P&T Committee Meeting Minutes
GHP Family
January 16, 2018

Present:	**Absent:**
Bret Yarczower, MD, MBA – Chair	Beverly Blaisure, MD
Jamie Miller, RPh – Secretary	Holly Bones, Pharm.D
Kristen Bender, Pharm.D – via phone	Kimberly Castelnovo, RPh
Dr. Kenneth Bertka, MD – via phone	Sandra Garrett, RPh, MBA
Rajneel Chohan Pharm.D.	Perry Meadows, MD
Dean Christian, MD	Thomas Morland, MD
Alyssa Cilia, RPh – via phone	Steven Moscello, RPh
Kimberly Clark, Pharm.D.	Jonas Pearson, MS, RPh
Kristi Clarke, Pharm. D. – via phone	Richard Silbert, MD
Michael Evans, Pharm.D. – via phone	Lori Zaleski, RPh
Patrick Ferguson, RPh, MBA – via phone	
Anthony Fanucci, Pharmacy Student – via phone	
Tricia Heitzman, Pharm.D.	
Jason Howay, Pharm.D. – via phone	
Keith Hunsicker, Pharm.D.	
Kelli Hunsicker, Pharm.D.	
Steven Kheloussi, Pharm.D. – via phone	
Phillip Krebs, R.EEG T.	
Justine Maley, Pharmacy Student – via phone	
Anastasia Mauger Pharm.D.	
Aubrielle Prater Pharm.D. – via phone	
Kristen Scheib, Pharm. D. – via phone	
William Seavey, Pharm.D. – via phone	
Michael Spishock RPh – via phone	
Todd Sponenberg, Pharm.D., RPh	
Kevin Szczecina, RPh – via phone	

Call To Order:
Dr. Bret Yarczower called the meeting to order at 1:03 p.m., Tuesday, January 16, 2018.

Review and Approval of Minutes:
Dr. Bret Yarczower asked for a motion or approval to accept the November 21, 2017 minutes as written. Kimberly Clark accepted the motion and Jamie Miller seconded the motion. None were opposed.

DRUG REVIEWS

YESCARTA (axicabtagene ciloleucel)

Review: Yescarta is indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.

Yescarta is the second U.S. FDA-approved gene therapy product after Kymriah (tisagenlecleucel). Yescarta is a genetically-modified autologous T-cell immunotherapy, also known as a chimeric antigen receptor T (CAR-T) cell therapy, which targets CD19, a protein expressed on the surface of B-cell leukemia and lymphoma cells. Each dose of Yescarta is a customized treatment created using an individual patient's own T-cells. The patient's T-cells are collected and sent to a manufacturing center where they are genetically modified to include a new gene that contains the CAR protein. Once modified, the CAR protein directs the T-cells to target and kill leukemia cells with CD19 on the surface. The modified cells are then infused back into the patient to kill the cancer cells. Yescarta is indicated to treat adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma (also known as transformed follicular lymphoma).

In the ZUMA-1 Study, 51% of patients who received treatment with Yescarta achieved complete remission (CR), with an overall response rate (ORR) of 72%. These responses are higher than those currently achievable with standard chemotherapies. As an example, integrated results from the SCHOLAR-1 meta-analysis of 635 patients with refractory aggressive DLBCL who had been treated with standard chemotherapy regimens demonstrated a 26% ORR and 8% CR rate. Yescarta may be a treatment option for patients who have failed second-line chemotherapies, those who have relapsed after stem cell transplantation (SCT), or those who are not candidates for a SCT. Treatment with Yescarta may be considered curative; however, long-term follow-up is necessary to determine the durability of the responses achieved in the pivotal clinical trial.

Yescarta maintains a black box warning for cytokine release syndrome (CRS) and neurological toxicities. There is an associated REMS program, called the Yescarta REMS. In addition to the black box warning, the package insert describes warnings and precautions including prolonged cytopenias, hypogammaglobulinemia, secondary malignancies (which should be monitored for the life of the patient and reported to the manufacturer upon discovery), and effects on the ability to drive and use machines.

Yescarta is only available for administration at authorized infusion centers as dictated by the manufacturer of the drug (Kite Pharma). NCCN guidelines for the use of Yescarta closely resemble the labeled indication of the drug.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, and Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: Dr. Yarczower questioned whether both Yescarta and Kymriah target CD19, which they both do. It was also questioned whether CAR-T therapies will be an opportunity for contracting in the future, but it's too soon to tell. Jamie Miller made a motion to accept the recommendations as written. Todd Sponenberg seconded the motion. None were opposed

Financial Discussion: No questions or comments. Tricia Heitzman made a motion to accept the criteria as written. Jamie Miller seconded the motion. None were opposed.

Outcome: For GHP Family, Yescarta will be covered as a medical benefit requiring prior authorization. The following criteria will apply:

Large B-Cell Lymphoma

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is 18 years of age or older **AND**
- Medical record documentation of one of the following diagnoses:
    - Relapsed or refractory diffuse large B-cell lymphoma (DLBCL) **OR**
    - Relapsed or refractory primary mediastinal large B-cell lymphoma **OR**
    - Relapsed or refractory high-grade B-cell lymphoma

  AND
- Medical record documentation of a therapeutic failure on two or more previous lines of therapy

AUTHORIZATION DURATION/QUANTITY LIMIT: One-time authorization for one administration of Yescarta.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

CALQUENCE (acalabrutinib)

Review: Calquence is a new Bruton tyrosine kinase (BTK) indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.

Calquence and its active metabolite inhibit Bruton tyrosine kinase (BTK) by covalently bonding to a cysteine residue at the active BTK site. This prevents activation of the signaling proteins CD86 and CD69, as well as inhibits proliferation and survival of malignant B cells. The only other therapy current in this class of medications and used to treat the same indication is Imbruvica (ibrutinib). Calquence shares many of the same warnings and precautions as Imbruvica; however, Imbruvica also has a warning and precaution for hypertension, tumor lysis syndrome, and embryo-fetal toxicity. Calquence and Imbruvica share the following warnings and precautions: hemorrhage, infections, cytopenia, second primary malignancies, atrial fibrillation and flutter. The liver is the primary site of metabolism and its active metabolite is termed ACP-5862 (major). Calquence is also a substrate of CYP3A, P-glycoprotein, and BCRP, weak inhibitor of CYP3A4/5, CYP2C8, and CYP2C9 and weak inducer of CYP1A2, CYP2B6, and CYP3A4. Calquence is minimally excreted in the urine - Renal: 12%; less than 1% as unchanged drug, fecal: 84%; less than 1% as unchanged drug, and the total body clearance: 159 L/hr. The elimination half-life is 0.9 hours and 6.9 hours for the major active metabolite ACP-5862.

Due to the potential for adverse reactions in a breastfed child from Calquence, advise lactating women not to breastfeed while taking Calquence and for at least 2 weeks after the final dose. Based on findings in animals, Calquence 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 Calquence 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 (see Data). Advise pregnant women of the potential risk to a fetus. Safety and effectiveness in pediatric patients have not been established.

The efficacy of Calquence was evaluated in a phase 2, open-label study in 124 patients with MCL who has received at least one prior therapy. After a median follow-up of 15.2 months, 81% of patients achieved an overall response, with 40% patients having a complete response, and 41% of patients with a partial response. At the time of evaluation, median duration of response was not yet reached: the 12-mo DOR was 72% (95% CI, 62%-80%). Based on this trial data, the National Comprehensive Cancer Network (NCCN) recently added Calquence to the NCCN Guidelines for B-cell Lymphomas V6.2017. The panel consensus was to include Calquence as a second-line therapy option for mantel cell lymphoma. This was added as a category 2A recommendation.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, and Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: It was recommended that member age greater than or equal to 18 years is added to the policy. Keith Hunsicker made a motion to accept the recommendations as amended. Todd Sponenberg seconded the motion. None were opposed.

Financial Discussion: It was recommended that the policy be updated to a quantity limit of two capsules per day. A quantity limit exception would be available for members who require four capsules per day due to drug interactions. Keith Hunsicker made a motion to accept the recommendations as amended. Dr. Dean Christian seconded the motion. None were opposed.

Outcome: For GHP Family, Calquence will be a pharmacy benefit. Calquence will be added to the GHP Family formularies on the Brand Tier. Calquence will require prior authorization with the following criteria:

- Medical record documentation that Calquence is prescribed by a hematologist/oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation a diagnosis of mantle cell lymphoma (MCL) **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to one prior therapy **AND**
- If the requested dose is 400 mg daily: Medical record documentation that the patient is using Calquence in combination with a strong CYP3A inducer, including but not limited to carbamazepine, enzalutamide, fosphenytoin, lumacaftor, mitotane, phenytoin, rifampin, St. John's Wort

  QUANTITY LIMIT: 2 capsules per day, 30 day supply per fill

  AUTHORIZATION DURATION: Each treatment period will be defined as 12 months. Subsequent approval after 12 months will require documentation of continued disease improvement or lack of disease progression.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

RENFLEXIS (infliximab-abda)

Review: Renflexis is the second-to-market infliximab biosimilar product (Reference Product - Remicade), following Inflectra. Renflexis carries the same FDA-approved indications as Inflectra, which are the same as Remicade (except for pediatric ulcerative colitis).

Renflexis follows weight-based dosing, which is specific to the indication being treated and ranges from 5mg/kg to 10mg/kg given every 8 weeks after the initial loading dose. Infliximab is a TNFα inhibitor, which inhibits the induction of proinflammatory cytokines (e.g. IL-1, IL-6), inhibits the enhancement of leukocyte migration, inhibits the activation of neutrophil and eosinophil functional activity, inhibits the induction of acute phase reactants and other liver proteins, and inhibits the induction of tissue degrading enzymes produced by synoviocytes and/or chondrocytes.

In clinical trials, Renflexis was proven to be pharmacokinetically equivalent to EU- and US- sourced infliximab. In a phase III randomized, double-blind, parallel group, multicenter study, Renflexis demonstrated similar efficacy and safety compared to EU sourced infliximab, showing a similar ACR20/50/70, DAS28, EULAR, major clinical response, and mTSS change between the Renflexis and EU sourced infliximab groups at Week 54. An extension study (to the above-mentioned trial) concluded that the above efficacy and safety results were maintained from Week 54 through Week 78. Immunogenicity results of Renflexis were comparable to those of EU- or US- sourced infliximab in all trials.

The safety profile, which consists of a black box warning for risk of malignancy and serious infections, is similar to that of Remicade and Inflectra. In addition to the black box warning, warnings and precautions of reactivation of tuberculosis and invasive fungal infections, risk of malignancies, hepatitis B reactivation, hepatotoxicity, heart failure, hematologic reactions, hypersensitivity reactions, neurologic reactions, use with anakinra, abatacept, or other biological therapeutics, switching between biological DMARDs, autoimmunity, and administration of live vaccines/therapeutic infectious agents are listed by the package insert.

Clinical guidelines recommend anti-TNF therapy after an inadequate response to other non-biologic DMARD therapies. The guidelines do not make recommendation of one anti-TNF product over another. Geisinger Health System prefers to use a biosimilar infliximab product as preferred therapy in new-start infliximab patients. For patients currently established on a particular infliximab product, the System does not routinely switch products, but will review patients on an individualized basis whether or not they are candidates for biosimilar therapy.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, and Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: No comments or questions. Kimberly Clark made a motion to accept the recommendations as written. Jamie Miller seconded the motion. None were opposed

Financial Discussion: No comments or questions. Jamie Miller made a motion to accept the recommendations as written. Dr. Dean Christian seconded the motion. None were opposed.

Outcome: For GHP Family, Renflexis will be covered as a medical benefit requiring prior authorization. Renflexis will be added to Medical Benefit Policy 5.0 as outlined below:

MBP 5.0

Remicade (infliximab), Inflectra (infliximab-dyyb), or Renflexis (infliximab-abda) will be considered medically necessary when all of the following criteria are met based on indication:

For Treatment of Rheumatoid Arthritis:

- Must be 18 years of age or greater **AND**
- Requesting provider must be a rheumatologist **AND**
- Diagnosis of moderate to severe rheumatoid arthritis according the American College of Rheumatology Criteria for the Classification and Diagnosis of Rheumatoid Arthritis **AND**
- Medical record documentation of an intolerance to, contraindication to, or therapeutic failure on a minimum 3-month trial of Humira* AND Enbrel* **AND**
- Continuation of effective dose of methotrexate during infliximab therapy **AND**
- For new start Remicade or Renflexis requests, medical record documentation of an intolerance to, contraindication to, or therapeutic failure on a minimum 3-month trial of Inflectra*

Recommended guidelines for use in the treatment of rheumatoid arthritis

- *3 mg/kg given as an intravenous infusion followed with additional similar doses at 2 and 6 weeks after the first infusion then every 8 weeks thereafter. Infliximab should be given in combination with methotrexate.*
- *For patients who have an incomplete response, consideration may be given to adjusting the dose up to 10 mg/kg or treating as often as every 4 weeks.*

For Treatment of Crohn's Disease, Pediatric Crohn's Disease, and/or Fistulizing Crohn's Disease:

- Must be 6 years of age or older; **AND**
- Prescription is written by a gastroenterologist **AND**
- Medical record documentation of a diagnosis of moderate to severe Crohn's disease **AND**
- One of the following:
    - Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Humira* **OR**
    - Physician documentation of Crohn's disease with actively draining fistulas.

  AND
- For new start Remicade or Renflexis requests, medical record documentation of an intolerance to, contraindication to, or therapeutic failure on a minimum 3-month trial of Inflectra*

Recommended guidelines for use in the treatment of Crohn's disease or fistulizing Crohn's disease:

- *5 mg/kg given intravenously as an induction regimen at 0, 2, and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks thereafter*
- *For adult members who respond and then lose response, consideration may be given to treatment with 10 mg/kg.*

For Treatment of Ulcerative Colitis:

- Must be at least 6 years of age **AND**
- Must be prescribed by a gastroenterologist **AND**
- Physician provided documentation of a diagnosis of moderate to severe ulcerative colitis **AND**
- Physician provided documentation of failure on, intolerance to, or contraindication to adequate trials of conventional therapy that include corticosteroids, aminosalicylates and immunomodulators (e.g. 6-mercaptopurine or azathioprine) **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to at least a 12-week trial of Humira* OR medical record documentation of age < 18 years **AND**
- For new start Remicade requests, medical record documentation of an intolerance to, contraindication to, or therapeutic failure on a minimum 3-month trial of Inflectra* OR medical record documentation of age <18 years **AND**
- For new start Renflexis requests, medical record documentation of an intolerance to,

contraindication to, or therapeutic failure on a minimum 3-month trial of Inflectra*

Recommended guidelines for the use in the treatment of ulcerative colitis

- *5 mg/kg as an intravenous infusion followed with additional similar doses at 2 and 6 weeks after the first infusion, then every 8 weeks thereafter.*

For Treatment of Ankylosing Spondylitis:

- Physician documentation of a diagnosis of ankylosing spondylitis **AND**
- Prescribing physician must be a rheumatologist **AND**
- Must be at least 18 years of age **AND**
- Medical record documentation of an intolerance to, contraindication to, or therapeutic failure on a minimum 3-month trial of Humira* **AND** Enbrel* **AND**
- For new start Remicade or Renflexis requests, medical record documentation of an intolerance to, contraindication to, or therapeutic failure on a minimum 3-month trial of Inflectra*

Recommended guidelines for use in ankylosing spondylitis

- *5mg/kg at 0, 2 and 6 weeks, then every 6 weeks thereafter*

For the treatment of Plaque Psoriasis:

- Prescribed by a dermatologist **AND**
- Insured individual must be at least 18 years of age **AND**
- Physician provided documentation of a diagnosis of moderate to severe plaque psoriasis characterized by greater than or equal to 5% body surface area involved or disease affecting crucial body areas such as the hands, feet, face, or genitals **AND**
- Medical record documentation of an inadequate response to, contraindication to, or failure on at least 3 months of Humira* and Enbrel* **AND**
- For new start Remicade or Renflexis requests, medical record documentation of an intolerance to, contraindication to, or therapeutic failure on a minimum 3-month trial of Inflectra*

Recommended guidelines for the use in the treatment of plaque psoriasis

- *5 mg/kg as an intravenous infusion followed with additional similar doses at 2 and 6 weeks after the first infusion, then every 8 weeks thereafter.*

For the treatment of Psoriatic Arthritis:

- Physician provided documentation of a diagnosis of moderately to severely active psoriatic arthritis which must include the following:
  - Documentation of either active psoriatic lesions or a documented history of psoriasis **AND**
- Must be prescribed by a rheumatologist or dermatologist **AND**
- Must be at least 18 years of age **AND**
- Medical record documentation of an inadequate response to, contraindication to, or failure on 12 weeks of Enbrel* AND Humira* **AND**
- For new start Remicade or Renflexis requests, medical record documentation of an intolerance to, contraindication to, or therapeutic failure on a minimum 3-month trial of Inflectra*

Recommended guidelines for the use in the treatment of psoriatic arthritis

- *5 mg/kg as an intravenous infusion followed with additional similar doses at 2 and 6 weeks after the first infusion, then every 8 weeks thereafter.*

AUTHORIZATION DURATION: Approval will be given for an initial duration of six (6) months. For continuation of coverage, medical record documentation of clinical improvement or

lack of progression in the signs and symptoms of the treated indication at six (6) months of infliximab therapy is required.

After the initial six (6) month approval, subsequent approvals for coverage will be for a duration of one (1) year. Reevaluation of coverage will be every one (1) year requiring medical record documentation of continued or sustained improvement in the signs and symptoms of the treated indication while on infliximab therapy.

LIMITATIONS: Inflectra and Renflexis are not approved for the use in pediatric ulcerative colitis due to orphan drug exclusivity for Remicade.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

NITYR (nitisinone)

Review: Nityr is a hydroxyphenyl-pyruvate dioxygenase inhibitor indicated for the treatment of hereditary tyrosinemia type 1 (HT-1) in combination with dietary restriction of tyrosine and phenylalanine.

Dosing for Nityr starts at 0.5 mg/kg twice daily and may be titrated up to a maximum dose of 2 mg/kg/day. Nityr is supplied through Diplomat Specialty Pharmacy as 2 mg, 5 mg, and 10 mg tablets that may be dissolved in water or crushed and mixed with applesauce. Patients with HT-1 have deficient fumarylacetoacetate hydrolase (FAH) enzyme levels, resulting in accumulation of toxic metabolites succinyl acetoacetate (SAA) and succinylacetone (SA). Nityr blocks 4-hydroxyphenyl-pyruvate (HPD) to prevent the production of SAA and SA. In clinical trials with another oral formulation of nitisinone, addition of nitisinone to dietary restriction of tyrosine and phenylalanine significantly decreased urine SA and increased the 2- and 4-year survival probabilities in patients with HT-1. There are no black box warnings or contraindications for Nityr, and the most common adverse events are elevated tyrosine levels, leukopenia, thrombocytopenia, and ocular disturbances. Nityr is the second available oral formulation of nitisinone, the only pharmacologic agent used in treatment of HT-1. Recommendations for the management of HT-1 advise starting nitisinone as soon as a diagnosis of HT-1 is suspected but do not indicate a preference of Nityr over Orfadin.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, and Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: Dr. Yarczower questioned whether there was a predictor to who doesn't do as well on therapy and also if they looked at increased levels of tyrosine and how that impacted patients. This information was not available as part of the clinical trial. No additional comments or questions. Keith Hunsicker made a motion to accept the recommendations as written. Dr. Dean Christian seconded the motion. None were opposed.

Financial Discussion: No comments or questions. Todd Sponenberg made a motion to accept the recommendations as written. Keith Hunsicker seconded the motion. None were opposed.

Outcome: For GHP Family, Nityr will be a pharmacy benefit. Nityr will be added to the GHP Family formularies on the Brand Tier. Nityr will require prior authorization with the following criteria:

- Prescription is written by specialist in medical genetics or metabolic diseases **AND**

- Medication is being used in combination with dietary restriction of tyrosine and phenylalanine **AND**
  Medical record documentation of hereditary tyrosinemia type 1 (HT-1) diagnosis established and supported by documentation of elevated plasma or urine succinylacetone (SA) levels

  AUTHORIZATION DURATION: Initial approval will be for 12 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional 12 months or less if the reviewing provider feels it is medically appropriate and will require medical record documentation of continued disease improvement or lack of disease progression. Nityr will no longer be covered if the member experiences unacceptable toxicity or worsening of disease.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

ORFADIN (nitisinone)

Review: Orfadin is a hydroxyphenyl-pyruvate dioxygenase inhibitor indicated for the treatment of hereditary tyrosinemia type 1 (HT-1) in combination with dietary restriction of tyrosine and phenylalanine.

Dosing for Orfadin starts at 0.5 mg/kg twice daily and may be titrated up to a maximum dose of 2 mg/kg/day. Orfadin is supplied through Dohmen Life Sciences Services as 2 mg, 5 mg, 10 mg, and 20 mg capsules and 4 mg/mL oral suspension. Patients with HT-1 have deficient fumarylacetoacetate hydrolase (FAH) enzyme levels, resulting in accumulation of toxic metabolites succinyl acetoacetate (SAA) and succinylacetone (SA). Orfadin blocks 4-hydroxyphenyl-pyruvate (HPD) to prevent the production of SAA and SA. In clinical trials, addition of Orfadin to dietary restriction of tyrosine and phenylalanine significantly decreased urine SA and increased the 2- and 4-year survival probabilities in patients with HT-1. There are no black box warnings or contraindications for Orfadin, and the most common adverse events are elevated tyrosine levels, leukopenia, thrombocytopenia, and ocular disturbances. Orfadin was the first available oral formulation of nitisinone, the only pharmacologic agent used in treatment of HT-1, and is the only product available as an oral suspension. Recommendations for the management of HT-1 advise starting Orfadin as soon as a diagnosis of HT-1 is suspected.
A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, and Other Considerations and a Financial Review Based on Cost Analysis were presented**.**

Clinical Discussion: No comments or questions. Dr. Dean Christian made a motion to accept the recommendations as written. Kimberly Clark seconded the motion. None were opposed.

Financial Discussion: No comments or questions. Keith Hunsicker made a motion to accept the recommendations as written. Dr. Dean Christian seconded the motion. None were opposed.

Outcome: For GHP Family, Orfadin will be a pharmacy benefit. Nityr will not be added to the GHP Family formulary. Orfadin will require prior authorization with the following criteria:

- Prescription is written by specialist in medical genetics or metabolic diseases **AND**
- Medication is being used in combination with dietary restriction of tyrosine and phenylalanine **AND**

Medical record documentation of hereditary tyrosinemia type 1 (HT-1) diagnosis established and supported by documentation of elevated plasma or urine succinylacetone (SA) levels **AND**

- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Nityr tablets

AUTHORIZATION DURATION: Initial approval will be for 12 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional 12 months or less if the reviewing provider feels it is medically appropriate and will require medical record documentation of continued disease improvement or lack of disease progression. Orfadin will no longer be covered if the member experiences unacceptable toxicity or worsening of disease.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

DUZALLO (lesinurad and allopurinol)

Review: Duzallo is a combination of lesinurad, a URAT1 inhibitor, and allopurinol, a xanthine oxidase inhibitor, and it is indicated for the treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid levels with a medically appropriate dose of allopurinol alone. Duzallo is not recommended for the treatment of asymptomatic hyperuricemia.

Duzallo is available as 200 mg lesinurad/200 mg allopurinol tablets and 200 mg lesinurad/300 mg allopurinol tablets. The recommended dose of Duzallo is one tablet orally once daily in the morning with food and water. Duzallo is not recommended for patients taking daily doses of allopurinol < 300 mg (or < 200 mg in those with a creatinine clearance < 60 mL/min). The total daily dose of allopurinol should be maintained at the time of Duzallo initiation There have been no phase 3 clinical trials with Duzallo. Bioequivalence of Duzallo to lesinurad and allopurinol (co-administered) was demonstrated and the efficacy of the combination was demonstrated in two phase 3 trials (Zurampic clinical trials). Duzallo has a Black Box Warning for risk of acute renal failure. Duzallo is contraindicated for patients with severe renal impairment, ESRD, kidney transplant recipients, dialysis, tumor lysis syndrome or Lesch-Nyhan syndrome, and/or known hypersensitivity to allopurinol. The most common adverse reactions (≥ 2% of patients treated with lesinurad in combination with a xanthine oxidase inhibitor and more frequently than on oxidase inhibitor alone) were headache, influenza, blood creatinine increased, and gastroesophageal reflux disease. Treatment with lesinurad and allopurinol was associated with an increased incidence of serum creatinine elevations. A higher incidence of renal-related adverse reactions, serum creatinine elevations, and serious adverse reactions (including acute renal failure) were observed with lesinurad 400 mg in combination with allopurinol. The highest incidence of these events occurred when lesinurad was given alone. Patients with moderate renal impairment had a higher occurrence of renal related adverse reactions compared to patients with mild renal impairment or normal renal function. Lesinurad/allopurinol use in patients with a creatinine clearance < 45 mL/min is limited and trended toward lower efficacy. Duzallo should not be started in patients with a creatinine clearance < 45 mL/min. There is no dose adjustment recommended for patients with a creatinine clearance 45 to < 60 mL/min, however more frequent monitoring is recommended. Duzallo has not been studied in patients with severe renal impairment (creatine clearance < 30 mL/min), ESRD, or those receiving dialysis and it is not expected to be effective in these patient populations. Duzallo is not recommended in patients with severe hepatic impairment. The safety and effectiveness of Duzallo in pediatric patients < 18 years have not been established. UpToDate recommends allopurinol as first-line anti-hyperuricemic therapy. Allopurinol is titrated until reach urate lowering goal < 6 mg/dL or for patients with tophaceous gout < 5 mg/dL. Febuxostat can be an alternative to allopurinol for patients who cannot tolerate or have therapeutic failure.

For patients who do not have moderate or severe renal impairment or uric acid overproduction, probenecid monotherapy can be used. For patients with advanced gout refractory to conventional treatment or severe tophaceous disease, pegloticase can be considered.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, and Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: No comments or questions. Keith Hunsicker made a motion to accept the recommendations as written. Tricia Heitzman seconded the motion. None were opposed.

Financial Discussion: No comments or questions. Kimberly Clark made a motion to accept the recommendations as written. Keith Hunsicker seconded the motion. None were opposed.

Outcome: For GHP Family, Duzallo will be a pharmacy benefit. Duzallo will not be added to the GHP Family formulary. Duzallo will require prior authorization with the following criteria:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of symptomatic hyperuricemia associated with gout **AND**
- Medical record documentation that patient has been on a medically appropriate dose of allopurinol of at least 300 mg (or at least 200 mg in patients with estimated creatinine clearance (eCLcr < 60 mL/min)) and did not achieve target serum uric acid levels **AND**
- Medical record documentation of an estimated creatinine clearance (eCLcr) ≥ 45 mL/min **AND**
- Medical record documentation that Duzallo is not being used in tumor lysis syndrome, Lesch-Nyhan syndrome, and kidney transplant recipients.

  QUANTITY LIMIT: 1 tablet per day

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

TREMFYA (guselkumab)

Review: Tremfya is an IL-23 inhibitor indicated for the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

Tremfya is administered subcutaneously at a dose of 100mg on weeks 0, 4 and every 8 weeks thereafter. In the clinical trials, VOYAGE-1 and VOYAGE-2, Tremfya achieved statistically significantly greater PASI90 and IGA response at week 16 compared to Humira. These responses were maintained through weeks 24 and 48. In the NAVIGATE trial, Tremfya achieved a statistically significantly greater IGA response at week 24 compared to Stelara. The safety profile of Tremfya is relatively benign, having warnings and precautions only significant for increased risk of infections, increased risk of latent TB reactivation, and live vaccinations. Physicians involved with the Geisinger Psoriasis ProvenCare recognized the advantageous statistical efficacy outcomes of Tremfya; however, the physicians noted that the measures utilized the in the manufacturer clinical trials differ than what is used in clinical practice (PASI90 was used in trials but BSA is used in practice), and the physicians noted that they have not found that one agent has shown clinical significance over another. The AAD guidelines recognize that IL- inhibitors demonstrate therapeutic efficacy in the treatment of psoriasis, however do not make recommendations for their use currently.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, and Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: No comments or questions. Tricia Heitzman made a motion to accept the recommendations as written. Dr. Dean Christian seconded the motion. None were opposed.

Financial Discussion: Phil Krebs questioned why light box therapy was not a required failure prior to approval of all biologics. It is something that will be considered as the ProvenCare Pathway continues to develop. Dr. Dean Christian made a motion to accept the recommendations as written. Tricia Heitzman seconded the motion. None were opposed.

Outcome: For GHP Family, Tremfya will be a pharmacy benefit. Tremfya will not be added to the GHP Family formularies. Tremfya will require prior authorization with the following criteria:

- Prescription written by a dermatologist **AND**
- Medical record documentation that the member is 18 years of age or older **AND**
- Medical record documentation of a diagnosis of moderate-to-severe plaque psoriasis with greater than or equal to 5% body surface area involved **OR** disease involving crucial areas of the body such as hands, feet, face, and/or genitals **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Humira **AND** Enbrel

  QUANTITY LIMIT: One time, one week authorization of 1 syringe (1mL) per 28 days. Remainder of 6-month authorization, 1 syringe (1mL) per 56 days. Subsequent authorizations will have a QL of 1 syringe per 56 days.

  AUTHORIZATION DURATION: Approval will be given for an initial duration of six (6) months. For continuation of coverage, medical record documentation of clinical improvement or lack of progression in the signs and symptoms of plaque psoriasis on six (6) months of guselkumab therapy is required.

  After the initial six (6) month approval, subsequent approvals for coverage will be for a duration of one (1) year. Reevaluation of coverage will be every one (1) year requiring medical record documentation of continued or sustained improvement in the signs and symptoms of plaque psoriasis while on guselkumab therapy.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

MYLOTARG (gemtuzumab ozogamicin)

Review: Mylotarg is indicated for the treatment of newly-diagnosed CD33-positive AML in adults and for relapsed or refractory CD33-positive AML in adults and in pediatric patients 2 years and older. For newly-diagnosed AML patients, Mylotarg is recommended in a combination regimen or as a single agent. For relapsed or refractory AML patients, Mylotarg is only recommended as a single-agent for treatment.

The dose of Mylotarg is based on BSA and differs for each indication and infused over 2 hours. The clinical trial program for Mylotarg consisted of two phase 3 studies for newly-diagnosed CD33-positive AML (ALFA-0701 for use in combination with chemotherapy, AML-19 for use as a single agent) and

one phase 2 study for relapsed or refractory CD33-positive AML (MyloFrance-1). The ALFA-0701 study demonstrated that the lower dose fractionated regimen of Mylotarg in combination with chemotherapy (daunorubicin and cytarabine) resulted in a clinically meaningful and statistically significant improvement in EFS by and RFS, with a trend towards improved OS. In the AML-19 study, Mylotarg achieved the primary endpoint of OS, with a hazard ratio (HR) of 0.69 (95% CI: 0.53, 0.90; p=0.005). Median OS was 4.9 months in the Mylotarg arm versus 3.6 months in the BSC arm. In the MyloFrance-1 study, lower fractionated doses of Mylotarg given as a monotherapy successfully induced a second remission in relapsed or refractory AML patients. Mylotarg carries a black box warning for hepatotoxicity, including severe or fatal hepatic veno-occlusive liver disease (VOD). Mylotarg is contraindicated in patients with a history of hypersensitivity to the active ingredients or any of its components or to any of the excipients. Mylotarg carries warning for infusion-related reactions, hemorrhage, and embryo-fetal toxicity. The most common adverse reactions (> 15%) were hemorrhage, infection, fever, nausea, vomiting, constipation, headache, increased AST, increased ALT, rash, and mucositis. When Mylotarg was first released in 2000, a dose of 9 mg/m2 on days 1 and 14 was recommended; however, post-marketing studies and confirmatory trials found this dose was associated with hematological toxicity (i.e., myelosuppression) and frequent liver toxicity (i.e., VOD). After Mylotarg was discontinued, positive data from a meta-analysis of individual patient data suggested clinical benefit when Mylotarg was delivered as a 3 mg/m2 dose on days 1, 4, and 7 (3-3-3 regimen) during induction and at a lower dose for consolidation or continuation therapy. These lower fractionated doses resulted in lower rates of VOD and hematologic toxicities. Mylotarg can cause embryo-fetal harm when administered to a pregnant woman. Females of reproductive potential should use effective contraception during treatment with Mylotarg and for at least 6 months after the last dose. Males with female partners of reproductive potential should use effective contraception during treatment and for at least 3 months after the last dose. Due to the potential risk for adverse reactions, women should not breastfeed during treatment with Mylotarg and for at least 1 month after the final dose. The safety and efficacy of Mylotarg in combination with daunorubicin and cytarabine have not been established in the pediatric patients with newly diagnosed de novo AML. Mylotarg as a single-agent for the treatment of relapsed or refractory AML, showed no difference in effectiveness observed by age, but elderly patients experienced a higher rate of fever and severe or greater infections. Mylotarg is a first-in-class therapy to target CD33 in AML patients. Mylotarg is the first therapy with an indication that includes pediatric AML.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, and Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: No comments or questions. Keith Hunsicker made a motion to accept the recommendations as written. Dr. Dean Christian seconded the motion. None were opposed.

Financial Discussion: The maximum approved length of therapy is as a single-agent for the treatment of newly-diagnosed AML and consists of 9-cycles. Jamie Miller made a motion to accept the recommendations as written. Phil Krebs seconded the motion. None were opposed.

Outcome: For GHP Family, Mylotarg will be covered as a medical benefit requiring prior authorization. The following criteria will apply:

Newly-diagnosed CD33-positive Acute Myeloid Leukemia

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of a diagnosis of newly diagnosed CD33-positive Acute Myeloid Leukemia **AND**
- Medical record documentation of the member being ≥ 18 years

Relapsed or refractory CD33-positive Acute Myeloid Leukemia

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of relapsed or refractory CD33-positive Acute Myeloid Leukemia **AND**
- Medical record documentation of the member being ≥ 2 years

AUTHORIZATION DURATION: If approved, authorization should be for a maximum of 9 cycles for an authorization duration of 12 months.

For requests exceeding the above limits, medical record documentation of the following is required:

- Peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

VYXEOS (daunorubicin/cytarabine liposomal)

Review: Vyxeos is a liposomal combination of daunorubicin, an anthracycline topoisomerase inhibitor, and cytarabine, a nucleoside metabolic inhibitor, that is indicated for the treatment of adults with newly-diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC). A full Vyxeos course consists of 1-2 cycles of Induction and up to 2 cycles of Consolidation at a dose and schedule specific to the cycle.

Based on the phase 2b and phase 3 trial results, Vyxeos resulted in improvement in remission rate (38% vs 26%, p-value= 0.005) and overall survival (9.6 months vs 5.9 months, p-value= 0.005, hazard ratio= 0.69) compared to the conventional 7+3 regimen. These results are significant as Vyxeos is the first drug to improve overall survival in the secondary AML population in decades.

The safety profile of Vyxeos is significant for a black box warning regarding the inability to interchange the dosing of Vyxeos with its individual components, daunorubicin and cytarabine. Vyxeos' safety profile is also significant for the risk for cardiotoxicity, severe or life-threatening hypersensitivity reactions, and serious or fatal hemorrhagic events which have been associated prolonged thrombocytopenia. The most common adverse reactions noted with Vyxeos were hemorrhage, rash, cough, and headache. Drug interactions with Vyxeos include cardiotoxic agents and hepatotoxic agents. Similar to cytarabine, Vyxeos can cause fetal harm if a pregnant woman is exposed to the drug. For that reason, pregnant woman should not receive treatment with Vyxeos.

Although Vyxeos combines two commonly used chemotherapies into a single formulation, this is the first therapy that has shown an improvement in survival in years among this high-risk patient population. Vyxeos could fill in a gap in treatment options for patients with t-AML or AML-MRC by providing patients with a treatment that does not require use of an ambulatory home-infusion pump.

At this time, the NCCN guidelines do not make specific recommendations for the use of Vyxeos. Specialist feedback from Ben Andrick (Clinical Pharmacist, GMC) indicates that Vyxeos is expected to have a niche in treating patients previously treated as well as older patients, with the ultimate goal being to transition patients to stem-cell transplant. Ben indicated that Vyxeos maintains the efficacy of a full anthracycline dose while administering only a fraction of the anthracycline dose that would be given in a

7+3 regimen. This allows for the treatment of patients that might be nearing their total cumulative lifetime anthracycline dose and older patients who cannot tolerate the 7+3 regimen. Ben struggles to justify the high cost of Vyxeos, and due to the limited efficacy data, cost, and inability to extrapolate the available statistically significant data to "clinical significance," Ben anticipates use of Vyxeos to be limited to those above-mentioned populations.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, and Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: No comments or questions. Dr. Dean Christian made a motion to accept the recommendations as written. Jamie Miller seconded the motion. None were opposed.

Financial Discussion: There was discussion regarding how inpatient costs associated with the 7+3 regimen could impact the significant cost differential. It was recommended to approve the criteria as presented and evaluate the cost for the next committee meeting. Tricia Heitzman made a motion to accept the recommendations as written. Kimberly Clark seconded the motion. None were opposed.

Outcome: For GHP Family, Vyxeos will be covered as a medical benefit requiring prior authorization. The following criteria will apply:

Acute Myeloid Leukemia (AML)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of age of ≥18 years **AND**
- Medical record documentation of one of the following diagnoses:
    - Newly-diagnosed therapy-related acute myeloid leukemia (t-AML) OR
    - AML with myelodysplasia-related changes (AML-MRC) **AND**
- Medical record documentation of rationale why 7+3 (cytarabine + daunorubicin) is not a medically appropriate treatment for the member (i.e. Unable to tolerate 7+3 regimen due to performance status or age, unable to administer full dose 7+3 regimen without exceeding maximum lifetime cumulative anthracycline dose, etc.)

  AUTHORIZATION DURATION: If approved, initial approval should be for a period of six (6) months. Subsequent approvals will be for an additional six (6) months and will require medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if the member experiences unacceptable toxicity or worsening of disease.

  Authorization of Vyxeos should not exceed four (4) cycles or the patient's maximum lifetime cumulative anthracycline dosage, whichever comes first. For requests exceeding the above limits, medical record documentation of the following is required:

  - Peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration and/or maximum cumulative anthracycline dose.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

BEVYXXA (betrixaban)

Review: Bevyxxa is a factor Xa (FXa) inhibitor indicated for the prophylaxis of venous thromboembolism (VTE) in adult patients hospitalized for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE.

Similar to other Factor Xa inhibitors and LMWH, Bevyxxa carries a black box warning for risk of spinal/ epidural hematoma occurrence in patients who are receiving neuraxial anesthesia or undergoing spinal puncture, and a contraindication in patients with active bleeding. All anticoagulants have warnings for risk of bleeding. Bevyxxa has a warning for increased risk of bleeding in patients with severe renal impairment and patients taking P-gp inhibitors. Bevyxxa is recommended to be dose adjusted in patients with CrCl>15ml/min to <30ml/min and while the indications do not align at this time, other Factor Xa inhibitors require dose adjustments based on differing levels of renal impairment. Bevyxxa is primarily excreted in the gut through the hepatobiliary route, via the P-gp efflux pump mostly as unchanged drug. Therefore, since it is primarily excreted through the GI tract, GI side effects may be more pronounced. Generally, drug interactions with P-gp inhibitors are reported with other Factor Xa inhibitors, although Bevyxxa has the advantage of a lack of CYP3A4 drug interactions. Similar to other Factor Xa inhibitors, Bevyxxa should be avoided with other anticoagulants and antiplatelets due to risk of bleeding.

Bevyxxa has not been evaluated in patients with hepatic impairment, because these patients may have intrinsic coagulation abnormalities. Therefore, Bevyxxa is not recommended in patients with hepatic impairment. There are no data with the use of Bevyxxa in pregnant women, but treatment with an anticoagulant is likely to increase the risk of hemorrhage during pregnancy and delivery. LMWH are the preferred agents for VTE prophylaxis during pregnancy. Safety and effectiveness in pediatric patients have not been established in Bevyxxa.

Efficacy analyses were performed based on the modified intention to treat (mITT) population. The mITT population consisted of all patients who had taken at least one dose of the study drug and had follow-up data assessments on one or more primary or secondary efficacy outcome components. Based on the results, extended duration Bevyxxa was associated with significantly less VTEs compared to standard duration enoxaparin. The events were driven by asymptomatic DVTs. A subgroup analysis showed patients who were randomized to receive 40 mg Bevyxxa (those with severe renal impairment or receiving P-gp inhibitors), had VTE rates similar to the enoxaparin arm.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, and Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: No comments or questions. Tricia Heitzman made a motion to accept the recommendations as written. Dr. Dean Christian seconded the motion. None were opposed.

Financial Discussion: There was discussion regarding the potential future approval of additional indications and whether Bevyxxa will compete with the other oral agents in this category. It's thought that it's likely, but no way to tell for sure. Kelli Hunsicker made a motion to accept the recommendations as written. Anastasia Mauger seconded the motion. None were opposed.

Outcome: For GHP Family, Bevyxxa will be a pharmacy benefit. Bevyxxa will be added to the Brand Tier of the GHP Family formulary. Bevyxxa will require prior authorization with the following criteria:

Extended duration prophylaxis of Venous Thromboembolism (VTE) for an acute medical illness due to moderate or severe restricted mobility and other risk factors for VTE:

- Member is at least 18 years of age **AND**
- Medical record documentation of a confirmed diagnosis of prophylaxis of venous thromboembolism (VTE) in adult patients hospitalized for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE **AND**
- Medical record documentation that the member has received Bevyxxa during hospitalization and will be continuing therapy following discharge from the hospital

QUANTITY LIMIT: 1 tablet per day (for all strengths)

AUTHORIZATION DURATION: 42 days

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

OZEMPIC (semaglutide)

Review: Ozempic is a GLP-1 agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Ozempic is a modified structure of Victoza, resulting in a higher resistance to degradation by DPP-4 and an increased affinity to albumin. As a result, Ozempic has a longer half-life than Victoza, extending to approximately 1 week compared to 13 hours for Victoza. Ozempic is available as 0.25mg-0.5mg/ injection and 1 mg/ injection pre-filled pens. The recommended starting dose of Ozempic is 0.25 mg given as a once-weekly subcutaneous injection for four weeks. After four weeks, the dose is increased to 0.5 mg once-weekly. If additional glycemic control is needed after four weeks on the 0.5 mg dose, the dosage may be increased to 1 mg once weekly.

Ozempic was studied as monotherapy, in combination with metformin, metformin and sulfonylureas, metformin and/or thiazolidinedione, and basal insulin in patients with T2DM. The efficacy of Ozempic was also compared to Januvia (sitagliptin), Bydureon (exenatide ER), Lantus (insulin glargine), and Trulicity. In patients with T2DM, Ozempic produced clinically relevant reductions from baseline in HbA1c compared to various treatment regimens and superior reductions in HbA1c compared to Bydureon and Trulicity. More weight loss (2-3kg more) was observed with Ozempic compared to Bydureon and Trulicity. SUSTAIN-6 evaluated the cardiovascular and other long-term outcomes of Ozempic in 3,297 T2DM patients at high cardiovascular risk. There was a statistically significant reduction in the primary composite endpoint (CV death, nonfatal MI, nonfatal stroke) with Ozempic compared to placebo. There was also a significant reduction in the expanded composite outcome (CV death, nonfatal MI, nonfatal stroke, revascularization, hospitalization for unstable angina or heart failure) with Ozempic. There was also a statistically lower incidence of nonfatal stroke with Ozempic. However, there was no significant difference in the rate of cardiovascular death between Ozempic and placebo.

Ozempic contains the same black box warning as other GLP-1 RAs (risk of thyroid C-cell tumors and contraindication for use in patients with a personal or family history of medullary thyroid carcinoma or Multiple Endocrine Neoplasia syndrome 2). Consistent with other GLP-1 RAs, warnings and precautions with Ozempic include risk of pancreatitis, risk of hypoglycemia with concomitant use of secretagogue or insulin, and monitoring of renal function in patients with renal impairment reporting severe adverse gastrointestinal reactions. Ozempic has an additional warning for increased risk in diabetic retinopathy complications. However, rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy and this has been well documented with the use of insulin. Patients with a history of diabetic retinopathy should be monitored for progression of diabetic retinopathy while using

Ozempic. The most common adverse reactions were mostly GI-related. Given the slow titration and slightly more discontinuations reported with Ozempic compared to Byetta and Trulicity, GI side effects might be more prominent with Ozempic, although these tend to be self-limiting. Ozempic should be discontinued at least 2 months before a planned pregnancy due to the long washout period for semaglutide. The safety and efficacy of Ozempic in pediatric patients have not been established. There are no dose adjustments recommended for renal or hepatic impairment.

Tanzeum will be discontinued by July 2018 due to declining sales. Thus, Ozempic will directly compete with the other two once-weekly GLP-1RAs: Trulicity and Bydureon. In clinical trials, Ozempic resulted it superior reductions in HbA1c compared to Bydureon and Trulicity. Additionally, Ozempic and Victoza are the only GLP-1 agonists with demonstrated CV risk reduction.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, and Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: Dr. Yarczower questioned the increased risk of diabetic retinopathy associated with Ozempic, but not other GLP-1 agonists. This is thought to be due to the rapid improvement in glucose which is seen with this product. A similar warning is included in the labeling of insulin products. This was reviewed by the FDA, but they felt the overall benefit of blood glucose reduction offsets the risk. Kimberly Clark made a motion to accept the recommendations as written. Keith Hunsicker seconded the motion. None were opposed.

Financial Discussion: The quantity limit was updated to include a limit specific to the 0.25mg/0.5 mg dose pen on 1.5 mL per 28 days (0.06 mL per day). Kimberly Clark made a motion to accept the recommendations as written. Dr. Dean Christian seconded the motion. None were opposed.

Outcome: For GHP Family, Ozempic will be a pharmacy benefit. Ozempic will be added to the Brand Tier of the GHP Family formulary. Ozempic will require step therapy with the following criteria:

- Medical record documentation of current utilization of metformin or intolerance to or contraindication to metformin

  QUANTITY LIMIT: 1 mg pen: 3 mL per 28 days (0.11 mL per day)
  0.25mg/0.5mg pen: 1.5 mL per 28 days (0.06 mL per day)

Additional Recommendations:

<u>Bydureon</u>

There are no changes recommended to formulary status at this time. However, the prior authorization criteria should be updated to the following:

- Medical record documentation of a diagnosis of Type 2 diabetes **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Victoza* **AND** Ozempic*

*Step therapy required

<u>Tanzeum</u>

There are no changes to formulary status at this time. Tanzeum should require a prior authorization for **<u>new starts only</u>** with the following criteria:

- Medical record documentation of a diagnosis of Type 2 diabetes **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Victoza* **AND** Ozempic*

*Step therapy required

Trulicity
There are no changes recommended to formulary status at this time. However, the prior authorization criteria should be updated to the following:

- Medical record documentation of a diagnosis of Type 2 diabetes **AND**
- Medical record documentation of patient age ≥ 18 years **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Victoza* **AND** Ozempic*

*Step therapy required

Adlyxin
There are no changes to formulary status at this time. However, the prior authorization criteria should be updated to the following:

- Medical record documentation of a diagnosis of Type 2 diabetes **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to metformin, Victoza*, **AND** Ozempic*

*Step therapy required

Byetta
There are no changed to formulary status at this time. However, the prior authorization criteria should be updated to the following:

- Medical record documentation of a diagnosis of Type 2 diabetes **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Victoza* **AND** Ozempic*

*Step therapy required

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

RITUXAN HYCELA (rituximab/hyaluronidase)

Review: Rituxan Hycela is a subcutaneously administered form of rituximab indicated for the treatment of chronic lymphocytic leukemia, follicular lymphoma, and diffuse large B-cell lymphoma. Rituxan Hycela is administered over 5 to 7 minutes at a fixed dose and schedule as determined by the patient's indication. Patients must receive at least 1 cycle of intravenously administered rituximab prior to receiving Rituxan Hycela. Rituxan Hycela follows the same mechanism of action as Rituxan, targeting the CD-20 antigen on the surface of pre-B and mature B-lymphocytes and inducing complement-dependent cytotoxicity. The hyaluronidase component of Rituxan Hycela increases the absorption rate of rituximab by temporarily increasing the permeability of subcutaneous tissue via depolymerization of hyaluronan. Rituxan Hycela carries a similar safety and efficacy profile as Rituxan. Rituxan Hycela was proven to be non-inferior to Rituxan in terms of pharmacokinetics, safety, and efficacy in clinical trials. While SQ and IV forms of rituximab are equivalent in terms of safety and efficacy, Rituxan Hycela provides favorable administration times compared to intravenously administered rituximab (5 to 7 minutes as opposed to several hours). NCCN recommends the use of Rituxan Hycela in place of IV rituximab after the initial IV rituximab infusion. Specialist feedback regarding the use of Rituxan Hycela is limited at this time due to lack of experience with the drug.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, and Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: The presented recommendations for CLL were updated to remove "Medical record documentation that member has been previously treated for CLL" and to add "or will receive" to the criterion regarding a cycle of intravenous Rituxan. Phil Krebs made a motion to accept the recommendations as amended. Tricia Heitzman seconded the motion. None were opposed.

Financial Discussion: There was discussion regarding the cost difference between Rituxan Hycela and Rituxan IV and how that can be variable as Rituxan IV dosing is weight based. Anastasia Mauger made a motion to accept the recommendations as written. Phil Krebs seconded the motion. None were opposed.

Outcome: For GHP Family, Rituxan Hycela will be covered as a medical benefit requiring prior authorization. The following criteria will apply:

Chronic Lymphocytic Leukemia (CLL)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of a diagnosis of Chronic Lymphocytic Leukemia (CLL) **AND**
- Medical record documentation that Rituxan Hycela is being given in combination with fludarabine and cyclophosphamide **AND**
- Medical record documentation that member has received and tolerated a minimum of one (1) cycle of intravenous rituximab (Rituxan)

Note: The FDA-approved dosage for CLL is 1,600mg/26,800units of Rituxan Hycela per dose.

Diffuse Large B-Cell Lymphoma (DLBCL)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of a diagnosis of Diffuse Large B-Cell Lymphoma (DLBCL) **AND**
- Medical record documentation that member has NOT received prior treatment for DLBCL **AND**
- Medical record documentation that Rituxan Hycela is being given in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or other anthracycline-based chemotherapy regimen **AND**
- Medical record documentation that member has received and tolerated a minimum of one (1) cycle of intravenous rituximab (Rituxan)

Note: The FDA-approved dosage for DLBCL is 1,400mg/23,400units of Rituxan Hycela per dose.

Follicular Lymphoma (FL)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of a diagnosis of Follicular Lymphoma (FL) **AND**
- Medical record documentation that member has received and tolerated a minimum of one (1) cycle of intravenous rituximab (Rituxan)

Note: The FDA-approved dosage for FL is 1,400mg/23,400units of Rituxan Hycela per dose. The schedule of Rituxan Hycela is specific to diagnosis.

Note: Rituxan Hycela has not been studied in and is not FDA-approved for non-malignant conditions. For this reason, Rituxan Hycela is considered off-label and investigational for use in non-malignant conditions and is not covered.

QUANTITY LIMIT: Authorizations should be entered by **GPID** with the following quantity limits (authorized strength will be dependent on diagnosis):

- Rituxan Hycela 1,400mg/23,400units: **4 vials (46.8mL) per 28 days**
- Rituxan Hycela 1,600mg/26,800units: **1 vial (13.4mL) per 28 days**

AUTHORIZATION DURATION: Initial approval will be for **6 months** or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional **12 months** or less if the reviewing provider feels it is medically appropriate and will require medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if patient experiences toxicity or worsening of disease. Requests exceeding the maximum FDA-approved treatment duration (listed below) will require the following:

- Medical record documentation of peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration.

Indication	Maximum Treatment Duration
Follicular Lymphoma (FL)	
Relapsed or Refractory	7 Weeks
Retreatment for Relapsed or Refractory	3 Weeks
Previously Untreated	21 Weeks (Seven 21-day cycles)
Non-progressing after first line CVP chemotherapy	2 Years (16 doses given once weekly for 4 weeks in 6-month intervals)
Diffuse Large B-Cell Lymphoma (DLBCL)	21 Weeks (Seven 21-day cycles)
Chronic Lymphocytic Leukemia (CLL)	5 Months (Five 28-day cycles)

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

CLASS REVIEW

ORAL ANTICOAGULANT CLASS REVIEW

Available oral anticoagulants

Medication	Generic	Manufacturer	How Supplied	FDA Approval Date
Coumadin	Warfarin, Jantoven	Bristol Myers Squibb	1mg, 2mg, 2.5mg, 3mg, 4mg, 5mg, 6mg, 7.5mg, 10mg tablets	June 8, 1954
Pradaxa	Dabigatran	Boehringer Ingelheim	75mg, 110mg, 150mg capsules	October 19, 2010
Xarelto	Rivaroxaban	Janssen Pharms	10mg, 15mg, 20mg tablets & starter pack for DVT/PE treatment	July 1, 2011
Eliquis	Apixaban	Bristol Myers Squibb	2.5mg & 5mg tablets	December 28, 2012
Savaysa	Edoxaban	Daiichi Sankyo Inc	15mg, 30mg, 60mg tablets	January 8, 2015

Review: There are four commercially available NOACs: Eliquis, Xarelto, Pradaxa, and Savaysa. Xarelto, Eliquis, and Savaysa are Factor Xa Inhibitors. Pradaxa is a direct thrombin inhibitor. Eliquis is available as 2.5 and 5 mg tablets. Xarelto is available as 10 mg, 15 mg, and 20 mg tablets. Xarelto is also available as a starter pack with 42, 15 mg tablets and 9, 20 mg tablets indicated for VTE treatment. Pradaxa is available as 75mg, 110 mg, and 150 mg capsules. Savaysa is available as 15mg, 30 mg, and 60 mg tablets. The dosages and length of therapy differ for each medication and with each indication. In general, Xarelto and Savaysa are taken once daily, except Xarelto is administered twice as a loading dose for VTE treatment. Most of the time Eliquis and Pradaxa are taken twice daily. However, Pradaxa is administered once daily for prophylaxis after a hip replacement. A parenteral anticoagulant is given for 5-10 days prior to Pradaxa or Savaysa for the treatment of VTE. A NOAC for prophylaxis of VTE after hip replacement is usually given for 28-38 days. A NOAC for prophylaxis of VTE after knee replacement is usually given for 10-14 days.

Eliquis, Xarelto, Pradaxa, Savaysa, and warfarin are indicated for the treatment of acute and recurrent VTE and to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation. Warfarin, Xarelto, and Eliquis are indicated for the prophylaxis of VTE in knee replacement. Warfarin, Xarelto, Eliquis, and Pradaxa are indicated for the prophylaxis of VTE in hip replacement. Only warfarin is indicated to reduce the risk of death, recurrent MI, and thromboembolic events after MI and for the prophylaxis and treatment of thrombotic complications associated with cardiac valve replacement.

In patients with atrial fibrillation Pradaxa was superior to warfarin in terms of stroke/systemic embolism prevention. Pradaxa had significantly lower rates of ischemic and hemorrhagic stroke compared to warfarin. Pradaxa was associated with higher rates of MI than warfarin. There was no difference between Pradaxa and warfarin for major bleeds, however Pradaxa had higher rates of GI bleeds. There was no difference in all-cause mortality between treatment groups.

In patients with atrial fibrillation, there was no difference in Xarelto and warfarin for the number of stroke/systemic embolisms. There was no difference in major bleeding between Xarelto and warfarin. However, Xarelto had higher rates of GI bleeds. There was no difference in all-cause mortality between groups.

In patients with atrial fibrillation, there was a significant reduction in stroke/systemic embolism in patients taking Eliquis compared to warfarin. Patients taking Eliquis also experienced less major bleeds. Eliquis use is associated with lower rates of all-cause mortality compared to warfarin. There was no difference in GI bleeds.

In patients with atrial fibrillation, there was no difference between Savaysa and warfarin in time to first stroke. Patients who were administered Savaysa had lower rates of major bleeds. Savaysa had higher rates of GI bleeds.

For VTE treatment, there was no difference between Pradaxa and warfarin for recurrent symptomatic VTE and related death. Pradaxa was superior to warfarin for major and clinically relevant non-major bleeds. Pradaxa also had a lower incidence of any bleed when compared to warfarin. However, there was a trend toward a higher incidence of GI hemorrhages with Pradaxa.

For VTE treatment, there was no difference between Xarelto and warfarin for symptomatic recurrent VTE. There was no difference in a first major bleed or clinically relevant nonmajor bleed. In the PE trial, there was significantly lower incidences of major bleeds observed with Xarelto compared to warfarin.

For VTE treatment, there was no difference between Eliquis and warfarin for recurrent symptomatic VTE and related death. Eliquis had a lower incidence of major and clinical relevant nonmajor bleeds when compared to warfarin.

For VTE treatment, there was no difference between Savaysa and warfarin for recurrent symptomatic VTE and related death. Savaysa had a lower incidence of clinically relevant major and nonmajor bleeds. However, there was no difference between treatment groups in terms of major bleeds.

For Ortho VTE prophylaxis, there was no significant different in total venous thromboembolic event and all-cause mortality when comparing Pradaxa to enoxaparin. Bleeding occurred more in the dabigatran group compared to enoxaparin.

For Ortho VTE prophylaxis, Xarelto had lower incidence of composite outcome (any DVT, nonfatal PE, or death from any cause) compared to enoxaparin. Major VTE occurred less in the Xarelto group. There was no difference in terms of bleeding when comparing Xarelto to enoxaparin.
For Ortho prophylaxis, Eliquis had a lower incidence of composite outcome (asymptomatic/symptomatic DVT, non-fatal PE, and all-cause death) compared to enoxaparin. There was no difference between Eliquis and enoxaparin in terms of major and clinically relevant non-major bleeds.

All NOACs carry warnings for bleeds and prosthetic heart valves. All NOACs have a black box warning for spinal/epidural hematoma and premature discontinuation increases the risk of thrombotic events. The most common adverse reaction for all NOACs is bleeding. Pradaxa, Xarelto, Savaysa are pregnancy category C. Eliquis is pregnancy category B. Warfarin is contraindicated in pregnancy, except if the patient has mechanical heart valves. All agents have dosing recommendations based on renal function (separated by indication), except warfarin. Savaysa has a unique recommendation in patients with atrial fibrillation, it should not be used in patients with CrCl > 95 ml/min due to increased risk of ischemic stroke. Xarelto and Savaysa should be avoided in patients with moderate or severe hepatic impairment. Eliquis should be avoided in severe hepatic impairment. Pradaxa does not require dose adjustment with hepatic impairment.

Geisinger completed a historical data pull of the previous 2 years. In patients with atrial fibrillation, there was no significant difference in bleeding and clotting events when comparing rivaroxaban to apixaban. There was a lower utilization of dabigatran, therefore it was not able to be compared.

For patients with a history of stroke/TIA and atrial fibrillation, the CHEST guidelines (9th edition) recommend dabigatran 150 mg BID over warfarin. For patients with VTE without cancer, the CHEST guidelines (10th edition) recommend new oral anticoagulants over warfarin. The ACC/AHA 2014 guidelines recommend warfarin (level A), dabigatran (level B), rivaroxaban (level B), apixaban (level B) for patients with atrial fibrillation (with history of stroke/TIA, or CHADSVASc score ≥ 2). The American Heart Association (2014) recommends the following for prevention of recurrent stroke in patients with nonvalvular AF (paroxysmal/permanent): warfarin (Class I; Level of Evidence A), apixaban (Class I; Level of Evidence A), and dabigatran (Class I; Level of Evidence B). Rivaroxaban is a reasonable option for prevention of recurrent stroke (Class IIa, Level of Evidence B).

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, and Other Considerations and a Financial Review Based on Cost Analysis were presented.

Formulary recommendations based on clinical review

Medication	Current Policy	Recommendations
Eliquis	No current criteria.	Eliquis is a pharmacy benefit and should remain on the formulary. No changes recommended at this time.
Xarelto	No current criteria.	Xarelto is a pharmacy benefit and should remain on the formulary. No changes recommended at this time.
Pradaxa	Prior authorization: • Medical record documentation of treatment to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation OR Medical record documentation of use for the treatment of deep vein thrombosis, pulmonary embolism, or for the reduction in the risk of recurrence of deep vein thrombosis and/or pulmonary embolism OR Medical record documentation of use for the prophylaxis of DVT and PE in patients who have undergone hip replacement surgery AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Eliquis AND Xarelto	Pradaxa is a pharmacy benefit and should remain on the formulary. Pradaxa will require step therapy. • Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Eliquis **OR** Xarelto
Savaysa	Non-formulary: • Medical record documentation of a diagnosis of stroke and systemic embolism risk reduction in patients with non-valvular atrial fibrillation **OR** • Medical record documentation that Savaysa is being used for treatment of deep vein thrombosis and/or pulmonary embolism AND one of the following:	Savaysa is a pharmacy benefit and should remain non-formulary. No changes to policy recommended at this time.

	o Patient weight greater than 60 kg **OR** o Patient weight less than or equal to 60 kg AND Savaysa being dosed as 30 mg per day **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Eliquis **AND** Xarelto	

Clinical Discussion: A committee member questioned the rationale for requiring a step through Eliquis and Xarelto. This is required for a multitude of reasons: renal implications (rivaroxaban can now be used through dialysis), less GI bleeding risk with the Xa inhibitors, and the fact that the Xa inhibitors have more FDA approved indications. Todd Sponenberg made a motion to accept the recommendations as written. Kimberly Clark seconded the motion. None were opposed.

Formulary Recommendations Based on Cost Review

Medication	Current Formulary Status	Recommendations
Eliquis	Brand Tier	No changes recommended to formulary status at this time. Quantity Limit: 2.5mg tablets: 2 tablets per day 5 mg tablets: 4 tablets per day
Xarelto	Brand Tier	No changes recommended to formulary status at this time. Quantity Limit: 10 mg & 20 mg tablet: 1 tablet per day 15 mg tablet: 2 tablets per day
Pradaxa	Brand Tier	No changes recommended to formulary status at this time. Quantity Limit: 2 capsules per day
Savaysa	Non-formulary	No changes recommended to formulary status at this time. Quantity Limit: 1 tablet per day

Financial Discussion: No comments or questions. Kimberly Clark made a motion to accept the recommendations as written. Dr. Dean Christian seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

FAST FACTS

SUTENT (sunitinib malate)

Updated Indication: Sutent, a kinase inhibitor, is indicated for adjuvant treatment of adult patients at high risk of recurrent renal cell carcinoma, RCC, following nephrectomy.

Previous Indication:

- Treatment of gastrointestinal stromal tumor (GIST) after disease progression on or intolerance to imatinib
- Treatment of advanced renal cell carcinoma (RCC)
- Treatment of progressive, well-differentiated pancreatic neuroendocrine tumors (pNET) in patients with unresectable locally advanced or metastatic disease

Recommendation: No changes are recommended to the formulary placement of Sutent at this time. It is recommended a quantity limit of 1 capsule per day, 30 days per fill for all strengths be added. It is recommended that the Sutent prior authorization criteria be updated to ensure a smoother review process:

Gastrointestinal Stromal Tumor (GIST)

- Prescription is written by an oncologist **OR** gastroenterologist **AND**
- Medical record documentation of a diagnosis of gastrointestinal stromal tumor (GIST) **AND**
- Medical record documentation of therapeutic failure on, contraindication to, or intolerance to imatinib (Gleevec*)

Pancreatic Neuroendocrine Tumors (pNET)

- Prescription is written by an oncologist **AND**
- Medical record documentation of a diagnosis of progressive, well-differentiated pancreatic neuroendocrine tumors (pNET) in patients with unresectable locally advanced or metastatic disease

Advanced Renal Cell Carcinoma (RCC)

- Prescription is written by an oncologist **AND**
- Medical record documentation of a diagnosis of advanced renal cell carcinoma

Renal Cell Carcinoma, adjuvant treatment:

- Prescription is written by an oncologist **AND**
- Medical record documentation of adult patient at high risk of recurrent renal cell carcinoma, RCC, following nephrectomy

  NOTE: In clinical trials, high risk disease was defined as a score of greater than or equal to T3 on the University of California Los Angeles Integrated Staging System and/or node positive tumors.

No changes to authorization duration to the applicable policies are recommended at this time.

Discussion: It was recommended that a note be added to define high risk of recurrence for the renal cell carcinoma indication.

Outcome: Anastasia Mauger made a motion to accept the recommendations as amended. Todd Sponenberg seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

LILETTA (levonorgestrel-releasing intrauterine system)

Updated Indication: Liletta is a sterile, levonorgestrel-releasing intrauterine system indicated for prevention of pregnancy for up to 4 years.

Previous Indication*:* Liletta is a sterile, levonorgestrel-releasing intrauterine system indicated for prevention of pregnancy for up to 3 years.

Recommendation: Liletta is currently available via the medical benefit and does not require prior authorization. No changes are recommended at this time.

Discussion: No questions or comments.

Outcome: Tricia Heitzman made a motion to accept the recommendations as written. Phil Krebs seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

CUBICIN/CUBICIN RF (daptomycin)

Updated Indication: Cubicin and Cubicin RF are now indicated for the treatment of *Staphylococcus aureus* bloodstream infections (bacteremia) in pediatric patients (1 to 17 years of age).

Previous Indication: Cubicin and Cubicin RF were indicated for complicated skin and skin structure infections (cSSSI) in adult and pediatric patients (1 to 17 years of age) and *Staphylococcus aureus* bloodstream infections (bacteremia), in adult patients including those with right-sided infective endocarditis.

Recommendation: Cubicin, Cubicin RF, and daptomycin are medical benefit drugs not requiring prior authorization for GHP Family members. No changes are recommended at this time.

Discussion: No questions or comments.

Outcome: Phil Krebs made a motion to accept the recommendations as written. Kimberly Clark seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

RAPIVAB (peramivir)

Updated Indication: Rapivab is an influenza virus neuraminidase inhibitor indicated for the treatment of acute uncomplicated influenza in patients 2 years and older who have been symptomatic for no more than two days.

Previous Indication: Rapivab was indicated in patients 18 years and older.

Recommendation: Rapivab is a medical benefit and does not require prior authorization. No changes are recommended to the formulary placement of Rapivab at this time.

Discussion: No questions or comments.

Outcome: Kimberly Clark made a motion to accept the recommendations as presented. Kelli Hunsicker seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

CABOMETYX (cabozantinib)

Updated Indication: Cabometyx is a kinase inhibitor indicated for the treatment of patients with advanced renal cell carcinoma (RCC).

Previous Indication: Cabometyx is a kinase inhibitor indicated for the treatment of patients with advanced renal cell carcinoma (RCC) who have received prior antiangiogenic therapy.

Recommendation: There are no changes recommended formulary placement or quantity limits of Cabometyx recommended at this time. It is recommended that the following stricken through prior authorization criteria be removed to reflect the new indication:

- Prescription written by an oncologist **AND**
- Medical record documentation of use as a single agent for relapse or for surgically unresectable advanced or metastatic renal cell carcinoma ~~with predominant clear-cell histology~~ **AND**
- ~~Medical record documentation of a therapeutic failure on or intolerance to one prior anti-angiogenic therapy, including, but not limited to, Sutent (sunitinib), Votrient (pazopanib), Inlyta (axitinib), Nexavar (sorafenib), Avastin (bevacizumab), Afinitor (everolimus), or Torisel (temsirolimus) AND~~
- If the requested dose is 80 mg daily: Medical record documentation that the patient is using Cabometyx in combination with a strong CYP3A4 inducer, including but not limited to, rifampin, phenytoin, carbamazepine, phenobarbital, rifabutin, rifapentine, and St. John's Wort.

Discussion: Initial recommendations included an update to the prior failure criteria to reflect the NCCN recommendations. Cabometyx carries a category 2A recommendation for use as first line therapy, while it carries a category 1 recommendation for subsequent therapy. This change would have limited members to failure of a category 1 recommended first line agent if they were considered favorable risk and would have included a reference of category 1 therapies/risk determinants. It was decided to cover the product more broadly by sticking with the FDA approved indication, rather than the more limited NCCN approval.

Outcome: Todd Sponenberg made a motion to accept the recommendations as presented. Keith Hunsicker seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

SOMATULINE DEPOT (LANREOTIDE)

Updated Indication: Somatuline Depot, a somatostatin analog, is indicated for the treatment of adults with carcinoid syndrome; when used, it reduces the frequency of short-acting somatostatin analog rescue therapy.

Previous Indication:

- Long-term treatment of acromegalic patients who have had an inadequate response to or cannot be treated with surgery and/or radiotherapy
- Treatment of adult patients with unresectable, well- or moderately-differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival.

Recommendation: No changes recommended

Discussion: No questions or comments.

Outcome: Tricia Heitzman made a motion to accept the recommendations as written. Kimberly Clark seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

VICTOZA (liraglutide)

Updated Indication: Victoza is now indicated to reduce the risk of major adverse cardiovascular events, which include cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke, in adults with type 2 diabetes mellitus (T2DM) and established cardiovascular disease.

Previous Indication*:* Victoza was approved as an adjunct to diet and exercise to improve glycemic control in adults with T2DM.

Recommendation: No changes are recommended to the formulary placement of Victoza at this time.

Discussion: No questions or comments.

Outcome: Keith Hunsicker made a motion to accept the recommendations as written. Kimberly Clark seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

GAZYVA (obinutuzumab)

Updated Indication: Gazyva is now indicated, in combination with chemotherapy followed by Gazyva monotherapy in patients achieving at least a partial remission, for the treatment of adult patients with previously untreated stage II bulky, III or IV follicular lymphoma.

Previous Indication:

- in combination with chlorambucil, for the treatment of patients with previously untreated chronic lymphocytic leukemia.
- in combination with bendamustine followed by Gazyva monotherapy, for the treatment of patients with follicular lymphoma who relapsed after, or are refractory to, a rituximab-containing regimen.

Recommendation: Gazyva is currently covered as a medical benefit requiring prior authorization. It is recommended that the Gazyva prior authorization criteria for follicular lymphoma are updated to reflect the following changes to MBP 113.0

Follicular Lymphoma

• Medical record documentation of a diagnosis of follicular lymphoma AND

- For first line therapy:
  - Medical record documentation of previously untreated stage II bulky, III or IV follicular lymphoma AND
  - Medical record documentation that Gazyva will be used in combination with chemotherapy
  - OR
  - Medical record documentation that the patient has achieved at least a partial remission of stage II bulky, III, or IV follicular lymphoma if previously treated with at least 6 cycles of Gazyva in combination with chemotherapy AND
  - Medical record documentation that Gazyva will be used as monotherapy

- For second line or subsequent therapy:
  - Medical record documentation that the patient has relapsed after, or is refractory to, a rituximab-containing regimen. AND
  - Medical record documentation that Gazyva is being used in combination with bendamustine
  - OR
  - Medical record documentation that the patient achieved a complete response, partial response, or has stable disease after at least 6 cycles of Gazyva in combination with bendamustine AND
  - Medical record documentation that Gazyva will be used as monotherapy.

AUTHORIZATION DURATION for follicular lymphoma: Initial approval will be 6 months for this indication. The following criteria should apply to reauthorization requests for Gazyva:

- Medical record documentation that the patient achieved a complete response, partial response, or has stable disease after 6 cycles of Gazyva + bendamustine therapy OR after 6 cycles of Gazyva + chemotherapy **AND**

- Documentation that Gazyva will be used as monotherapy.

Subsequent authorization duration should be 24 months as data does not extend past this point.

*Note: In clinical trials for the treatment of stage II bulky, III or IV follicular lymphoma chemotherapy was defined as: CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone); CVP (cyclophosphamide, vincristine and prednisone); or bendamustine

Discussion: No questions or comments.

Outcome: Todd Sponenberg made a motion to accept the recommendations as written. Kelli Hunsicker seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

TIVICAY (dolutegravir)

Updated Indication: Tivicay is indicated in combination with dipivefrine as a complete regimen for the treatment of HIV-1 infection in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen for at least 6 months with no history of treatment failure or known substitutions associated with resistance to either antiretroviral agent.

Previous Indication: In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients weighing at least 30 kg.

Recommendation: Tivicay is available without restrictions for GHP Family members on the brand preferred tier with a quantity limit. No changes are recommended at this time.

Discussion: No questions or comments.

Outcome: Todd Sponenberg made a motion to accept the recommendations as presented. Tricia Heitzman seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

FASLODEX (fulvestrant)

Updated Indication: Faslodex is indicated for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer in combination with palbociclib or abemaciclib in women with disease progression after endocrine therapy.

Previous Indication: Treatment of HR-positive, HER2-negative advanced or metastatic breast cancer in combination with palbociclib in women with disease progression after endocrine therapy.

Other unchanged indications:

- Treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer in postmenopausal women not previously treated with endocrine therapy.
- Treatment of HR-positive advanced breast cancer in postmenopausal women with disease progression following endocrine therapy.

Recommendation: Faslodex is available as a medical benefit with no restrictions for GHP Family members. No changes are recommended at this time.

Discussion: No questions or comments.

Outcome: Kevin Szczecina made a motion to accept the recommendations as presented. Tricia Heitzman seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

SPRYCEL (dasatinib)

Updated Indication: Sprycel is now indicated for the treatment of pediatric patients with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase.

Previous Indication:

- Newly diagnosed adults with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase.
- Adults with chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib.
- Adults with Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) with resistance or intolerance to prior therapy.

Recommendation: There are no changes to formulary status recommended at this time. There are no age restrictions present in the current prior authorization criteria, however it is recommended to update the Sprycel policy to the following:

- Prescription must be written by a hematologist or oncologist **AND**
- Medical record documentation of the use of Sprycel to treat newly diagnosed Chronic Phase Ph+ CML **OR**
- Medical record documentation of the use of Sprycel to treat chronic, accelerated, or myeloid/lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib **OR**
- Medical record documentation of use of Sprycel to treat Ph+ ALL with resistance or intolerance to prior therapy

Discussion: No questions or comments.

Outcome: Tricia Heitzman made a motion to accept the recommendations as presented. Kevin Szczecina seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

TRIUMEQ (abacavir, dolutegravir, and lamivudine)

Updated Indication: Triumeq is indicated for the treatment of HIV-1 infection in adults and in pediatric patients weighing at least 40 kg. Triumeq is still not recommended alone in patients with resistance-associated integrase substitutions or clinically suspected integrase strand transfer inhibitor resistance because the dose of dolutegravir is insufficient in these subpopulations.

Previous Indication: For treatment of HIV-1 infection in adults.

Recommendation: Triumeq is available without restrictions for GHP Family members on the brand preferred tier with a quantity limit. No changes are recommended at this time.

Discussion: No questions or comments.

Outcome: Keith Hunsicker made a motion to accept the recommendations as presented. Todd Sponenberg seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

BOSULIF (bosutinib)

Updated Indication: Bosulif is indicated for the treatment of newly-diagnosed chronic phase Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML)

Note: This indication has been granted accelerated FDA approval based on molecular and cytogenic response rates. Continued approval may be dependent on verification and confirmation of clinical benefit in an ongoing long-term follow up trial.

Previous Indication: treatment of chronic, accelerated, or blast phase Ph+ CML with resistance or intolerance to prior therapy.

Updated Product Availability: 400 mg tablet

Previously available in 100 mg or 500 mg tablets.

Recommendation: There are no changes recommended to the formulary status or authorization duration at this time. It is recommended that the underlined prior authorization criteria are added to the existing policy and quantity limits are updated as follows:

- Must be prescribed by a hematologist/oncologist **AND**
- <u>Medical record documentation of use of Bosulif to treat newly-diagnosed chronic phase Ph+ chronic myelogenous leukemia **OR**</u>
- Medical record documentation of chronic, accelerated, or blast phase Ph+ chronic myelogenous leukemia **AND** medical record documentation of therapeutic failure on, intolerance to, or contraindication to one prior therapy (imatinib, Sprycel, Tasigna)

QUANTITY LIMIT UPDATES:

- 100 mg tablets – 3 tablets per day
- 400 mg tablets – 1 tablet per day
- 500 mg tablets – 1 tablet per day

Discussion: No questions or comments.

Outcome: Kelli Hunsicker made a motion to accept the recommendations as presented. Keith Hunsicker seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

ZELBORAF (vemurafenib)

Updated Indication: Zelboraf (vemurafenib) is indicated for the treatment of patients with Erdheim-Chester Disease (ECD) with BRAF V600 mutation. This is the first FDA-approved treatment for ECD.

Previous Indication: treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test.

Recommendation: There are no changes to formulary status recommended at this time for all lines of business. It is recommended that the Zelboraf policies be updated to reflect the new indication as underlined below:

- Prescription written by an oncologist or dermatologist **AND**
- Medical record documentation of unresectable or metastatic melanoma **OR**
- Medical record documentation of Erdheim-Chester (ECD) **AND**
- Medical record documentation of an FDA-approved test documenting the presence of the BRAF V600E mutation

  NOTE: The FDA-approved test is the Cobas® 4800 BRAF V600 Mutation Test

  QUANTITY LIMIT: 240 tablets per 30 days

  AUTHORIZATION DURATION: Each treatment period will be defined as twelve (12) months. Re-review will occur every twelve (12) months. Zelboraf will no longer be covered if there is medical record documentation of disease progression.

Discussion: No questions or comments.

Outcome: Keith Hunsicker made a motion to accept the recommendations as presented. Kevin Szczecina seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

ALECENSA (alectinib)

Updated Indication: Alecensa is a kinase inhibitor indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test.

Previous Indication: treatment of patients who had progressed on or were intolerant to crizotinib.

Recommendation: No changes are recommended to existing formulary status, quantity limits, or authorization durations. It is recommended that Alecensa policies (362.0, 1289.0F, 453.0D) for all the lines of business are updated as follows:

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of a diagnosis of ALK-positive, metastatic non-small cell lung cancer ~~**AND**~~
- ~~Medical record documentation that Alecensa is being used as subsequent therapy after documented failure on, intolerance to, or contraindication to Xalkori (crizotinib) therapy **AND**~~

Discussion: No questions or comments.

Outcome: Kelli Hunsicker made a motion to accept the recommendations as presented. Tricia Heitzman seconded the motion. None were opposed.

Additional Recommendations: It is recommended that the following language is added to Xalkori and Zykadia policies for all lines of business:

- When requested for first-line treatment of ALK-positive, metastatic non-small cell lung cancer: Medical record documentation of therapeutic failure on, intolerance to or contraindication to Alecensa if clinically appropriate

Discussion: No questions or comments.

Outcome: Kelli Hunsicker made a motion to accept the recommendations as presented. Aubrielle Prater seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

VIMPAT (lacosamide)

Updated Indication: Vimpat is indicated for the treatment of partial-onset seizures in patients 4 years of age and older. As the safety of Vimpat injection has not been established in pediatric patients, Vimpat injection is indicated for the treatment of partial-onset seizures in adult patients (17 years of age and older).

Previous Indication: Vimpat is indicated as monotherapy or adjunctive therapy in patients with partial-onset seizures. Vimpat injection is indicated as short-term replacement when oral administration is not feasible.

Recommendation: There are no changes recommended to the formulary status of Vimpat at this time. It is recommended that the prior authorization criteria and formulary alternatives are updated to account for the new age approval:

- Medical record documentation of partial-onset seizures in patients ≥4 years old **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to 3 formulary alternatives

Formulary alternatives:

- For patients > 4 years of age: carbamazepine, gabapentin, lamotrigine IR, levetiracetam IR, oxcarbazepine, phenobarbital, phenytoin, topiramate IR, topiramate ER*
- Additional formulary alternatives for patients over certain ages:
  - Divalproex (10+), levetiracetam ER (12+), Gabitril (12+), lamotrigine ER (13+), felbamate (14+), zonisamide (16+), and Lyrica (18+)
    (*Prior authorization required)

Discussion: No questions or comments.

Outcome: Kevin Szczecina made a motion to accept the recommendations as presented. Todd Sponenberg seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

ISENTRESS (raltegravir)

Updated Indication: Isentress is indicated for the treatment of HIV-1 infection in combination with other antiretroviral agents in pediatric patients weighing at least 2 kg.

Previous Indication: For treatment of HIV-1 infection in combination with other antiretroviral agents in adult patients and pediatric patients 4 weeks and older.

Recommendation: Isentress is available without restrictions for GHP Family members on the brand preferred tier with a quantity limit. No changes are recommended at this time.

Discussion: No questions or comments.

Outcome: Kevin Szczecina made a motion to accept the recommendations as presented. Tricia Heitzman seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

UPDATES

ENTRESTO (sacubitril/valsartan)

Recommendation: Based on feedback from Geisinger Cardiology, criteria for Entresto included a requirement that there be medical record documentation of an LVEF of ≤ 35%, which matched the amended trial inclusion criteria. Pharmacists at Pennsylvania Department of Human Services (DHS) questioned this requirement due to studies that show a benefit with beginning therapy in those with an LVEF of ≤ 40%. After consulting with Nathan Sauers, Clinical Pharmacist at Geisinger Medical Center, it is now recommended that the LVEF required for treatment with Entresto be raised to ≤ 40%. Additionally, GHP data shows that members with a diagnosis of heart failure who are compliant to Entresto have lower costs of care than those who are not compliant.

Discussion: No comments or questions.

Outcome: Aubrielle Prater made a motion to accept the presented recommendations. Keith Hunsicker seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

ORKAMBI (lumacaftor/ivacaftor) AND KALYDECO (ivacaftor)

Recommendation: Currently, the initial authorization for Orkambi and Kalydeco is given for two months, but Geisinger's Cystic Fibrosis (CF) Clinic schedules a follow-up appointment at two months. To better align with Geisinger's CF Clinic, it is recommended that the existing initial authorization be changed to four months for all lines of business.

Discussion: No questions or comments.

Outcome: Tricia Heitzman made a motion to accept the presented recommendations. Kevin Szczecina seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

HEPATITIS C TREATMENT UPDATE

Review: The American Academy for the Study of Liver Disease (AASLD) recommends and Pennsylvania Department of Human Services required the following changes to treatment guidelines:

- Persons with Hepatitis C should be evaluated for other conditions that may accelerate liver fibrosis, including Hepatitis B Virus (HBV) and Human Immunodeficiency Virus – 1 (HIV) infections
- Removal of all references to specific prescribers of Hepatitis C Agents.

Recommendations: It is recommended that the GHP Family policies for Technivie, Viekira Pak, Daklinza, Epclusa, Harvoni, Sovaldi, Vosevi, Olysio, Zepatier, Mavyret and Direct Acting Antivirals be updated as follows:

- Remove "Is prescribed by a board-certified gastroenterology, hepatology, infectious disease or transplant specialist"

- Add “Has documented completion of Hepatitis B immunization series or Hepatitis B screening (sAb/sAg and cAb/cAg) AND quantitative HBV DNA if positive for Hepatitis B sAg or cAb or cAg AND if there is detectable HBV DNA will be treated for Hepatitis B or if negative for hepatitis B sAb is being vaccinated against Hepatitis B **AND** has a documented HIV screening (HIV Ag/Ab) and if confirmed positive by HIV-1/HIV-2 differentiation immunoassay is being treated for HIV or is not being treated for HIV and there is medical record documentation of the rationale for not being treated”

Discussion: No questions or comments.

Outcome: Aubrielle Prater made a motion to accept the presented recommendations. Anastasia Mauger seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

2018 GHP FAMILY FORMULARY

Review: The HealthChoices contract requires annual approval of the Managed Care Organizations Pharmacy Formulary by the Plan’s Pharmacy and Therapeutics Committee.

Recommendations: It is recommended that the 2018 GHP Family Formulary be approved by the Committee.

Discussion: No questions or comments.

Outcome: Aubrielle Prater made a motion to accept the presented recommendations. Tricia Heitizman seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

GHP FAMILY FORMULARY UPDATE

Recommendations: It is recommended that pentazocine 50 mg/naloxone 0.5 mg tablets be added to the GHP Family Formulary on the generic tier with a quantity limit of three (3) tablets per day.

Discussion: No questions or comments.

Outcome: Aubrielle Prater made a motion to accept the presented recommendations. Keith Hunsicker seconded the motion. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

RESULTS OF ELECTRONIC VOTE

SHINGRIX (zoster vaccine recombinant, adjuvanted)

The following recommendations were approved electronically by the P&T Committee on December 28, 2017 with 25 votes of approval.

Review: Shingrix is indicated for prevention of herpes zoster (shingles) in adults aged 50 years and older. In clinical trials Shingrix demonstrated efficacy against shingles greater than 90% across all age groups, as well as sustained efficacy over a follow-up period of 4 years. This is in comparison to Zostavax which has an overall efficacy rate of 51%, and only 18% in the cohort of patients over the age of 80 years. Shingrix has been recommended by ACIP as the preferred zoster vaccine for adults aged 50 years and older. It is recommended for patients who are vaccine naïve as well as patients who have previously received the Zostavax vaccine.

Outcome: Shingrix will be covered as a preventive medical benefit for members age 50 years and older. Shingrix will be limited to coverage of one vaccine course (two vaccine series) per lifetime.

Additionally, it is recommended that a limit of once vaccine per lifetime is added to Zostavax. Continued coverage of Zostavax will be evaluated at a later date, pending recommendations from the CDC.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

Meeting adjourned at 5:01 pm.

Future Scheduled Meetings
Tuesday, March 20, 2018 at 1:00 HCN3A & 3B Conference room

All of these meetings are scheduled to be held at Geisinger Health Plan, Hughes Center North and South Buildings; 108 Woodbine Lane; Danville, PA 17821.