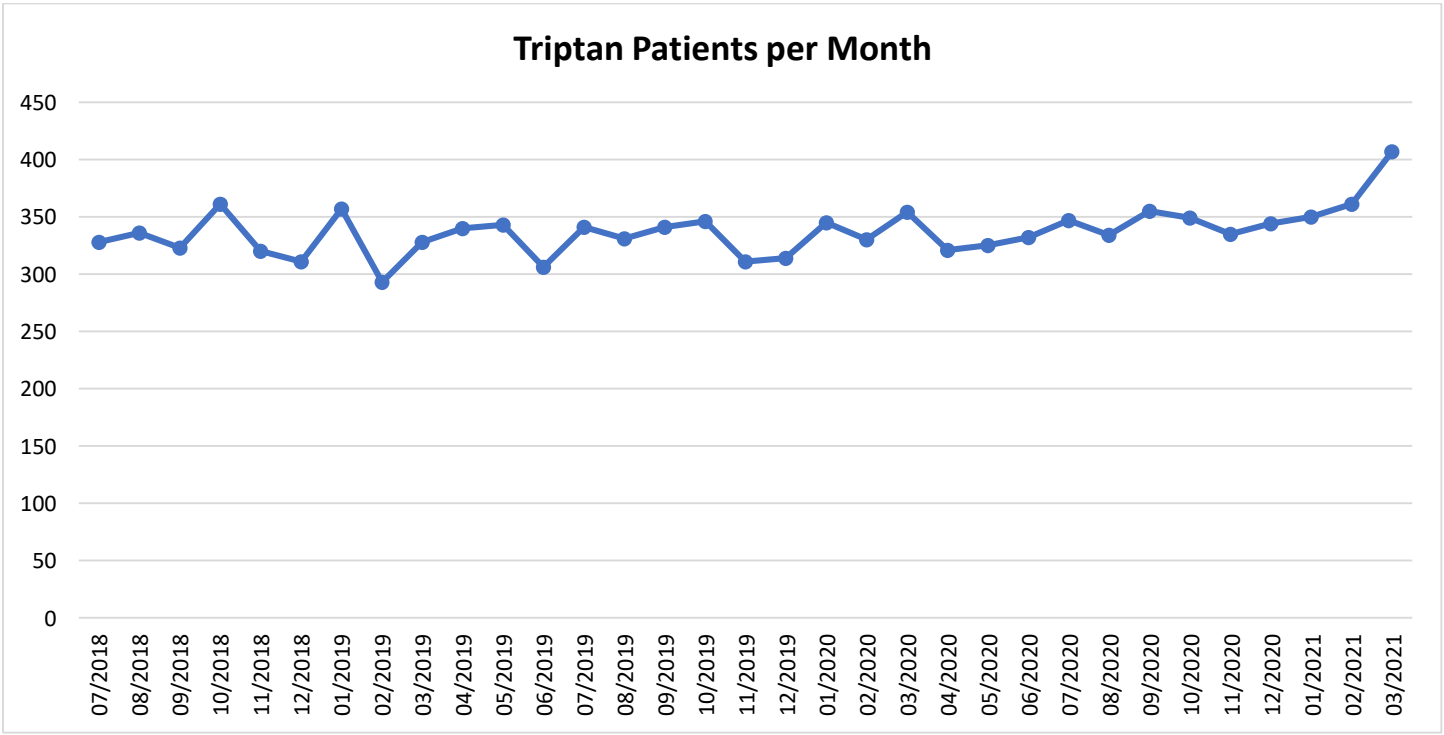

CGRP Inhibitor Claims per Month
45
40
35
30
25
20
15
10
5
0
07/2018
08/2018
09/2018
10/2018
11/2018
12/2018
01/2019
02/2019
03/2019
04/2019
05/2019
06/2019
07/2019
08/2019
09/2019
10/2019
11/2019
12/2019
01/2020
02/2020
03/2020
04/2020
05/2020
06/2020
07/2020
08/2020
09/2020
10/2020
11/2020
12/2020
01/2021
02/2021
03/2021
Aimovig
Emgality
Ajovy


CGRP Inhibitor Patients per Month
45
40
35
30
25
20
15
10
5
0
07/2018
08/2018
09/2018
10/2018
11/2018
12/2018
01/2019
02/2019
03/2019
04/2019
05/2019
06/2019
07/2019
08/2019
09/2019
10/2019
11/2019
12/2019
01/2020
02/2020
03/2020
04/2020
05/2020
06/2020
07/2020
08/2020
09/2020
10/2020
11/2020
12/2020
01/2021
02/2021
03/2021
Aimovig
Emgality
Ajovy


Non-Triptan Treatments Claims per Month
16
14
12
10
8
6
4
2
0
02/2020
03/2020
04/2020
05/2020
06/2020
07/2020
08/2020
09/2020
10/2020
11/2020
12/2020
01/2021
02/2021
03/2021
Nurtec
Ubrelvy
Reyvow


Non-Triptan Treatment Patients per Month
14
12
10
8
6
4
2
0
02/2020
03/2020
04/2020
05/2020
06/2020
07/2020
08/2020
09/2020
10/2020
11/2020
12/2020
01/2021
02/2021
03/2021
Nurtec
Ubrelvy
Reyvow


Triptan Claims per Month
600
500
400
300
200
100
0
Axis Title
07/2018
08/2018
09/2018
10/2018
11/2018
12/2018
01/2019
02/2019
03/2019
04/2019
05/2019
06/2019
07/2019
08/2019
09/2019
10/2019
11/2019
12/2019
01/2020
02/2020
03/2020
04/2020
05/2020
06/2020
07/2020
08/2020
09/2020
10/2020
11/2020
12/2020
01/2021
02/2021
03/2021
Axis Title


Triptan Patients per Month
450
400
350
300
250
200
150
100
50
0
07/2018
08/2018
09/2018
10/2018
11/2018
12/2018
01/2019
02/2019
03/2019
04/2019
05/2019
06/2019
07/2019
08/2019
09/2019
10/2019
11/2019
12/2019
01/2020
02/2020
03/2020
04/2020
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07/2020
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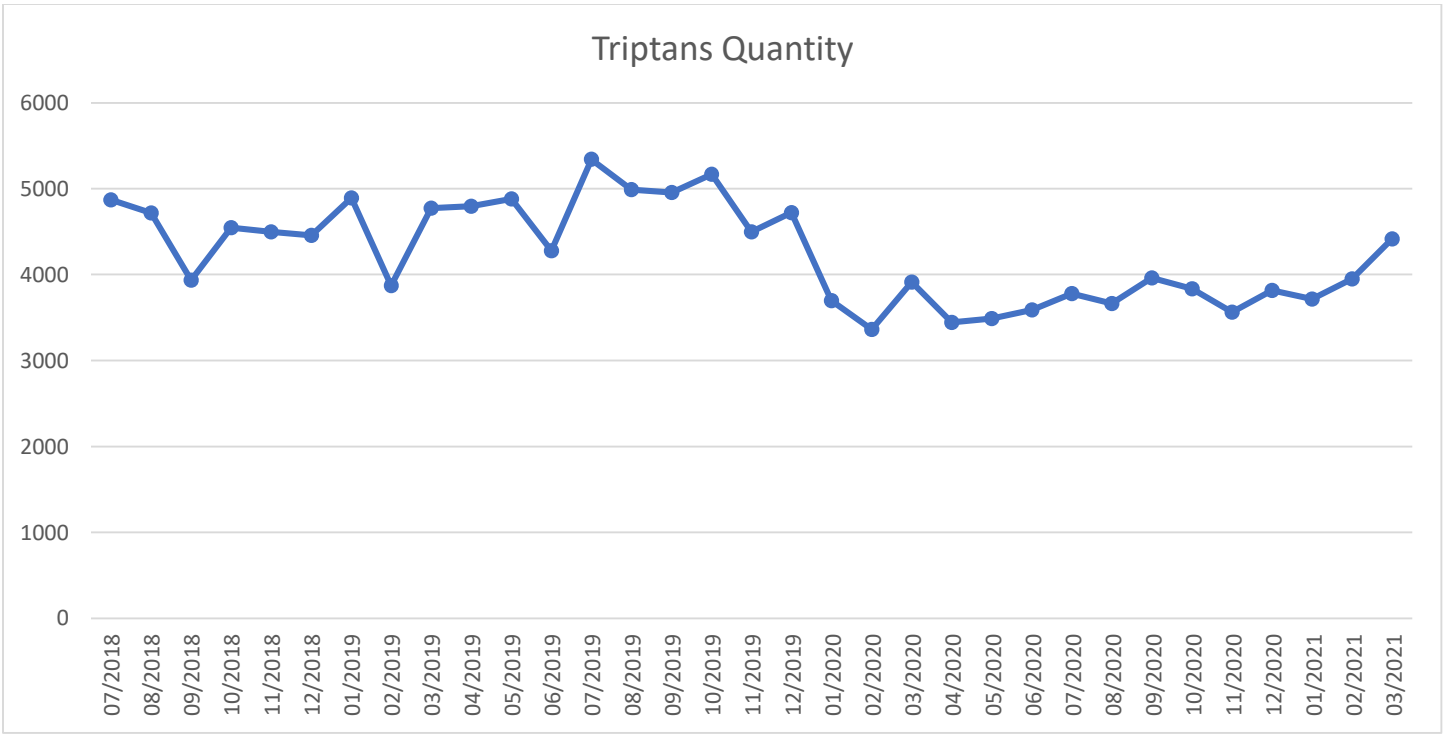
09/2020
10/2020
11/2020
12/2020
01/2021
02/2021
03/2021


Triptans Quantity
6000
5000
4000
3000
2000
1000
0
07/2018
08/2018
09/2018
10/2018
11/2018
12/2018
01/2019
02/2019
03/2019
04/2019
05/2019
06/2019
07/2019
08/2019
09/2019
10/2019
11/2019
12/2019
01/2020
02/2020
03/2020
04/2020
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07/2020
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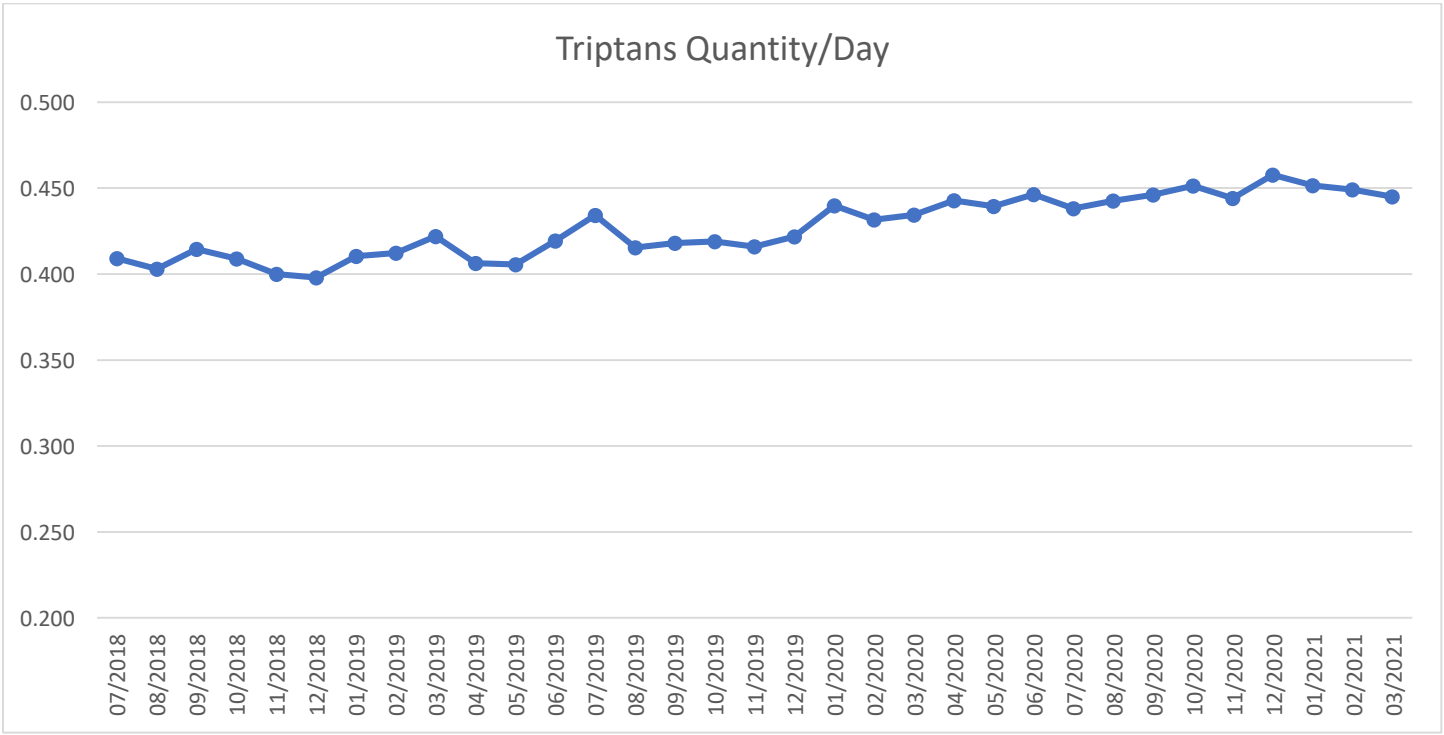
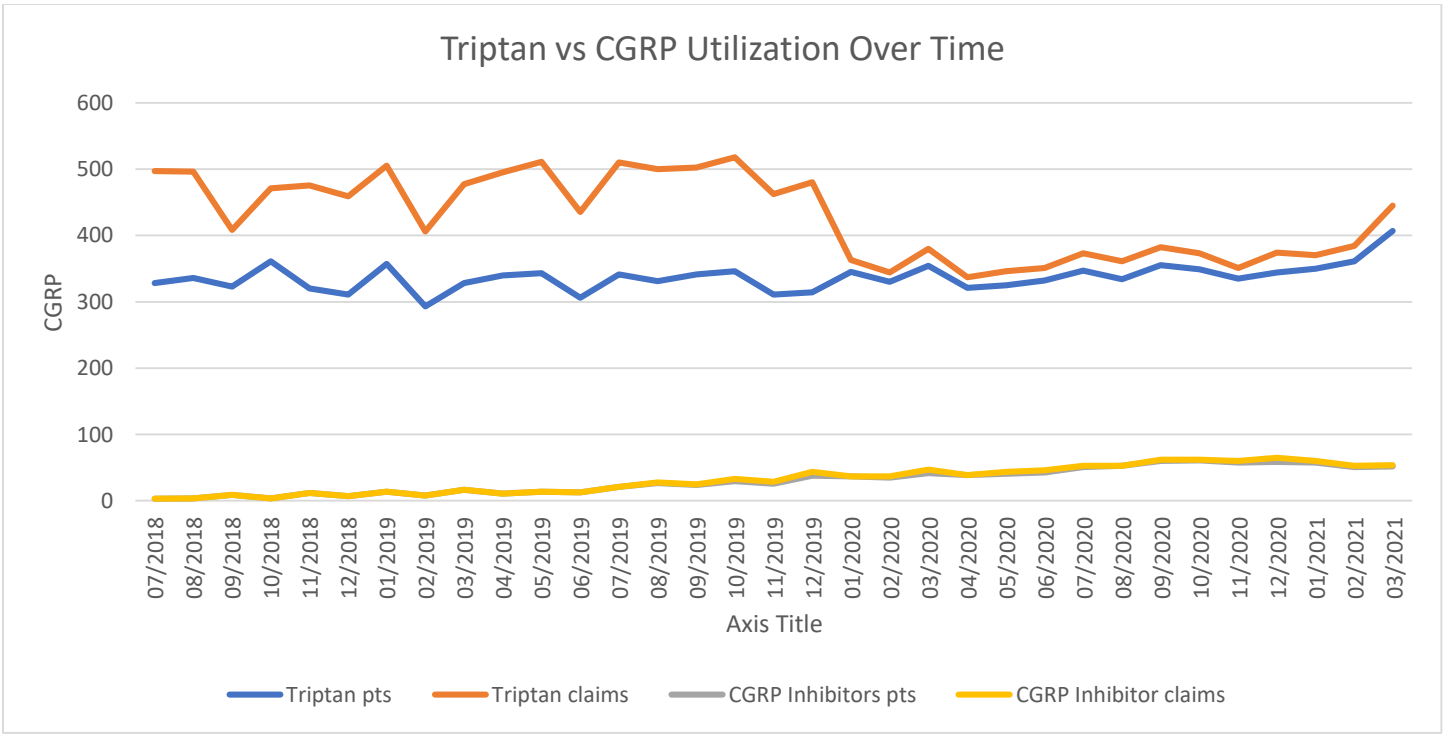
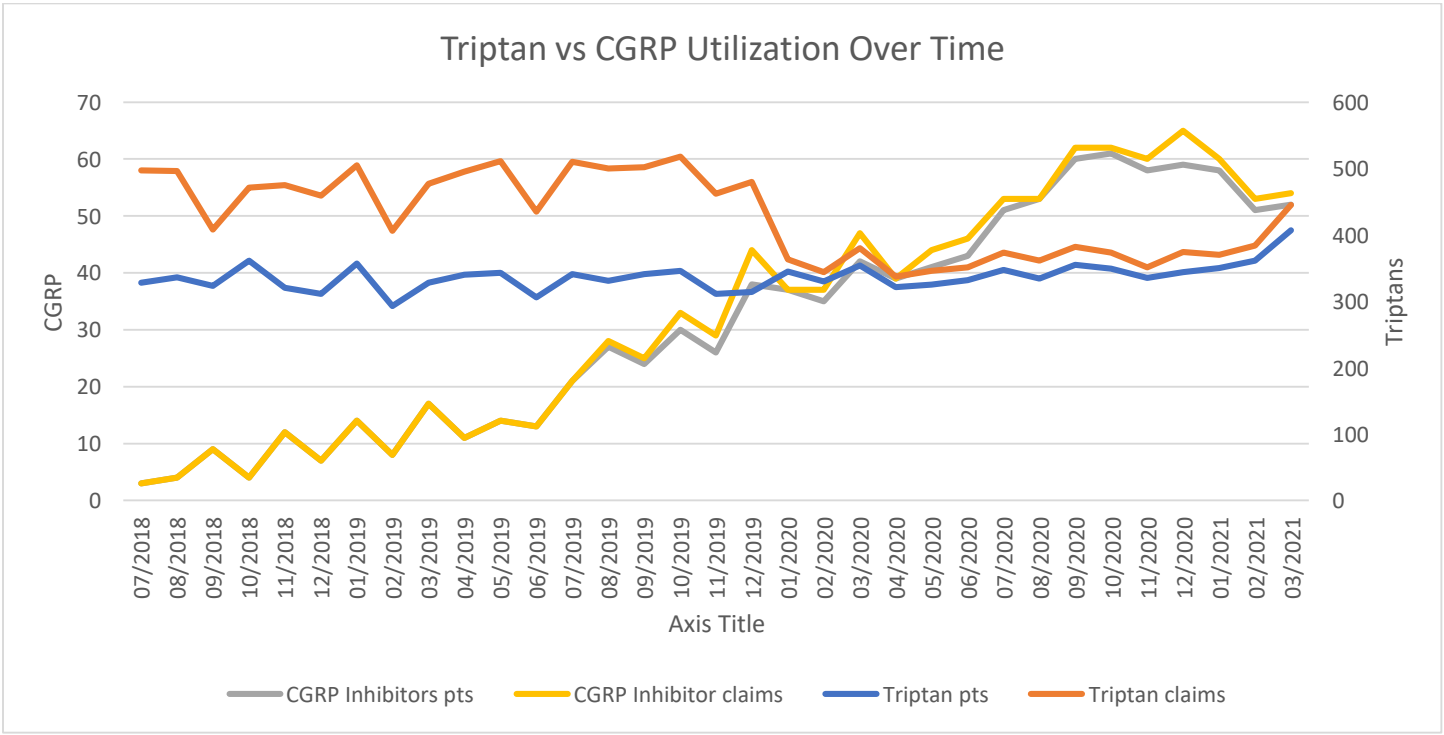
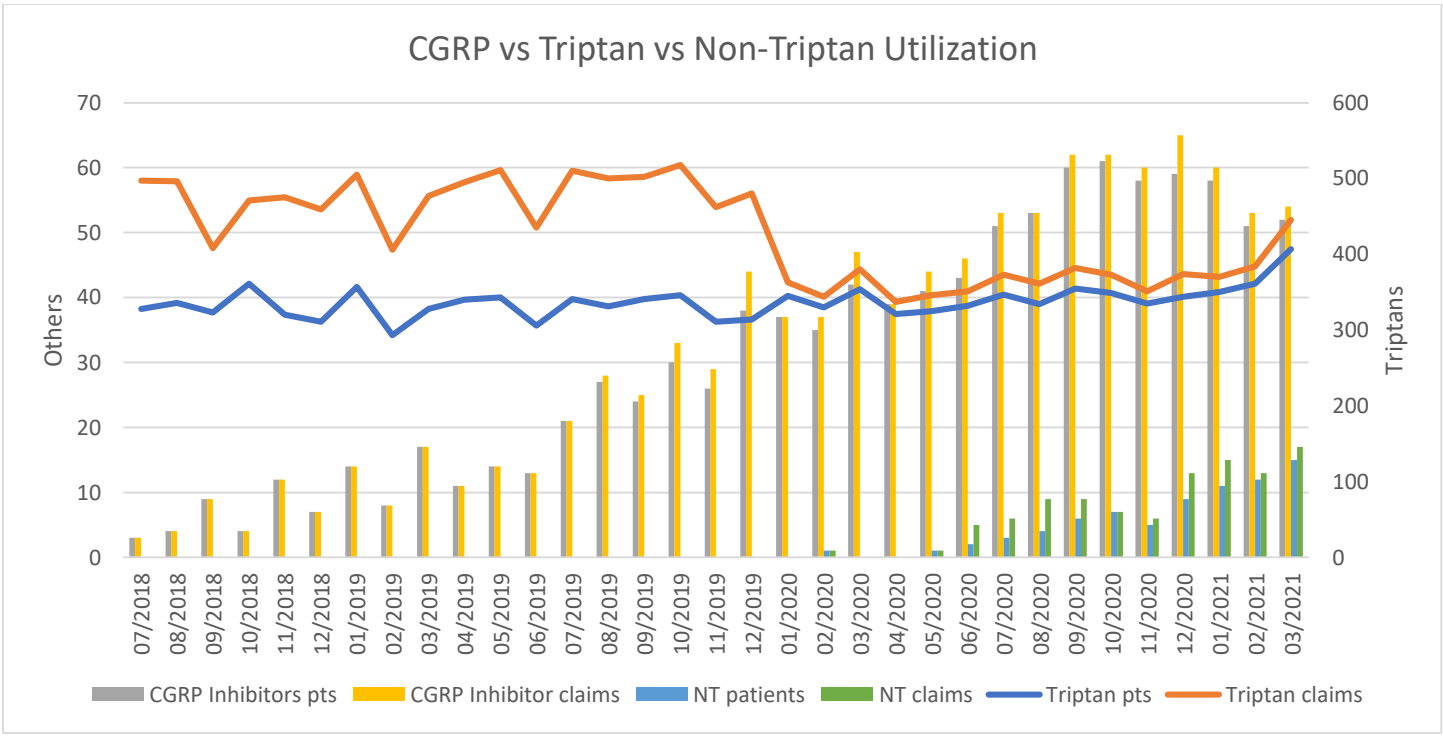
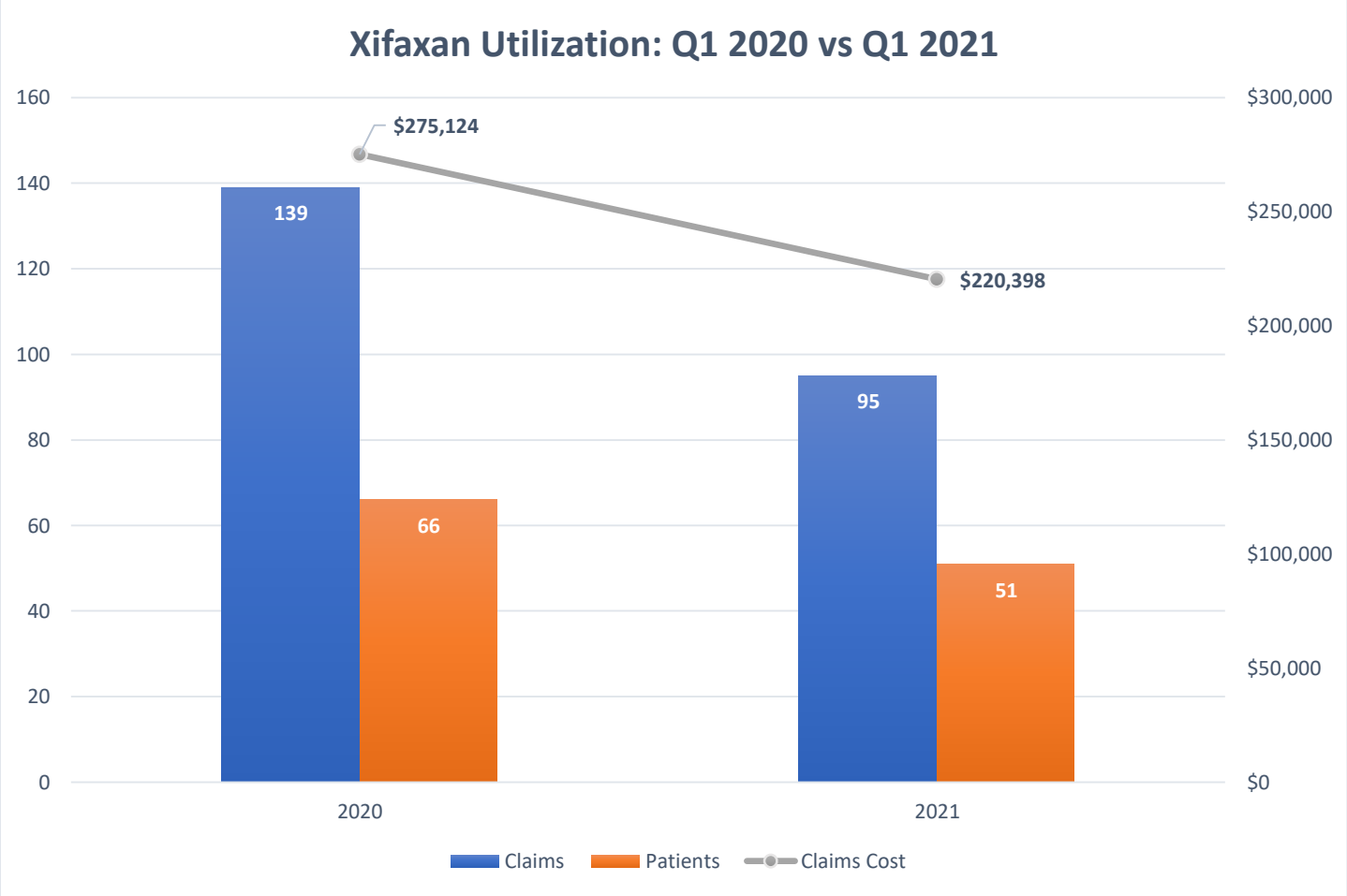
09/2020
10/2020
11/2020
12/2020
01/2021
02/2021
03/2021


Triptans Quantity/Day
0.500
0.450
0.400
0.350
0.300
0.250
0.200
07/2018
08/2018
09/2018
10/2018
11/2018
12/2018
01/2019
02/2019
03/2019
04/2019
05/2019
06/2019
07/2019
08/2019
09/2019
10/2019
11/2019
12/2019
01/2020
02/2020
03/2020
04/2020
05/2020
06/2020
07/2020
08/2020
09/2020
10/2020
11/2020
12/2020
01/2021
02/2021
03/2021

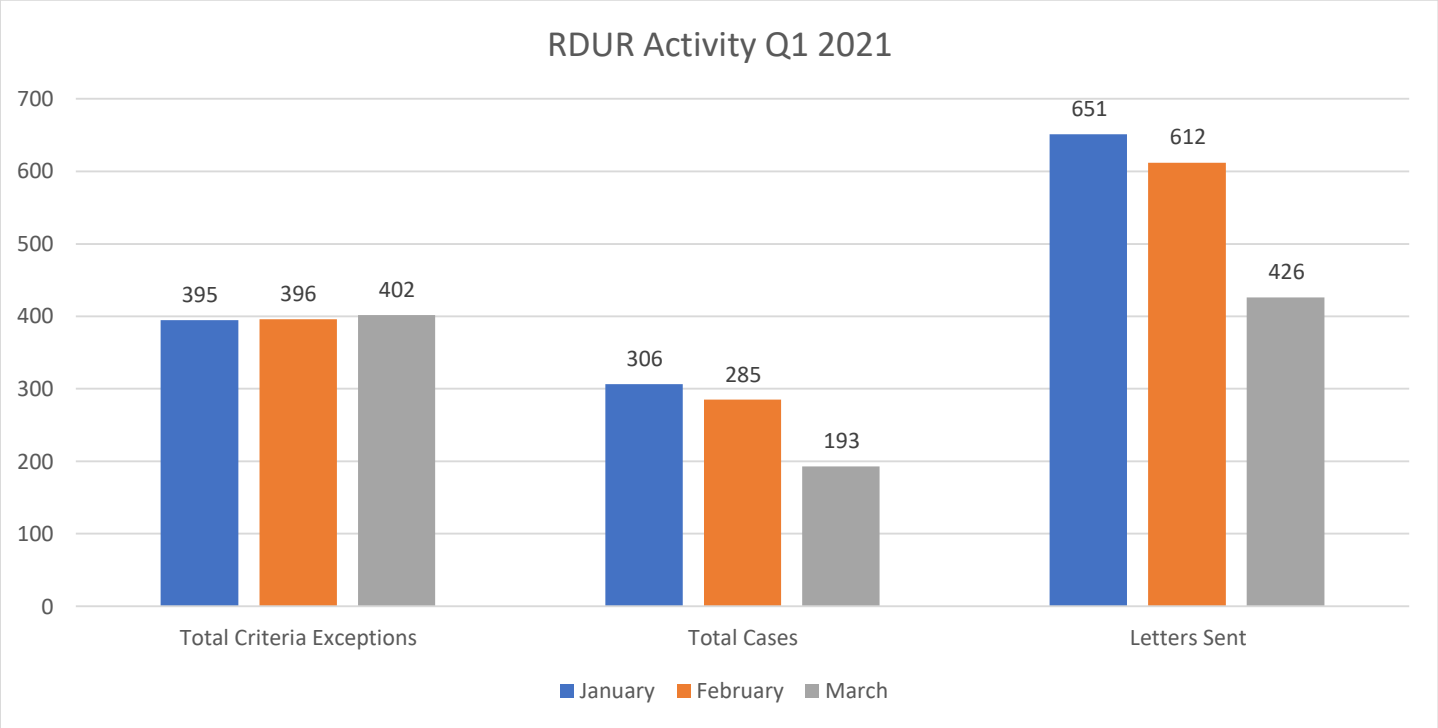

Triptan vs CGRP Utilization Over Time
600
500
400
300
200
100
0
CGRP
07/2018
08/2018
09/2018
10/2018
11/2018
12/2018
01/2019
02/2019
03/2019
04/2019
05/2019
06/2019
07/2019
08/2019
09/2019
10/2019
11/2019
12/2019
01/2020
02/2020
03/2020
04/2020
05/2020
06/2020
07/2020
08/2020
09/2020
10/2020
11/2020
12/2020
01/2021
02/2021
03/2021
Axis Title
Triptan pts
Triptan claims
CGRP Inhibitors pts
CGRP Inhibitor claims


Triptan vs CGRP Utilization Over Time
70
60
50
40
30
20
10
0
CGRP
600
500
400
300
200
100
0
Triptans
07/2018
08/2018
09/2018
10/2018
11/2018
12/2018
01/2019
02/2019
03/2019
04/2019
05/2019
06/2019
07/2019
08/2019
09/2019
10/2019
11/2019
12/2019
01/2020
02/2020
03/2020
04/2020
05/2020
06/2020
07/2020
08/2020
09/2020
10/2020
11/2020
12/2020
01/2021
02/2021
03/2021
Axis Title
CGRP Inhibitors pts
CGRP Inhibitor claims
Triptan pts
Triptan claims


CGRP vs Triptan vs Non-Triptan Utilization
Others
Triptans
70
60
50
40
30
20
10
0
600
500
400
300
200
100
0
07/2018
08/2018
09/2018
10/2018
11/2018
12/2018
01/2019
02/2019
03/2019
04/2019
05/2019
06/2019
07/2019
08/2019
09/2019
10/2019
11/2019
12/2019
01/2020
02/2020
03/2020
04/2020
05/2020
06/2020
07/2020
08/2020
09/2020
10/2020
11/2020
12/2020
01/2021
02/2021
03/2021
CGRP Inhibitors pts
CGRP Inhibitor claims
NT patients
NT claims
Triptan pts
Triptan claims


Xifaxan Utilization: Q1 2020 vs Q1 2021
160
140
120
100
80
60
40
20
0
$300,000
$250,000
$200,000
$150,000
$100,000
$50,000
$0
$275,124
$220,398
139
66
95
51
2020
2021
Claims
Patients
Claims Cost

RDUR Activity Overview: Q1 2021



January Cases by Type of Criteria			
Classification of Criteria	**Criteria Description**	**# of Cases**	**% of Cases**
Clinical Appropriateness	HYPERTENSION	34	11.11%
	RENAL IMPAIRMENT	4	1.31%
	ADVERSE FETAL EFFECTS	1	0.33%
	RESPIRATORY DEPRESSION	5	1.63%
	CONGESTIVE HEART FAILURE	2	0.65%
	INAPPROPRIATE THERAPY FOR ELDERLY	11	3.59%
	OVERUTILIZATION	2	0.65%
	DISEASE STATE MANAGEMENT	43	14.05%
	COST CONTROL	4	1.31%
	INAPPROPRIATE MIGRAINE THERAPY	5	1.63%
	INAPPROPRIATE PEDIATRIC THERAPY	30	9.80%
	INAPPROPRIATE THERAPY	2	0.65%
	QT PROLONGATION	1	0.33%
	INAPPROPRIATE USE OF LABA	1	0.33%
	SEDATIVE USE IN ADHD	41	13.40%
	TOPICAL CORTICOSTEROIDS IN PEDIATRIC PATIENTS	2	0.65%
	INAPPROPRIATE LIDODERM USE	50	16.34%
	INAPPROPRIATE PPI DURATION/USE	68	22.22%

February Cases by Type of Criteria			
Classification of Criteria	**Criteria Description**	**# of Cases**	**% of Cases**
Drug/Drug Conflicts	ADD. ANTICHOLINERGIC EFFECTS	15	5.26%
	DUPLICATE ANTIPSYCHOTIC THERAPY	38	13.33%
	THERAPEUTIC DUPLICATION OF ANXIOLYTIC AGENTS	18	6.32%
	DISEASE STATE MANAGEMENT	33	11.58%
	THERAPEUTIC DUPLICATION OF ANTIHISTAMINES	17	5.96%
	THERAPEUTIC DUPLICATION OF ANTICHOLINERGIC BRONCHODILATORS	6	2.11%
Clinical Appropriateness	DELAYED GASTRIC EMPTYING	13	4.56%
	INCREASED CANCER RISK	25	8.77%
	INCREASED LDL-C LEVELS	28	9.82%
	CONTRAINDICATION	2	0.70%
	PATIENT AT RISK OF ASCVD AND NOT ON STATIN	68	23.85%
	ARTHRALGIA	7	2.46%
	OPIOID USE IN PEDIATRIC PATIENTS	3	1.05%
	BEERS CRITERIA	2	0.70%
	INAPPROPRIATE STIRIPENTOL REGIMEN	1	0.35%
	INCREASED RISK OF LOWER LIMB AMPUTATION	9	3.16%

March Cases by Type of Criteria			
Classification of Criteria	**Criteria Description**	**# of Cases**	**% of Cases**
Drug/Disease Interaction	BETA BLOCKERS + RESPIRATORY DISEASE	38	19.69%
	RENAL IMPAIRMENT	57	29.53%
	LITHIUM TOXICITY	2	1.04%
	ARRHYTHMIAS	9	4.66%
	GASTROINTESTINAL DISORDER	32	16.58%
	COUGH	9	4.66%
	HORMONE EFFECTS	29	15.03%
	RENAL INSUFFICIENCY	5	2.59%
	URINARY RETENTION	12	6.22%

NORTH DAKOTA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
2ND QUARTER 2021

Criteria Recommendations ***Approved Rejected***

1. Tolvaptan / Therapeutic Appropriateness _____ _____
Alert Message: The safety and effectiveness of Jynarque (tolvaptan) in pediatric patients have not been established.

Drugs/Diseases

Util A	Util B	Util C
Tolvaptan		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Jynarque Prescribing Information, Oct. 2020, Otsuka America Pharmaceuticals, Inc.

2. Tolvaptan / Therapeutic Appropriateness _____ _____
Alert Message: Jynarque (tolvaptan) is contraindicated in patients with a history, signs or symptoms of significant liver impairment or injury. Tolvaptan can cause serious and potentially fatal liver injury. This contraindication does not apply to uncomplicated polycystic liver disease.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Tolvaptan	Liver Impairment	Cystic Liver Disease

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Jynarque Prescribing Information, Oct. 2020, Otsuka America Pharmaceuticals, Inc.

3. Tolvaptan / Contraindicated Conditions _____ _____
Alert Message: Jynarque (tolvaptan) is contraindicated in patients with uncorrected abnormal blood sodium concentrations, unable to sense or respond to thirst, hypovolemia, uncorrected urinary outflow obstruction, or anuria. Tolvaptan increases free water clearance and, as a result, may cause dehydration, hypovolemia, and hypernatremia.

Drugs/Diseases

Util A	Util B	Util C
Tolvaptan	Anuria	
	Hypovolemia	
	Urinary Tract Obstruction	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Jynarque Prescribing Information, Oct. 2020, Otsuka America Pharmaceuticals, Inc.

4. Tolvaptan / Strong CYP3A Inhibitors _____ _____

Alert Message: The coadministration of Jynarque (tolvaptan) with strong CYP3A inhibitors is contraindicated. Tolvaptan is a CYP3A4 substrate, and concurrent use with a strong CYP3A inhibitor has been shown to increase tolvaptan exposure, increasing the risk of tolvaptan-related adverse effects.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Jynarque Prescribing Information, Oct. 2020, Otsuka America Pharmaceuticals, Inc.

5. Tolvaptan / Moderate CYP3A Inhibitors _____ _____

Alert Message: The coadministration of Jynarque (tolvaptan) with moderate CYP3A inhibitors should be avoided. If concurrent use cannot be avoided, reduce the tolvaptan dose per the official prescribing information. Tolvaptan is a CYP3A substrate, and concurrent use with a moderate CYP3A inhibitor can result in increased tolvaptan exposure, increasing the risk of tolvaptan-related adverse effects.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Jynarque Prescribing Information, Oct. 2020, Otsuka America Pharmaceuticals, Inc.

6. Tolvaptan / Strong CYP3A Inducers _____ _____

Alert Message: The coadministration of Jynarque (tolvaptan) with strong CYP3A inducers should be avoided. Tolvaptan is a CYP3A4 substrate, and coadministration with a CYP3A4 inducer can lead to a reduction in the plasma concentration of tolvaptan and decreased effectiveness of treatment.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Jynarque Prescribing Information, Oct. 2020, Otsuka America Pharmaceuticals, Inc.

7. Tolvaptan / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Available data with Jynarque (tolvaptan) use in pregnant women are insufficient to determine if there is a drug-associated risk of adverse developmental outcomes. In animal studies, tolvaptan has been shown to have adverse effects on the fetus when given to pregnant animals at maternally toxic doses. Advise pregnant patients of the potential risk to the fetus.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Jynarque Prescribing Information, Oct. 2020, Otsuka America Pharmaceuticals, Inc.

8. Tolvaptan / Therapeutic Appropriateness _____ _____

Alert Message: There are no data on the presence of Jynarque (tolvaptan) in human milk, the effects on the breastfed infant, or the effects on milk production. Tolvaptan is present in rat milk. When a drug is present in animal milk, it is possible that the drug will be present in human milk, but relative levels may vary. Because of the potential for serious adverse reactions, including liver toxicity, electrolyte abnormalities (e.g., hypernatremia), hypotension, and volume depletion in breastfed infants, advise women not to breastfeed during treatment with tolvaptan.

Drugs/Diseases

Util A	Util B	Util C
Tolvaptan	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Jynarque Prescribing Information, Oct. 2020, Otsuka America Pharmaceuticals, Inc.

9. 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.

10. Rosuvastatin Sprinkle / Overuse _____ _____

Alert Message: Ezallor Sprinkle (rosuvastatin) may be over-utilized. The recommended maximum dosage of rosuvastatin is 40 mg once daily.

Drugs/Diseases

Util A	Util B	Util C (Negating)	
Rosuvastatin sprinkle		CKD Stage 4 & 5	Gemfibrozil
		ESRD	Glecaprevir/Pibrentasvir
		Atazanavir	Lopinavir/rtv
		Cyclosporine	Regorafenib
		Darolutamide	Sofosbuvir/Velpatasvir
		Elbasvir/Grazoprevir	Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir

Max Dose: 40 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ezallor Prescribing Information, Sept. 2020, Sun Pharmaceuticals Industries.

11. Rosuvastatin Sprinkle / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Ezallor Sprinkle (rosuvastatin) have not been established in pediatric patients.

Drugs/Diseases

Util A	Util B	Util C
Rosuvastatin Sprinkle		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ezallor Prescribing Information, Sept. 2020, Sun Pharmaceuticals Industries.

12. Rosuvastatin Sprinkle / Hepatic Impairment _____ _____

Alert Message: Ezallor Sprinkle (rosuvastatin) use is contraindicated in patients with active liver disease, which may include unexplained persistent elevations of hepatic transaminase levels.

Drugs/Diseases

Util A	Util B	Util C (Include)
Rosuvastatin sprinkle		Hepatic Impairment

Max Dose
References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ezallor Prescribing Information, Sept. 2020, Sun Pharmaceuticals Industries.

13. Rosuvastatin Sprinkle / Severe Renal Impairment _____ _____

Alert Message: For patients with severe renal impairment (CLcr < 30 mL/min/1.73 m2) not on hemodialysis, dosing of Ezallor Sprinkle (rosuvastatin) should be started at 5 mg once daily and not exceed 10 mg once daily.

Drugs/Diseases

Util A	Util B	Util C (Include)
Rosuvastatin sprinkle		CKD Stage 4 & 5 ESRD

Max Dose: 10 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ezallor Prescribing Information, Sept. 2020, Sun Pharmaceuticals Industries.

14. Rosuvastatin Sprinkle / Gemfibrozil _____ _____

Alert Message: Due to the observed increased risk of myopathy/rhabdomyolysis, the concurrent use of Ezallor Sprinkle (rosuvastatin) with gemfibrozil should be avoided. If concomitant use cannot be avoided, initiate rosuvastatin at 5 mg once daily. The dose of rosuvastatin should not exceed 10 mg once daily.

Drugs/Diseases

Util A	Util B	Util C
Rosuvastatin sprinkle	Gemfibrozil	

Max Dose: 10 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ezallor Prescribing Information, Sept. 2020, Sun Pharmaceuticals Industries.

15. Rosuvastatin Sprinkle / Cyclosporine _____ _____

Alert Message: The dose of Ezallor Sprinkle (rosuvastatin) should not exceed 5 mg once daily when coadministered with cyclosporine. Rosuvastatin is a BCRP and OATP1B1 substrate, and concurrent use with cyclosporine, a BCRP and OATP1B1 transport inhibitor, has been shown to elevate 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 sprinkle	Cyclosporine	

Max Dose: 5 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ezallor Prescribing Information, Sept. 2020, Sun Pharmaceuticals Industries.

16. Rosuvastatin Sprinkle / Darolutamide _____ _____

Alert Message: The dose of Ezallor Sprinkle (rosuvastatin) should not exceed 5 mg once daily when co-administered with Nubeqa (darolutamide). Rosuvastatin is a BCRP substrate, and concurrent use with darolutamide, a BCRP transport inhibitor, has been shown to elevate 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 sprinkle	Darolutamide	

Max Dose: 5 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ezallor Prescribing Information, Sept. 2020, Sun Pharmaceuticals Industries.

17. Rosuvastatin Sprinkle / Regorafenib _____ _____

Alert Message: The dose of Ezallor Sprinkle (rosuvastatin) should not exceed 10 mg once daily when co-administered with regorafenib. Rosuvastatin is a BCRP substrate, and concurrent use with regorafenib, a BCRP transport inhibitor, has been shown to elevate 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 sprinkle	Regorafenib	

Max dose: 10 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ezallor Prescribing Information, Sept. 2020, Sun Pharmaceuticals Industries.

18. Rosuvastatin Sprinkle / Lopinavir & Atazanavir _____ _____

Alert Message: The dose of Ezallor Sprinkle (rosuvastatin) should not exceed 10 mg once daily when co-administered with lopinavir/ritonavir or ritonavir-boosted atazanavir. Lopinavir and atazanavir are OATP1B1 transport inhibitors, 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 sprinkle	Atazanavir Lopinavir/Ritonavir	

Max Dose: 10 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ezallor Prescribing Information, Sept. 2020, Sun Pharmaceuticals Industries.

19. Rosuvastatin Sprinkle / Viekira Pak _____ _____

Alert Message: The dose of Ezallor Sprinkle (rosuvastatin) should not exceed 10 mg per day when co-administered with ombitasvir/paritaprevir/ritonavir/dasabuvir (Viekira Pak). 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 sprinkle	Ombitasvir/paritaprevir/ritonavir/dasabuvir	

Max Dose: 10 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ezallor Prescribing Information, Sept. 2020, Sun Pharmaceuticals Industries.

20. Rosuvastatin Sprinkle / Elbasvir/Grazoprevir _____ _____

Alert Message: The dose of Ezallor Sprinkle (rosuvastatin) should not exceed 10 mg 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 sprinkle	Elbasvir/Grazoprevir	

Max Dose: 10 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ezallor Prescribing Information, Sept. 2020, Sun Pharmaceuticals Industries.

21. Rosuvastatin Sprinkle / Sofosbuvir/Velpatasvir _____ _____

Alert Message: The dose of Ezallor Sprinkle (rosuvastatin) should not exceed 10 mg 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 sprinkle	Sofosbuvir/Velpatasvir	

Max Dose: 10 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ezallor Prescribing Information, Sept. 2020, Sun Pharmaceuticals Industries.

22. Rosuvastatin Sprinkle / Glecaprevir/Pibrentasvir _____ _____

Alert Message: The dose of Ezallor Sprinkle (rosuvastatin) should not exceed 10 mg 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 sprinkle	Glecaprevir/Pibrentasvir	

Max Dose: 10 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ezallor Prescribing Information, Sept. 2020, Sun Pharmaceuticals Industries.

23. Rosuvastatin Sprinkle / Atazanavir/Cobicistat _____ _____

Alert Message: The dose of Ezallor Sprinkle (rosuvastatin) should not exceed 10 mg once daily when co-administered with Evotaz (atazanavir/cobicistat). The components of the antiretroviral 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 sprinkle	Atazanavir/Cobicistat	

Max Dose: 10 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ezallor Prescribing Information, Sept. 2020, Sun Pharmaceuticals Industries.

24. Rosuvastatin Sprinkle / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Ezallor Sprinkle (rosuvastatin) is contraindicated for use in pregnant patients since safety in these patients has not been established, and there is no apparent benefit to therapy with rosuvastatin during pregnancy. Because HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, rosuvastatin may cause fetal harm when administered to pregnant patients. Rosuvastatin should be discontinued as soon as pregnancy is recognized.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ezallor Prescribing Information, Sept. 2020, Sun Pharmaceuticals Industries.

25. Rosuvastatin Sprinkle / Therapeutic Appropriateness _____ _____

Alert Message: Ezallor Sprinkle (rosuvastatin) use is contraindicated during breastfeeding. Limited data indicate that rosuvastatin is present in human milk. There is no available information on the effects of the drug on the breastfed infant or the effects of the drug on milk production. Because of the potential for serious adverse reactions in a breastfed infant, advise patients that breastfeeding is not recommended during treatment with rosuvastatin.

Drugs/Diseases

Util A	Util B	Util C
Rosuvastatin sprinkle	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ezallor Prescribing Information, Sept. 2020, Sun Pharmaceuticals Industries.

26. Eptinezumab / Overuse _____ _____

Alert Message: Vyepti (eptinezumab) may be over-utilized. The recommended dosage of eptinezumab is 100 mg administered by intravenous infusion every 3 months. Some patients may benefit from a dosage of 300 mg administered by intravenous infusion every 3 months.

Drugs/Diseases

Util A	Util B	Util C
Eptinezumab		

Max Dose: 300mg/3 months

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.
Vyepti Prescribing Information, Feb. 2020, Lundbeck Seattle BioPharmaceuticals, Inc.

27. Eptinezumab / Therapeutic Appropriateness _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Eptinezumab		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.
Vyepti Prescribing Information, Feb. 2020, Lundbeck Seattle BioPharmaceuticals, Inc.

28. Eptinezumab/ Non-adherence _____ _____
Alert Message: Based on refill history, your patient may be underutilizing Vyepti (eptinezumab). 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
Eptinezumab		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med.2005;353:487-97.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Vyepti Prescribing Information, Feb. 2020, Lundbeck Seattle BioPharmaceuticals, Inc.

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

Drugs/Diseases

Util A	Util B	Util C
Rimegepant		

Max Dose: 75 mg/day

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

30. Opicapone / Overuse _____ _____
Alert Message: Ongentys (opicapone) may be over-utilized. The recommended dosage of opicapone is 50 mg once daily at bedtime.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Opicapone		Hepatic Impairment

Max Dose: 50 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ongentys Prescribing Information, April 2020, Neurocrine Biosciences, Inc.

31. Opicapone / Overuse – Hepatic Impairment _____ _____

Alert Message: Ongentys (opicapone) may be over-utilized. The recommended dosage of opicapone in patients with moderate hepatic impairment (Child-Pugh B) is 25 mg once daily at bedtime. In a pharmacokinetic study, the mean overall opicapone plasma exposure (AUC) in subjects with moderate hepatic impairment increased by 84%. Opicapone has not been studied in patients with severe hepatic impairment (Child-Pugh C), and its use should be avoided in this population.

Drugs/Diseases

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

Max Dose: 25 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ongentys Prescribing Information, April 2020, Neurocrine Biosciences, Inc.

32. Opicapone / Therapeutic Appropriateness _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Opicapone		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ongentys Prescribing Information, April 2020, Neurocrine Biosciences, Inc.

33. Opicapone / Therapeutic Appropriateness _____ _____

Alert Message: The use of Ongentys (opicapone) should be avoided in patients with end-stage renal disease (ESRD) (CLcr < 15 mL/min). No dosage adjustment is required for patients with mild, moderate, or severe renal impairment. However, because of the potential for increased exposure, monitor patients with severe renal impairment for adverse reactions and discontinue opicapone if tolerability issues arise.

Drugs/Diseases

Util A	Util B	Util C
Opicapone	ESRD	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ongentys Prescribing Information, April 2020, Neurocrine Biosciences, Inc.

34. Opicapone / Non-Selective MAO Inhibitors _____ _____

Alert Message: The concurrent use of Ongentys (opicapone) with non-selective MAO inhibitors is contraindicated. Both opicapone and non-selective MAO inhibitors (e.g., phenelzine, isocarboxazid, and tranylcypromine) inhibit catecholamine metabolism, leading to increased levels of catecholamines. Concomitant use may increase the risk of possible arrhythmias, increased heart rate, and excessive changes in blood pressure.

Drugs/Diseases

Util A	Util B	Util C
Opicapone	Isocarboxazid	
	Phenelzine	
	Tranylcypromine	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ongentys Prescribing Information, April 2020, Neurocrine Biosciences, Inc.

35. Opicapone / Catecholamine Secreting Neoplasm _____ _____

Alert Message: Ongentys (opicapone) use is contraindicated in patients with a history of pheochromocytoma, paraganglioma, or other catecholamine secreting neoplasms.

Drugs/Diseases

Util A	Util B	Util C (Include)
Opicapone		Malignant Neoplasm of Adrenal Gland
		Benign Neoplasm of Adrenal Gland

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ongentys Prescribing Information, April 2020, Neurocrine Biosciences, Inc.

36. Opicapone / COMT Substrates _____ _____

Alert Message: Possible arrhythmias, increased heart rate, and excessive changes in blood pressure may occur with concomitant use of Ongentys (opicapone) and drugs metabolized by COMT (e.g., ephedrine, epinephrine, and methyldopa), regardless of the route of administration (including inhalation). Monitor patients treated concomitantly with opicapone and drugs metabolized by COMT.

Drugs/Diseases

Util A	Util B	Util C
Opicapone	Ephedrine	
	Epinephrine	
	Methyldopa	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ongentys Prescribing Information, April 2020, Neurocrine Biosciences, Inc.

37. Opicapone / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no adequate data on the developmental risk associated with the use of Ongentys (opicapone) in pregnant patients. In animal studies, oral administration of opicapone during pregnancy resulted in adverse effects on embryofetal development (increased incidence of fetal abnormalities) at clinically relevant plasma exposures in one of two species tested. In addition, opicapone is always given concomitantly with levodopa/carbidopa, which is known to cause developmental toxicity in rabbits.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ongentys Prescribing Information, April 2020, Neurocrine Biosciences, Inc.

38. Opicapone / Lactation _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Opicapone	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ongentys Prescribing Information, April 2020, Neurocrine Biosciences, Inc.

39. Opicapone / Therapeutic Appropriateness _____ _____

Alert Message: A review of the patient's drug history did not reveal a current prescription for levodopa/carbidopa. Ongentys (opicapone) is indicated as adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease experiencing "off " episodes.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Opicapone		Carbidopa/Levodopa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ongentys Prescribing Information, April 2020, Neurocrine Biosciences, Inc.

40. Opicapone / Hallucinations & Psychosis _____ _____

Alert Message: Hallucinations (auditory hallucinations, visual hallucinations, mixed hallucinations) have been reported in patients receiving Ongentys (opicapone). Patients with a major psychotic disorder ordinarily should not be treated with opicapone because of the risk of exacerbating the psychosis with an increase in central dopaminergic tone. Consider stopping opicapone if hallucinations or psychotic-like behaviors occur.

Drugs/Diseases

Util A	Util B	Util C
Opicapone	Hallucinations	
	Delusions	
Psychosis		

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ongentys Prescribing Information, April 2020, Neurocrine Biosciences, Inc.

41. Opicapone / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Ongentys (opicapone). 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
Opicapone		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med. 2005;353:487-97.
Grosset D, Antonini A, Canesi M, et al. Adherence to Antiparkinson Medication in a Multicenter European Study. Movement Disord. 2009. Vol 24, No. 6:826-832.
Straka I, Minár M, Škorvánek M, et al. Adherence to Pharmacotherapy in Patients With Parkinson's Disease Taking Three and More Daily Doses of Medication. Front Neurol. 2019;10:799. Published 2019 Jul 31. doi:10.3389/fneur.2019.00799

42. Viloxazine / Overuse _____ _____

Alert Message: Qelbree (viloxazine) may be over-utilized. The recommended maximum daily dose of viloxazine is 400 mg once daily.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Viloxazine		Chronic Kidney Disease Stage 4
		Chronic Kidney Disease Stage 5

Max Dose: 400 mg/day

References:
Qelbree Prescribing Information, April 2021, Supernus Pharmaceuticals.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

43. Viloxazine / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Qelbree (viloxazine) have not been established in pediatric patients younger than 6 years old.

Drugs/Diseases

Util A	Util B	Util C
Viloxazine		

Age Range: 0 – 5 yoa

References:
Qelbree Prescribing Information, April 2021, Supernus Pharmaceuticals.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

44. Viloxazine / Overuse Renal Impairment _____ _____

Alert Message: Qelbree (viloxazine) may be over-utilized. The recommended maximum daily dose of viloxazine in patients with severe renal impairment (eGFR < 30 mL/min/1.73m2), is 200 mg once daily. No dosage adjustment is recommended in patients with mild to moderate (eGFR of 30 to 89 mL/min/1.73m2) renal impairment.

Drugs/Diseases

Util A	Util B	Util C (Include)
Viloxazine		Chronic Kidney Disease Stage 4
		Chronic Kidney Disease Stage 5

Max Dose: 200 mg/day

References:
Qelbree Prescribing Information, April 2021, Supernus Pharmaceuticals.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

45. Viloxazine / Therapeutic Appropriateness (Black Box Warning) _____ _____

Alert Message: In clinical studies, higher rates of suicidal thoughts and behavior were reported in pediatric patients with ADHD treated with Qelbree (viloxazine) than in patients treated with placebo. Closely monitor all viloxazine-treated patients for clinical worsening, and emergence of suicidal thoughts and behaviors.

Drugs/Diseases

Util A	Util B	Util C (Include)
Viloxazine		Suicide, Attempt
		Suicidal Ideation
		History of Self Harm

Age Range: 6 - 17 yoa

References:
Qelbree Prescribing Information, April 2021, Supernus Pharmaceuticals..
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

46. Viloxazine / Therapeutic Appropriateness _____ _____

Alert Message: The effect of hepatic impairment on the pharmacokinetics of Qelbree (viloxazine) is unknown. Viloxazine use is not recommended in patients with hepatic impairment.

Drugs/Diseases

Util A	Util B	Util C
Viloxazine	Hepatic Impairment	

References:
Qelbree Prescribing Information, April 2021, Supernus Pharmaceuticals.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

47. Viloxazine / Heart Rate and Blood Pressure Increases _____ _____

Alert Message: Qelbree (viloxazine) can cause an increase in heart rate and diastolic blood pressure. Assess heart rate and blood pressure prior to initiating treatment with viloxazine, following increases in dosage, and periodically while on therapy.

Drugs/Diseases

Util A	Util B	Util C
Viloxazine	Hypertension	

References:
Qelbree Prescribing Information, April 2021, Supernus Pharmaceuticals.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

48. Viloxazine / MAO Inhibitors _____ _____

Alert Message: Qelbree (viloxazine) is contraindicated in patients receiving concomitant treatment with monoamine oxidase inhibitors (MAOI), or within 14 days following discontinuing an MAOI, because of an increased risk of hypertensive crisis.

Drugs/Diseases

Util A	Util B	Util C
Viloxazine	Isocarboxazid	
	Phenelzine	
	Rasagiline	
	Safinamide	
	Selegiline	
	Tranylcypromine	

References:
Qelbree Prescribing Information, April 2021, Supernus Pharmaceuticals.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

49. Viloxazine / Sensitive/NTI CYP1A2 Substrates _____ _____

Alert Message: Qelbree (viloxazine) is contraindicated in patients receiving concomitant administration of sensitive CYP1A2 substrates or CYP1A2 substrates with a narrow therapeutic range. Viloxazine is a strong CYP1A2 inhibitor. Concomitant use of viloxazine significantly increases the total exposure, but not peak exposure, of sensitive CYP1A2 substrates, which may increase the risk of adverse reactions associated with these CYP1A2 substrates.

Drugs/Diseases

Util A	Util B	Util C
Viloxazine	Alosetron	
	Duloxetine	
	Ramelteon	
	Tasimelteon	
	Tizanidine	
	Theophylline	

References:
Qelbree Prescribing Information, April 2021, Supernus Pharmaceuticals.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

50. Viloxazine / Mania or Hypomania _____ _____

Alert Message: Noradrenergic drugs, such as Qelbree (viloxazine), may induce a manic or mixed episode in patients with bipolar disorder. Prior to initiating treatment with viloxazine, screen patients to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a personal or family history of suicide, bipolar disorder, and depression.

Drugs/Diseases

Util A	Util B	Util C (Include)
Viloxazine		Bipolar Disorder
		Depression
		History of Self Harm
		Suicide, Attempt
		Suicidal Ideation

References:
Qelbree Prescribing Information, April 2021, Supernus Pharmaceuticals.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

51. Viloxazine / Moderately Sensitive CYP1A2 Substrates _____ _____

Alert Message: The concurrent use of Qelbree (viloxazine) with a moderately sensitive CYP1A2 substrate is not recommended. Dose reduction of the CYP1A2 substrate may be warranted if coadministration is necessary. Viloxazine is a strong CYP1A2 inhibitor, and concomitant use of viloxazine increases the total exposure, but not peak exposure, of sensitive CYP1A2 substrates, which may increase the risk of adverse reactions associated with these CYP1A2 substrates.

Drugs/Diseases

Util A	Util B	Util C
Viloxazine	Clozapine	
	Pirfenidone	

References:

Qelbree Prescribing Information, April 2021, Supernus Pharmaceuticals.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

52. Viloxazine / CYP3A4 Substrates _____ _____

Alert Message: The concurrent use of Qelbree (viloxazine) with a CYP3A4 substrate may increase the exposure of the CYP3A4 substrate. Dose reduction of the CYP3A4 substrate may be warranted if coadministration is necessary. Viloxazine is a weak inhibitor of CYP3A4 inhibitor. Monitor patients for adverse reactions and adjust the dosage of CYP3A4 substrates, as clinically indicated.

Drugs/Diseases

Util A	Util B					Util C
Viloxazine	Amiodarone	Buprenorphine	Budesonide	Etoposide	Dexamethasone	
	Fentanyl	Cabozantinib	Buspirone	Estrogens	Dexlansoprazole	
	Midazolam	Disopyramide	Cariprazine	Copanlisib	Quinidine	
	Abemaciclib	Amlodipine	Ceritinib	Crizotinib	Diazepam	
	Acalabrutinib	Aripiprazole	Chlordiazepoxide	Dabrafenib	Diltiazem	
	Oxycodone	Bedaquiline	Cilostazol	Saxagliptin	Rilpivirine	
	Hydrocodone	Bortezomib	Avanafil	Dapsone	Tolterodine	
	Tacrolimus	Bosutinib	Citalopram	Darifenacin	Duvelisib	
	Cyclosporine	Brexpiprazole	Cariprazine	Darunavir	Efavirenz	
	Fluticasone	Brigatinib	Clonazepam	Dasatinib	Elbasvir/Grazoprevir	
	Escitalopram	Bromocriptine	Clorazepate	Eletriptan	Everolimus	
	Felodipine	Encorafenib	Eplerenone	Erlotinib	Estazolam	
	Estradiol	Eszopiclone	Ethosuximide	Vilazodone	Flurazepam	
	Fosamprenavir	Gefitinib	Glasdegib	Guanfacine	Haloperidol	
	Idelalisib	Imatinib	Isradipine	Itraconazole	Ixabepilone	
	Ketoconazole	Lapatinib	Larotrectinib	Levomilnacipran	Macitentan	
	Maraviroc	Mefloquine	Lurasidone	Midostaurin	Mifepristone	
	Mirtazapine	Nelfinavir	Netupitant	Nevirapine	Nifedipine	
	Nilotinib	Nisoldipine	Ospemifene	Paclitaxel	Palbociclib	
	Panobinostat	Pazopanib	Pimavanserin	Valbenazine	Tadalafil	
	Quetiapine	Ranolazine	Regorafenib	Ribociclib	Rifabutin	
	Roflumilast	Romidepsin	Ruxolitinib	Saquinavir	Sildenafil	
	Silodosin	Solifenacin	Sunitinib	Suvorexant	Ibrutinib	
	Tasimelteon	Temsirolimus	Ticagrelor	Tipranavir	Lomitapide	
	Toremifene	Trabectedin	Trazodone	Triazolam	Lovastatin	
	Verapamil	Vardenafil	Vemurafenib	Venlafaxine	Simvastatin	
	Vinblastine	Vincristine	Vinorelbine	Zolpidem	Sirolimus	

References:

Qelbree Prescribing Information, April 2021, Supernus Pharmaceuticals.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

53. Viloxazine / CYP2D6 Substrates _____ _____

Alert Message: The concurrent use of Qelbree (viloxazine) with a CYP2D6 substrate may increase the exposure of the CYP2D6 substrate. Viloxazine is a weak inhibitor of CYP2D6. Monitor patients for adverse reactions and adjust the dosage of CYP2D6 substrates, as clinically indicated.

Drugs/Diseases

Util A	Util B	Util C
Viloxazine	Atomoxetine	
	Desipramine	
	Dextromethorphan	
	Nortriptyline	
	Metoprolol	
	Nebivolol	
	Perphenazine	
	Tolterodine	
	Venlafaxine	
	Risperidone	

References:
Qelbree Prescribing Information, April 2021, Supernus Pharmaceuticals.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

54. Viloxazine / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on findings from animal reproduction studies, Qelbree (viloxazine) may cause maternal harm when used during pregnancy. Discontinue viloxazine when pregnancy is recognized unless the benefits of therapy outweigh the potential risk to the mother. Available data from case series with viloxazine use in pregnant patients are insufficient to determine a drug-associated risk of major birth defects, miscarriage, or adverse maternal outcomes.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Qelbree Prescribing Information, April 2021, Supernus Pharmaceuticals.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

55. Viloxazine / Lactation _____ _____

Alert Message: There are no data on the presence of Qelbree (viloxazine) in human milk, the effects on the breastfed infant, or the effects on milk production. Viloxazine is likely present in rat 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 viloxazine and any potential adverse effects on the breastfed child from viloxazine or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Viloxazine	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Qelbree Prescribing Information, April 2021, Supernus Pharmaceuticals.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

56. Vorinostat / Overuse _____ _____
Alert Message: Zolinza (vorinostat) may be over-utilized. The recommended dose of vorinostat is 400 mg orally once daily with food.

Drugs/Diseases

Util A	Util B	Util C
Vorinostat		

Max Dose: 40 mg/day

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

57. Vorinostat / Therapeutic Appropriateness _____ _____
Alert Message: The safety and effectiveness of Zolinza (vorinostat) in pediatric patients have not been established.

Drugs/Diseases

Util A	Util B	Util C
Vorinostat		

Age Range: 0 – 17 yoa

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

58. Vorinostat / Pulmonary Embolism _____ _____
Alert Message: Pulmonary embolism occurred in 5% (4/86) of patients receiving Zolinza (vorinostat), and deep vein thrombosis has also been reported. Monitor patients for signs and symptoms of these events, particularly in patients with a prior history of thromboembolic events.

Drugs/Diseases

Util A	Util B	Util C (Include)
Vorinostat		Embolism
		Thrombosis

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

59. Vorinostat / Gastrointestinal Toxicity _____ _____

Alert Message: Gastrointestinal disturbances, including nausea, vomiting, and diarrhea, have been reported with Zolinza (vorinostat) use and may require the use of antiemetic and antidiarrheal medications. Fluid and electrolytes should be replaced to prevent dehydration. Pre-existing nausea, vomiting, and diarrhea should be adequately controlled before beginning therapy with Zolinza (vorinostat).

Drugs/Diseases

Util A	Util B	Util C
Vorinostat	Diarrhea	
	Nausea	
	Vomiting	

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

60. Vorinostat / Hyperglycemia _____ _____

Alert Message: Zolinza (vorinostat) may cause hyperglycemia. Monitor serum glucose every 2 weeks during the first 2 months of therapy and monthly thereafter.

Drugs/Diseases

Util A	Util B	Util C (Include)
Vorinostat		Diabetes

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

61. Vorinostat / Warfarin _____ _____

Alert Message: Prolongation of prothrombin time (PT) and International Normalized Ratio (INR) were observed in patients receiving Zolinza (vorinostat) concomitantly with coumarin-derivative anticoagulants. Physicians should monitor PT and INR more frequently in patients concurrently administered vorinostat and coumarin derivatives.

Drugs/Diseases

Util A	Util B	Util C
Vorinostat	Warfarin	

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

62. Vorinostat / Valproic Acid _____ _____

Alert Message: Severe thrombocytopenia and gastrointestinal bleeding have been reported with concomitant use of Zolinza (vorinostat) and other HDAC inhibitors (e.g., valproic acid). Monitor platelet count every 2 weeks for the first 2 months.

Drugs/Diseases

Util A	Util B	Util C
Vorinostat	Valproic Acid	

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

63. Vorinostat / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on its mechanism of action and findings from animal studies, Zolinza (vorinostat) can cause fetal harm when administered to a pregnant woman. There are insufficient data on vorinostat use in pregnant women to inform a drug-associated risk of major birth defects and miscarriage. In animal reproduction studies, administration of vorinostat to pregnant rats and rabbits during the period of organogenesis caused adverse developmental outcomes at maternal exposures approximately 0.5 times the human exposure based on AUC0-24 hours. Advise pregnant women of the potential risk to a fetus.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Vorinostat	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.

64. Vorinostat / Therapeutic Appropriateness _____ _____

Alert Message: There are no data on the presence of Zolinza (vorinostat) or its metabolites in human milk, the effects on a breastfed child, or the effects on milk production. Because many drugs are excreted in human milk and because of the potential for serious adverse drug reactions in a nursing child, advise lactating patients not to breastfeed during treatment with vorinostat and for at least 1 week after the last dose.

Drugs/Diseases

Util A	Util B	Util C
Vorinostat	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

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

65. Vorinostat / Therapeutic Appropriateness _____ _____
Alert Message: Advise females of reproductive potential to use effective contraception during treatment with Zolinza (vorinostat) and for at least 6 months after the last dose.

Drugs/Diseases
Util A Util B Util C
Vorinostat

Gender: Female
Age Range: 11 – 50 yoa

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

66. Vorinostat / Therapeutic Appropriateness _____ _____
Alert Message: Advise males with female partners of reproductive potential to use effective contraception and to avoid fathering a child during treatment with Zolinza (vorinostat) and for at least 3 months after the last dose.

Drugs/Diseases
Util A Util B Util C
Vorinostat

Gender: Male

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

67. Vorinostat / Non-adherence _____ _____
Alert Message: Based on refill history, your patient may be under-utilizing Zolinza (vorinostat). 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
Vorinostat

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.

68. Ivosidenib / Overuse _____ _____

Alert Message: Tibsovo (ivosidenib) may be over-utilized. The recommended dose of ivosidenib is 500 mg taken orally once daily until disease progression or unacceptable toxicity.

Drugs/Diseases

Util A	Util B	Util C
Ivosidenib		

Max Dose: 500 mg/day

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

69. Ivosidenib / Therapeutic Appropriateness _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Ivosidenib		

Age Range: 0 – 17 yoa

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

70. Ivosidenib / Differentiation Syndrome (Black Box Warning) _____ _____

Alert Message: Patients treated with Tibsovo (ivosidenib) have experienced differentiation syndrome, which can be fatal or life-threatening if not treated. Symptoms may include; fever, dyspnea, hypoxia, pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, hypotension, or renal dysfunction. If differentiation syndrome is suspected, administer corticosteroid therapy as instructed in the official prescribing information and initiate hemodynamic monitoring until symptom resolution. Interrupt ivosidenib if severe signs and/or symptoms persist for more than 48 hours after initiation of systemic corticosteroids.

Drugs/Diseases

Util A	Util B		Util C
Ivosidenib	Dyspnea	Pericardial Effusion	
	Edema	Pleural Effusion	
	Fever	Renal Dysfunction	
	Hypoxia		

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

71. Ivosidenib / QT Prolongation _____ _____

Alert Message: Patients treated with Tibsovo (ivosidenib) can develop QT (QTc) prolongation and ventricular arrhythmias. In patients with congenital long QTc syndrome, congestive heart failure, electrolyte abnormalities, or those taking medications known to prolong the QTc interval, more frequent monitoring may be necessary. Interrupt ivosidenib if QTc increases to greater than 480 msec and less than 500 msec. Interrupt and reduce ivosidenib if QTc increases to greater than 500 msec. Permanently discontinue ivosidenib in patients who develop QTc interval prolongation with signs or symptoms of life-threatening arrhythmia.

Drugs/Diseases

Util A	Util B	Util C
Ivosidenib	Long QT Syndrome	
	Heart Failure	
	Arrhythmias	

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

72. Ivosidenib / Gillian-Barre Syndrome & Symptoms _____ _____

Alert Message: Guillain-Barre syndrome has occurred in patients treated with Tibsovo (ivosidenib) in the clinical study. Monitor patients taking Tibsovo (ivosidenib) for the onset of new signs or symptoms of motor and/or sensory neuropathy such as unilateral or bilateral weakness, sensory alterations, paresthesias, or difficulty breathing. Permanently discontinue ivosidenib in patients who are diagnosed with Guillain-Barre syndrome.

Drugs/Diseases

Util A	Util B	Util C
Ivosidenib	Gillian Barre Syndrome	
	Dyspnea	
	Paresthesias	
	Weakness	

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

73. Ivosidenib / Strong CYP3A4 Inhibitors _____ _____

Alert Message: Co-administration of Tibsovo (ivosidenib) with strong CYP3A4 inhibitors increased ivosidenib plasma concentrations. Increased ivosidenib plasma concentrations may increase the risk of QTc interval prolongation. If a strong CYP3A4 inhibitor must be coadministered, reduce the ivosidenib dose to 250 mg once daily. If the strong inhibitor is discontinued, increase the ivosidenib dose (after at least 5 half-lives of the strong CYP3A4 inhibitor) to the recommended dose of 500 mg once daily.

Drugs/Diseases

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

Max Dose: 250 mg/day

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

74. Ivosidenib / Moderate CYP3A4 Inhibitors _____ _____

Alert Message: Co-administration of Tibsovo (ivosidenib) with moderate CYP3A4 inhibitors increased ivosidenib plasma concentrations. Increased ivosidenib plasma concentrations may increase the risk of QTc interval prolongation. If a moderate CYP3A4 inhibitor must be coadministered, monitor the patient for QT prolongation.

Drugs/Diseases

Util A	Util B		Util C
Ivosidenib	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.

75. Ivosidenib / Strong CYP3A4 Inducers _____ _____

Alert Message: The concurrent administration of Tibsovo (ivosidenib) with strong CYP3A4 inducers should be avoided. Ivosidenib is a CYP3A4 substrate and concomitant use with strong CYP3A4 inducers is predicted to decrease ivosidenib steady-state AUC by 33%.

Drugs/Diseases

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

References:

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

76. Ivosidenib / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Tibsovo (ivosidenib). 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
Ivosidenib		

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.

77. Ivosidenib / QT Prolongation Drugs _____ _____

Alert Message: Patients treated with Tibsovo (ivosidenib) can develop QT (QTc) prolongation and ventricular arrhythmias, therefore concurrent administration of ivosidenib with medications that prolong the QT interval should be avoided. If co-administration of a QTc prolonging drug is unavoidable, monitor patients for increased risk of QTc interval prolongation.

Drugs/Diseases

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

References:

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

78. Ivosidenib / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on animal embryo-fetal toxicity studies, Tibsovo (ivosidenib) may cause fetal harm when administered to a pregnant patient. There are no available data on ivosidenib use in pregnant patients to inform a drug-associated risk of major birth defects and miscarriage. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, advise the patient of the potential risk to a fetus.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Ivosidenib	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.

79. Ivosidenib / Lactation _____ _____

Alert Message: There are no data on the presence of Tibsovo (ivosidenib) or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production. Because many drugs are excreted in human milk and because of the potential for adverse reactions in breastfed children, advise patients not to breastfeed during treatment with ivosidenib and for at least 1 month after the last dose.

Drugs/Diseases

Util A	Util B	Util C
Ivosidenib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

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

80. Encorafenib / Overuse _____ _____

Alert Message: Braftovi (encorafenib) may be over-utilized. The recommended maximum dose of encorafenib is 300 mg (four 75 mg capsules) orally once daily in combination with cetuximab until disease progression or unacceptable toxicity.

Drugs/Diseases

Util A	Util B	Util C (Include)
Encorafenib		Cetuximab

Max Dose: 300 mg/day

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