DUR Board Meeting
September 4, 2019
Heritage Center

North Dakota Medicaid
DUR Board Meeting Agenda
Brynhild Haugland Room
State Capitol
600 East Boulevard Avenue
Bismarck, ND
September 4, 2019
1:00 pm

1. Administrative items
    - DHS announcements

2. Old business
    - Review and approval of June 2019 meeting minutes
    - Budget update
    - Review top 25 drugs for second quarter of 2019
    - Prior authorization/PDL update
    - Second review of short-acting opioid analgesic agents
    - Second review of agents for the treatment of thrombocytopenia
    - Second review of agents for the treatment of interstitial cystitis
    - Second review of agents for the treatment of narcolepsy
    - Sanford Medicaid Expansion update

3. New business
    - Review of antifungal agents for aspergillus and candidiasis infections
    - Report on utilization data from select drugs and drug classes
    - DUR Board discussion regarding medication adherence
    - Retrospective DUR criteria recommendations
    - Case Reviews
    - Upcoming meeting date/agenda.
        - Next meeting is December 4, 2019 in the Brynhild Haugland Room

4. Adjourn

Please remember to silence all cellular phones during the meeting.

Drug Utilization Review (DUR) Meeting Minutes
June 5, 2019

Members Present: Michael Quast, Gabriela Balf, Tanya Schmidt, Andrea Honeyman, Peter Woodrow, Jesse Rue, LeNeika Roehrich, Kayli Bardell, Michael Quast, Jeffrey Hostetter

Members Absent: Michael Booth, Russ Sobotta, Laura Schield, Katie Kram

Medicaid Pharmacy Department: Brendan Joyce, Alexi Murphy

Old Business

Chair L. Roehrich called the meeting to order at 1:07 p.m. Chair L. Roehrich asked for a motion to approve the minutes of the December meeting. T. Schmidt moved that the minutes be approved and G. Balf seconded the motion. Chair L. Roehrich called for a voice vote to approve the minutes. The motion passed with no audible dissent.

Review Top 15 Therapeutic Categories/Top 25 Drugs

B. Joyce presented the quarterly review of the top 15 therapeutic classes by total cost of claims, top 25 drugs based on number of claims, and top 25 drugs based on claims cost for the 1st quarter of 2019.

PDL/PA Criteria Updates

A. Murphy shared with the Board all of changes made to the Preferred Drug List since the most recent version of the Preferred Drug List was posted. Notable changes included removing PA requirements a number of COPD inhalers and adding numerous agents to recently DUR Board approved PA class criteria. 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 Sivextro and Nuzyra

A motion and second was made at the December meeting to place Sivextro and Nuzyra on prior authorization. The topics were brought up for a second review. J. Hostetter made a motion to amend the prescriber requirements to include following stewardship or per protocol, and J. Rue seconded the motion. Chair L. Roehrich called for a voice vote to approve the amendment, and the motion passed with no audible dissent. Chair L. Roehrich called for a voice vote to approve the amended criteria, and the motion passed with no audible dissent.

Second Review of Estrogen Agents

A motion and second was previously made to place estrogen agents on prior authorization. The topic was brought up for a second review. There was no public comment. Chair L. Roehrich called for a voice vote and the motion passed with no audible dissent.

Second Review of Agents for Treatment of Osteoporosis

A motion and second was made at the December meeting to place agents for the treatment of osteoporosis on prior authorization. The topic was brought up for a second review. P. Woodrow made a motion to amend the criteria to account for FRAX scores to be included and considered, and J. Hostetter seconded the motion. Chair L. Roehrich called for a voice vote to approve the

amendment, and the motion passed with no audible dissent. There was no public comment. Chair L. Roehrich called for a voice vote to approve the amended criteria, and the motion passed with no audible dissent.

Second Review of Agents for the Treatment of Hyperkalemia
A motion and second was made at the December meeting to place agents for the treatment of hyperkalemia on prior authorization. The topic was brought up for a second review. There was no public comment. Chair L. Roehrich called for a voice vote and the motion passed with no audible dissent.

Second Review of Agents for the Treatment of Parkinsons's Disease
A motion and second was made at the December meeting to place agents for the treatment of Parkinson's disease on prior authorization. The topic was brought up for a second review. There was no public comment. Chair L. Roehrich called for a voice vote and the motion passed with no audible dissent.

New Business
Review of Short Acting Opioids
A. Murphy presented a review of short-acting opioid agents to the Board. A motion was made by M. Quast to create PA criteria for the use of these agents and manage these medications through prior authorization. The motion was seconded by J. Rue. This topic will be reviewed at the next meeting.

Review of Agents for Treatment of Thrombocytopenia
A. Murphy presented a review of agents for treatment of thrombocytopenia to the Board. A motion was made by J. Hostetter. Woodrow to create PA criteria for the use of this agent and manage this medication through prior authorization. The motion was seconded by J. Rue. This topic will be reviewed at the next meeting.

Review of Agents for Treatment of Interstitial Cystitis
A. Murphy presented a review of agents for treatment of interstitial cystitis to the Board. A motion was made by P. Woodrow to create a new PA criteria class and manage these medications through prior authorization. The motion was seconded by J. Rue. This topic will be reviewed at the next meeting.

Review of Agents for Treatment of Narcolepsy
A. Murphy presented a review of agents for treatment of hyperkalemia to the Board. A motion was made by J. Rue to create a new PA criteria class and manage these medications through prior authorization. The motion was seconded by G. Balf. This topic will be reviewed at the next meeting.

Report on Utilization of Benzodiazepines and Opioids Concurrently
To reduce the risk of respiratory depression, a claims processing edit was put in place limiting the concurrent use of these agents to requiring a prior authorization in 2018. T. DeRuiter presented utilization data showing the number of FFS patients receiving an opioid and benzodiazepine concurrently from 2018 to 2019. The data showed that the number of patients receiving an agent from both of these drug classes was reduced by ~50% since this edit was put in place.

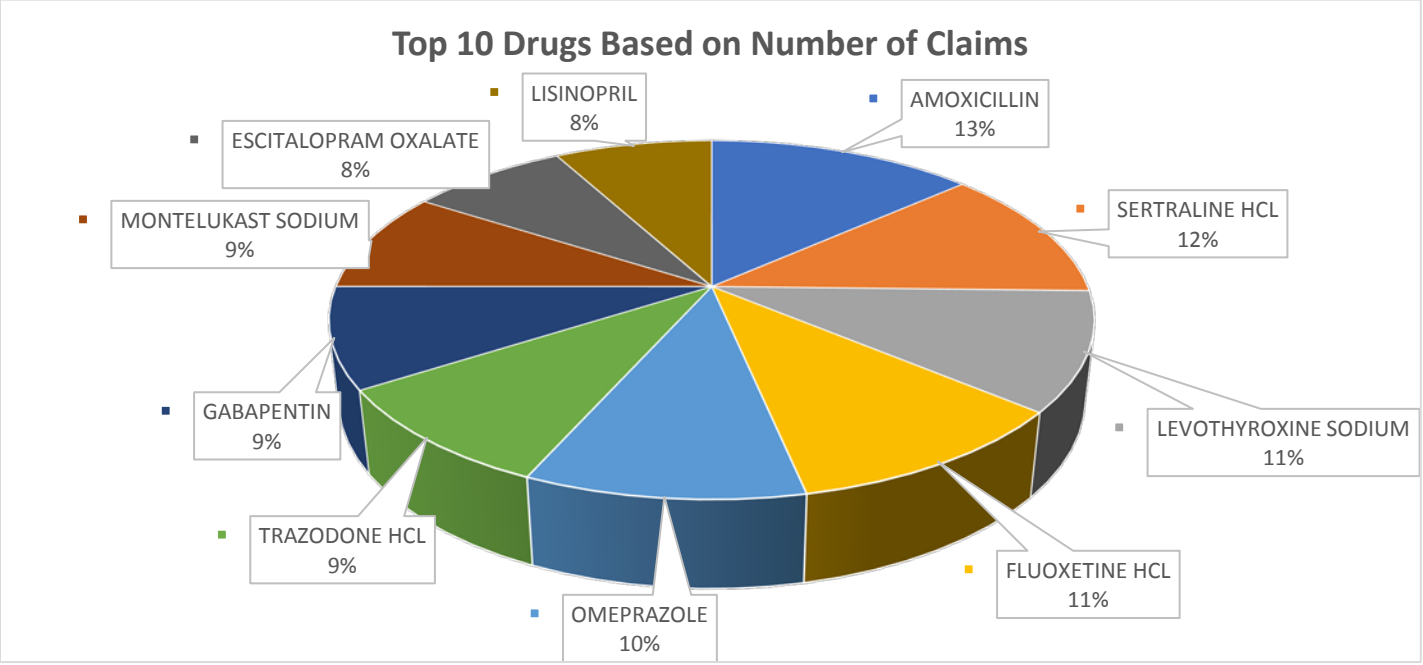
Retrospective Drug Utilization Review (RDUR) Criteria Recommendations
The recommended RDUR criteria enclosed in the packet were developed from product information provided by the manufacturers and are usually consistent with new indications, new drugs added, and new warnings. These proposed criteria will be added to the current set of criteria and will be used in future DUR cycles. J. Hostetter moved to amend the new criteria as stated above and approve it. J. Rue seconded the motion. The motion passed with no audible dissent.

Adjournment and Upcoming Meeting Date
Chair L. Roehrich adjourned the meeting at 2:45 pm. The next DUR Board meeting will be held September 4, 2019 at 1:00 pm at the State Capitol building in the Brynhild -Haugland room.

TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 04/01/2019 – 06/30/2019

Drug	AHFS Class	Claims	Claims Cost	Patients	Cost Per Claim	% Total Claims
AMOXICILLIN	PENICILLIN ANTIBIOTICS	2,951	$112,358.97	2,756	$38.07	2.13%
SERTRALINE HCL	ANTIDEPRESSANTS	2,616	$59,423.73	1,149	$22.72	1.89%
LEVOTHYROXINE SODIUM	THYROID AGENTS	2,348	$45,020.71	855	$19.17	1.70%
FLUOXETINE HCL	ANTIDEPRESSANTS	2,328	$40,012.16	1,014	$17.19	1.68%
OMEPRAZOLE	PROTON-PUMP INHIBITORS	2,192	$42,181.41	995	$19.24	1.58%
TRAZODONE HCL	ANTIDEPRESSANTS	2,027	$38,873.32	887	$19.18	1.46%
GABAPENTIN	ANTICONVULSANTS, MISC	1,993	$46,446.36	867	$23.30	1.44%
MONTELUKAST SODIUM	LEUKOTRIENE MODIFIERS	1,990	$43,819.73	1,005	$22.02	1.44%
ESCITALOPRAM OXALATE	ANTIDEPRESSANTS	1,749	$40,011.21	833	$22.88	1.26%
LISINOPRIL	ACE INHIBITORS	1,744	$53,336.34	758	$30.58	1.26%
ATORVASTATIN CALCIUM	STATINS	1,728	$46,295.00	723	$26.79	1.25%
VYVANSE	AMPHETAMINES	1,708	$406,421.89	686	$237.95	1.23%
HYDROCODONE-APAP	OPIATE AGONISTS	1,564	$33,578.89	1,002	$21.47	1.13%
CLONIDINE HCL	CENTRAL ALPHA-AGONISTS	1,488	$25,296.12	622	$17.00	1.08%
RISPERIDONE	ANTIPSYCHOTIC AGENTS	1,443	$21,399.41	472	$14.83	1.04%
PROAIR HFA	SABAS	1,412	$107,212.00	1,394	$75.93	1.02%
DULOXETINE HCL	ANTIDEPRESSANTS	1,401	$32,096.94	544	$22.91	1.01%
CONCERTA	CNS STIMULANTS	1,396	$460,715.08	575	$330.03	1.01%
FLUTICASONE PROPIONATE	CORTICOSTEROIDS (EENT)	1,340	$31,147.39	930	$23.24	0.97%
ASPIRIN EC	NSAIDS	1,339	$55,531.24	520	$41.47	0.97%
METFORMIN HCL	BIGUANIDES	1,324	$23,476.60	582	$17.73	0.96%
LAMOTRIGINE	ANTICONVULSANTS, MISC	1,321	$24,277.39	451	$18.38	0.95%
AMOXICILLIN-CLAVULANATE	PENICILLIN ANTIBIOTICS	1,295	$53,582.26	1,219	$41.38	0.94%
CETIRIZINE HCL	ANTIHISTAMINES	1,259	$44,983.43	740	$35.73	0.91%
ARIPIPRAZOLE	ANTIPSYCHOTIC AGENTS	1,257	$28,185.31	517	$22.42	0.91%

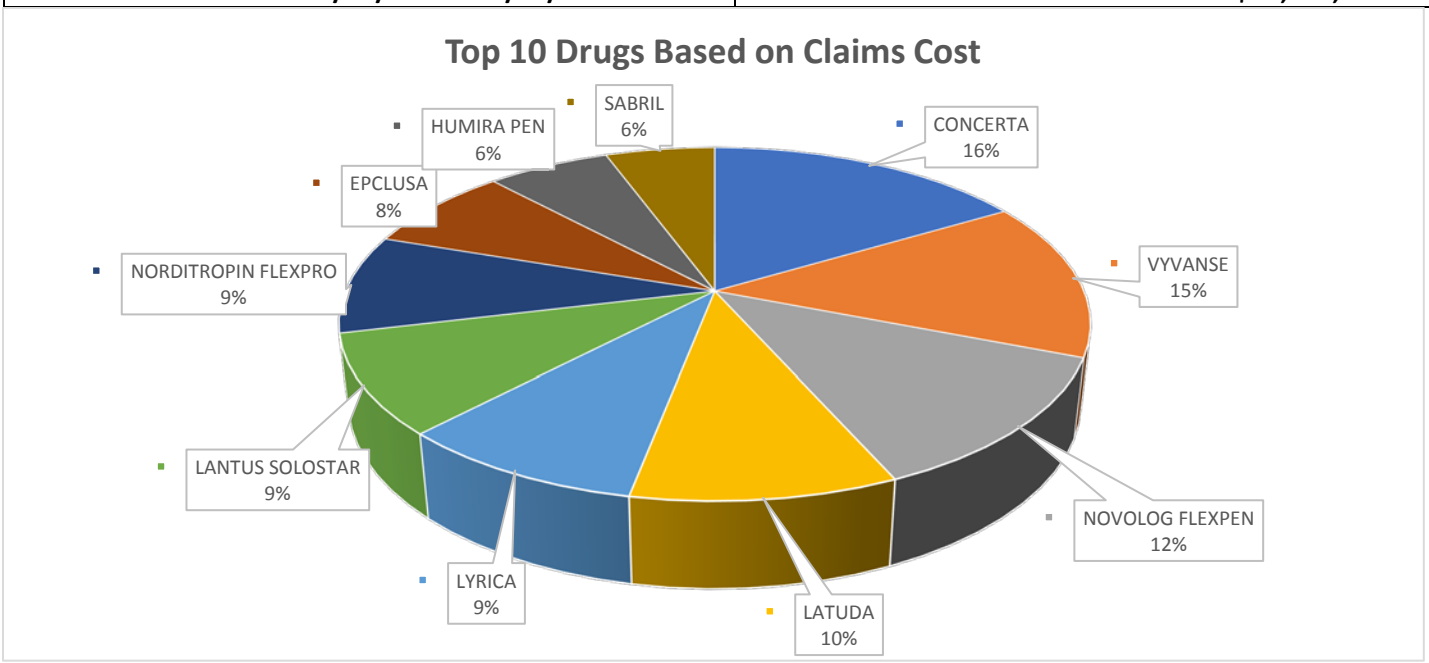
Total Claims From 04/01/2019 – 06/30/2019	**138,365**



TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 04/01/2019 – 06/30/2019

Drug	AHFS Class	Claims Cost	Claims	Patients	Cost Per Claim	% Total Cost
CONCERTA	CNS STIMULANTS	$460,715.08	1,396	575	$330.03	3.81%
VYVANSE	CNS STIMULANTS	$406,421.89	1,708	686	$237.95	3.36%
NOVOLOG FLEXPEN	INSULINS	$347,521.87	606	320	$573.47	2.88%
LATUDA	ANTIPSYCHOTIC AGENTS	$271,119.92	395	140	$686.38	2.24%
LYRICA	ANTICONVULSANTS, MISC	$254,692.27	525	213	$485.13	2.11%
LANTUS SOLOSTAR	INSULINS	$254,003.07	568	286	$447.19	2.10%
NORDITROPIN FLEXPRO	PITUITARY	$253,628.51	73	33	$3,474.36	2.10%
EPCLUSA	HCV ANTIVIRALS	$218,961.99	9	6	$24,329.11	1.81%
HUMIRA PEN	IMMUNOMODULATORS	$176,790.38	32	14	$5,524.70	1.46%
SABRIL	ANTICONVULSANTS, MISC	$157,489.36	9	4	$17,498.82	1.30%
INVEGA SUSTENNA	ANTIPSYCHOTIC AGENTS	$145,398.65	74	31	$1,964.85	1.20%
GENVOYA	ANTIRETROVIRALS	$144,140.90	124	52	$1,162.43	1.19%
ADVAIR DISKUS	INHALED CORTICOSTEROIDS	$140,359.64	382	200	$367.43	1.16%
VIMPAT	ANTICONVULSANTS, MISC	$125,599.57	203	59	$618.72	1.04%
LEVEMIR FLEXTOUCH	INSULINS	$120,746.57	304	172	$397.19	1.00%
FOCALIN XR	CNS STIMULANTS	$116,244.44	344	142	$337.92	0.96%
AMOXICILLIN	PENICILLIN ANTIBIOTICS	$112,358.97	2,951	2,756	$38.07	0.93%
PROAIR HFA	BETA-ADRENERGIC AGONISTS	$107,212.00	1,412	1,394	$75.93	0.89%
FLOVENT HFA	INHALED CORTICOSTEROIDS	$106,661.65	479	303	$222.68	0.88%
MAVYRET	HCV ANTIVIRALS	$102,857.48	8	6	$12,857.19	0.85%
COSENTYX PEN (2 PENS)	IMMUNOMODULATORS	$101,317.03	18	9	$5,628.72	0.84%
ABILIFY MAINTENA	ANTIPSYCHOTIC AGENTS	$98,984.50	48	18	$2,062.18	0.82%
NOVOLOG	INSULINS	$92,575.40	179	89	$517.18	0.77%
SYMBICORT	INHALED CORTICOSTEROIDS	$91,588.98	292	168	$313.66	0.76%
COSENTYX PEN	IMMUNOMODULATORS	$91,474.83	9	4	$10,163.87	0.76%

Total Claims Cost From 04/01/2019 – 06/30/2019	**$12,087,420.13**



PDL Update

ADDED TO PA	
Drug	**Criteria Category**
APOKYN	Parkinson's Disease
ASMANEX TWISTHALER	Inhaled Corticosteroids
BAXDELA	Antibiotics - Resistance Prevention
CANDESARTAN - HCTZ	ARBs (Angiotensin Receptor Blockers)
CEQUA	Ophthalmic – Dry Eye Syndrome
DUOBRII	Antipsoriatics – Topical
DUOPA	Parkinson's Disease
ESTRADIOL VAGINAL CREAM	Estrogens
ESTRADIOL VAGINAL TABLET	Estrogens
ESTRADIOL PATCH	Estrogens
EVENITY	Osteoporosis
FEMRING	Estrogens
FORTEO	Osteoporosis
GOCOVRI	Parkinson's Disease
INBRIJA	Parkinson's Disease
LEVORPHANOL	Opioid Analgesics – Long Acting
LOKELMA	Hyperkalemia
MAVENCLAD	Multiple Sclerosis - Oral Non-Interferons
MIACALCIN	Osteoporosis
MINOSTAR	Estrogens
NASCOBAL	Preferred Dosage Forms
NATROBA	Lice
NEOMYCIN/POLYMYXIN B/GRAMICIDIN DROPS	Ophthalmic Anti-Infectives
NEULASTA	Hematopoietic, Colony Stimulating Factors
NORGESIC FORTE	Skeletal Muscle Relaxants
NUPLAZID	Parkinson's Disease
NUZYRA	Antibiotics - Resistance Prevention
OSMOLEX ER	Parkinson's Disease
OTOVEL	Otic Anti-infectives – Fluoroquinolones
OXERVATE	Meds over $3000/month
PRAMIPEXOLE ER	Parkinson's Disease
PREFEST	Estrogens
RASAGILINE	Parkinson's Disease
RYTARY	Parkinson's Disease
SIVEXTRO	Antibiotics - Resistance Prevention
SKYRIZI	Cytokine Modulators
TOLCAPONE	Parkinson's Disease
TOLTERODINE	Urinary Antispasmodics
TOLTERODINE ER	Urinary Antispasmodics
TREPROSTINIL	Pulmonary Hypertension - Prostacyclins
TYMLOS	Osteoporosis
VELTASSA	Hyperkalemia
XADAGO	Parkinson's Disease

Removed from PA	
Drug	**Criteria Category**
ARMODAFINIL	Nuvigil
BELBUCA	Opioid Analgesics – Long Acting
CANDESARTAN	ARBs (Angiotensin Receptor Blockers)
DALIRESP	COPD - PDE4-Inhibitor
DICLOFENAC	NSAIDS
ETODOLAC	NSAIDS
FULPHILA	Ophthalmic Glaucoma - Beta Blockers
GENTAK	Tardive Dyskinesia
JENTADUETO XR	Diabetes - DPP4-Inhibitors
MODAFINIL	Nuvigil
NYSTATIN-TRIAMCINOLONE	Antifungals - Topical
OLOPATADINE 0.2%	Ophthalmic - Antihistamines
ORALAIR	Allergen Extracts
ORAVIG	Noxafil & Tolsura
ORENITRAM	Pulmonary Hypertension - Prostacyclins
OXAPROZIN	NSAIDS
PIROXICAM	NSAIDS
PRASUGREL	Platelet Aggregation Inhibitors
REVATIO	Pulmonary Hypertension - PDE-5 Inhibitors
SILDENAFIL	Pulmonary Hypertension - PDE-5 Inhibitors
SYMJEPI	Epinephrine Autoinjectors
TADALAFIL	Pulmonary Hypertension - PDE-5 Inhibitors
TOLMETIN	NSAIDS
TYVASO	Pulmonary Hypertension - Prostacyclins
UDENYCA	Hematopoietic, Colony Stimulating Factors
UPTRAVI	Pulmonary Hypertension - Prostacyclins
VENTAVIS	Pulmonary Hypertension - Prostacyclins
ZALAPAR	Parkinson’s Disease
ZORVOLEX	NSAIDS

SHORT-ACTING OPIOID ANALGESIC AGENTS

- **Criteria for coverage of Subsys, Fentora, Lazanda, Actiq, and Abstral:**
  - The patient's age must be within label recommendations
  - The patient must have a diagnosis of cancer pain
  - The patient must currently be on around the clock opioid therapy for at least a week, as evidenced by paid claims or pharmacy print-outs
    - The around the clock opioid therapy must be equivalent to 60 mg oral morphine daily, 25 mcg transdermal fentanyl/hour, 30mg oxycodone daily, 8 mg of oral hydromorphone daily, or equianalgesic dose of another opioid daily
- **Criteria for coverage of ALL other non-preferred short-acting opioid analgesics:**
  - Initial Criteria:
    - The patient must have required around-the-clock pain relief for the past 90 days, as evidenced by paid claims or pharmacy print-outs
    - The prescriber must attest that they have reviewed the past 3 months of the patient's North Dakota PDMP reports
    - The patient must have not achieved therapeutic goal with non-narcotic medication (NSAIDs, TCAs, SNRIs, Corticosteroids, etc.) and non-medication alternatives (Weight Loss, Physical Therapy, Cognitive Behavioral Therapy, etc.)
    - The prescription must be written by or in consultation with an oncologist or pain management specialist with a pain management contract (with treatment plan including goals for pain and function, and urine and/or blood screens)
  - Additional criteria for coverage of Oxycodone IR:
    - The above Initial Criteria must be met
    - The patient must currently be on a long-acting opioid analgesic that provides a daily Morphine Equivalent Dose (MED) which meets requirements below (based on requested strength), as evidenced by paid claims or pharmacy print-outs:
      - **Oxycodone 15 mg tablet**: long-acting opioid must provide ≥150 mg MED per day
      - **Oxycodone 20 mg tablet**: long-acting opioid must provide ≥200 mg MED per day
      - **Oxycodone 30 mg tablet**: long-acting opioid must provide ≥300 mg MED per day
  - Additional criteria for coverage of Meperidine, butalbital-codeine products:
    - The above Initial Criteria must be met
    - Clinical justification must be provided explaining why the patient is unable to use other opioid and non-opioid analgesic products (subject to clinical review).
  - Renewal Criteria:
    - Documentation noting progress toward therapeutic goal must be included with request (including pain level and function).

health information designs

Opioid Analgesics
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 long-acting opioid analgesic must meet the following criteria:

- Patient must have required around-the-clock pain relief for the past 90 days
- The past 3 months of North Dakota PDMP reports must have been reviewed by the prescriber.
- Patient must be in consult with oncologist or pain management specialist with a pain management contract (with treatment plan including goals for pain and function, and urine and/or blood screens) if:
  - Cumulative daily dose of narcotics exceed 90 MED/day
  - Patient is using benzodiazepine concurrently with narcotic medication
- Patient must have not achieved therapeutic goal with non-narcotic medication (NSAIDs, TCAs, SNRIs, Corticosteroids, etc.) and non-medication alternatives (Weight Loss, Physical Therapy, Cognitive Behavioral Therapy, etc.)

*** For additional and agent-specific criteria, please see criteria for coverage in the Preferred Drug List at www.hidesigns.com/assets/files/ndmedicaid/NDPDL.pdf**

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name	Pain, Palliative Care, or Oncology/Hematology Specialist involved in therapy (if not treating physician):		
Prescriber NPI	Telephone Number	Fax Number	
Requested Opioid Analgesic:	**Diagnosis for use of opioid(s) in this patient:**		
List All Failed/Current Medications: □ NSAIDs □ TCAs □ SNRIs □ Corticosteroids □ Weight Loss □ Physical Therapy □ Cognitive Behavioral Therapy □ Other:	**Dose and Frequency:**	**Start/End Date:**	**Reason for failure:**

Qualifications for coverage:	
Has the past 3 months of North Dakota PDMP reports must have been reviewed by the prescriber?	□ YES □ NO
Has the provider established a realistic treatment plan with the patient, addressing expected outcomes and limitations of therapy in totally eliminating pain?	□ YES □ NO
Does the patient undergo routine drug screens?	□ YES □ NO

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

□ Patient's treatment plan including an evaluation of effectiveness and plans for continuation/discontinuation
□ Clinical documentation of previously tried and failed non-opioid therapies.

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.*

INTERSTITIAL CYSTITIS

- **Elmiron:**
  - Initial Criteria: Duration of Approval = 3 months
    - The prescriber must attest that all other potential causes for bladder pain/discomfort have been ruled out.
    - The patient must have a diagnosis of pain or discomfort due to interstitial cystitis.
    - The patient must be 16 years of age or older.
    - The patient must have not experienced adequate symptom relief after implementing self-care practices and behavior modification (e.g. avoiding food/beverages and activities that exacerbate symptoms, fluid management, etc).
    - The patient must have failed a 30-day trial of amitriptyline, as evidenced by paid claims or pharmacy print-outs.
  - Renewal Criteria: Duration of approval = 12 months
    - The patient must have experienced a significant reduction in bladder pain/discomfort since initiating therapy (supported by clinical documentation).

PREFERRED AGENTS	NON-PREFERRED AGENTS
amitriptyline	ELMIRON (pentosan polysulfate sodium)

NARCOLEPSY

- **Criteria for coverage for all non-preferred agents:**
  - The patient must have an FDA-approved indication for use (meets label recommendations for diagnosis and age).
- **Additional criteria for coverage of Xyrem**
  - The patient must be experiencing one of the following, and meet any additional criteria for coverage (if applicable):
    - Cataplexy
    - Excessive Daytime Sleepiness:
      - The patient must have failed 30-day trials of modafinil and at least 1 additional CNS stimulant indicated for treatment of narcolepsy, as evidenced by paid claims or pharmacy print-outs
- **Additional criteria for coverage of Sunosi**
  - The patient must meet have a diagnosis of Narcolepsy or obstructive sleep apnea.
  - The patient must have failed 30-day trials of each preferred agent, as evidenced by paid claims or pharmacy print-outs
  - Provider must submit documentation of prior treatment failure, as evidenced by documentation of one of the following, while on prior treatments:
    - Multiple Sleep Latency Test (MSLT) <8 minutes
    - EPWORTH sleepiness scale score ≥10

PREFERRED AGENTS	NON-PREFERRED AGENTS
modafinil	SUNOSI
NUVIGIL (armodafinil)	XYREM

THROMBOCYTOPENIA

- **Criteria for initial and renewal requests for all agents and indications**
  - The patient must have an FDA-approved indication for use (meets label recommendations for diagnosis and age).
  - Documentation of the patient's current platelet count must be attached to the request
- **Chronic immune thrombocytopenia (ITP)**
  - Criteria for coverage of Promacta, Doptelet, Nplate, and Tavalisse:
    - **Initial Criteria:**
      - The provider must attest that the patient's degree of thrombocytopenia and clinical condition increase the risk for bleeding
      - The patient must have experienced an inadequate response after one of the following (A or B):
        A. The patient must have failed a trial of appropriate duration of a corticosteroid or immunoglobulins as evidenced by paid claims or pharmacy print outs
        B. The patient must have undergone a splenectomy
    - **Renewal Criteria:**
      - The patient must be experiencing a significant increase in platelet count and bleeding reduction risk on therapy (supported by documentation)
      - If on maximum dose: The patient's platelet count must have increased to a level sufficient to avoid clinically important bleeding after the recommended duration for the product*
        * Promacta, Nplate, Doptelet: 4 weeks
        * Tavalisse: 12 weeks

- **Chronic liver disease-associated thrombocytopenia**
  - Criteria for coverage of Doptelet and Mulpleta
    - The patient must have a diagnosis of chronic liver disease
    - The patient must be scheduled to undergo a procedure that puts the patient at risk of bleeding
      - The prescriber must include documentation of the name and scheduled date of the procedure
    - The provider must indicate the date therapy will be initiated and discontinued*
      * Doptelet: given from 10-13 to 5-8 days prior to procedure
      * Mulpleta: given from 8-14 to 2-8 days prior to procedure

- **Chronic hepatitis C infection-associated thrombocytopenia**
  - Criteria for coverage of Promacta
    - The patient must have a diagnosis of hepatitis C and be currently receiving or planning to initiate interferon-based treatment
      - Prescriber must attest that the patient's degree of thrombocytopenia prevents continuation or initiation of interferon

- **Aplastic anemia**
  - Criteria for coverage of Promacta
    - One of the following must be met (A or B):
      A. The patient must be receiving Promacta as first-line treatment in combination with standard immunosuppressive therapy (e.e. corticosteroid, Atgam, cyclosporin)
      B. The patient must have had an insufficient response to treatment with prior immunosuppressive therapy

health information designs

General
Prior Authorization Form

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

Prior Authorization Vendor for ND

ND Medicaid requires that patients receiving a prescription for non-preferred medications to meet specific diagnosis and step-therapy requirements. Criteria for agents requiring prior authorization can be found at one of the following locations:

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

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

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name	Specialist involved in therapy (if not treating physician)		
Prescriber NPI	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage:	**Diagnosis for this request:**		
List all failed medications:		**Start Date:**	**End Date:**

Additional Qualifications for Coverage (e.g. medical justification explaining inability to meet required trials)

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

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

Prescriber (or Staff) / Pharmacy Signature**	Date

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

Part II: TO BE COMPLETED BY PHARMACY

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

SANFORD HEALTH PLAN

PBM Quarterly Review: Mid-Year 2019
Prepared by: Axia Strategies

Medicaid

AXIA STRATEGIES

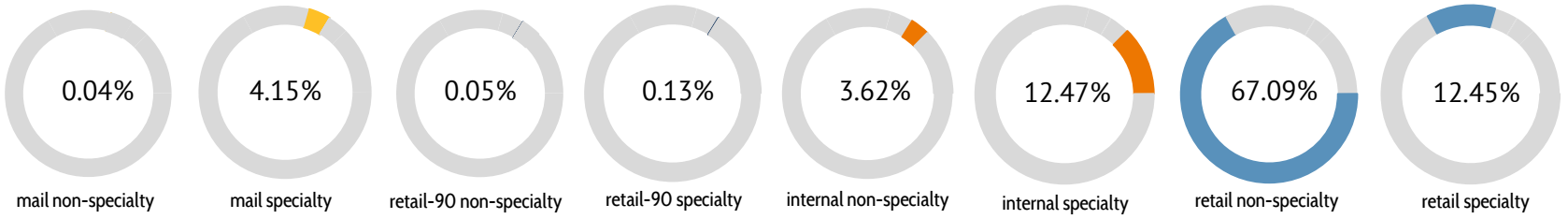
SPECIALTY & NON-SPECIALTY: SUMMARY

	Mid-Year 2018	Mid-Year 2019	Trend
membership			
Avg. Members / Month	20,325	19,226	-5.4%
Total Utilizing Members	15,279	15,020	-1.7%
utilization			
Total Rx Volume	219,806	208,976	-4.9%
% Specialty Rx Volume	0.5%	0.6%	7.5%
Rx Volume / Member	10.8	10.9	0.5%
Generic Dispensing Rate	86.0%	86.1%	0.0%
Mail Dispensing Rate	0.1%	0.1%	-33.2%
cost			
Total Gross Cost	$17,888,055	$17,437,974	-2.5%
Total Plan Cost	$17,816,282	$17,129,452	-3.9%
% Specialty Plan Cost	26.5%	29.2%	10.3%
Plan Cost PMPM	$146.09	$148.49	1.6%
Member Cost Share %	0.4%	0.4%	1.6%
Non-SRx Mbr Cost Share %	0.5%	0.5%	5.1%
Specialty Mbr Cost Share %	0.0%	0.0%	0.8%

Costs & Trends

- SHP's total Rx volume fell by 10,830 claims, which was a decrease of 4.9% over the prior period
- SHP total plan cost decreased by 3.9% to $17,129,452 for Mid-Year 2019
- Plan cost on a PMPM basis increased by 1.6%
- Specialty plan cost continues to make up a large portion of total spend at 29.2% for Mid-Year 2019
- Member cost share is currently 0.4%, which represents a positive trend of 1.6% from Mid-Year 2018

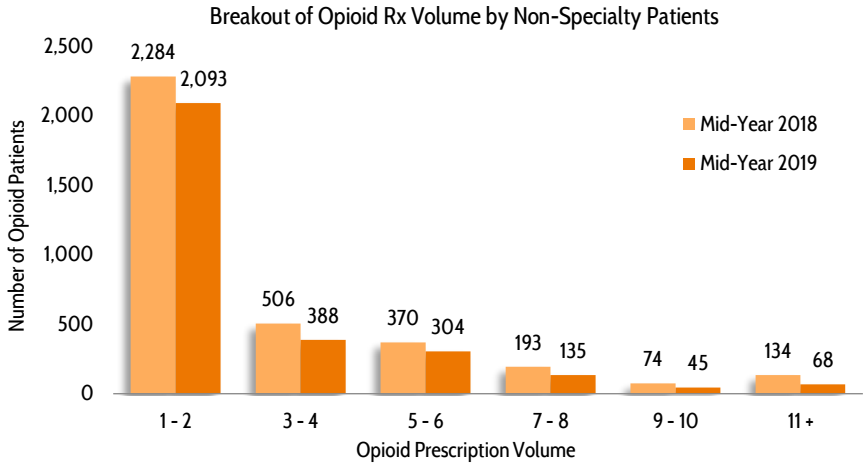
Breakout of Total Plan Costs: Mid-Year 2019



NON-SPECIALTY: SUMMARY

network pharmacies	Mid-Year 2018	Mid-Year 2019	Trend
utilization			
Avg. Members / Month	20,325	19,226	-5.4%
Total Rx Volume	218,635	207,779	-5.0%
Rx Volume / Member	10.8	10.8	0.5%
Generic Dispensing Rate	86.3%	86.4%	0.1%
cost			
Total Gross Cost	$13,164,264	$12,367,949	-6.0%
Total Plan Cost	$13,098,325	$12,126,749	-7.4%
Plan Cost PMPM	$107.41	$105.12	-2.1%
Member Cost Share %	0.5%	0.5%	5.1%

Opioids



	Total Rx Volume	Total # of Patients	Avg. Days Supply/Rx
Mid-Year 2018	10,741	3,561	13.2
Mid-Year 2019	7,964	3,033	12.4

Top 10 New Drugs by Total Plan Cost: Non-Specialty

Drug Name	Common Indication	Drug Type	Rx Volume	# Patients	Total Plan Cost
Bupropion Hydrochloride E	Depression	Generic	3699	1053	$79,361
Concerta	Attention Disorders	Brand	192	56	$71,188
Albuterol Sulfate Hfa	Asthma	Brand	1611	1018	$70,669
Fluticasone Propionate/Sa	Asthma	Generic	379	191	$70,546
Wixela Inhub	Asthma	Generic	125	69	$19,922
Ingrezza	Tardive Dyskinesia	Brand	3	1	$19,529
Advair Hfa	Asthma	Brand	48	26	$19,277
Aprepitant	Nausea/Vomiting	Generic	24	1	$13,140
Buprenorphine Hydrochlori	Pain	Generic	59	30	$10,928
Lotronex	Gi Disorders	Brand	5	1	$10,204

* Indicates that the product has been used in compounds during the reporting time period

NON-SPECIALTY Rx
AWP Prices: Then & Now

48%

The baseline AWP/unit **increased** for 479 drugs (48% of the claims dispensed during both periods)

The average AWP/unit increase was $2.60.

Top 10 Non-Specialty Drugs: By Dollar Increase in Average AWP Per Unit

			Rx Volume	Total AWP	Avg. AWP/Unit		
Drug Name	Drug Type	Common Indication	Mid-Year 2019		Mid-Year 2018	Mid-Year 2019	$ Change
INVEGA SUSTENNA	Brand	ANTIPSYCHOTICS	72	$201,178	$1,997	$2,132	$134
ZYPREXA RELPREVV	Brand	MENTAL/NEURO DISORDERS	27	$29,063	$1,011	$1,101	$90
ARISTADA	Brand	MENTAL/NEURO DISORDERS	22	$61,563	$874	$953	$80
RISPERDAL CONSTA	Brand	MENTAL/NEURO DISORDERS	41	$55,658	$972	$1,008	$36
BYETTA	Brand	DIABETES	29	$27,142	$507	$532	$24
EPINEPHRINE	Brand	ANAPHYLAXIS	102	$42,705	$188	$210	$22
VICTOZA	Brand	DIABETES	652	$621,112	$108	$123	$15
BYDUREON PEN	Brand	DIABETES	216	$181,380	$198	$210	$12
NUVARING	Brand	CONTRACEPTIVES	217	$43,120	$186	$195	$10
SPIRIVA RESPIMAT	Brand	COPD	109	$56,174	$119	$129	$10

31%

The baseline AWP/unit **decreased** for 316 drugs (31% of the claims dispensed during both periods)

The average AWP/unit decrease was $0.80.

Top 10 Non-Specialty Drugs: By Dollar Decrease in Average AWP Per Unit

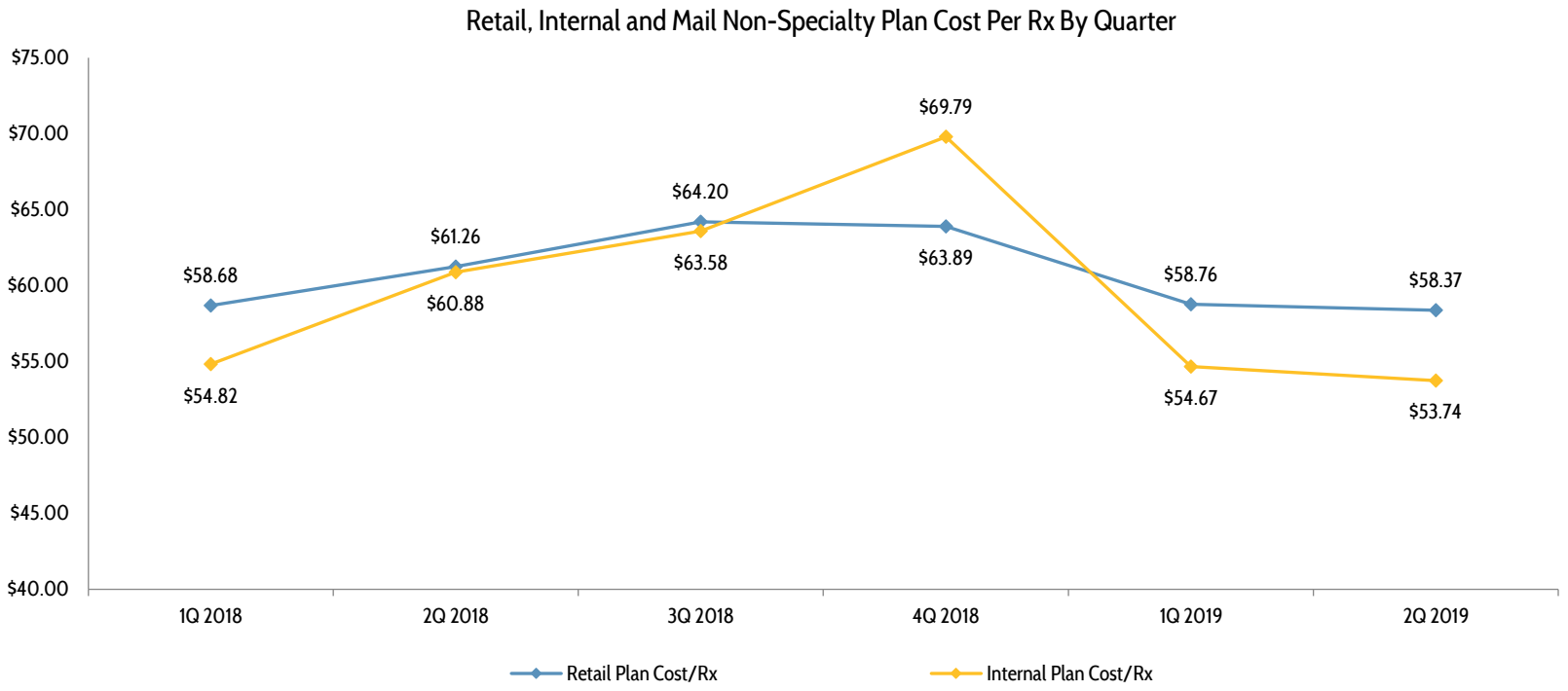
			Rx Volume	Total AWP	Avg. AWP/Unit		
Drug Name	Drug Type	Common Indication	Mid-Year 2019		Mid-Year 2018	Mid-Year 2019	$ Change
NALTREXONE HCL	Generic*	MENTAL/NEURO DISORDERS	360	$28,663	$28	$3	-$25
OLOPATADINE HCL	Generic	EYE CONDITIONS	139	$31,525	$47	$38	-$9
ABILIFY MAINTENA	Brand	MENTAL/NEURO DISORDERS	93	$230,885	$2,437	$2,431	-$6
PALIPERIDONE ER	Generic	ANTIPSYCHOTICS	80	$71,576	$33	$31	-$2
METHYLPHENIDATE HYDROCHLO	Generic	ATTENTION DISORDERS	472	$70,608	$5	$4	-$1
ESOMEPRAZOLE MAGNESIUM	Generic	ULCER DISEASE	322	$79,406	$9	$8	-$1
MIDODRINE HCL	Generic	LOW BLOOD PRESSURE	72	$25,779	$5	$5	-$1
RANITIDINE HCL	Generic	ULCER DISEASE	468	$36,489	$3	$2	-$1
SUMATRIPTAN SUCCINATE	Generic	MIGRAINE HEADACHES	658	$153,436	$26	$26	-$1
ONDANSETRON ODT	Generic	NAUSEA/VOMITING	999	$537,773	$26	$25	-$1

* Indicates that the product has been used in compounds during the reporting time period

** Top drugs tables reviewed only the top 200 non-specialty drugs by total AWP

NON-SPECIALTY: SUMMARY

Non-Specialty Claims by Quarter												
	Rx Volume				Plan Cost/Rx				Member Cost/Rx			
	Retail	Retail-90	Internal	Mail	Retail	Retail-90	Internal	Mail	Retail	Retail-90	Internal	Mail
1Q 2018	103,683	37	5,951	0	$58.68	$335.24	$54.82	$0.00	$0.29	$0.57	$0.22	$0.00
2Q 2018	102,753	40	6,171	0	$61.26	$136.86	$60.88	$0.00	$0.31	$0.23	$0.23	$0.00
3Q 2018	99,765	38	5,592	0	$64.20	$139.48	$63.58	$0.00	$0.32	$0.47	$0.23	$0.00
4Q 2018	100,620	28	5,625	0	$63.89	$132.58	$69.79	$0.00	$0.31	$0.32	$0.25	$0.00
1Q 2019	97,154	53	5,641	25	$58.76	$80.66	$54.67	$305.57	$0.32	$0.11	$0.24	$0.60
2Q 2019	99,063	54	5,789	0	$58.37	$67.53	$53.74	$0.00	$0.30	$0.06	$0.24	$0.00



NON-SPECIALTY:

Top 25 Drugs by Gross Cost

Top 25 Non-Specialty Drugs by Gross Cost

Rank '18	Rank '19	Drug Name	Drug Type	Common Indication	Rx Volume Mid-Year 2018	Rx Volume Mid-Year 2019	Rx Volume Trend	Total Gross Cost Mid-Year 2018	Total Gross Cost Mid-Year 2019	Total Gross Cost Trend	Total Plan Cost Mid-Year 2018	Total Plan Cost Mid-Year 2019	Total Plan Cost Trend
1	1	NOVOLOG FLEXPEN	Brand	DIABETES	1,545	1,368	-11.5%	$870,390	$761,698	-12.5%	$867,198	$754,585	-13.0%
2	2	LYRICA	Brand	SEIZURES	1,294	1,084	-16.2%	$617,137	$547,953	-11.2%	$614,098	$537,114	-12.5%
4	3	LANTUS SOLOSTAR	Brand	DIABETES	1,281	1,286	0.4%	$473,851	$485,532	2.5%	$470,590	$479,136	1.8%
5	4	VICTOZA	Brand	DIABETES	572	652	14.0%	$391,752	$474,519	21.1%	$390,318	$459,146	17.6%
3	5	LEVEMIR FLEXTOUCH	Brand	DIABETES	1,010	910	-9.9%	$476,636	$428,907	-10.0%	$475,094	$425,671	-10.4%
7	6	LATUDA	Brand	MENTAL/NEURO DISORDERS	265	333	25.7%	$316,125	$389,607	23.2%	$315,555	$363,415	15.2%
11	7	ZUBSOLV	Brand	OPIOID DEPENDENCE	985	1,494	51.7%	$199,333	$279,705	40.3%	$197,167	$275,619	39.8%
8	8	XIFAXAN	Brand	INFECTIONS	136	128	-5.9%	$279,390	$265,090	-5.1%	$279,081	$264,790	-5.1%
16	9	JARDIANCE	Brand	DIABETES	378	623	64.8%	$147,835	$246,102	66.5%	$146,935	$241,797	64.6%
9	10	SYMBICORT	Brand	ASTHMA	812	750	-7.6%	$251,547	$243,710	-3.1%	$249,363	$238,544	-4.3%
10	11	VYVANSE	Brand	ATTENTION DISORDERS	779	812	4.2%	$220,419	$232,643	5.5%	$218,607	$221,838	1.5%
20	12	ABILIFY MAINTENA	Brand	MENTAL/NEURO DISORDERS	61	93	52.5%	$122,341	$180,633	47.6%	$122,185	$175,136	43.3%
13	13	CONTOUR NEXT BLOOD GLUCOS	Brand	DIABETES	1,864	1,846	-1.0%	$161,744	$178,777	10.5%	$156,767	$172,175	9.8%
28	14	INVEGA SUSTENNA	Brand	ANTIPSYCHOTICS	44	72	63.6%	$91,579	$158,161	72.7%	$91,456	$157,972	72.7%
23	15	ELIQUIS	Brand	ANTICOAGULANT	253	359	41.9%	$104,265	$152,964	46.7%	$103,608	$151,573	46.3%
14	16	SPIRIVA HANDIHALER	Brand	COPD	445	410	-7.9%	$160,060	$146,838	-8.3%	$158,827	$143,660	-9.5%
12	17	JANUVIA	Brand	DIABETES	490	363	-25.9%	$194,299	$142,025	-26.9%	$193,057	$141,008	-27.0%
30	18	BYDUREON PEN	Brand	DIABETES	136	216	58.8%	$84,876	$134,266	58.2%	$84,600	$133,063	57.3%
15	19	NOVOLOG	Brand	DIABETES	303	228	-24.8%	$159,804	$131,940	-17.4%	$159,075	$126,286	-20.6%
18	20	GABAPENTIN	Generic	SEIZURES	6,624	5,991	-9.6%	$138,935	$110,671	-20.3%	$138,935	$110,493	-20.5%
39	21	TRINTELLIX	Brand	DEPRESSION	177	286	61.6%	$63,344	$103,702	63.7%	$62,921	$98,583	56.7%
27	22	XARELTO	Brand	ANTICOAGULANT	226	244	8.0%	$94,486	$102,406	8.4%	$93,850	$97,182	3.6%
17	23	PROAIR HFA	Brand	ASTHMA	2,449	1,378	-43.7%	$141,022	$92,123	-34.7%	$135,451	$88,182	-34.9%
35	24	ANORO ELLIPTA	Brand	COPD	177	226	27.7%	$70,336	$89,257	26.9%	$69,829	$88,618	26.9%
42	25	LEVOTHYROXINE SODIUM	Generic*	THYROID DISORDERS	4,041	3,999	-1.0%	$59,921	$83,783	39.8%	$59,921	$83,516	39.4%

* Indicates that the product has been used in compounds during the reporting time period

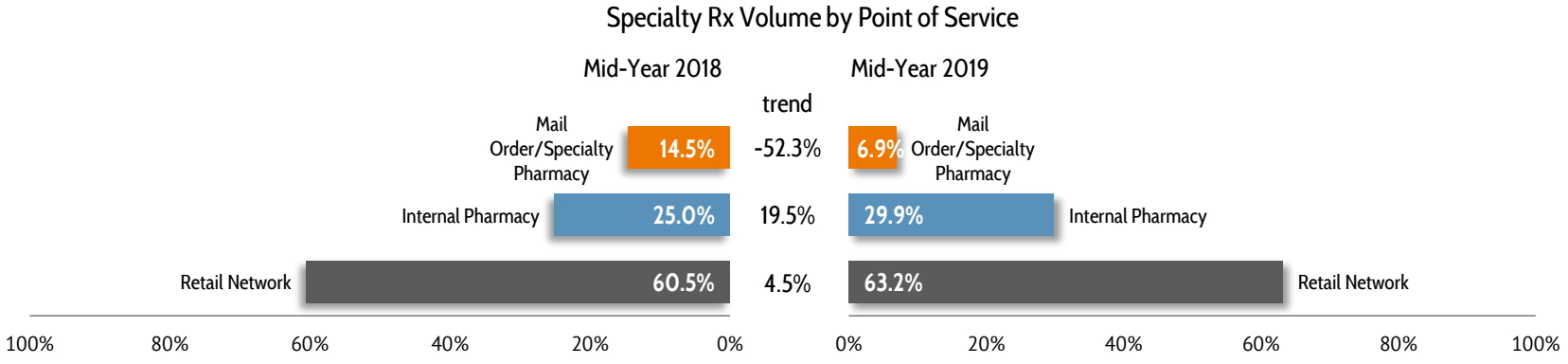
SPECIALTY: SUMMARY

	Mid-Year 2018	Mid-Year 2019	Trend
membership			
Avg. Members / Month	20,325	19,226	-5.4%
Total Utilizing Members	323	328	1.5%
utilization			
Total Rx Volume	**1,171**	**1,197**	**2.2%**
Retail Network SRx Volume	708	756	6.8%
Internal Pharmacy SRx Volume	293	358	22.2%
Mail Order SRx Volume	170	83	-51.2%
Rx Volume/Utilizing SRx Member	3.6	3.6	0.7%
Generic Dispensing Rate	28.7%	29.3%	2.2%
cost			
Total Gross Cost	$4,723,791	$5,070,025	7.3%
Total Plan Cost	$4,717,958	$5,002,703	6.0%
Plan Cost PMPM	**$38.69**	**$43.37**	**12.1%**
Retail Network	$16.56	$18.49	11.7%
Internal Pharmacy	$12.91	$18.52	43.4%
Mail Order/SRx Pharmacy	$9.22	$6.17	-33.1%
Member Cost Share $	$2,094	$2,265	8.2%
Member Cost Share %	**0.0%**	**0.0%**	**0.8%**
Retail Network	0.1%	0.1%	12.1%
Internal Pharmacy	0.0%	0.0%	-7.4%
Mail Order/SRx Pharmacy	0.0%	0.0%	-29.7%

Top 10 New Drugs by Total Plan Cost: Specialty

Drug Name	Common Indication	Drug Type	Rx Volume	# Patients	Total Plan Cost
Bexarotene	Cancer	Generic	6	1	$161,314
Symdeko	Cystic Fibrosis	Brand	4	1	$93,065
Imbruvica	Cancer	Brand	6	1	$72,540
Letairis	Pulmonary Hypertension	Brand	7	2	$70,527
Sutent	Cancer	Brand	4	1	$68,318
Taltz	Psoriasis	Brand	6	1	$60,678
Gleevec	Cancer	Brand	5	1	$49,086
Lynparza	Cancer	Brand	4	2	$42,651
Dupixent	Atopic Dermatitis	Brand	10	3	$33,895
Kuvan	Endocrine Disorders	Brand	2	1	$32,571

* Indicates that the product has been used in compounds during the reporting time period



SPECIALTY Rx
AWP Prices: Then & Now

66%

The baseline AWP/unit **increased** for 41 drugs (66% of the claims dispensed during both periods)

The average AWP/unit increase was $132.46.

Top 10 Specialty Drugs: By Dollar Increase in Average AWP Per Unit

			Rx Volume	Total AWP	Avg. AWP/Unit		
Drug Name	Drug Type	Common Indication	Mid-Year 2019		Mid-Year 2018	Mid-Year 2019	$ Change
STELARA	Brand	RHEUMATOID ARTHRITIS	6	$132,028	$24,701	$26,406	$1,704
HUMIRA PEN-CD/UC/HS START	Brand	ULCER DISEASE	2	$37,254	$2,923	$3,725	$802
HUMIRA PEN-PS/UV STARTER	Brand	RHEUMATOID ARTHRITIS	5	$62,089	$2,923	$3,684	$761
NATPARA	Brand	HYPOPARATHYROIDISM	5	$58,810	$5,609	$5,830	$221
PROMACTA	Brand	BLOOD CELL DEFICIENCY	2	$32,095	$330	$519	$189
HUMIRA PEN	Brand	RHEUMATOID ARTHRITIS	137	$968,590	$2,923	$3,104	$181
HUMIRA	Brand	RHEUMATOID ARTHRITIS	31	$228,488	$2,923	$3,104	$181
AVONEX PEN	Brand	MULTIPLE SCLEROSIS	3	$24,933	$8,148	$8,311	$163
AVONEX	Brand	MULTIPLE SCLEROSIS	1	$8,311	$8,148	$8,311	$163
SPRYCEL	Brand	CANCER	4	$65,697	$392	$547	$155

15%

The baseline AWP/unit **decreased** for 9 drugs (15% of the claims dispensed during both periods)

The average AWP/unit decrease was $27.63.

Top 10 Specialty Drugs: By Dollar Decrease in Average AWP Per Unit

			Rx Volume	Total AWP	Avg. AWP/Unit		
Drug Name	Drug Type	Common Indication	Mid-Year 2019		Mid-Year 2018	Mid-Year 2019	$ Change
REPATHA SURECLICK	Brand	HIGH BLOOD CHOLESTEROL	10	$7,802	$670	$483	-$188
TEMOZOLOMIDE	Generic	CANCER	10	$43,099	$288	$256	-$31
ENOXAPARIN SODIUM	Generic	DVT/ANTICOAGULATION	72	$100,257	$86	$69	-$17
TENOFOVIR DISOPROXIL FUMA	Generic	HIV	16	$13,827	$40	$31	-$9
SIROLIMUS	Generic	TRANSPLANT	8	$5,339	$17	$14	-$3
MYCOPHENOLATE MOFETIL	Generic	TRANSPLANT	77	$63,531	$7	$6	$0
TRETINOIN	Generic	ACNE	106	$22,133	$5	$5	$0
CAPECITABINE	Generic	CANCER	8	$25,730	$39	$39	$0
ENTECAVIR	Generic	HEPATITIS B	6	$7,998	$44	$44	$0
-	-	-	-	-	-	-	-

* Indicates that the product has been used in compounds during the reporting time period

** Top drugs tables reviewed only the top 200 specialty drugs by total AWP

SPECIALTY:

Top 25 Drugs by Gross Cost

Top 25 Specialty Drugs by Gross Cost

Rank '18	Rank '19	Drug Name	Drug Type	Common Indication	Rx Volume Mid-Year 2018	Rx Volume Mid-Year 2019	Rx Volume Trend	Total Gross Cost Mid-Year 2018	Total Gross Cost Mid-Year 2019	Total Gross Cost Trend	Total Plan Cost Mid-Year 2018	Total Plan Cost Mid-Year 2019	Total Plan Cost Trend
1	1	HUMIRA PEN	Brand	RHEUMATOID ARTHRITIS	159	137	-13.8%	$829,642	$790,012	-4.8%	$829,270	$767,586	-7.4%
22	2	COSENTYX SENSOREADY PEN	Brand	PSORIASIS	9	68	655.6%	$58,369	$470,956	706.9%	$58,336	$470,752	707.0%
3	3	MAVYRET	Brand	HEPATITIS C	32	36	12.5%	$431,285	$437,113	1.4%	$431,219	$437,026	1.3%
2	4	EPCLUSA	Brand	HEPATITIS C	17	14	-17.6%	$436,760	$286,189	-34.5%	$436,715	$286,147	-34.5%
4	5	GILENYA	Brand	MULTIPLE SCLEROSIS	35	30	-14.3%	$276,676	$240,229	-13.2%	$276,574	$240,139	-13.2%
19	6	HUMIRA	Brand	RHEUMATOID ARTHRITIS	14	31	121.4%	$69,779	$187,337	168.5%	$69,758	$187,244	168.4%
6	7	ENBREL SURECLICK	Brand	RHEUMATOID ARTHRITIS	27	33	22.2%	$132,858	$165,856	24.8%	$132,777	$165,775	24.9%
-	8	BEXAROTENE	Generic	CANCER	0	6	-	$0	$161,314	-	-	$161,314	-
5	9	COPAXONE	Brand	MULTIPLE SCLEROSIS	31	18	-41.9%	$224,035	$123,909	-44.7%	$224,005	$123,855	-44.7%
7	10	AUBAGIO	Brand	MULTIPLE SCLEROSIS	19	17	-10.5%	$125,432	$115,397	-8.0%	$125,375	$115,346	-8.0%
27	11	STELARA	Brand	RHEUMATOID ARTHRITIS	2	6	200.0%	$42,489	$106,936	151.7%	$42,477	$106,918	151.7%
13	12	STRIBILD	Brand	HIV	27	31	14.8%	$85,853	$94,347	9.9%	$85,787	$94,290	9.9%
-	13	SYMDEKO	Brand	CYSTIC FIBROSIS	0	4	-	$0	$93,077	-	-	$93,065	-
24	14	GENVOYA	Brand	HIV	18	29	61.1%	$51,373	$85,255	66.0%	$51,319	$67,861	32.2%
8	15	TRUVADA	Brand	HIV	69	45	-34.8%	$116,974	$75,674	-35.3%	$116,791	$75,548	-35.3%
-	16	IMBRUVICA	Brand	CANCER	0	6	-	$0	$72,558	-	-	$72,540	-
-	17	LETAIRIS	Brand	PULMONARY HYPERTENSION	0	7	-	$0	$70,548	-	-	$70,527	-
15	18	REVLIMID	Brand	CANCER	6	7	16.7%	$85,126	$70,360	-17.3%	$85,108	$70,339	-17.4%
-	19	SUTENT	Brand	CANCER	0	4	-	$0	$68,330	-	-	$68,318	-
25	20	XELJANZ	Brand	RHEUMATOID ARTHRITIS	12	14	16.7%	$50,510	$61,310	21.4%	$50,474	$61,268	21.4%
-	21	TALTZ	Brand	PSORIASIS	0	6	-	$0	$60,696	-	-	$60,678	-
-	22	KUVAN	Brand	ENDOCRINE DISORDERS	0	2	-	$0	$53,606	-	-	$32,571	-
20	23	TRIUMEQ	Brand	HIV	23	19	-17.4%	$66,136	$53,320	-19.4%	$66,085	$50,505	-23.6%
12	24	SPRYCEL	Brand	CANCER	9	4	-55.6%	$91,055	$52,812	-42.0%	$91,037	$52,800	-42.0%
42	25	NATPARA	Brand	HYPOPARATHYROIDISM	2	5	150.0%	$19,294	$49,547	156.8%	$19,288	$49,532	156.8%

* Indicates that the product has been used in compounds during the reporting time period

SPECIALTY & NON-SPECIALTY:

Top 20 High Cost Claimants

Top 20 High Cost Claimants by Total YTD Plan Cost										
		2019 Totals		Patient's Highest Cost Drug: 2019						
Patient Rank '19	New to List*	Total Rx Volume	Total Plan Cost	Drug Name	Common Indication	Rx Volume	Plan Cost	% Patient's Total Plan Cost	Specialty Indicator	Drug Type
1	Yes	76	$175,759	BEXAROTENE	CANCER	6	$161,314	91.8%	Specialty	Generic
2	Yes	41	$109,558	SYMDEKO	CYSTIC FIBROSIS	4	$93,065	84.9%	Specialty	Brand
3	Yes	13	$85,504	STELARA	RHEUMATOID ARTHRITIS	4	$85,363	99.8%	Specialty	Brand
4	Yes	42	$75,725	IMBRUVICA	CANCER	6	$72,540	95.8%	Specialty	Brand
5	Yes	10	$73,154	EPCLUSA	HEPATITIS C	3	$72,987	99.8%	Specialty	Brand
6	Yes	45	$72,200	REVLIMID	CANCER	7	$70,339	97.4%	Specialty	Brand
7	Yes	55	$71,955	GILENYA	MULTIPLE SCLEROSIS	7	$55,466	77.1%	Specialty	Brand
8	Yes	24	$69,307	SUTENT	CANCER	4	$68,318	98.6%	Specialty	Brand
9	Yes	7	$60,744	TALTZ	PSORIASIS	6	$60,678	99.9%	Specialty	Brand
10	Yes	40	$59,810	EPCLUSA	HEPATITIS C	2	$48,658	81.4%	Specialty	Brand
11	Yes	43	$56,598	HUMIRA PEN	RHEUMATOID ARTHRITIS	6	$40,394	71.4%	Specialty	Brand
12	Yes	17	$56,544	COSENTYX SENSOREADY PEN	PSORIASIS	1	$43,052	76.1%	Specialty	Brand
13	Yes	50	$54,446	LETAIRIS	PULMONARY HYPERTENSION	5	$50,116	92.0%	Specialty	Brand
14	Yes	29	$52,952	HUMIRA	RHEUMATOID ARTHRITIS	9	$50,496	95.4%	Specialty	Brand
15	Yes	5	$52,867	SPRYCEL	CANCER	4	$52,800	99.9%	Specialty	Brand
16	Yes	85	$52,791	HUMIRA	RHEUMATOID ARTHRITIS	5	$50,459	95.6%	Specialty	Brand
17	Yes	34	$50,948	GLEEVEC	CANCER	5	$49,086	96.3%	Specialty	Brand
18	Yes	11	$50,561	HUMIRA PEN	RHEUMATOID ARTHRITIS	5	$50,469	99.8%	Specialty	Brand
19	Yes	11	$50,535	HUMIRA PEN	RHEUMATOID ARTHRITIS	7	$50,446	99.8%	Specialty	Brand
20	Yes	40	$50,236	NATPARA	HYPOPARATHYROIDISM	5	$49,532	98.6%	Specialty	Brand

* Indicates that this patient was not on the top 20 high cost claimant list as of year end 2018

REVIEW OF ANTIFUNGAL AGENTS FOR ASPERGILLUS AND CANDIDA INFECTIONS

ASPERGILLUS AND CANDIDA INFECTIONS:

- Both are broad terms to describe a host of fungal infections caused by species of Aspergillus or Candida.
- These infections are most common in immunosuppressed patients, most commonly:
  - Hematopoietic cell transplant (HCT) recipients
  - Solid organ transplant (especially lung, heart-lung, and liver) recipients
  - Patients who experience prolonged neutropenia
  - Patients with hematologic malignancies
  - Patients with AIDs
- **Aspergillus**:
  - Invasive aspergillosis most frequently occurs in the lungs or sinuses after inhalation, although, less commonly, disease can spread from the gastrointestinal tract or result from direct inoculation into the skin.
    - "aspergillosis" refers to illness due to allergy, airway or lung invasion, cutaneous infection, or extrapulmonary dissemination caused by species of Aspergillus, most commonly A. fumigatus, A. flavus, and A. terreus
    - Aspergillus species are ubiquitous in nature, and inhalation is common
      - Tissue invasion is uncommon (typically due to immunosuppression)
  - Invasive focal infections most often occur after spreading in the blood or when anatomic abnormalities or devices are present
- **Candida**:
  - The clinical manifestations of infection with Candida species range from local mucous membrane infections to widespread dissemination with multisystem organ failure
  - The different Candida species are capable of producing all of the clinical syndromes (infection with Candida albicans is the most common)
    - The most benign infections are characterized by local overgrowth on mucous membranes (oropharyngeal involvement, vaginitis) as a result of changes in the normal flora.
  - More extensive persistent mucous membrane infections occur in individuals with deficiencies in cell-mediated immunity, in which widespread visceral dissemination occurs after Candida species gain access to the bloodstream

TREATMENT:

- **Candida:**
  - **General Guideline Recommendations**
    - **Treatment** options depend on the type of infection (location, species, and susceptibility), but generally, the Infectious Diseases Society of America (IDSA) recommendations that fall under outpatient (pharmacy) care include the following:
      - **Oropharyngeal candidiasis (thrush):** Topical antifungal agents (Nystatin or clotrimazole lozenges)
      - **Other candida infections:** systemic azole antifungals and echinocandins (caspofungin, micafungin, and anidulafungin)
    - **Prophylaxis** recommendations are for use of fluconazole or an echinocandin.
- **Aspergillus:**
  - **General Guideline Recommendations**
    - **Treatment** options depend on the type of infection (location, species, and susceptibility), but generally, the Infectious Diseases Society of America (IDSA) recommendations that fall under outpatient (pharmacy) care include the following:
      - **Triazoles — Triazole antifungal agents include voriconazole, posaconazole, itraconazole, and fluconazole**
    - **Prophylaxis:** posaconazole, voriconazole, itraconazole, micafungin, and caspofungin

- **Newer agents**
  - **Cresemba (isavuconazonium)**
    - Azole antifungal derivative, indicated for the treatment of invasive aspergillosis in adults
  - **Noxafil (posaconazole)**
  - Suspension formulation of posaconazole
    - Indicated for prophylaxis of invasive Aspergillus and Candida infections in patients 13 years and older, and Treatment of oropharyngeal candidiasis, including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole in patients 13 years and older
  - **Tolsura (itraconazole):**
    - Formulation of itraconazole in a 65 mg capsule
    - Indications for the following:
      - **Blastomycosis**, pulmonary and extrapulmonary
      - **Histoplasmosis**, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis
      - **Aspergillosis**, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy

COST

Drug	Strength	Package Size	AWP Pkg Price	AWP Unit Price
CLOTRIMAZOLE LOZENGE	10 mg	140	408.84	2.92
CRESEMBA	186 mg caps	14	1555.09	111.08
FLUCONAZOLE TABLET	50, 100, 150, 200 mg tablet	various	Various	1.02-14.32
ITRACONAZOLE SOLUTION	10 mg/mL	3 supp	347.12	2.31
ITRACONAZOLE CAPSULE	100 mg	various	various	5.66-24.06
NYSTATIN SUSPENSION	100,000 u/mL	various	various	0.24-0.28
NOXAFIL	40 mg/mL	105 mL	1,727.46	82.23
TOLSURA	65 mg	60 caps	2,482.25	41.37
VORICONAZOLE	50, 200 mg tab	various	various	19.87-139.31

CURRENT UTILIZATION

ND Medicaid Utilization (08/01/18 – 07/31/19)			
Label Name	**Rx Num**	**Quantity**	**Total Reimb Amt**
CLOTRIMAZOLE LOZENGE	46	2,778	$2,128.83
CRESEMBA	0	0	0
FLUCONAZOLE TABLET	1,879	6,408	$39,399.15
FLUCONAZOLE SUSPENSION	237	9,720	$6,087.24
ITRACONAZOLE SOLUTION	1	28	$67.30
ITRACONAZOLE CAPSULE	22	2.472	$5,428.83
NYSTATIN SUSPENSION	588	65,386	$18,374.01
NOXAFIL	0	0	0
TOLSURA	0	0	0
VORICONAZOLE	22	1,455	$9,161.23

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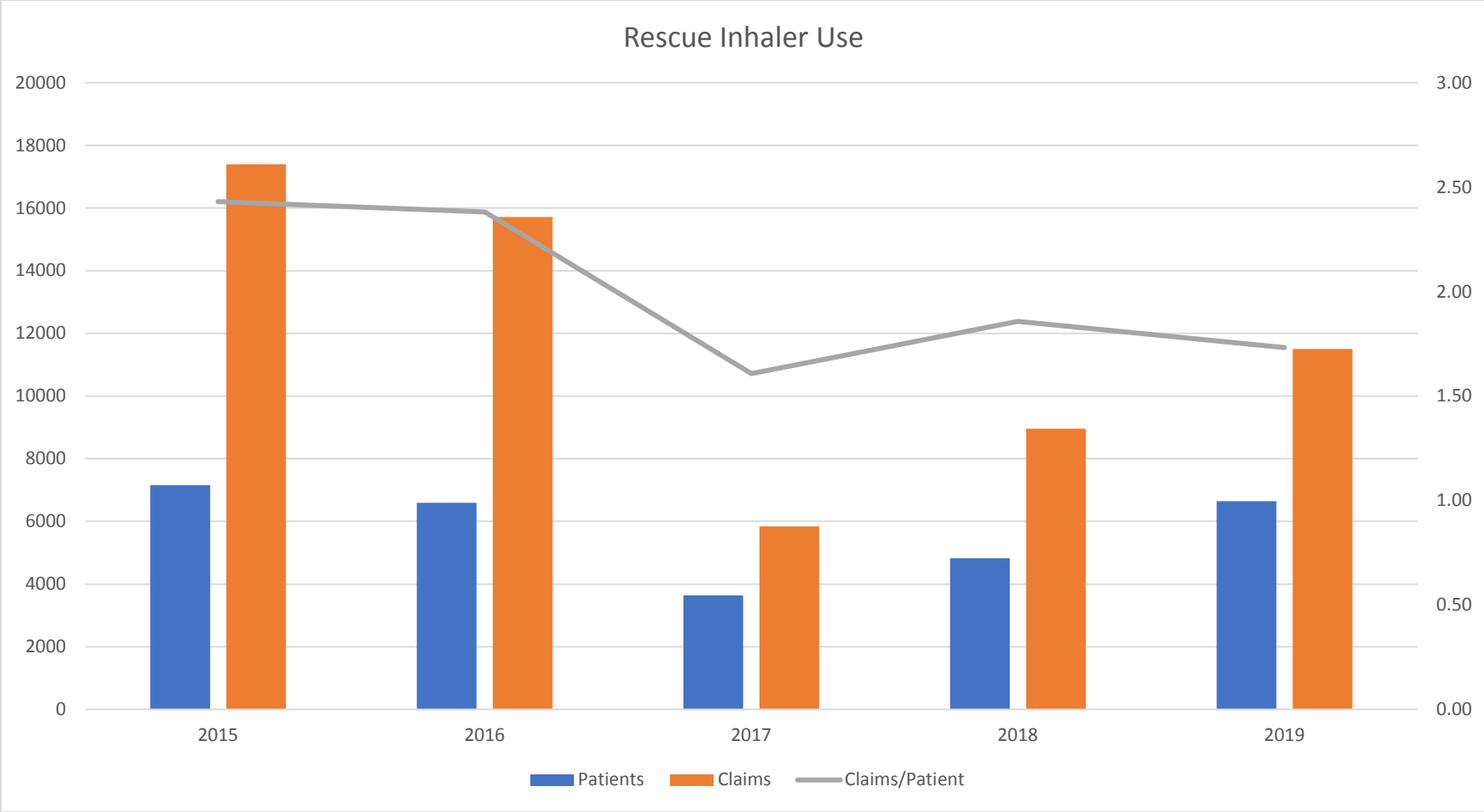
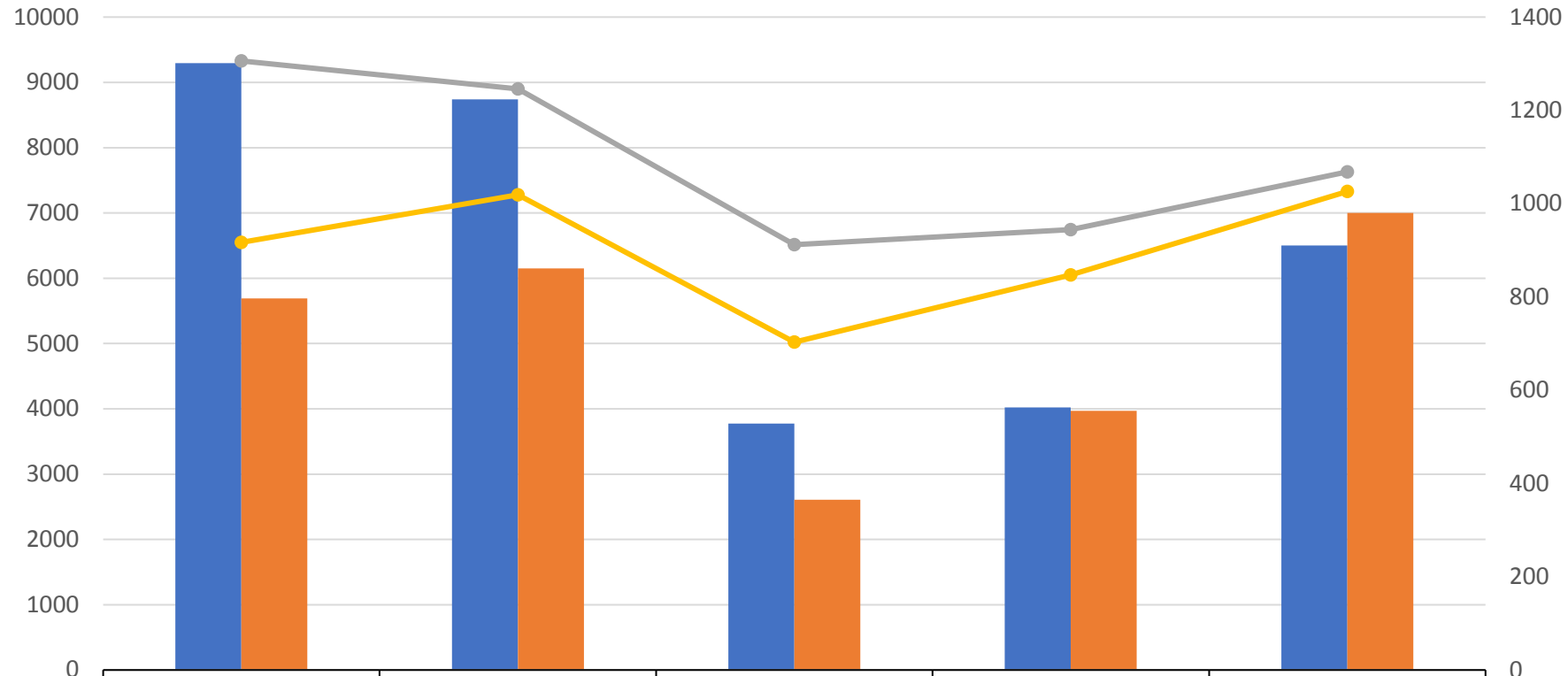
3. Pappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, Reboli AC, Schuster MG, Vazquez JA, Walsh TJ, Zaoutis TE. Clinical practice guideline for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. Clinical Infectious Diseases. 2015 Dec 16;62(4):e1-50.


Rescue Inhaler Use
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
3.00
2.50
2.00
1.50
1.00
0.50
0.00
2015
2016
2017
2018
2019
Patients
Claims
Claims/Patient

Adderall vs. Vyvanse Utilization Over 5 Years



	2015	2016	2017	2018	2019
Adderall (rx)	9296	8739	3776	4022	6503
Vyvanse (rx)	5689	6150	2608	3970	7001
Adderall (pts)	1306	1246	912	944	1068
Vyvanse (pts)	917	1019	703	847	1026

NORTH DAKOTA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
3RD QUARTER 2019

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

1. Esketamine / Overutilization _____ _____

Alert Message: The recommended maximum maintenance dosage of Spravato (esketamine) is 84 mg once weekly. Evidence of therapeutic benefit should be evaluated at the end of the induction phase to determine the need for continued treatment.

Drugs/Diseases

Util A	Util B	Util C
Esketamine		

Max Dose: 84 mg once weekly

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Spravato Prescribing Information, March 2019, Janssen Pharmaceuticals, Inc.

2. Esketamine / Antidepressants (Negating) _____ _____

Alert Message: A review of the patient's drug profile does not reveal a prescription for an oral antidepressant. Spravato (esketamine) is approved to be used in conjunction with an oral antidepressant.

Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Esketamine		Antidepressants

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Spravato Prescribing Information, March 2019, Janssen Pharmaceuticals, Inc.

3. Esketamine / Contraindications _____ _____

Alert Message: Spravato (esketamine) is contraindicated in patients with; aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial, and peripheral arterial vessels), arteriovenous malformation, or a history of intracerebral hemorrhage.

Drugs/Diseases

Util A	Util B	Util C
Esketamine	Abdominal Aortic Aneurysm	
	Thoracic Aortic Aneurysm	
	Peripheral Arterial Vessels	
	Arteriovenous Malformation	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Spravato Prescribing Information, March 2019, Janssen Pharmaceuticals, Inc.

Criteria Recommendations *Approved* *Rejected*

4. Esketamine / Contraindications _____ _____

Alert Message: Spravato (esketamine) is contraindicated in patients with a history of intracerebral hemorrhage. Esketamine causes increases in the systolic and/or diastolic blood pressure at all recommended doses. In clinical trials, approximately 8% to 17% of esketamine-treated patients and 1% to 3% of placebo-treated patients experienced an increase of more than 40 mmHg in systolic BP and/or 25 mmHg in diastolic BP in the first 1.5 hours after administration at least once during the first 4 weeks of treatment.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Esketamine		History of Intracranial Hemorrhage

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Spravato Prescribing Information, March 2019, Janssen Pharmaceuticals, Inc.

5. Esketamine / CNS Depressants _____ _____

Alert Message: Concomitant use of Spravato (esketamine) with CNS depressants (e.g., benzodiazepines, opioids, alcohol) may increase sedation. Closely monitor the patient for sedation with concomitant use of esketamine with CNS depressants.

Drugs/Diseases

Util A	Util B	Util C
Esketamine	Benzodiazepines	
	Opioids	
	Skeletal Muscle Relaxants	
	Sedative/Hypnotics	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Spravato Prescribing Information, March 2019, Janssen Pharmaceuticals, Inc.

6. Esketamine / Dissociation (Black Box Warning) _____ _____

Alert Message: Given its potential to induce dissociative effects, carefully assess patients with psychosis before administering Spravato (esketamine). Treatment with esketamine should be initiated only if the benefit outweighs the risk. Because of the risks of dissociation and sedation, patients must be monitored by a healthcare provider for at least 2 hours at each treatment session, followed by an assessment to determine when the patient is considered clinically stable and ready to leave the healthcare setting.

Drugs/Diseases

Util A	Util B	Util C
Esketamine		

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Spravato Prescribing Information, March 2019, Janssen Pharmaceuticals, Inc.

Criteria Recommendations *Approved* *Rejected*

7. Esketamine / Abuse and Misuse (Black Box Warning) _____ _____

Alert Message: Spravato (esketamine) contains esketamine, a Schedule III controlled substance (CIII), and may be subject to abuse and diversion. Assess each patient's risk for abuse or misuse prior to prescribing esketamine and monitor all patients receiving esketamine for the development of these behaviors or conditions, including drug-seeking behavior, while on therapy. Individuals with a history of drug abuse or dependence are at greater risk.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Esketamine		Drug Abuse
		Drug Dependence

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Spravato Prescribing Information, March 2019, Janssen Pharmaceuticals, Inc.

8. Esketamine / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on published findings from pregnant animals treated with ketamine, the racemic mixture of arketamine and esketamine, Spravato (esketamine) may cause fetal harm when administered to pregnant women. Advise pregnant women of the potential risk to an infant exposed to esketamine in utero. Advise women of reproductive potential to consider pregnancy planning and prevention.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Spravato Prescribing Information, March 2019, Janssen Pharmaceuticals, Inc.

9. Esketamine / Lactation _____ _____

Alert Message: Spravato (esketamine) is present in human milk. There are no data on the effects of esketamine on the breastfed infant or on milk production. Published studies in juvenile animals report neurotoxicity. Because of the potential for neurotoxicity, advise patients that breastfeeding is not recommended during treatment with esketamine.

Drugs/Diseases

Util A	Util B	Util C
Esketamine	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Spravato Prescribing Information, March 2019, Janssen Pharmaceuticals, Inc.

Criteria Recommendations *Approved* *Rejected*

10. Esketamine / Hypertension _____ _____

Alert Message: Spravato (esketamine) can cause increases in systolic and/or diastolic blood pressure (BP) at all recommended doses. Increases in BP peak approximately 40 minutes after esketamine administration and last approximately 4 hours. Carefully assessed to determine whether the potential benefits of esketamine therapy outweigh its risks.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Esketamine		Hypertension

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Spravato Prescribing Information, March 2019, Janssen Pharmaceuticals, Inc.

11. Esketamine /Therapeutic Appropriateness _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Esketamine		

Age Range: 0 - 17 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Spravato Prescribing Information, March 2019, Janssen Pharmaceuticals, Inc.

12. Esketamine / Therapeutic Appropriateness _____ _____

Alert Message: The mean Spravato (esketamine) AUC and t1/2 values were higher in patients with moderate hepatic impairment compared to those with normal hepatic function. Esketamine-treated patients with moderate hepatic impairment may need to be monitored for adverse reactions for a longer period of time. Esketamine has not been studied in patients with severe hepatic impairment (Child-Pugh class C). Use in this population is not recommended.

Drugs/Diseases

Util A	Util B	Util C
Esketamine		

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Spravato Prescribing Information, March 2019, Janssen Pharmaceuticals, Inc.

13. Esketamine / Psychostimulants _____ _____

Alert Message: Concomitant use of Spravato (esketamine) with psychostimulants (e.g., amphetamines, methylphenidate, modafinil, armodafinil) may increase blood pressure. Closely monitor blood pressure with concomitant use of esketamine with psychostimulants.

Drugs/Diseases

Util A	Util B	Util C
Esketamine	Amphetamine	
	Dextroamphetamine	
	Lisdexamfetamine	
	Methylphenidate	
	Dexmethylphenidate	
	Modafinil	
	Armodafinil	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Spravato Prescribing Information, March 2019, Janssen Pharmaceuticals, Inc.

14. Esketamine / MAO Inhibitors _____ _____

Alert Message: Concomitant use of Spravato (esketamine) with monoamine oxidase inhibitors (MAOIs) may increase blood pressure. Closely monitor blood pressure with concomitant use of esketamine with MAOIs.

Drugs/Diseases

Util A	Util B	Util C
Esketamine	Isocarboxazid	
	Phenelzine	
	Tranylcypromine	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Spravato Prescribing Information, March 2019, Janssen Pharmaceuticals, Inc.

15. Doravirine / Overutilization _____ _____

Alert Message: Pifeltro (doravirine) may be over-utilized. The recommended dosage of doravirine is 100 mg orally once daily.

Drugs/Diseases

Util A	Util B	Util C
Doravirine		

Max Dose: 1 tablet/day

References:
Pifeltro Prescribing Information, August 2018, Merck Sharp & Dohme Corp.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

16. Doravirine / Nonadherence _____ _____

Alert Message: Based on the refill history, your patient may be under-utilizing Pifeltro (doravirine). Nonadherence to antiretroviral therapy may result in insufficient plasma levels and partial suppression of viral load leading to the development of resistance, HIV progression, and increased mortality.

Drugs/Diseases

Util A	Util B	Util C
Doravirine		

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents. Department of Health and Human Services. October 25, 2018. Available at: http://www.aidsinfo.nih.gov/guidelines/ht,l/1/adult-and-adolescent-arv/0
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Schaecher KL. The Importance of Treatment Adherence in HIV. Am J Manag Care. 2013 Sep;19(12 Suppl):231-7.

17. Doravirine / Rifabutin _____ _____

Alert Message: If Pifeltro (doravirine) is co-administered with rifabutin, increase the doravirine dosage to one tablet twice daily (approximately 12 hours apart) for the duration of rifabutin co-administration.

Drugs/Diseases

Util A	Util B	Util C
Doravirine	Rifabutin	

References:

Pifeltro Prescribing Information, August 2018, Merck Sharp & Dohme Corp.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

18. Doravirine / Contraindicated Drugs _____ _____

Alert Message: The concurrent use of Pifeltro (doravirine) with a drug that is a strong CYP3A4 inducer is contraindicated. Doravirine is a CYP3A4 substrate, and co-administration with a strong CYP3A4 inducer may result in a significant decrease in doravirine plasma concentrations, a decrease doravirine efficacy, and possible development of resistance. At least a 4-week cessation period is recommended for the strong inducer prior to initiation of doravirine.

Drugs/Diseases

Util A	Util B	Util C
Doravirine	Enzalutamide	
	Carbamazepine	
	Oxcarbazepine	
	Phenobarbital	
	Phenytoin	
	Rifampin	
	Rifapentine	
	Mitotane	

References:

Pifeltro Prescribing Information, August 2018, Merck Sharp & Dohme Corp.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

19. Doravirine / Therapeutic Appropriateness _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Doravirine		

Age Range: 0 – 17 yoa

References:

Pifeltro Prescribing Information, August 2018, Merck Sharp & Dohme Corp.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

20. Doravirine / Therapeutic Appropriateness _____ _____

Alert Message: Monotherapy with an NNRTI is not recommended in HIV-1-infected patients. Drug-resistant virus emerges rapidly when an NNRTI is administered as single agent therapy. Achieving viral suppression requires the use of antiretroviral (ARV) regimens with at least two, and preferably three, active drugs from two or more ARV drug classes.

Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Doravirine		All Other Antiretrovirals

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Pifeltro Prescribing Information, August 2018, Merck Sharp & Dohme Corp.
Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents. Department of Health and Human Services. Oct. 25, 2018. Available at: http://www.aidsinfo.nih.gov/guidelines/ht,l/1/adult-and-adolescent-arv/0

21. Doravirine / Efavirenz _____ _____

Alert Message: The concurrent use of Pifeltro (doravirine) with an efavirenz-containing drug is not recommended. Doravirine is a CYP3A substrate, and co-administration with efavirenz, a CYP3A4 inducer, may result in decreased doravirine exposure and decreased doravirine efficacy. Both drugs are non-nucleoside reverse transcriptase inhibitors, and the concomitant use represents unnecessary duplication of therapy.

Drugs/Diseases

Util A	Util B	Util C
Doravirine	Efavirenz	
	Efavirenz/Lamivudine/Tenofovir Dis	
	Efavirenz/Emtricitabine/Tenofovir Dis	

References:

Pifeltro Prescribing Information, August 2018, Merck Sharp & Dohme Corp.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

22. Doravirine / Etravirine _____ _____

Alert Message: The concurrent use of Pifeltro (doravirine) with (Intelence) etravirine is not recommended. Doravirine is a CYP3A substrate, and co-administration with etravirine, a CYP3A4 inducer, may result in decreased doravirine exposure and decreased doravirine efficacy. Both drugs are non-nucleoside reverse transcriptase inhibitors, and the concomitant use represents unnecessary duplication of therapy.

Drugs/Diseases

Util A	Util B	Util C
Doravirine	Etravirine	

References:
Pifeltro Prescribing Information, August 2018, Merck Sharp & Dohme Corp.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

23. Doravirine / Nevirapine _____ _____

Alert Message: The concurrent use of Pifeltro (doravirine) with nevirapine is not recommended. Doravirine is a CYP3A substrate, and co-administration with nevirapine, a CYP3A4 inducer, may result in decreased doravirine exposure and decreased doravirine efficacy. Both drugs are non-nucleoside reverse transcriptase inhibitors, and the concomitant use represents unnecessary duplication of therapy.

Drugs/Diseases

Util A	Util B	Util C
Doravirine	Nevirapine	

References:
Pifeltro Prescribing Information, August 2018, Merck Sharp & Dohme Corp.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

24. Delstrigo / Overutilization _____ _____

Alert Message: Delstrigo (doravirine/lamivudine/tenofovir disoproxil fumarate) may be over-utilized. The recommended dosage of doravirine 100 mg/lamivudine 300 mg/tenofovir disoproxil fumarate 300 mg is one tablet once daily.

Drugs/Diseases

Util A	Util B	Util C
Doravirine/Lamivudine/Tenofovir DF		

Max Dose: 1 tablet/day

References:
Delstrigo Prescribing Information, August 2018, Merck Sharp & Dohme Corp.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

Criteria Recommendations *Approved* *Rejected*

25. Delstrigo / Nonadherence _____ _____

Alert Message: Based on the refill history, your patient may be under-utilizing Delstrigo (doravirine/lamivudine/tenofovir disoproxil fumarate). Nonadherence to antiretroviral therapy may result in insufficient plasma levels and partial suppression of viral load leading to the development of resistance, HIV progression, and increased mortality.

Drugs/Diseases

Util A	Util B	Util C
Doravirine/Lamivudine/Tenofovir DF		

References:

Delstrigo Prescribing Information, August 2018, Merck Sharp & Dohme Corp.
Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents. Department of Health and Human Services. Octeber25, 2018. Available at: http://www.aidsinfo.nih.gov/guidelines/ht,l/1/adult-and-adolescent-arv/0
Nachega JB, Marconi VC, van Zyl GU, et al. HIV Treatment Adherence, Drug Resistance, Virologic Failure: Evolving Concepts. Infect Disord Drug Targets. 2011 April;11(2):167-174.
Schaecher KL. The Importance of Treatment Adherence in HIV. Am J Manag Care. 2013 Sep;19(12 Suppl):231-7.

26. Delstrigo / Renal Impairment _____ _____ _____

Alert Message: Delstrigo (doravirine/lamivudine/tenofovir disoproxil fumarate) is not recommended in patients with estimated creatinine clearance less than 50 mL/min. Doravirine/lamivudine/tenofovir disoproxil fumarate is a fixed-dose combination tablet, and the dosage of lamivudine and tenofovir cannot be adjusted.

Drugs/Diseases

Util A	Util B	Util C
Doravirine/Lamivudine/Tenofovir DF	CKD 3, 4, 5 ESRD	

References:

Delstrigo Prescribing Information, August 2018, Merck Sharp & Dohme Corp.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

27. Delstrigo / Rifabutin / Doravirine (Negating) _____ _____

Alert Message: If Delstrigo (doravirine/lamivudine/tenofovir disoproxil fumarate) is co-administered with rifabutin, take one tablet of doravirine/lamivudine/tenofovir disoproxil once daily, followed by one tablet of doravirine 100 mg approximately 12 hours after the fixed-dose combination product for the duration of rifabutin co-administration. Doravirine is a CYP3A4 substrate, and concurrent use with a CYP3A4 inducer may decrease doravirine exposure, resulting in potential loss of virologic response.

Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Doravirine/Lamivudine/Tenofovir DF	Rifabutin	Doravirine

References:

Delstrigo Prescribing Information, August 2018, Merck Sharp & Dohme Corp.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

28. Delstrigo / Contraindicated Drugs _____ _____

Alert Message: The concurrent use of Delstrigo (doravirine/lamivudine/tenofovir disoproxil fumarate) with a drug that is a strong CYP3A4 inducer is contraindicated. The doravirine component of the fixed-dose combination product is a CYP3A substrate, and co-administration with a strong CYP3A4 inducer may result in a significant decrease in doravirine plasma concentrations, a decrease doravirine efficacy, and possible development of resistance. At least a 4-week cessation period is recommended for the strong inducer prior to initiation of doravirine/lamivudine/tenofovir disoproxil fumarate.

Drugs/Diseases

Util A	Util B	Util C
Doravirine/Lamivudine/Tenofovir DF	Enzalutamide	
	Carbamazepine	
	Oxcarbazepine	
	Phenobarbital	
	Phenytoin	
	Rifampin	
	Rifapentine	
	Mitotane	

References:
Delstrigo Prescribing Information, August 2018, Merck Sharp & Dohme Corp.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

29. Delstrigo / Ledipasvir/Sofosbuvir _____ _____

Alert Message: The concurrent use of Delstrigo (doravirine/lamivudine/tenofovir disoproxil fumarate) with ledipasvir/sofosbuvir may result in elevated tenofovir disoproxil plasma concentrations. Monitor the patient for adverse reactions associated with tenofovir disoproxil fumarate.

Drugs/Diseases

Util A	Util B	Util C
Doravirine/Lamivudine/Tenofovir DF	Ledipasvir/Sofosbuvir	

References:
Delstrigo Prescribing Information, August 2018, Merck Sharp & Dohme Corp.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

30. Delstrigo / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Delstrigo (doravirine/lamivudine/tenofovir disoproxil fumarate) in pediatric patients less than 18 years of age have not been established.

Drugs/Diseases

Util A	Util B	Util C
Doravirine/Lamivudine/Tenofovir DF		

Age Range: 0 – 17 yoa

References:
Delstrigo Prescribing Information, August 2018, Merck Sharp & Dohme Corp.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

31. Delstrigo / Therapeutic Appropriateness _____ _____

Alert Message: Delstrigo (doravirine/lamivudine/tenofovir disoproxil) is a complete regimen for the treatment of HIV-1 infection, co-administration with other antiretroviral medications for the treatment of HIV-1 infection is not recommended.

Drugs/Diseases

Util A	Util B	Util C
Doravirine/Lamivudine/Tenofovir DF	All Other Antiretrovirals	

References:

Delstrigo Prescribing Information, August 2018, Merck Sharp & Dohme Corp.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

32. Metformin - All / Vitamin B 12 _____ _____

Alert Message: The use of metformin is associated with vitamin B12 deficiency. Certain individuals (those with inadequate vitamin B12 or calcium intake or absorption) appear to be predisposed to developing subnormal vitamin B12 levels. Consider measuring hematologic parameters on an annual basis and vitamin B12 at 2 to 3-year intervals in patients receiving a metformin-containing medication and manage any abnormalities.

Drugs/Diseases

Util A	Util B	Util C
Metformin		

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Facts & Comparisons, 2019 Updates, Wolters Kluwer Health.
Aroda VR, Edelstein SL. Goldberg RB, et al., Long-term Metformin Use and Vitamin B12 Deficiency in the Diabetes Prevention Program Outcomes Study. J Clin Endocrinol Metab. 2016 Apr;101(4):1754-1761.

33. DPP-4 Inhibitors / Bullous Pemphigoid _____ _____

Alert Message: Postmarketing cases of bullous pemphigoid requiring hospitalization have been reported with DPP-4 inhibitor use (sitagliptin, saxagliptin, linagliptin, and alogliptin). In reported cases, patients typically recovered with topical or systemic immunosuppressive treatment and discontinuation of the DPP-4 inhibitor. Tell patients to report the development of blisters or erosions while receiving a DPP-4 inhibitor containing medication. If bullous pemphigoid is suspected, the DPP-4 inhibitor should be discontinued, and referral to a dermatologist should be considered for diagnosis and appropriate treatment.

Drugs/Diseases

Util A	Util B	Util C
Sitagliptin	Bullous Pemphigoid	
Saxagliptin		
Linagliptin		
Alogliptin		

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Facts & Comparisons, 2019 Updates, Wolters Kluwer Health.

34. Galcanezumab-gnlm / Overutilization _____ _____

Alert Message: Emgality (galcanezumab-gnlm) may be over-utilized. The recommended dosage of galcanezumab-gnlm for the treatment of episodic cluster headaches is 300 mg (three consecutive 100 mg subcutaneous injections) at the onset of the cluster period, then monthly until the end of the cluster period.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Galcanezumab-gnlm		Cluster Headache

Max Dose: 3 pens per month

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Emgality Prescribing Information, June 2019, Eli Lilly and Company.

35. Galcanezumab-gnlm / Overutilization _____ _____

Alert Message: Emgality (galcanezumab-gnlm) may be over-utilized. The recommended dosage of galcanezumab-gnlm for the preventative treatment of migraine in adults is 240 mg once as a loading dose, followed by doses of 120 mg injected subcutaneously once monthly.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Galcanezumab-gnlm		Migraine

Max Dose:1 pen per month after loading dose

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Emgality Prescribing Information, June 2019, Eli Lilly and Company.

36. Pitavastatin / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Livalo (pitavastatin) have not been established in pediatric patients younger than 8 years of age with HeFH or in pediatric patients with other types of hyperlipidemia (other than HeFH).

Drug/Disease:

Util A	Util B	Util C
Pitavastatin		

Age Range: 0 - 7 yoa

References:
Livalo Prescribing Information, May 2019, Kowa Pharmaceuticals America, Inc.
Facts & Comparisons, 2019 Updates, Wolters Kluwer Health.

37. Pitavastatin / Overuse _____ _____

Alert Message: The recommended maximum dose of Zypitamag (pitavastatin magnesium) is 4 mg once daily. Doses exceeding 4 mg per day have been associated with an increased risk for severe myopathy in premarketing clinical studies.

Drug/Disease:

Util A	Util B	Util C **(Negate)**
Pitavastatin		Severe Renal Impairment
		Hemodialysis

Max Dose: 4 mg per day

References:
Zypitamag Prescribing Information, August 2018, Medicure.

38. Pitavastatin / Moderate to Severe Renal Impairment & ESRD _____ _____

Alert Message: The recommended maximum dose of Zypitamag (pitavastatin magnesium) in patients with moderate and severe renal impairment (GFR 30-59 mL/min/1.73m2 and 15-29 mL/min/1.73m2 not receiving hemodialysis, respectively) as well as end-stage renal disease receiving hemodialysis is 2 mg once daily.

Drug/Disease:

Util A	Util B	Util C **(Include)**
Pitavastatin		Severe Renal Impairment
		Hemodialysis

Max Dose: 2 mg/day

References:
Zypitamag Prescribing Information, August 2018, Medicure.

39. Pitavastatin / Cyclosporine _____ _____

Alert Message: Co-administration of Zypitamag (pitavastatin magnesium) with cyclosporine is contraindicated. The concurrent use of these agents has been shown to cause significant increases the AUC (4.6-fold increase) and Cmax (6.6-fold increase) of pitavastatin.

Drug/Disease:

Util A	Util B	Util C
Pitavastatin	Cyclosporine	

References:
Zypitamag Prescribing Information, August 2018, Medicure.

40. Pitavastatin / Active Liver Disease _____ _____

Alert Message: Zypitamag (pitavastatin magnesium) is contraindicated in patients with active liver disease, which may include unexplained persistent transaminase elevations.

Drug/Disease:

Util A	Util B	Util C
Pitavastatin	Hepatitis	
	Cirrhosis	
	Hemochromatosis	
	Non-alcoholic Fatty Liver Disease	
	Hepatic Cancer	
	Wilson's Disease	
	Budd-Chiari Syndrome	
	Gilbert's Syndrome	

References:
Zypitamag Prescribing Information, August 2018, Medicure.

41. Erythromycin / Pitavastatin _____ _____

Alert Message: In patients taking erythromycin, the dose of Zypitamag (pitavastatin magnesium) should not exceed 1 mg per day. In clinical trials, concurrent use of pitavastatin 4 mg QD with erythromycin 500 mg QID for 6 days resulted in a significant increase in pitavastatin exposure (2.8-fold increase in AUC and 3.6-fold increase in Cmax).

Drug/Disease:

Util A	Util B	Util C
Erythromycin	Pitavastatin 2 & 4 mg	

References:
Zypitamag Prescribing Information, August 2018, Medicure.

42. Pitavastatin / Rifampin _____ _____

Alert Message: In patients taking rifampin, the dose of Zypitamag (pitavastatin magnesium) should not exceed 2 mg once daily. In clinical trials, concurrent use of pitavastatin 4 mg QD with rifampin 600 mg QID for 5 days resulted in a significant increase in pitavastatin exposure (29% increase in AUC and 2.0-fold increase in Cmax).

Drug/Disease:

Util A	Util B	Util C
Pitavastatin	Rifampin	

Max Dose: 2 mg/day

References:
Zypitamag Prescribing Information, August 2018, Medicure.

43. Pitavastatin / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Zypitamag (pitavastatin magnesium) in pediatric patients have not been established.

Drug/Disease:

Util A	Util B	Util C
Pitavastatin		

Age Range: 0 - 17 yoa

References:
Zypitamag Prescribing Information, August 2018, Medicure.

44. Dapagliflozin-Saxagliptin-Metformin / Overutilization _____ _____

Alert Message: Qternmet XR (dapagliflozin/saxagliptin/metformin) may be over-utilized. The recommended maximum daily dose of dapagliflozin/saxagliptin/metformin is 10 mg dapagliflozin/5 mg saxagliptin/2000 metformin once daily.

Drugs/Diseases

Util A	Util B	Util C **(Negate)**
Dapagliflozin/Saxagliptin/Metformin		CKD Stage 3, 4 & 5 ESRD Dialysis

Max Dose: 10 mg/5 mg/2000mg per day

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Qternmet XR Prescribing Information, June 2019, AstraZeneca.

45. Dapagliflozin-Saxagliptin-Metformin / CKD Stage 3, 4 & 5 & ESRD _____ _____

Alert Message: Qternmet XR (dapagliflozin/saxagliptin/metformin) use is contraindicated in patients with moderate to severe renal impairment (eGFR < 45 mL/min/1.73m2), end-stage renal disease or on dialysis. The dapagliflozin component of the combo product causes intravascular volume contraction and can cause renal impairment.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Dapagliflozin/Saxagliptin/Metformin		CKD Stage 3, 4 & 5 ESRD Dialysis

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Qternmet XR Prescribing Information, June 2019, AstraZeneca.

46. Dapagliflozin-Saxagliptin-Metformin/ Therapeutic Appropriateness _____ _____

Alert Message: Qternmet XR (dapagliflozin/saxagliptin/metformin) use is contraindicated in patients with ketoacidosis. Reports of ketoacidosis, a serious life-threatening condition requiring urgent hospitalization, have been identified in postmarketing surveillance in patients with type 1 and type 2 diabetes mellitus receiving sodium glucose cotransporter-2 (SGLT2) inhibitors, including dapagliflozin. Fatal cases of ketoacidosis have been reported in patients taking dapagliflozin. Dapagliflozin/saxagliptin/metformin is not indicated for the treatment of patients with type 1 diabetes mellitus.

Drugs/Diseases

Util A	Util B	Util C
Dapagliflozin/Saxagliptin/Metformin	Ketoacidosis	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Qternmet XR Prescribing Information, June 2019, AstraZeneca.

47. Dapagliflozin-Saxagliptin-Metformin / Strong CYP3A4/5 Inhibitors _____ _____

Alert Message: Do not co-administer Qternmet XR (dapagliflozin/saxagliptin/metformin) with strong CYP3A4/5 inhibitors (e.g., ketoconazole, atazanavir, nefazodone, ritonavir, and clarithromycin). The saxagliptin component of the combo product is a CYP3A4/5 substrate and use with a strong CYP3A4/5 inhibitor is expected to result in a significant increase in saxagliptin plasma concentrations.

Drugs/Diseases

Util A	Util B		Util C
Dapagliflozin/Saxagliptin/Metformin	Itraconazole	Indinavir	
	Ketoconazole	Nelfinavir	
	Atazanavir	Telithromycin	
	Clarithromycin	Nefazodone	
	Saquinavir	Cobicistat	
	Ritonavir		

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Qternmet XR Prescribing Information, June 2019, AstraZeneca.

48. Dapagliflozin-Saxagliptin-Metformin/ Insulin & Insulin Secretagogues _____ _____

Alert Message: The concurrent use of Qternmet XR (dapagliflozin/saxagliptin/metformin) with insulin or an insulin secretagogue can increase the risk of hypoglycemia. A lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when used in combination with dapagliflozin/saxagliptin/metformin.

Drugs/Diseases

Util A	Util B	Util C
Dapagliflozin/Saxagliptin/Metformin	Insulin	
	Chlorpropamide	
	Tolbutamide	
	Tolazamide	
	Glyburide	
	Glipizide	
	Glimepiride	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Qternmet XR Prescribing Information, June 2019, AstraZeneca.

49. Dapagliflozin-Saxagliptin-Metformin/ Bladder Cancer _____ _____

Alert Message: In clinical trials, an increased occurrence of bladder cancer was observed in subjects receiving dapagliflozin (0.17%) as compared to placebo (0.03%). Qternmet XR (dapagliflozin/saxagliptin/metformin) should not be used in patients with active bladder cancer and used with caution in patients with a prior history of bladder cancer.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Dapagliflozin/Saxagliptin/Metformin		Neoplasm of Bladder
		History of Malignant Neoplasm of Bladder

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Qternmet XR Prescribing Information, June 2019, AstraZeneca.

50. Dapagliflozin-Saxagliptin-Metformin/ Hypotension (Loop Diuretics) _____ _____

Alert Message: The dapagliflozin component of Qternmet XR (dapagliflozin/saxagliptin/metformin) can cause osmotic diuresis which can lead to volume depletion and hypotension, particularly in patients with impaired renal function, elderly patients or patients on loop diuretics. Before initiating a dapagliflozin-containing agent in a patient with one or more of these characteristics, volume status should be assessed and corrected. Patients should be monitored for signs and symptoms during therapy.

Drugs/Diseases

Util A	Util B	Util C
Dapagliflozin/Saxagliptin/Metformin	Furosemide	
	Torsemide	
	Ethacrynate	
	Bumetanide	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Qternmet XR Prescribing Information, June 2019, AstraZeneca.

51. Dapagliflozin-Saxagliptin-Metformin / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Qternmet XR (dapagliflozin/saxagliptin/metformin) in patients under 18 years of age have not been established.

Drugs/Diseases

Util A	Util B	Util C
Dapagliflozin/Saxagliptin/Metformin		

Age Range: 0 - 17 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Qternmet XR Prescribing Information, June 2019, AstraZeneca.

52. Dapagliflozin-Saxagliptin-Metformin / Therapeutic Appropriateness _____ _____

Alert Message: The use of Qternmet XR (dapagliflozin/saxagliptin/metformin) can cause an increase in LDL-C levels. Patients receiving dapagliflozin/saxagliptin/metformin should have their LDL-C monitored and treated per standard of care.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Dapagliflozin/Saxagliptin/Metformin		Hypercholesterolemia

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Qternmet XR Prescribing Information, June 2019, AstraZeneca.

53. Dapagliflozin-Saxagliptin-Metformin / Nonadherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Qternmet XR (dapagliflozin/saxagliptin/metformin). Nonadherence to the prescribed dosing regimen may result in sub-therapeutic effects, which may lead to decreased outcomes and additional healthcare costs.

Drugs/Diseases

Util A	Util B	Util C
Dapagliflozin/Saxagliptin/Metformin		

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Ho PM, Rumsfeld JS, Masoudi FA, et al., Effect of Medication Nonadherence in Diabetes Mellitus. Cardiology Review, April 2007.
Currie CJ, Peyrot M, Morgan CL, et al. The Impact of Treatment Noncompliance on Mortality in People With Type 2 Diabetes. Diabetes Care 35:1279-1284, June 2012.
Qternmet XR Prescribing Information, June 2019, AstraZeneca.

54. Dapagliflozin-Saxagliptin-Metformin / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on animal data showing renal effects, from dapagliflozin, Qternmet XR (dapagliflozin/saxagliptin/metformin) is not recommended during the second and third trimesters of pregnancy. The limited available data with dapagliflozin and saxagliptin in pregnant women are not sufficient to determine a drug-associated risk for major birth defects or miscarriage. During pregnancy, consider appropriate alternative therapies.

Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Dapagliflozin/Saxagliptin/Metformin	Pregnancy	Delivery Abortion Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Qternmet XR Prescribing Information, June 2019, AstraZeneca.
American College of Obstetricians and Gynecologists (ACOG), Committee on Practice Bulletins - Obstetrics. Practice Bulletin No. 137: Gestational Diabetes Mellitus. Obstet Gynecol. 2013:122(2 Pt 1):406-416.
Blumer I, Hadar E, Hadden DR, et al. Diabetes and Pregnancy: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2013;98(11):406-416.

55. Dapagliflozin-Saxagliptin-Metformin /OAT2 & MATE Inhibitors _____ _____

Alert Message: Concurrent use of Qternmet XR (dapagliflozin/saxagliptin/metformin) with drugs that interfere with common renal tubular transport systems involved in the renal elimination of metformin (e.g., OCT2 and MATE inhibitors) may result in reduced metformin clearance and increased risk of metformin-related adverse effects (e.g., lactic acidosis). Consider the benefits and risks of concomitant use.

Drugs/Diseases

Util A	Util B	Util C
Dapagliflozin/Saxagliptin/Metformin	Ranolazine Vandetanib Dolutegravir Cimetidine	

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Qternmet XR Prescribing Information, June 2019, AstraZeneca.

56. Dapagliflozin-Saxagliptin-Metformin / Alcohol Use _____ _____

Alert Message: Alcohol is known to potentiate the effect of metformin on lactate metabolism. Patients should be warned against excessive alcohol intake (ethanol intoxication) while taking a metformin-containing medication due to the increased risk for lactic acidosis.

Drugs/Diseases

Util A	Util B	Util C
Dapagliflozin/Saxagliptin/Metformin	Alcohol Related	Disorders

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Qternmet XR Prescribing Information, June 2019, AstraZeneca.

57. Dapagliflozin-Saxagliptin-Metformin / Lactation _____ _____

Alert Message: Because of the potential for serious adverse reactions in a breastfed infant, advise women that use of Qternmet XR (dapagliflozin/saxagliptin/metformin) is not recommended while breastfeeding. There is limited information regarding the presence of dapagliflozin/saxagliptin/metformin or its components (dapagliflozin, saxagliptin, and metformin) in human milk, the effects on the breastfed infant, or the effects on milk production. Limited published studies report that metformin is present in human milk.

Drugs/Diseases

Util A	Util B	Util C
Dapagliflozin/Saxagliptin/Metformin	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Qternmet XR Prescribing Information, June 2019, AstraZeneca.

58. Lamivudine/Tenofovir Disoproxil / Overutilization _____ _____

Alert Message: The recommended dosage of Cimduo (lamivudine/tenofovir disoproxil fumarate) in HIV-1-infected adult and pediatric patients weighing at least 35 kg is one tablet taken orally once daily with or without food.

Drugs/Diseases

Util A	Util B	Util C
Lamivudine/Tenofovir Disoproxil		

Max dose: 1 tablet/day

References:
Cimduo Prescribing Information, Feb. 2018, Mylan Specialty LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

59. Lamivudine/Tenofovir Disoproxil / Renal Impairment _____ _____

Alert Message: Because Cimduo (lamivudine/tenofovir disoproxil fumarate) is a fixed-dose combination tablet and cannot be dose adjusted, it is not recommended for use in patients with impaired renal function (creatinine clearance less than 50 mL/min) or patients with end-stage renal disease (ESRD) requiring hemodialysis. The tenofovir disoproxil fumarate (TDF) component of the combination antiretroviral agent is primarily eliminated by the kidney. Renal impairment, including cases of acute renal failure and Fanconi syndrome, has been reported with the use of TDF.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Lamivudine/Tenofovir Disoproxil		CKD 3, 4, & 5 ESRD Dialysis

References:
Cimduo Prescribing Information, Feb. 2018, Mylan Specialty LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

60. Lamivudine/Tenofovir Disoproxil / Lactic Acidosis or Hepatomegaly _____ _____

Alert Message: Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs and other antiretrovirals. Treatment with the nucleoside analog should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations).

Drugs/Diseases

Util A	Util B	Util C
Lamivudine/Tenofovir Disoproxil	Lactic Acidosis Hepatomegaly	

References:
Cimduo Prescribing Information, Feb. 2018, Mylan Specialty LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

61. Lamivudine/Tenofovir Disoproxil / Pancreatitis _____ _____

Alert Message: Cimduo (lamivudine/tenofovir disoproxil fumarate), should be used with caution in pediatric patients with a history of prior antiretroviral nucleoside exposure, a history of pancreatitis, or other significant risk factors for the development of pancreatitis. Pancreatitis, which has been fatal in some cases, has been observed in antiretroviral nucleoside-experienced pediatric subjects receiving lamivudine alone or in combination with other antiretroviral agents. Treatment with lamivudine/tenofovir disoproxil fumarate should be stopped immediately if clinical signs, symptoms, or laboratory abnormalities suggestive of pancreatitis occur.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Lamivudine/Tenofovir Disoproxil		Pancreatitis

References:
Cimduo Prescribing Information, Feb. 2018, Mylan Specialty LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

62. Lamivudine/Tenofovir Disoproxil / Bone Effects _____ _____

Alert Message: In clinical trials in HIV-1-infected adults, tenofovir disoproxil fumarate (TDF) was associated with slightly greater decreases in bone mineral density (BMD) and increases in biochemical markers of bone metabolism, suggesting increased bone turnover relative to comparators. For patients receiving Cimduo (lamivudine/tenofovir disoproxil fumarate), assessment of BMD should be considered for adults who have a history of pathologic bone fracture or other risk factors for osteoporosis or bone loss. If bone abnormalities are suspected, then appropriate consultation should be obtained.

Drugs/Diseases

Util A	Util B	Util C
Lamivudine/Tenofovir Disoproxil	Osteoporosis w/ Fractures	
	Osteoporosis w/o Fractures	

References:

Cimduo Prescribing Information, Feb. 2018, Mylan Specialty LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

63. Lamivudine/Tenofovir Disoproxil / Atazanavir + Ritonavir _____ _____

Alert Message: When atazanavir is co-administered with Cimduo (lamivudine/tenofovir disoproxil fumarate), it is recommended that atazanavir 300 mg is given with ritonavir 100 mg. Tenofovir disoproxil fumarate should not be coadministered with atazanavir without ritonavir.

Drugs/Diseases

Util A	Util B	Util C **(Negate)**
Lamivudine/Tenofovir Disoproxil	Atazanavir	Ritonavir

References:

Cimduo Prescribing Information, Feb. 2018, Mylan Specialty LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

64. Lamivudine/Tenofovir Disoproxil / Lopinavir/Ritonavir _____ _____

Alert Message: The concurrent use of lopinavir/ritonavir with tenofovir disoproxil fumarate (TDF) has been shown to increase TDF concentrations. Patients receiving Cimduo (lamivudine/tenofovir disoproxil fumarate) concomitantly with lopinavir/ritonavir should be monitored for TDF-associated adverse reactions. Lamivudine/TDF should be discontinued in patients who develop TDF-associated adverse reactions.

Drugs/Diseases

Util A	Util B	Util C
Lamivudine/Tenofovir Disoproxil	Lopinavir/rtv	

References:

Cimduo Prescribing Information, Feb. 2018, Mylan Specialty LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

65. Lamivudine/Tenofovir Disoproxil / Atazanavir or Darunavir + Ritonavir _____ _____

Alert Message: Atazanavir coadministered with ritonavir and darunavir coadministered with ritonavir have been shown to increase tenofovir disoproxil fumarate (TDF) concentrations. Patients receiving Cimduo (lamivudine/tenofovir disoproxil fumarate) concomitantly with atazanavir and ritonavir or darunavir and ritonavir should be monitored for TDF-associated adverse reactions. Lamivudine/TDF should be discontinued in patients who develop TDF-associated adverse reactions.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Lamivudine/Tenofovir Disoproxil	Atazanavir Darunavir	Ritonavir

References:
Cimduo Prescribing Information, Feb. 2018, Mylan Specialty LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

66. Lamivudine/Tenofovir Disoproxil / Sofosbuvir/Velpatasvir _____ _____

Alert Message: Coadministration of tenofovir disoproxil fumarate (TDF), a component of Cimduo (lamivudine/tenofovir disoproxil fumarate), and Epclusa (sofosbuvir/velpatasvir) has been shown to increase TDF exposure. In patients receiving TDF concomitantly with sofosbuvir/velpatasvir, monitor for adverse reactions associated with TDF.

Drugs/Diseases

Util A	Util B	Util C
Lamivudine/Tenofovir Disoproxil	Sofosbuvir/Velpatasvir	

References:
Cimduo Prescribing Information, Feb. 2018, Mylan Specialty LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

67. Lamivudine/Tenofovir Disoproxil / Ledipasvir/Sofosbuvir w/o RTV _____ _____

Alert Message: Coadministration of tenofovir disoproxil fumarate (TDF), a component of Cimduo (lamivudine/tenofovir disoproxil fumarate), and Harvoni (ledipasvir/sofosbuvir) has been shown to increase TDF exposure. In patients receiving (lamivudine/TDF concomitantly with ledipasvir/sofosbuvir without an HIV-1 protease inhibitor/ritonavir or an HIV-1 protease inhibitor/cobicistat combination, monitor for adverse reactions associated with TDF.

Drugs/Diseases

Util A	Util B	Util C **(Negate)**
Lamivudine/Tenofovir Disoproxil	Ledipasvir/Sofosbuvir	Ritonavir Cobicistat

References:
Cimduo Prescribing Information, Feb. 2018, Mylan Specialty LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

68. Lamivudine/Tenofovir Disoproxil / Ledipasvir/Sofosbuvir w/ RTV _____ _____

Alert Message: Coadministration of tenofovir disoproxil fumarate (TDF), a component of Cimduo (lamivudine/tenofovir disoproxil fumarate), and Harvoni (ledipasvir/sofosbuvir) has been shown to increase TDF exposure. In patients receiving lamivudine/TDF, concomitantly with ledipasvir/sofosbuvir and an HIV-1 protease inhibitor/ritonavir or an HIV-1 protease inhibitor/cobicistat combination, consider an alternative HCV or antiretroviral therapy, as the safety of increased TDF concentrations in this setting has not been established.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Lamivudine/Tenofovir Disoproxil	Ledipasvir/Sofosbuvir	Ritonavir
		Cobicistat

References:
Cimduo Prescribing Information, Feb. 2018, Mylan Specialty LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

69. Lamivudine/Tenofovir Disoproxil / Drugs that Reduce Renal Function _____ _____

Alert Message: Co-administration of Cimduo (lamivudine/tenofovir disoproxil fumarate) with drugs that reduce renal function or compete for active tubular secretion may increase serum concentrations of the tenofovir component of the combination antiretroviral and/or increase the concentrations of other renally eliminated drugs. Tenofovir disoproxil fumarate (TDF) is principally eliminated by the kidney by glomerular filtration and active renal tubular secretion.

Drugs/Diseases

Util A	Util B	Util C
Lamivudine/Tenofovir Disoproxil	Adefovir	
	Cidofovir	
	Acyclovir	
	Valacyclovir	
	Valganciclovir	

References:
Cimduo Prescribing Information, Feb. 2018, Mylan Specialty LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

70. Lamivudine/Tenofovir Disoproxil / NSAIDs _____ _____

Alert Message: The use of Cimduo (lamivudine/tenofovir disoproxil fumarate) should be avoided with concurrent or recent use of a nephrotoxic agent (e.g., high-dose or multiple non-steroidal anti-inflammatory drugs). Cases of acute renal failure after initiation of high dose or multiple NSAIDs have been reported in HIV-infected patients with risk factors for renal dysfunction who appeared stable on tenofovir disoproxil fumarate. Some patients required hospitalization and renal replacement therapy. Alternatives to NSAIDs should be considered, if needed, in patients at risk for renal dysfunction.

Drugs/Diseases

Util A	Util B	Util C
Lamivudine/Tenofovir Disoproxil	NSAIDs	

References:
Cimduo Prescribing Information, Feb. 2018, Mylan Specialty LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

71. Lamivudine/Tenofovir Disoproxil / Nephrotoxic Agents _____ _____

Alert Message: The use of Cimduo (lamivudine/tenofovir disoproxil fumarate) should be avoided with concurrent or recent use of a nephrotoxic agent. Renal impairment, including cases of acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia), has been reported with the use of tenofovir disoproxil fumarate (TDF). Coadministration of TDF with nephrotoxic agents may increase the risk nephrotoxicity.

Drugs/Diseases

Util A	Util B		Util C
Lamivudine/Tenofovir Disoproxil	ACE Inhibitor	Pamidronate	
	ARBs	Probenecid	
	Methotrexate	Tacrolimus	
	Cyclosporine	Zoledronic Acid	
	Penicillins	Salicylates	
	Amikacin		

References:
Cimduo Prescribing Information, Feb. 2018, Mylan Specialty LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

72. Lamivudine/Tenofovir Disoproxil / Nonadherence _____ _____

Alert Message: Based on the refill history, your patient may be underutilizing Cimduo (lamivudine/tenofovir disoproxil fumarate). Nonadherence to antiretroviral therapy may result in insufficient plasma levels and partial suppression of viral load leading to the development of resistance, HIV progression, and increased mortality.

Drugs/Diseases

Util A	Util B	Util C
Lamivudine/Tenofovir Disoproxil		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Beer L, Heffelfinger J, Frazier E, et al. Use of and Adherence to Antiretroviral Therapy in a Large U.S. Sample of HIV-Infected Adults in Care, 2007-2008. Open AIDS J.2012;6:213-223.
Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents. Department of Health and Human Services. October 25, 2018. Available at: http://www.aidsinfo.nih.gov/contentfiles/adultandadolescentgl.pdf.
Panel on Antiretroviral Therapy and Medical Management of HIV-Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. April 16, 2018. Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/pediatricguidelines.pdf

73. Acalabrutinib / Overutilization _____ _____

Alert Message: The recommended dose of Calquence (acalabrutinib) is 100 mg taken approximately every 12 hours until disease progression or unacceptable toxicity.

Drugs/Diseases

Util A	Util B	Util C
Acalabrutinib		

Max Dose: 200 mg/day

References:
Calquence Prescribing Information, Oct. 2017, AstraZeneca.
Clinical Pharmacology 2019, Elsevier/Gold Standard.

74. Acalabrutinib / Strong CYP3A4 Inhibitors _____ _____

Alert Message: Coadministration of Calquence (acalabrutinib), a CYP3A4 substrate, with strong CYP3A4 inhibitors should be avoided. Concurrent use of these agents may cause increased acalabrutinib plasma concentrations and result in acalabrutinib toxicity. Alternatively, if the CYP3A4 inhibitor will be used short-term, interrupt acalabrutinib therapy.

Drugs/Diseases

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

References:
Calquence Prescribing Information, Oct. 2017, AstraZeneca.
Clinical Pharmacology 2019, Elsevier/Gold Standard.

75. Acalabrutinib / Moderate CYP3A4 Inhibitors _____ _____

Alert Message: Coadministration of Calquence (acalabrutinib), a CYP3A4 substrate, with moderate CYP3A4 inhibitors may increase acalabrutinib plasma concentrations and result in acalabrutinib toxicity. If acalabrutinib is co-administered with a moderate CYP3A4 inhibitor, reduce the acalabrutinib dose to 100 mg once daily.

Drugs/Diseases

Util A	Util B		Util C
Acalabrutinib	Aprepitant	Ciprofloxacin	
	Crizotinib	Imatinib	
	Diltiazem	Cyclosporine	
	Verapamil	Dronedarone	
	Fluconazole	Erythromycin	
	Fluvoxamine	Fosamprenavir	

Max Dose: 100 mg/day

References:
Calquence Prescribing Information, Oct. 2017, AstraZeneca.
Clinical Pharmacology 2019, Elsevier/Gold Standard.

76. Acalabrutinib / Strong CPY3A4 Inducers _____ _____

Alert Message: Coadministration of Calquence (acalabrutinib), a CYP3A4 substrate, with strong CYP3A4 inducers should be avoided. Concurrent use of these agents may cause decreased acalabrutinib plasma concentrations and result in reduced acalabrutinib activity. If a strong CYP3A4 inducer cannot be avoided, increase the acalabrutinib dose to 200 mg twice daily.

Drugs/Diseases

Util A	Util B	Util C
Acalabrutinib	Carbamazepine	
	Phenytoin	
	Phenobarbital	
	Rifampin	
	Enzalutamide	
	Mitotane	

References:
Calquence Prescribing Information, Oct. 2017, AstraZeneca.
Clinical Pharmacology 2019, Elsevier/Gold Standard.

77. Acalabrutinib / Proton Pump Inhibitors _____ _____

Alert Message: Concurrent use of Calquence (acalabrutinib) with a proton pump inhibitor should be avoided. Co-administration of these agents may result in decreased acalabrutinib plasma concentrations. Acalabrutinib solubility decreases with increasing pH. If treatment with a gastric acid reducing agents is required, consider an H2-receptor antagonist or an antacid.

Drugs/Diseases

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

References:
Calquence Prescribing Information, Oct. 2017, AstraZeneca.
Clinical Pharmacology 2019, Elsevier/Gold Standard.

78. Acalabrutinib / H2-Receptor Antagonists _____ _____

Alert Message: Concurrent use of Calquence (acalabrutinib) with an H2-receptor antagonist may decrease acalabrutinib plasma concentrations. Acalabrutinib solubility decreases with increasing pH. If the use of an H2-receptor antagonist is required, administer acalabrutinib 2 hours before taking an H2-receptor antagonist.

Drugs/Diseases

Util A	Util B	Util C
Acalabrutinib	Cimetidine	
	Famotidine	
	Ranitidine	
	Nizatidine	

References:
Calquence Prescribing Information, Oct. 2017, AstraZeneca.
Clinical Pharmacology 2019, Elsevier/Gold Standard.

79. Acalabrutinib / Antacids _____ _____

Alert Message: Concurrent use of Calquence (acalabrutinib) with an antacid may decrease acalabrutinib plasma concentrations. Acalabrutinib solubility decreases with increasing pH. If the use of an antacid is required, separate the dosing of acalabrutinib and the antacid by at least 2 hours.

Drugs/Diseases

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

References:
Calquence Prescribing Information, Oct. 2017, AstraZeneca.
Clinical Pharmacology 2019, Elsevier/Gold Standard.

80. Acalabrutinib / Therapeutic Appropriateness _____ _____

Alert Message: The safety and efficacy of Calquence (acalabrutinib) in pediatric patients have not been established.

Drugs/Diseases

Util A	Util B	Util C
Acalabrutinib		

Age Range: 0 – 17 yoa

References:
Calquence Prescribing Information, Oct. 2017, AstraZeneca.
Clinical Pharmacology 2019, Elsevier/Gold Standard.

81. Acalabrutinib / Lactation _____ _____

Alert Message: No data are available regarding the presence of Calquence (acalabrutinib) or its active metabolite in human milk, its effects on the breastfed child, or on milk production. Acalabrutinib and its active metabolite were present in the milk of lactating rats. Due to the potential for adverse reactions in a breastfed child from acalabrutinib, advise lactating women not to breastfeed while taking acalabrutinib and for at least 2 weeks after the final dose.

Drugs/Diseases

Util A	Util B	Util C
Acalabrutinib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Calquence Prescribing Information, Oct. 2017, AstraZeneca.
Clinical Pharmacology 2019, Elsevier/Gold Standard.

82. Acalabrutinib / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on findings in animals, Calquence (acalabrutinib) may cause fetal harm when administered to a pregnant woman. There are no available data in pregnant women to inform the drug-associated risk. In animal reproduction studies, administration of acalabrutinib to pregnant rabbits during organogenesis resulted in reduced fetal growth at maternal exposures (AUC) approximately 4 times exposures in patients at the recommended dose of 100 mg twice daily. Advise pregnant women of the potential risk to a fetus.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Calquence Prescribing Information, Oct. 2017, AstraZeneca.
Clinical Pharmacology 2019, Elsevier/Gold Standard.

83. Acalabrutinib / Infections _____ _____

Alert Message: Serious infections (bacterial, viral or fungal), including fatal events and opportunistic infections have occurred in the combined safety database of 612 patients with hematologic malignancies treated with Calquence (acalabrutinib) monotherapy. Monitor patients for signs and symptoms of infection and treat as medically appropriate. Consider prophylaxis in patients who are at increased risk for opportunistic infections.

Drugs/Diseases

Util A	Util B		Util C
Acalabrutinib	Pneumonia	Cryptococcosis	
	Herpes Zoster	Cytomegalovirus	
	Urinary Tract Infection	Hepatitis	
	Esophageal Candidiasis	Fever	
	Acute Histoplasmosis	Pneumocystosis	

References:
Calquence Prescribing Information, Oct. 2017, AstraZeneca.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

84. Acalabrutinib / Atrial Fib & Flutter / Afib Tx (negating) _____ _____

Alert Message: In the combined safety database of 612 patients with hematologic malignancies treated with Calquence (acalabrutinib) monotherapy, atrial fibrillation and atrial flutter of any grade occurred in 3% of patients, and Grade 3 in 1% of patients. Monitor for atrial fibrillation and atrial flutter and manage as appropriate.

Drugs/Diseases

Util A	Util B	Util C **(Negating)**		
Acalabrutinib	Atrial Fibrillation	Apixaban	Dofetilide	Flecainide
	Atrial Flutter	Dabigatran	Dronedarone	Propranolol
		Digoxin	Edoxaban	Propafenone
		Diltiazem	Sotalol	
		Quinidine	Rivaroxaban	
		Verapamil	Warfarin	

References:
Calquence Prescribing Information, Oct. 2017, AstraZeneca.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

85. Acalabrutinib / Bleeding _____ _____

Alert Message: Serious hemorrhagic events, including fatal events, have occurred with Calquence (acalabrutinib) therapy. Grade 3 or higher bleeding events, including gastrointestinal, intracranial, and epistaxis have been reported in 2% of patients. The mechanism for the bleeding events is not well understood. Acalabrutinib may further increase the risk of hemorrhage in patients receiving antiplatelet or anticoagulant therapies, and patients should be monitored for signs of bleeding.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Acalabrutinib	Anticoagulants	Gastrointestinal Bleeding
	Antiplatelets	Intracranial Bleeding
		Epistaxis

References:
Calquence Prescribing Information, Oct. 2017, AstraZeneca.
Clinical Pharmacology 2019, Elsevier/Gold Standard.

86. Clobazam / Overutilization (≥ 10 yoa) _____ _____

Alert Message: Sympazan (clobazam) may be over-utilized. Patients weighing greater than 30 kg should have therapy initiated at 5 mg twice daily and titrated as tolerated to a maximum of 40 mg (20 mg twice daily). Patients weighing 30 kg or less should have clobazam therapy initiated at 5 mg daily and titrated as tolerated to 20 mg (10 mg twice daily).

Drugs/Diseases
Util A Util B Util C
Clobazam

Max Dose: 40 mg/day
Age Range: ≥ 10 yoa

References:
Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

87. Clobazam / Overutilization (2-9 yoa) _____ _____

Alert Message: Sympazan (clobazam) may be over-utilized. Patients weighing 30 kg or less should have clobazam therapy initiated at 5 mg daily and titrated as tolerated to 20 mg daily. Patients weighing greater than 30 kg should have therapy initiated at 10 mg daily and titrated as tolerated to a maximum of 40 mg daily.

Drugs/Diseases
Util A Util B Util C
Clobazam

Max Dose: 20 mg/day
Age Range: 2-9 yoa

References:
Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

88. Clobazam / TA - Therapeutic Appropriateness (<2 yoa) _____ _____

Alert Message: The safety and effectiveness of Sympazan (clobazam) in patients less than 2 years of age have not been established.

Drugs/Diseases
Util A Util B Util C
Clobazam

Age Range: 0-1 yoa

References:
Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

89. Clobazam / Nonadherence _____ _____

Alert Message: Based on the refill history, your patient may be underutilizing Sympazan (clobazam). Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs. If the patient is discontinuing clobazam, it should be withdrawn gradually by decreasing the total daily dose by 5 - 10 mg/day on a weekly basis until discontinued in order to avoid seizure occurrence or withdrawal symptoms.

Drugs/Diseases

Util A	Util B	Util C
Clobazam		

References:

Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Faught E, Duh MS, Weiner JR, et al. Nonadherence to Antiepileptic Drugs and Increased Mortality, Findings from the RANSOM Study. Neurology 2008;71(20): 1572-1578.
Hodges JC, Treadwell J, Malphrus AD, et al., Identification and Prevention of Antiepileptic Drug Noncompliance: The Collaborative Use of State-Supplied Pharmaceutical Data. ISRN Pediatr. 2014 Feb 19:1-8.
Viswanathan M, Golin CE, Jones DC, et al., Interventions to Improve Adherence to Self-administered Medications for Chronic Disease in the United States: A Systemic Review. Ann Intern Med. 2012:157:785-792.

90. Clobazam / Moderate & Strong CYP2C19 Inhibitors _____ _____

Alert Message: Sympazan (clobazam) is a CYP2C19 substrate, and concurrent use with a strong or moderate CYP2C19 inhibitor may result in increased exposure to the active metabolite of clobazam (N-desmethylclobazam). Dosage adjustment of clobazam may be necessary.

Drugs/Diseases

Util A	Util B	Util C
Clobazam	Fluconazole	
	Fluvoxamine	
	Ticlopidine	
	Omeprazole	
	Esomeprazole	
	Fluoxetine	
	Voriconazole	

References:

Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

91. Clobazam / CNS Depressants _____ _____

Alert Message: Sympazan (clobazam) has a CNS depressant effect, and concurrent use with other CNS depressants may result in potentiated depressants effects.

Drugs/Diseases

Util A	Util B	Util C
Clobazam	Narcotics	
	Barbiturates	
	Benzodiazepines	
	Sedative/Hypnotics	
	Muscle Relaxants	
	Antihistamines	
	Antipsychotics	

References:

Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

92. Clobazam / CYP3A4 Metabolized Hormonal Contraceptives _____ _____

Alert Message: Sympazan (clobazam) is a weak CYP3A4 inducer and concurrent use with CYP3A4-mediated hormonal contraceptives may diminish the effectiveness of the contraceptive agent. The manufacturer recommends the use of additional non-hormonal form of contraception when using clobazam.

Drugs/Diseases

Util A	Util B	Util C
Clobazam	CYP3A4 Metabolized Hormonal Contraceptives	

References:
Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

93. Clobazam / Substance Abuse _____ _____

Alert Message: Sympazan (clobazam) should be used with caution in patients with a history of substance abuse because of the predisposition of such patients to habituation and dependence. Clobazam is a benzodiazepine. In clinical trials, cases of dependency were reported following abrupt discontinuation of clobazam.

Drugs/Diseases

Util A	Util B	Util C
Clobazam	Substance Abuse	

References:
Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

94. Clobazam / CYP2D6 Metabolized Drugs _____ _____

Alert Message: Sympazan (clobazam) is a CYP2D6 inhibitor, and concurrent use with drugs metabolized by CYP2D6 may cause increased plasma concentrations of the substrate. Dosage adjustment of the CYP2D6 substrate may be required.

Drugs/Diseases

Util A	Util B			Util C
Clobazam	Dextromethorphan	Aripiprazole	Paroxetine	Ondansetron
	Atomoxetine	Carvedilol	Donepezil	Promethazine
	Metoprolol	Duloxetine	Propafenone	Chlorpheniramine
	Nebivolol	Flecainide	Propranolol	
	Perphenazine	Fluoxetine	Risperidone	
	Tolterodine	Fluvoxamine	Tamoxifen	
	Venlafaxine	Haloperidol	Timolol	
	Thioridazine	Mexiletine	Tramadol	
	Tricyclic Antidepressants	Oxycodone	Amphetamine	

References:
Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

95. Clobazam / Alcohol Abuse/Dependence _____ _____

Alert Message: A review of the patient's diagnostic profile reveals that they may consume alcohol. The concurrent use of Sympazan (clobazam) with alcohol has been reported to increase the maximum plasma exposure of clobazam by approximately 50%. Caution patients against the use of alcohol while taking clobazam.

Drugs/Diseases

Util A	Util B	Util C
Clobazam	Alcohol Dependence	
	Acute Alcohol Intoxication	
	Other/Unspecified Alcohol Dependence	

References:

Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

96. Cariprazine / Overutilization _____ _____

Alert Message: Vraylar (cariprazine) may be over-utilized. The manufacturer's recommended maximum daily dose of cariprazine for the treatment of depressive episodes associated with bipolar 1 disorder is 3 mg once daily.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Cariprazine		Bipolar Depression

Max Dose: 3 mg/day

References:

Vraylar Prescribing Information, May 2019, Allergan.
Clinical Pharmacology, 2019, Elsevier/Gold Standard.

97. Nuedexta / Elderly _____ _____

Alert Message: A review of the patient's diagnostic profile does not reveal a recent diagnosis of pseudobulbar affect. Nuedexta (dextromethorphan/quinidine) should be used with caution in older patients because it has limited efficacy in alleviating behavioral symptoms of dementia in patients without pseudobulbar affect and because it potentially increases the risk for falls and drug-drug interactions.

Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Dextromethorphan/quinidine		Pseudobulbar Affect

Age Range: ≥ 65 yoa

References:

2019 American Geriatrics Society Beers Criteria Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019;67(4):674-694.

98. Rivaroxaban / Elderly _____ _____

Alert Message: Xarelto (rivaroxaban) should be used with caution for the treatment of venous thromboembolism or atrial fibrillation in patients 75 years or older. This patient population may be at increased risk of both thrombotic and bleeding events.

Drugs/Diseases

Util A	Util B	Util C
Rivaroxaban		

Age Range: ≥ 75 yoa

References:

2019 American Geriatrics Society Beers Criteria Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019;67(4):674-694.

99. TMP-SMX / Elderly _____ _____

Alert Message: Trimethoprim-Sulfamethoxazole should be used with caution by older patients with reduced kidney function and taking an angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) because of an increased risk of hyperkalemia.

Drugs/Diseases

Util A	Util B	Util C
Trimethoprim-Sulfamethoxazole	ACE Inhibitors	
	ARBs	
	Renal Impairment	

Age Range: ≥ 75 yoa

References:

2019 American Geriatrics Society Beers Criteria Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019;67(4):674-694.

100. Tramadol / Elderly _____ _____

Alert Message: Tramadol-containing medication should be used with caution in older patients because tramadol may exacerbate or cause hyponatremia or SIADH. Sodium levels should be monitored closely when starting or changing tramadol dosages in this patient population.

Drugs/Diseases

Util A	Util B	Util C
Tramadol		

Age Range: ≥ 65 yoa

References:

2019 American Geriatrics Society Beers Criteria Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019;67(4):674-694.

101. Glimepiride / Elderly _____ _____

Alert Message: Glimepiride-containing medications can produce severe prolonged hypoglycemia in older adults. If no contraindications exist, consider discontinuing the glimepiride-containing agent and switching to a short-acting sulfonylurea (e.g., glipizide) or metformin.

Drugs/Diseases
Util A Util B Util C
Glimepiride

Age Range: ≥ 65 yoa

References:
2019 American Geriatrics Society Beers Criteria Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019;67(4):674-694.
American Diabetes Association (ADA). 12. Older Adults: Standards of Medical Care-2019. Diabetes Care. 2019 Jan;42(Suppl 1):S139.-147. Available at: http://care.diabetesjournals.org/content/42//Supplement_1

102. Oxaprozin / Overutilization _____ _____

Alert Message: In pediatric patients 6 to 16 years of age with juvenile rheumatoid arthritis, oxaprozin dosing is weight based. In children, doses greater than 1,200 mg have not been studied. The recommended once-daily dose of oxaprozin for pediatric patients weighing 22 to 31 kg is 600 mg and 900 mg once daily for patients weighing 32 to 54 kg. For patients weighing 55 kg or more, the dose is 1200 mg once daily.

Drugs/Diseases
Util A Util B Util C
Oxaprozin

Age Range: 6 - 16 yoa
Max Dose: 1200 mg/day

References:
Daypro Prescribing Information, May 2016, Pfizer.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Facts & Comparisons, 2019 updates, Wolters Kluwer Health.

103. Oxaprozin / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of oxaprozin have not been established in pediatric patients below 6 years of age.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases
Util A Util B Util C
Oxaprozin

Age Range: 0 - 5 yoa

References:
Daypro Prescribing Information, May 2016, Pfizer.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Facts & Comparisons, 2019 updates, Wolters Kluwer Health.

104. Meloxicam Tabs & ODT / Overutilization - Hemodialysis _____ _____
Alert Message: Meloxicam may be over-utilized. The maximum recommended daily dose of meloxicam in adults on hemodialysis is 7.5 mg.

Drugs/Diseases

Util A	Util B	Util C (**Include)**
Meloxicam Tabs & ODT		Hemodialysis

Max Dose: 7.5 mg/day
Age Range: 18 - 999 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Facts & Comparisons, 2019 Updates, Wolters Kluwer Health.

105. Meloxicam Tabs & ODT / Overutilization _____ _____
Alert Message: Meloxicam may be over-utilized. The maximum recommended daily dose of meloxicam in pediatric patients with juvenile rheumatoid arthritis who weigh greater than or equal to 60 kg is 7.5 mg. Meloxicam should not be used in children who weigh less than 60 kg.

Drugs/Diseases

Util A	Util B	Util C
Meloxicam Tabs & ODT		

Max Dose: 7.5 mg/day
Age Range: 2 – 17 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Facts & Comparisons, 2019 Updates, Wolters Kluwer Health.

106. Meloxicam Tabs & ODT / Overutilization _____ _____
Alert Message: The safety and effectiveness of meloxicam tablets in pediatric patients under 2 years of age have not been established.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C
Meloxicam Tabs & ODT		

Age Range: 0 - 1 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Facts & Comparisons, 2019 Updates, Wolters Kluwer Health.

107. Meloxicam Capsule / Therapeutic Appropriateness _____ _____
Alert Message: The safety and effectiveness of Vivlodex (meloxicam) in pediatric patients have not been established.

Drugs/Diseases

Util A	Util B	Util C
Meloxicam Caps		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Facts & Comparisons, 2019 Updates, Wolters Kluwer Health.

108. Meloxicam - All / Severe Renal Disease _____ _____

Alert Message: Avoid the use of meloxicam in patients with advanced renal disease unless the benefits are expected to outweigh the risk of worsening renal function. Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. No information is available from controlled clinical studies regarding the use of meloxicam in patients with advanced renal disease. The renal effects of meloxicam may hasten the progression of renal dysfunction in patients with pre-existing renal disease.

Drugs/Diseases

Util A	Util B	Util C **(Negate)**
Meloxicam - All	CKD Stage 4	Hemodialysis
	CKD Stage 5	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Facts & Comparisons, 2019 Updates, Wolters Kluwer Health.

109. Meloxicam Capsules 10 mg / Overutilization - Hemodialysis _____ _____

Alert Message: Vivlodex (meloxicam capsules) may be over-utilized. The maximum recommended daily dose of meloxicam in adults on hemodialysis is 5 mg.

Drugs/Diseases

Util A	Util B	Util C
Meloxicam Caps 10mg	Hemodialysis	

Max Dose: 5 mg/day

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Facts & Comparisons, 2019 Updates, Wolters Kluwer Health.

110. Canagliflozin - All / Black Box Warning _____ _____

Alert Message: An approximately 2-fold increased risk of lower limb amputations has been associated with canagliflozin use in patients with type 2 diabetes who have either established cardiovascular disease or who are at risk for cardiovascular disease. Before initiating a canagliflozin-containing product, consider factors in the patient history that may predispose to the need for amputations, such as a history of prior amputation, peripheral vascular disease, neuropathy and diabetic foot ulcers. Counsel patients about the importance of routine preventative foot care.

Drugs/Diseases

Util A	Util B	Util C
Canagliflozin		
Canagliflozin/Metformin		

Reference:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Facts & Comparisons, 2019 Updates, Wolters Kluwer Health.
MedWatch: FDA Drug Safety Communication: FDA Confirms Increased Risk of Leg and Foot Amputations with the Diabetes Medicine Canagliflozin (Invokana, Invokamet, Invokamet XR). [5-16-2017].
Available at: https://www.fda.gov/Drugs/DrugSafety/ucm557507.htm

111. Ribociclib;Letrozole / Overutilization _____ _____

Alert Message: The recommended dose of Kisqali Femara Co-Pack (ribociclib;letrozole) is 600 mg (three 200 mg film-coated tablets) of ribociclib taken orally, once daily for 21 consecutive days followed by 7 days off ribociclib treatment resulting in a complete cycle of 28 days. The letrozole 2.5 mg tablet is to be taken once daily throughout the 28-day cycle.

Drugs/Diseases

Util A	Util B	Util C
Ribociclib;Letrozole		

Max Dose: 600 mg/day ribociclib; 2.5mg letrozole

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Kisqali Femara Co-Pack Prescribing Information, Feb. 2019, Novartis Pharmaceuticals Corp.

112. Ribociclib;Letrozole / Strong CYP3A4 Inhibitors _____ _____

Alert Message: Concurrent use of Kisqali Femara Co-Pack (ribociclib;letrozole) with a strong CYP3A4 inhibitor may increase exposure to ribociclib, increasing the risk of ribociclib toxicity (e.g., QT prolongation). Concomitant use of these drugs should be avoided. Consider alternative therapies that do not strongly inhibit CYP3A4. If coadministration of ribociclib with a strong CYP3A4 inhibitor cannot be avoided, reduce the dose of ribociclib to 400 mg once daily.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Kisqali Femara Co-Pack Prescribing Information, Feb. 2019, Novartis Pharmaceuticals Corp.

113. Ribociclib;Letrozole / Strong CYP3A4 Inducers _____ _____

Alert Message: Concurrent use of Kisqali Femara Co-Pack (ribociclib;letrozole) with a strong CPY3A4 inducer should be avoided as concomitant use may result in decreased ribociclib concentrations and reduce efficacy. Consider an alternative concomitant medication with no or minimal potential to induce CYP3A4.

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

Util A	Util B		Util C
Ribociclib;Letrozole	Carbamazepine	Rifampin	
	Phenobarbital	Enzalutamide	
	Primidone	Phenytoin	
	Mitotane		

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Kisqali Femara Co-Pack Prescribing Information, Feb. 2019, Novartis Pharmaceuticals Corp.

114. Ribociclib;Letrozole / CYP3A4 Substrates with NTI _____ _____

Alert Message: Caution is recommended when Kisqali Femara Co-Pack (ribociclib;letrozole) is administered with drugs that are CYP3A4 substrates with a narrow therapeutic index. The ribociclib component in the co-packaged product is a CYP3A4 inhibitor. The dose of a sensitive CYP3A4 substrate with a narrow therapeutic index may need to be reduced as ribociclib can increase substrate exposure.

Drugs/Diseases

Util A	Util B	Util C
Ribociclib;Letrozole	Cyclosporine	
	Dihydroergotamine	
	Ergotamine	
	Everolimus	
	Fentanyl	
	Pimozide	
	Quinidine	
	Sirolimus	
	Tacrolimus	
	Midazolam	

References:

IBM Micromedex DRUDEX (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA, 2019.
Kisqali Femara Co-Pack Prescribing Information, Feb. 2019, Novartis Pharmaceuticals Corp.

115. Ribociclib;Letrozole / QT Prolongation _____ _____

Alert Message: Avoid using Kisqali Femara Co-Pack (ribociclib;letrozole) with drugs known to prolong the QT interval due to an increased risk of QT prolongation. The ribociclib component in the co-packaged product has been shown to prolong the QT interval in a concentration-dependent manner.

Drugs/Diseases

Util A	Util B				Util C
Ribociclib;Letrozole	Albuterol	Disopyramide	Imipramine	Pazopanib	Vardenafil
	Alfuzosin	Deutetrabenazine	Pentamidine	Tizanidine	Venlafaxine
	Amantadine	Dolasetron	Pimavanserin	Tolterodine	Ziprasidone
	Amiodarone	Doxepin	Itraconazole	Posaconazole	
	Amitriptyline	Ketoconazole	Procainamide	TMP/SMZ	
	Amphetamine	Lapatinib	Propafenone	Trimipramine	
	Arsenic Trioxide	Efavirenz	Levalbuterol	Protriptyline	
	Asenapine	Eliglustat	Levofloxacin	Quetiapine	
	Atazanavir	Erythromycin	Lithium	Quinidine	
	Atomoxetine	Escitalopram	Metaproterenol	Ranolazine	
	Azithromycin	Felbamate	Methadone	Risperidone	
	Ceritinib	Flecainide	Midostaurin	Ritonavir	
	Chloroquine	Fluconazole	Moxifloxacin	Salmeterol	
	Chlorpromazine	Fluoxetine	Maprotiline	Sertraline	
	Ciprofloxacin	Foscarnet	Nilotinib	Solifenacin	
	Citalopram	Fosphenytoin	Dofetilide	Sotalol	
	Clarithromycin	Galantamine	Nortriptyline	Sunitinib	
	Clomipramine	Gemifloxacin	Octreotide	Tacrolimus	
	Clozapine	Granisetron	Ofloxacin	Tamoxifen	
	Dasatinib	Haloperidol	Ondansetron	Terbutaline	
	Desipramine	Mexiletine	Paliperidone	Trazodone	
	Diphenhydramine	Iloperidone	Paroxetine	Vandetanib	

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Kisqali Femara Co-Pack Prescribing Information, Feb. 2019, Novartis Pharmaceuticals Corp.

116. Ribociclib;Letrozole / QT Prolongation _____ _____

Alert Message: Avoid the use of Kisqali Femara Co-Pack (ribociclib;letrozole) in patients who already have or who are at significant risk for developing QT prolongation. The ribociclib component of the co-packaged product has been shown to prolong the QT interval in a concentration-dependent manner. Based on the observed QT prolongation during treatment, ribociclib may require dose interruption, reduction, or discontinuation.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Ribociclib;Letrozole		Long QT Syndrome
		Congestive Heart Failure
		Unstable Angina
		Bradyarrhythmias
		Myocardial Infarction
		Hypomagnesemia
		Hypokalemia

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Kisqali Femara Co-Pack Prescribing Information, Feb. 2019, Novartis Pharmaceuticals Corp.

117. Ribociclib;Letrozole / Therapeutic Appropriateness _____ _____

Alert Message: Advise women of reproductive potential to use effective contraception during therapy with Kisqali Femara Co-Pack (ribociclib;letrozole) and for at least 3 weeks after the last dose. Based on findings from animal studies and the mechanisms of action, ribociclib;letrozole can cause fetal harm when administered to a pregnant woman.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Ribociclib;Letrozole		Contraceptives

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Kisqali Femara Co-Pack Prescribing Information, Feb. 2019, Novartis Pharmaceuticals Corp.

118. Ribociclib;Letrozole / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on findings from animal studies and the mechanisms of action, Kisqali Femara Co-Pack (ribociclib;letrozole) can cause fetal harm when administered to a pregnant woman. Advise pregnant women of potential risk to a fetus.

Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Ribociclib;Letrozole	Pregnancy	Miscarriage
		Delivery
		Abortion

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Kisqali Femara Co-Pack Prescribing Information, Feb. 2019, Novartis Pharmaceuticals Corp.

119. Ribociclib;Letrozole / Lactation _____ _____

Alert Message: It is not known if the components of Kisqali Femara Co-Pack (ribociclib;letrozole) are present in human milk. There are no data on the effects of ribociclib or letrozole on the breastfed infant or on milk production. Because of the potential for serious adverse reactions in breastfed infants from these drugs, advise lactating women not to breastfeed while taking ribociclib;letrozole therapy and for at least 3 weeks after the last dose.

Drugs/Diseases

Util A	Util B	Util C
Ribociclib;Letrozole	Lactation	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Kisqali Femara Co-Pack Prescribing Information, Feb. 2019, Novartis Pharmaceuticals Corp.

120. Ribociclib;Letrozole / Therapeutic Appropriateness _____ _____

Alert Message: The safety and efficacy of Kisqali Femara Co-Pack (ribociclib;letrozole) in pediatric patients have not been established.

Drugs/Diseases

Util A	Util B	Util C
Ribociclib;Letrozole		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Kisqali Femara Co-Pack Prescribing Information, Feb. 2019, Novartis Pharmaceuticals Corp.