Proposed Formulary Changes

Kentucky Medicaid
Effective 7/1/2017

Table 1: Summary of Medicaid PDL proposed designation as **Preferred**

Drug Name	Ingredients	Dosage Form	Strength(s)	Notes	P&T Decision
Neulasta Onpro	pegfilgastrim	Prefilled syringe with on-body injector	6 mg/0.6 mL	Medical benefit only	Approved

Table 2: Summary of Medicaid PDL proposed designation as **Non-Preferred**

Drug Name	Ingredients	Dosage Form	Strength(s)	Notes	P&T Decision
Adlyxin	Lixisenatide	Solution for subcutaneous infusion	50 mcg/mL 100 mcg/mL	Preferred agents: Victoza Trulicity	Approved
Cuvitru	Immune globulin	Solution for subcutaneous infusion	1 g/5 mL 2 g/10 mL 4 g/20 mL 8 g/40 mL	Medical benefit only	Approved
Exondys 51	Eteplirsen	Solution	100 mg/2 mL 500 mg/10 mL	Medical benefit only	Approved
Nexium	Esomeprazole	Capsule	20 mg 40 mg	Prescription strength formulations only.	Approved
Prevacid	Lansoprazole	Capsule	15 mg 30 mg	Prescription strength formulations only.	Approved
Xiidra	Lifitegrast	Ophthalmic solution	5% (50 mg/mL)	Preferred agent: 30 day trial of OTC artificial tears used QID routinely	Approved

New Drugs Reviewed Q1 2017

Adlyxin (lixisenatide)

Therapeutic Class: GLP-1 Agonist
FDA indication: Type 2 Diabetes Mellitus
Formulary Recommendations: Non-preferred
Rationale: Established class of drugs. In studies reduction in A1C and weight appears to be inferior to other GLP-1 agonist. In addition, it requires daily administration versus other weekly GLP-1 agonists. Another consideration is the release of Soliqua, Sanofi's lixisenatide and insulin glargine combination product which may be a more cost-effective utilization of the lixisenatide agent.
P&T Decision: Approved

Cuvitru (Immune Globulin Subcutaneous)

Therapeutic Class: Blood product derivative: Immune Globulin
FDA indication: Primary Humoral Immunodeficiency Syndrome
Formulary Recommendations: Non-preferred, medical benefit
Rationale: Similar product, Hizentra, (indication, approval in age 2, route of administration, AWP) is currently a preferred product.
P&T Decision: Approved

Exondys 51 (eteplirsen)

Therapeutic Class: Antisense oligonucleoside
FDA indication: Duchenne Muscular Dystrophy (DMD)
Formulary Recommendation: Non-preferred, medical benefit
Rationale: Provisional approval by FDA with ongoing studies requested. Approval based on a small study with questionable clinical significance and more data is necessary to draw conclusions on clinical outcomes.
P&T Decision: Approved

Xiidra (lifitegrast)

Therapeutic Class: Lymphocyte function-associated antigen 1 (LFA-1) antagonist
FDA indication: Dry eye disease
Formulary Recommendation: Non-Preferred
Rationale: OTC artificial tears are appropriate first-line therapy and Xiidra should be reserved for second line and refractory dry eye disease not relieved by OTC artificial tears.
P&T Decision: Approved

Pharmacy &Therapeutics Committee Summary Review
Adlyxin® (lixisenatide) – Sanofi Aventis

Prepared by: Jacob Coleman PharmD Candidate 2017

Presentation Date: 3/30/2017

Therapeutic Class: GLP-1 Agonist

FDA Approval Date: 07/27/16

FDA Indication: Type 2 diabetes mellitus

Comparable Formulary Products: Victoza (liraglutide), Trulicity (dulaglutide)

Proposed Designation & Rationale

Recommendation: Non-Preferred

- Criteria for use: 30 day trial of: Victoza or Trulicity (which require a 30 day trial of metformin or metformin ER)
- Approval duration: 1 year

Clinical Implications/Place in Therapy:
Lixisenatide is the newest addition to the GLP-1 agonist family of antidiabetic agents. GLP-1 agonists are typically prescribed following a trial of metformin. Metformin is first-line and is an inexpensive oral option for patients with type 2 diabetes. Advantages to utilizing Adlyxin include relatively lower cost and ease of administration compared with other GLP-1 agonists. Additionally, Adlyxin appears to have better safety profile compared with other agents and has not been associated with the increased risk of thyroid cancer reported with liraglutide use. Disadvantages include apparent inferior reductions in HbA1c and body weight compared with other GLP-1 agonists (especially liraglutide), making Adlyxin a less favorable option. Adlyxin requires daily dosing while dulaglutide and exenatide are available as once weekly injections. Overall, there is a lack of clear benefit in adding Adlyxin as a formulary product.

Another consideration is the release of Soliqua, Sanofi's lixisenatide and insulin glargine combination product. This new product is priced at the same AWP as Adlyxin and may be a more cost-effective utilization of the lixisenatide agent

Clinical Pharmacology: Lixisenatide is a glucagon-like peptide-1 agonist. It increases glucose-dependent insulin release, decreases glucagon secretion, and slows gastric emptying.

Notable Pharmacokinetics:

- Time to peak concentration: 1 to 3.5 hours
- Absorption rate is not altered based on injection site (abdomen, thigh, or arm)
- Volume of distribution: ~100 L
- Half-life: 3 hours
- Increased area under the curve (34%-124%) in patients with renal impairment
- No dosage adjustment required in renal or hepatic impairment; however, use is not recommended in patients with end stage renal disease

Efficacy:[2-5]

Table 1. Lixisenatide as monotherapy

Trial Design	Randomized, double-blind, placebo-controlled 12-week clinical trial		
Population	Patients with Type 2 diabetes mellitus inadequately controlled with diet and exercise alone		
Groups	Placebo (n=122)	Lixisenatide once-daily 2-step (10 mcg for 1 week, 15 mcg for 1 week, and then 20 mcg; n = 120)	Lixisenatide once-daily 1-step (10 mcg for 2 weeks and then 20 mcg; n = 119)
Outcomes	Primary: Reduction in HbA1c from baseline to week 12 Secondary: Percentage of patients achieving an HbA1c <7.0% or ≤6.5%; change in fasting plasma glucose, 2-hour post prandial glucose, glucose excursions, and body weight		
Results			

Outcome	Placebo	Lixisenatide two-step	Lixisenatide one-step
HbA1c, baseline	8.07%	7.98%	8.06%
HbA1c, change	-0.19%	-0.73%	-0.85%
Achieved HbA1c <7%	26.8%	52.2%	46.5%
Achieved HbA1c ≤6.5%	12.5%	31.9%	25.4%
Fasting Plasma Glucose, change	+1.5 mg/dL	-14.7 mg/dL	-18.3 mg/dL
2-hour PPG, change	-0.65 mg/dL	-4.51 mg/dL	-5.47 mg/dL
2-hour glucose excursion	-0.67 mg/dL	-3.77 mg/dL	-4.36 mg/dL
Body weight, change	-2.0 kg	-2.0 kg	-1.9 kg

Results were significantly improved in both lixisenatide groups compared with placebo for all outcomes listed above with the exception of body weight reduction. Overall, lixisenatide resulted in a -0.65% change in HbA1c compared with placebo ($p < 0.0001$). Lixisenatide is efficacious as monotherapy in patients inadequately controlled with diet and exercise alone.

Adverse event	Placebo	Lixisenatide groups
Any adverse events	55 (45.1%)	128 (53.6%)
Serious adverse events	5 (4.1%)	1 (0.4%)
Gastrointestinal disorders	17 (13.9%)	77 (32.2%)
Nausea	5 (4.1%)	53 (22.2%)
Headache	14 (11.5%)	19 (7.9%)
Vomiting	0	17 (7.1%)
Dizziness	3 (2.5)	13 (5.4)
Nasopharyngitis	4 (3.3%)	11 (4.6)
Symptomatic hypoglycemia	2 (1.6%)	4 (1.7%)

Table 2. Lixisenatide in combination with metformin

Trial Design	Randomized, double-blind, placebo-controlled 24-week clinical trial		
Population	Patients aged 24-79 with Type 2 diabetes mellitus currently receiving at least 1.5 g/day of metformin as monotherapy (for at least 3 months) and with HbA1c 7-10%		
Groups	Placebo (n=160)	Lixisenatide once-daily 2-step (10 mcg for 1 week, 15 mcg for 1 week, and then 20 mcg; n = 161)	Lixisenatide once-daily 1-step (10 mcg for 2 weeks and then 20 mcg; n = 161)
Outcomes	Primary: Reduction in HbA1c from baseline to week 24 Secondary: Percentage of patients achieving an HbA1c <7.0% or ≤6.5%; change in fasting plasma glucose, 2-hour post prandial glucose, and body weight; and percentage of patients receiving rescue therapy		

Results

Outcome	Placebo	Lixisenatide two-step	Lixisenatide one-step
HbA1c, baseline	8.03%	8.10%	7.99%
HbA1c, change	-0.42%	-0.83%	-0.92%
Achieved HbA1c <7%	24.1%	42.1%	47.4%
Achieved HbA1c ≤6.5%	7.6%	20.4%	25.6%
Fasting Plasma Glucose, change versus placebo	0.11 mg/dL	-0.56 mg/dL	-0.53 mg/dL
Patients receiving rescue therapy	4.4%	3.1%	1.3%
Body weight, change	-1.63 kg	-2.68 kg	-2.63 kg

All outcome measures were significantly improved in both lixisenatide groups compared with placebo. Lixisenatide is efficacious in combination with metformin in patients inadequately controlled with metformin alone. One- and two-step regimens were similar in terms of both efficacy and tolerability.

Adverse event	Placebo	Lixisenatide two-step	Lixisenatide one-step
Any adverse event	105 (65.6%)	114 (70.8%)	109 (67.7%)
Serious adverse events	4 (2.5%)	7 (4.3%)	5 (3.1%)
Gastrointestinal disorders	35 (21.9%)	76 (47.2%)	67 (41.6%)
Nausea	7 (4.4%)	57 (35.4%)	42 (26.1%)
Vomiting	0	25 (15.5%)	19 (11.8%)
Diarrhea	14 (8.8%)	20 (12.4%)	10 (6.2%)
Symptomatic hypoglycemia	1 (0.6%)	4 (2.5%)	3 (1.9%)
Severe hypoglycemia	2 (1.3%)	7 (4.3%)	7 (4.3%)

The clinical trials summarized above, and others, have demonstrated the safety and efficacy of lixisenatide as monotherapy and in combination with other antidiabetic agents. Of note, two clinical trials compared the efficacy and safety of lixisenatide against other agents in the same class:

- Once-daily liraglutide versus lixisenatide as add-on to metformin in type 2 diabetes: a 26-week randomized controlled clinical trial
  - Lixisenatide 20 mcg once daily was compared with liraglutide 1.8 mg once daily as add-on to metformin (n = 404)
  - Liraglutide reduced HbA1c significantly more than lixisenatide: -1.81% versus -1.24% ($p < 0.0001$)
  - More patients achieved HbA1c <7% and ≤6.5% in the liraglutide group (74.2% and 54.6%) versus the lixisenatide group (45.5% and 26.2%)
  - Liraglutide reduced fasting plasma glucose more than lixisenatide
  - Both agents caused similar reductions in body weight (−4.3 kg for liraglutide, −3.7 kg for lixisenatide; $p = 0.23$)
  - Lixisenatide has not been compared with the 1.2 mg dose of liraglutide (a common maintenance dose)
  - Adlyxin has not been associated with higher risk for thyroid cancer (rare cases have occurred in patients on liraglutide)
- Efficacy and safety of lixisenatide once daily versus exenatide twice daily in type 2 diabetes inadequately controlled on metformin: a 24-week, randomized, open-label, active-controlled study
  - Lixisenatide 20 mcg once daily was compared with exenatide 10 mcg twice daily as add-on to metformin (n = 634)
  - Lixisenatide demonstrated non-inferiority in HbA1c reduction versus exenatide (-0.79% vs. -0.96%, respectively) with a treatment difference of 0.17% (95% CI, 0.033-0.297), meeting the predefined non-inferiority upper CI margin of 0.4%
  - Achievement of HbA1c <7% (48.5% lixisenatide and 49.8% exenatide) and ≤6.5% (28.5% lixisenatide and 35.4% exenatide) was similar between groups
  - Weight reduction was greater in the exenatide group: -2.96 kg for lixisenatide and -3.98 kg for exenatide (1.02 kg difference; 95% CI 0.456–1.581)
  - In the lixisenatide group, fewer participants experienced symptomatic hypoglycemia (2.5% vs. 7.9%; $p < 0.05$), with fewer gastrointestinal events (especially nausea; 24.5% vs. 35.1%; $p < 0.05$)

Ongoing Clinical Trials:

- NCT02767596 Evaluation of Lixisenatide Efficacy in Diabetes Mellitus Type 2 With Failure of Other GLP-1 Analog
- NCT02308254 Drug Trial of Lixisenatide on Gastric Emptying and Blood Pressure Drops in Type 2 Diabetics and Healthy People
- NCT02941367 Safety Assessment of Lyxumia (Lixisenatide) and Sulfonylurea as Add-on Treatment to Basal Insulin in Uncontrolled Patients With Type 2 Diabetes Mellitus Who Elect to Fast During Ramadan
- NCT02803918 A Study on Safety, Pharmacokinetics and Pharmacodynamics of Lixisenatide in Pediatric Patients With Type 2 Diabetes Mellitus
- NCT02749890 Efficacy and Safety of the Insulin Glargine/Lixisenatide Fixed Ratio Combination (LixiLan) to Lixisenatide on Top of Oral Anti-diabetic Drugs (OADs) With Type 2 Diabetes in Japan (LIXILAN JP-O1)

Contraindications:

Contraindicated in patients with a hypersensitivity to Adlyxin or any product components.

Warnings/Precautions:

- Anaphylaxis and other serious hypersensitivity reactions have occurred following administration.

- Pancreatitis may occur in patients on Adlyxin. Consider alterative therapy in patients with a history of pancreatitis.
- Hypoglycemia may occur with concomitant use of a sulfonylurea or basal insulin. Consider reducing the Adlyxin dose in these patients.
- Acute kidney injury may occur. Monitor renal function in patients with renal impairment. Not recommended in patients with end stage renal disease.
- The development of antibodies to Adlyxin may occur. If treatment is ineffective or allergic reactions occur, consider alternative therapy.
- Clinical trials have not demonstrated macrovascular benefit with Adlyxin.

Drug Interactions:
- Adlyxin delays gastric emptying and may alter the absorption of oral medications. Oral medications should be administered at least 1 hour prior to Adlyxin to reduce this effect.
- Oral contraceptives should be taken at least 1 hour prior to or 11 hours after Adlyxin administration.

Common Adverse Effects:
- Nausea
- Vomiting
- Headache
- Diarrhea
- Dizziness
- Hypoglycemia

Safety:
- Adlyxin has not been studied in patients with a history of pancreatitis, with gastroparesis, or with concomitant short acting insulin.
- Adlyxin is not indicated to treat type 1 diabetes mellitus or diabetic ketoacidosis

Dosage:
- Adlyxin is supplied in a disposable single-patient use pen containing 14 doses of 0.2 mL (3 mL total solution)
    - The green starter pen contains 50 mcg/mL of lixisenatide
    - The burgundy maintenance pen contains 100 mcg/mL of lixisenatide
- Initiate at 10 mcg once daily for 14 days. Starting on day 15, increase dosage to 20 mcg once daily
- Administer within one hour before the first meal of the day

Administration:[6]
- To be injected subcutaneously in the abdomen, thigh, or upper arm
- Prior to first injection, the Adlyxin pen must be activated:
    - Pull off cap and check pen for clear and colorless liquid
    - Screw needle on and remove needle caps
    - Pull the injection button out firmly until it stops
    - Firmly press and hold the injection button to remove the liquid
- Daily use of the pen:
    - Pull off cap and check pen
    - Attach a new needle and remove needle caps
    - Pull the injection button out
    - Choosing injection site
    - Press and hold (2 seconds) the injection button to inject the dose
    - Remove and throw away needle after each injection
- In an open-label pilot study (n = 30), lixisenatide, liraglutide, and exenatide pen devices were compared for the following outcomes: time taken to complete a series of tasks, number of user errors (successful performance), and user satisfaction rating.
    - Tasks were completed faster ($p < 0.001$) with lixisenatide pen versus the exenatide pen
    - Successful performance rates were higher ($p < 0.001$) with lixisenatide pen versus the exenatide pen
    - Liraglutide was not significantly different versus the exenatide pen for time taken to complete a series of tasks or successful performance rates
    - Overall, user satisfaction was higher for the lixisenatide and liraglutide pens versus the exenatide pen ($p < 0.001$)

Special Drug Monitoring:
Monitor renal function in patients with renal impairment and in patients reporting severe gastrointestinal reactions. Adlyxin is not recommended in patients with end stage renal disease.

Handling and Preparation:

- Must be refrigerated at 2°C to 8°C. Do not freeze.
- Store in original carton until time of administration to protect from light.
- After first use, store below 30°C.
- Discard pen 14 days after first use.

Financial Impact:[7-9]

- According to the CDC, 29.1 million people or 9.3% of the United States population have diabetes.
- One pharmacoeconomic analysis in the U.K. concluded that weekly exenatide is more cost-effective than dulaglutide, liraglutide 1.2 mg, liraglutide 1.8 mg, or lixisenatide for the treatment of type 2 diabetes not adequately controlled with metformin. The analysis simulated costs and quality-adjusted life years, and indirectly compared efficacy and safety.

Product Name	AWP for 1-month supply	Package size	Formulary Status
Adlyxin (lixisenatide)	$ 668.64	2 pens; 28 doses	*Proposed: Non-Preferred*
Trulicity (dulaglutide)	$ 751.20	4 pens; 4 doses	Preferred; Step-therapy
Victoza (liraglutide) 1.2 mg dose	$ 598.10	2 pens; 30 doses	Preferred; Step-therapy
Victoza (liraglutide) 1.8 mg dose	$ 897.16	3 pens; 30 doses	Preferred; Step-therapy
Byetta (exenatide)	$ 801.94	1 pen; 60 doses	Non-preferred
Bydureon (exenatide)	$ 747.35	4 pens; 4 doses	Non-preferred

References:

1. Adlyxin [package insert]. Bridgewater, NJ: Sanofi-Aventis U.S.; 2016.
2. Fonseca VA, Alvarado-ruiz R, Raccah D, et al. Efficacy and safety of the once-daily GLP-1 receptor agonist lixisenatide in monotherapy: a randomized, double-blind, placebo-controlled trial in patients with type 2 diabetes (GetGoal-Mono). *Diabetes Care*. 2012;35(6):1225-31.
3. Bolli GB, Munteanu M, Dotsenko S, et al. Efficacy and safety of lixisenatide once daily vs. placebo in people with Type 2 diabetes insufficiently controlled on metformin (GetGoal-F1). *Diabet Med*. 2014;31(2):176-84.
4. Nauck M, Rizzo M, Johnson A, Bosch-traberg H, Madsen J, Cariou B. Once-Daily Liraglutide Versus Lixisenatide as Add-on to Metformin in Type 2 Diabetes: A 26-Week Randomized Controlled Clinical Trial. *Diabetes Care*. 2016;39(9):1501-9.
5. Rosenstock J, Raccah D, Korányi L, et al. Efficacy and safety of lixisenatide once daily versus exenatide twice daily in type 2 diabetes inadequately controlled on metformin: a 24-week, randomized, open-label, active-controlled study (GetGoal-X). *Diabetes Care*. 2013;36(10):2945-51.
6. Stauder U, Enginee D, Elton H, Penfornis A, Edelman S. Comparative Assessment of Lixisenatide, Exenatide, and Liraglutide Pen Devices: A Pilot User-Based Study. *J Diabetes Sci Technol*. 2014;8(1):123-131.
7. 2014 National Diabetes Statistics Report. Centers for Disease Control and Prevention https://www.cdc.gov/diabetes/data/statistics/2014statisticsreport.html. Updated 2014. Accessed January 26, 2017.
8. Huetson P, Palmer JL, Levorsen A, Fournier M, Germe M, Mcleod E. Cost-effectiveness of once daily GLP-1 receptor agonist lixisenatide compared to bolus insulin both in combination with basal insulin for the treatment of patients with type 2 diabetes in Norway. *J Med Econ*. 2015;18(8):573-85.
9. Red Book Online [database online]. Ann Arbor, MI: Truven Health Analytics Inc. http:// www.micromedexsolutions.com. Updated 2017. Accessed January 26, 2017.

Pharmacy &Therapeutics Committee Summary Review
Cuvitru® (Immune Globulin Subcutaneous) – Shire PLC

Prepared by: Nikolas James, PharmD Candidate 2017 **Presentation Date:** 3/30/2017

Therapeutic Class: Blood product derivative: Immune Globulin **FDA Approval Date:** 9/13/16

FDA Indication: Primary Humoral Immunodeficiency Syndrome – replacement therapy in adults and pediatric patients 2 years and older

Comparable Products:

- **Preferred:** Carimune NF, Cytogam, Flebogamma, Gamastan S/D, Gammagard, Gamunex-C, Hizentra, Privigen
- **Non-Preferred:** Bivigam, Gammagard S/D, Gammaked, Gammaplex, Hyqvia, Octagam

Proposed Designation & Rationale

Recommendation: Non-preferred, Medical benefit only

- Criteria for use:
  - Required diagnosis: Primary humoral immunodeficiency syndrome
  - Refer to Immune Globulin policy

Clinical Implications/Place in Therapy:
Cuvitru seems to be a very well tolerated subcutaneous infusion immune globulin that offers fewer infusions sites and shorter infusion durations (if tolerated) due to its lack of proline. As it is a new brand name product in the market, its AWP is considerably high than other comparable formulary products. Hizentra (approved in 2010) is currently our preferred subcutaneous infusion with the same indication for patients two and older at the same AWP.

Clinical Pharmacology: supplies a broad spectrum of opsonizing and neutralizing IgG antibodies against a wide variety of bacterial and viral agents; also contains a spectrum of antibodies capable of interacting with and altering the activity of cells of the immune system as well as antibodies capable of reacting with cells such as erythrocytes. The role of these antibodies and the mechanisms of action of IgG in CUVITRU have not been fully elucidated

Notable Pharmacokinetics:

Absorption: AUC= 115g*days/L	Metabolism: Time to peak = ~4.4 days
Distribution: V_d = 0.05 to 0.13 L/kg	Excretion: Apparent clearance= 1.86 mL/kg/day

Efficacy: (*insert footnote with appropriate AMA citation)*

Trial Design/ Population	Groups	Outcomes	Results
Prospective, open-label, non-controlled, multicenter clinical study in North America Age range: 2 and older	N= 77 adult and pediatric subjects (53 adults, 6 adolescents, 15 children) Median maximum infusion rate was 60mL/hr/site	Determine efficacy, tolerability, and PK	• Total # of subject-years on treatment = 83.70 • Annual rate of any infections (per subject-year) = 2.41 • SF-36 Physical Component Score difference 0.89 (p=0.067) • SF-36 Mental Component Score difference 1.31 (p=0.976) • Total score (PedsQL) difference 1.09 (p=0.449) • Treatment Interference difference (LQI) 1.5 (p=0.008) • Convenience (TSQM-9) difference 11.11 (p<0.001) • Dose adjustment factor is 145% of the IGIV by comparing AUC_{SC} with AUC_{IV}
Prospective, open-label, non-controlled, multi-center study conducted in Europe Age range: 2 and older	N = 48 adult and pediatric subjects	Evaluate efficacy, safety, tolerability and PK	• Geometric mean trough levels was 827mg/dL • Mean dose of 0.125 +/- 0.042 g/kg/week shown to be effective in subjects aged 2 and older • Annual rate of any infections (rate per subject-year = 4.38

Conclusion: Pharmacokinetic properties were determined in order to know appropriate dosing and conversion from IVIG. Cuvitru is well tolerated with minimum side effects and safe and effective in ages 2 and older.

Ongoing Clinical Trials: none

Contraindications: Anaphylactic or severe systemic hypersensitivity to immune globulin or any component of the formulation; IgA deficiency (with anti-IgA antibodies and history of hypersensitivity)

Warnings/Precautions:

- **Anaphylaxis/hypersensitivity reactions**: Hypersensitivity and anaphylactic reactions can occur (some severe); patients with anti-IgA antibodies are at greater risk; a severe fall in blood pressure may rarely occur with anaphylactic reaction; discontinue therapy and institute immediate treatment (including epinephrine 1 mg/mL) should be available.
- **Aseptic meningitis**: Aseptic meningitis syndrome (AMS) has been reported with immune globulin administration; may occur with high doses (≥1 g/kg) and/or rapid infusion. Syndrome usually appears within several hours to 2 days following treatment; usually resolves within several days after product is discontinued. Patients with a migraine history may be at higher risk for AMS.
- **Hematoma**: Increased risk of hematoma formation when administered subcutaneously for the treatment of ITP.
- **Hemolysis**: Intravenous immune globulin has been associated with antiglobulin hemolysis (acute or delayed); monitor for signs of hemolytic anemia. Cases of hemolysis-related renal dysfunction/failure or disseminated intravascular coagulation (DIC) have been reported. Risk factors associated with hemolysis include high doses (≥2 g/kg) given either as a single administration or divided over several days, underlying associated inflammatory conditions, and non-O blood type (FDA, 2012).
- **Hyperproteinemia**: Hyperproteinemia, increased serum viscosity, and hyponatremia may occur; distinguish hyponatremia from pseudohyponatremia to prevent volume depletion, a further increase in serum viscosity and a higher risk of thrombotic events.
- **Infusion reactions**: Patients should be monitored for adverse events during and after the infusion. Stop administration with signs of infusion reaction (fever, chills, nausea, vomiting, and rarely shock). Risk may be increased with initial treatment, when switching brands of immune globulin, and with treatment interruptions of >8 weeks.
- **Pulmonary edema**: Monitor for transfusion-related acute lung injury (TRALI); noncardiogenic pulmonary edema has been reported with immune globulin use. TRALI is characterized by severe respiratory distress, pulmonary edema, hypoxemia, normal left ventricular function, and fever in the presence of normal left ventricular function. Usually occurs within 1 to 6 hours after infusion.
- **Renal impairment**: **[US Boxed Warning]:** IV administration only: Acute renal dysfunction (increased serum creatinine, oliguria, acute renal failure, osmotic nephrosis) can rarely occur and has been associated with fatalities; usually within 7 days of use (more likely with products stabilized with sucrose). Use with caution in the elderly, patients with renal disease, diabetes mellitus, overweight, hypovolemia, volume depletion, sepsis, paraproteinemia, and nephrotoxic medications due to risk of renal dysfunction. In patients at risk of renal dysfunction, ensure adequate hydration prior to administration; the dose rate of infusion and concentration of solution should be minimized. Assess renal function prior to treatment and periodically thereafter. Discontinue if renal function deteriorates.
- **Thromboembolic events**: **[US Boxed Warning]:** Thrombosis may occur with immune globulin products even in the absence of risk factors for thrombosis. For patients at risk of thrombosis (e.g., advanced age, history of atherosclerosis, impaired cardiac output, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling central vascular catheters, hyperviscosity, and cardiovascular risk factors), administer at the minimum dose and infusion rate practicable. Ensure adequate hydration before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity such as those with cryoglobulins, fasting chylomicronemia/severe hypertriglyceridemia, or monoclonal gammopathies**.**
- **Elderly**: Use with caution in the elderly; may be at increased risk for renal dysfunction/failure and thromboembolic events
- **Subcutaneous administration**: Some clinicians may administer intravenous immune globulin products as a subcutaneous infusion based on patient tolerability and clinical judgment. SubQ infusion should begin 1 week after the last IV dose; dose should be individualized based on clinical response and serum IgG trough concentrations. Consider premedicating with acetaminophen and diphenhydramine
- **Vaccinations**: Response to live vaccinations may be impaired
- **Pregnancy Risk Factor: C**

Drug Interactions:

- Estrogen Derivatives – may enhance the thrombogenic effect of IG

Common Adverse Effects:

- Common reactions (>10%)
    - CNS: Headache (16% to 48%)
    - GI: Nausea (3% to 18%)
    - Local: Erythema (51%), Infusion site reaction (100%), Pain at injection site (13%), Swelling at injection site (68%), Warm sensation at injection site (16%)
    - Miscellaneous: Fever (6% to 16%)

Safety:

- No known safety issues

Dosage/Administration:

- Individualize dose based on the patient's clinical response to therapy and serum IgG trough levels.
- Primary Humoral Immunodeficiency:
  - Initial dosage:
    - For patients switching from another immune globulin SQ product;
      - WEEKLY DOSING: the dose is the same as the prior SQ weekly dose in grams
      - BIWEEKLY DOSING: multiply the calculated weekly dose (in grams) by 2
      - FREQUENT DOSING (2-7 times/week): Divide the calculated weekly dose (in grams) by the desired number of administration times/week
    - For patients switching from IVIG or IG/hyaluronidase SQ (Hyqvia):
      - Begin treatment one week after patient's last IVIG or Hyqvia infusion
      - WEEKLY DOSING: Divide the previous immune globulin IV or Hyqvia dose (in grams) by the number of weeks between IV doses, then multiply this dose by 1.3 (dose adjustment factor)
      - BIWEEKLY DOSING: Multiply the calculated weekly dose (in grams) by 2
      - FREQUENT DOSING: Divide the calculated weekly dose (in grams) by the desired number of times per week
  - Must be used in ≤ 4 simultaneous injection sites (spaced 4 inches apart or more)
  - Maximum infusion rate: 10 to 20mL/hour per injection site (for first 2 injections); may be increased to 60mL/hour per injection site (as tolerated) for subsequent infusions
  - Maximum infusion volume:
    - Patients < 40kg: 20mL per injection site (first 2 infusions); may be increased to 60mL/hour per site for subsequent infusions
    - Patients ≥ 40kg: 60mL per injection site

Special Drug Monitoring:

- Monitor renal function, urine output, IgG concentrations; infusion-related adverse reactions, anaphylaxis, signs and symptoms of hemolysis; blood viscosity; presence of antineutrophil and anti-HLA antibodies; volume status; neurologic symptoms; pulmonary adverse reactions; and clinical response
- Monitor IgG trough levels every 2-3 months before/after conversion from IV; SQ infusions provide more constant IgG levels than IVIG

Handling and Preparation:

- Initial dose should be administered in a healthcare setting capable of providing monitoring and treatment in the event of a hypersensitivity. Using aseptic technique, follow the infusion device manufacturer's instructions for filling the reservoir and preparing the pump. Remove air from administration set and needle by priming. After the sites are clean and dry, insert subcutaneous needle and prime administration set. Attach sterile needle to administration set, gently pull back on the syringe to assure a blood vessel has not been inadvertently accessed (do not use needle and tubing if blood present).
- Do not dilute for Cuvitru

Financial Impact:

- Primary humoral immunodeficiency syndrome is considered fairly uncommon. Only ~50,000 diagnosed each year in the United States.
- Comparison of other immune globulin products for subcutaneous infusion

Product Name	AWP for 1-month supply	Formulary Status
Cuvitru (Immune Globulin SQ)	$ 7,056.00	***Proposed: Non-preferred***
Gammagard	$ 5,486.60	Preferred with PA
Gamunex-C	$ 4,431.35	Preferred with PA
Hizentra	$ 7,056.00	Preferred with PA
Hyqvia	$ 7,770.00	Non-preferred
Gammaked	$ 5,191.90	Non-preferred

Note: Typical dosing is 0.4-0.6g/kg every 28 days for Primary Immunodeficiency Disorders; in the chart above pricing was based on 0.5g/kg (70kg). Pricing will vary greatly per patient depending on what dose they are being converted from.

References:

1. Cuvitru (immune globulin subcutaneous [human]) [prescribing information]. Westlake Village, CA: Baxalta US Inc; September
2. Sacher RA, IVIG Advisory Panel. Intravenous immunoglobulin consensus statement. J Allergy Clin Immunol, 2001; 108(4 Suppl):S139-46.
3. Red Book Online [database online]. Ann Arbor, MI: Truven Health Analytics Inc. http:// www.micromedexsolutions.com. Updated 2017. Accessed March 9, 2017.

Pharmacy &Therapeutics Committee Summary Review
Exondys 51® (eteplirsen) – Sarepta Therapeutics

Prepared by: Elise Smith PharmD. Candidate 2017

Presentation Date: 3/30/17

Therapeutic Class: Antisense oligonucleoside

FDA Approval Date: September 19, 2016

FDA Indication: Duchenne muscular dystrophy (DMD)

Comparable Formulary Products: None

Proposed Designation & Rationale

Recommendation: Non-preferred, medical benefit

- Criteria for use:
  - Required diagnosis: Duchenne Muscular Dystrophy
  - Genetic test demonstrating each patient's DMD case is amenable to exon 51 skipping
  - Member is currently taking a corticosteroid or has contraindication to corticosteroids
  - Patient is ambulatory
  - Approval duration: 6 months
  - Reauthorization: Member meets above and continues to be ambulatory, reapprove for 6 months

Clinical Implications/Place in Therapy:

- First in class therapy for DMD with no other drugs available on the market and a novel mechanism of action. Steroids are the only available, and optional, treatment for DMD and there are no curative options.
- Eteplirsen was studied in a small longitudinal of 12 patients and there were questions regarding how much dystrophin was produced by eteplirsen treatment and if that correlated to clinical outcomes.
- The drug was approved provisionally by the FDA with a request for a larger phase III clinical trial for safety and efficacy which is ongoing. More clinical data is needed to assess the clinical significance of the benefits provided by eteplirsen.

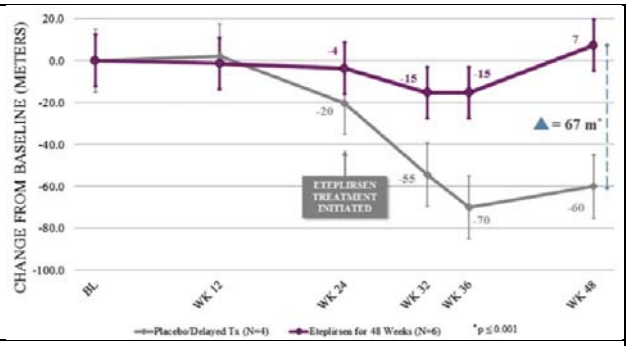
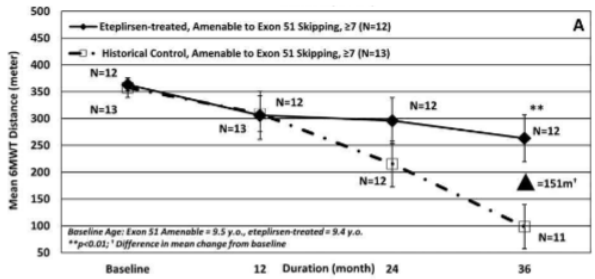
Clinical Pharmacology: Binds to exon 51 of dystrophin mRNA resulting in exclusion of this exon during mRNA procession. Skipping this exon adjusts the mRNA reading frame and allows for production of a functional dystrophin protein.

Notable Pharmacokinetics[1]:

- V_{dss}: 600 mL/kg
- Protein binding: 6-17%
- $T_{1/2}$: 3-4 hrs
- Time to peak: 1.1-1.2 hrs
- Excretion: renal

Efficacy[2,3,4]:

Trial Design/ Population	Groups	Outcomes	Results
Single-blind, placebo-controlled, dose-escalation study. Patients with DMD amenable to exon 51 skipping with preservation (grade 1-3) of the extensor digitorum brevis (EDB) muscle.	N=7 AVI-4658 0.09mg in 900µL 0.9% saline: N=2 AVI-4658 0.9mg in 900µL 0.9% saline: N=5 In these patients, active drug was injected into one foot and the other foot was injected with 0.9% saline	Outcomes: % of myofibers showing increased expression of dystrophin and mean intensity of dystrophin	In the muscles where AVI-4658 was injected, 44-79% of myofibers had increased expression of dystrophin. In the AVI-4658 treated muscles, the mean intensity of dystrophin staining ranged from 22-32% of a healthy range which is 17% greater than the intensity in the saline treated muscle.
24 week, randomized, double-blind, placebo-controlled study.	N=12 Placebo N=4 Eteplirsen 30mg/kg/week N=4	1° Outcome: 6-Minute Walk	24 weeks after initiating eteplirsen therapy, eteplirsen patients had a 67.3m walking advantage over placebo patients in the 6MWT.

Patients with DMD amenable to exon 51 skipping.	Eteplirsen 50mg/kg/week N=4	Test (6MWT) distance	
36 month, open label, historically controlled study. Continuation of the 24 week study. Patients with DMD amenable to exon 51 skipping.	N=25 Eteplirsen: N=12 (all patients from the previous study) Historical controls (HC): N=13 Mean age= 9.3 years, mean height= 123.7cm, mean weight= 31.52kg, time since DMD diagnosis= 56.4 months	1° Outcome: 6MWT distance	At 36 months, eteplirsen patients had a 151m (p<0.01) advantage compared to HC during 6MWT and experienced less loss of ambulation. At 36 months 2/12 patients treated with eteplirsen lost ambulation while 6/13 HC patients lost ambulation.  | Month | 12 | 24 | 36 | |---|---|---|---| | Eteplirsen-treated (N) | 12 | 12 | 12 | | Historical Control (N) | 13 | 12 | 11 | | Delta* (m) | -9 | 75 | 151 | | P-Value | NS | NS | <0.01 | *Difference in mean change from baseline 

Conclusion[5]: The data supporting Exondys 51® is not robust. Its clinical trials have been extremely small and its largest study used historical controls in place of a placebo group. These studies suggest that eteplirsen can improve functional dystrophin production, improve 6MWT scores compared to placebo, and slow the rate of loss of ambulation, but these benefits have not been adequately proven because of the weaknesses of the clinical trials. Dystrophin is the protein that is dysfunctional in DMD patients and correcting the production of the protein is thought to be a way to cure the disease, but the study evaluating eteplirsen's effects on dystrophin was not tied to any clinical outcomes and the clinical significance of a 17% increase in dystrophin production is questionable. It is noteworthy that the approval of eteplirsen by the FDA was controversial; the advisory panel recommended against approval. The committee voted 7-3 that there was not adequate evidence to show the drug is effective and 7-6 that there wasn't enough evidence to show it increased dystrophin levels. It has also been suggested that the Center for Drug Evaluation and Research Director, Janet Woodcock, who recommended approval of the drug was concerned that not approving eteplirsen would bankrupt Sarepta Therapeutics Inc., preventing future research.

Ongoing Clinical Trials[6]:

- Confirmatory Study of Eteplirsen in DMD Patients. NCT02255552
- Efficacy, Safety, and Tolerability Rollover Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy. NCT01540409
- Safety Study of Eteplirsen to Treat Advanced Stage Duchenne Muscular Dystrophy. NCT02286947
- Safety Study of Eteplirsen to Treat Early Stage Duchenne Muscular Dystrophy. NCT02420379

Contraindications: No contraindications

Warnings/Precautions: No warnings

Drug Interactions: No known significant interactions

Common Adverse Effects[1]:
- Equilibrium disturbance (38%)
- Vomiting (38%)
- Contact dermatitis (25%)
- Excoriation (≥10%)
- Skin rash (≥10%)
- Bruise (≥10%)
- Arthralgia (≥10%)
- Upper respiratory tract infection (≥10%)

Safety: No known safety concerns

Dosage/Administration[7]:
- Dose: 30mg/kg IV once weekly
- Administer intravenously over 35-60min
- Complete infusion within 4hrs of dilution
- Before and after administration, flush IV access line with 0.9% saline
- Do not administer other medications via the same IV line
- If a dose is missed, administer as soon as possible after the scheduled dose

Special Drug Monitoring: None

Handling and Preparation[7]:
- Store at 2-8°C
- Protect from light
- Store in original container
- Allow eteplirsen vials to warm to room temperature prior to dilution
- Use a 21-gauge or smaller non-coring needle to withdraw the necessary volume of eteplirsen and dilute in 0.9% saline to a total volume of 100-150mL
- Gently invert each vial 2-3 times to mix contents; do not shake
- If diluted solution cannot be used immediately, it may be stored at 2-8°C for up to 24hrs
- Discard unused eteplirsen

Financial Impact[8,9,10]:
- Prevalence of DMD: 1 in 3500 male births
- Prevalence of mutation amenable to exon 51 skipping: 13% of DMD cases
- Pricing:
    - Exondys 51® 50mg/1mL 10mL package
        - WAC package price = $8000.00
        - AWP package price = $9600.00
        - AWP unit price = $960.00
    - Exondys 51® 50mg/1mL 2mL package
        - WAC package price = $1600.00
        - AWP package price = $1920.00
        - AWP unit price = $960.00

References:

1. LexiComp Online. Eteplirsen. Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc. Updated October 25, 2016.
2. Mendell J, Rodino-Klapac L, Sahenk Z, et al. Eteplirsen for the treatment of Duchenne Muscular Dystrophy. *Ann Neurol*. 2013; 74: 637-647
3. Mendell J, Goemans N, Lowes L, et al. Longitudinal effect of eteplirsen versus historical control on ambulation in Duchenne Muscular Dystrophy. *Ann Neurol.* 2016; 79: 257-271.

4. Kinali M, Arechavala-Gomeza V, Feng L, et al. Local restoration of dystrophin expression with the morpholino oligomer ACI-4658 in Duchenne muscular dystrophy: a single-blind, placebo-controlled, dose-escalation, proof-of-concept study. *Lancet Neurol.* 8 Oct 2009; 8(10): 918-928.
5. Johnson C. FDA committee votes against approval of controversial muscular dystrophy drug. *The Washington Post*. 25 Apr 2016. Available from: https://www.washingtonpost.com/news/wonk/wp/2016/04/25/fda-committee-votes-against-approval-of-controversial-muscular-dystrophy-drug/?utm_term=.8f194d09b1c1
6. US National Institutes of Health. Eteplirsen. *Clinical Trials.gov.* Available at: http://www.clinicaltrials.gov. Accessed 7 Feb 2017.
7. Exondys 51 [package insert]. Cambridge, MA. Sarepta Therapeutics: 2016.
8. Prevalence of Duchenne/Becker Muscular Dystrophy among males ages 5—24 years --- four states, 2007. *MMWR*. 16 Oct 2009; 58(40): 1119-1122.
9. Red Book Online [database online]. Exondys 51. Accessed: 7 Feb 2017. Available from: http://www.micromedexsolutions.com/
10. Exon-skipping for Duchenne. Sarepta Therapeutics. 2016. Accessed: 16 Feb 2017. Available from: http://www.sarepta.com/pipeline/exon-skipping-duchenne
11. Darras BT, et al. Dystrophinopathies. In: Pagon RA, et al., editors. In: ed. Pagon RA, et al. GeneReviews. Seattle, WA: University of Washington, Seattle; 2016.

Pharmacy &Therapeutics Committee Summary Review
Xiidra® (lifitegrast) – Shire US Inc

Prepared by: Elise Smith PharmD. Candidate 2017 **Presentation Date:** 3/30/2017

Therapeutic Class: Lymphocyte function-associated antigen 1 (LFA-1) antagonist FDA Approval Date: July 12, 2016

FDA Indication: Dry eye disease

Comparable Formulary Products: Restasis, artificial tears

Proposed Designation & Rationale

Recommendation: Non-Preferred

- Criteria for use:
  - Diagnosis: Dry eye disease
  - Must use OTC artificial tears routinely QID for a trial period of at least 30 days (dates must be specified on request or supported by claims history)

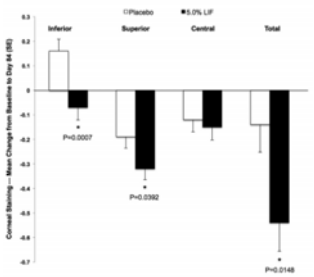
Clinical Implications/Place in Therapy:
Lifitegrast is a 1st in class therapy for dry eye disease. As lifitegrast is significantly more expensive than OTC artificial tears, it should not be a preferred first-line therapy. However, for patients who have inadequate symptom relief with artificial tears, lifitegrast appears to be an appropriate, efficacious secondary therapy. Lifitegrast's competitor, Restasis®, is limited in treating dry eye disease as it is indicated to increase tear production not the symptoms associated with dry eye disease. Restasis® also has a long set of action (up to 16 weeks) and many patients discontinue its use due to burning sensation where lifitegrast has shown efficacy within 6 to 12 weeks, or sooner.

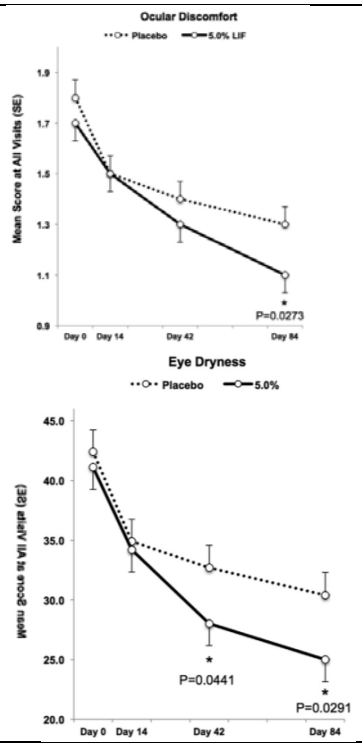
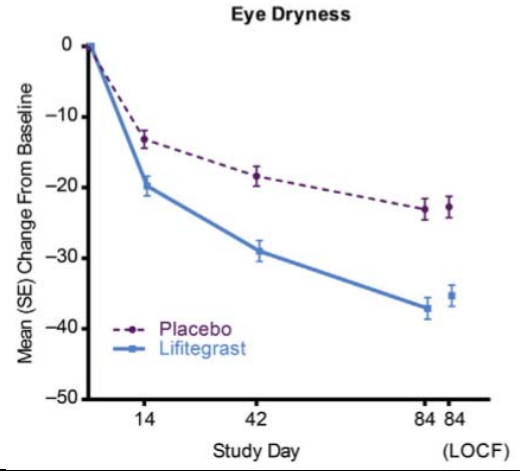
Clinical Pharmacology[1]: Lifitegrast binds to the integrin LFA-1 and blocks the interaction of LFA-1 with its cognate ligand intercellular adhesion molecule-1 (ICAM-1)

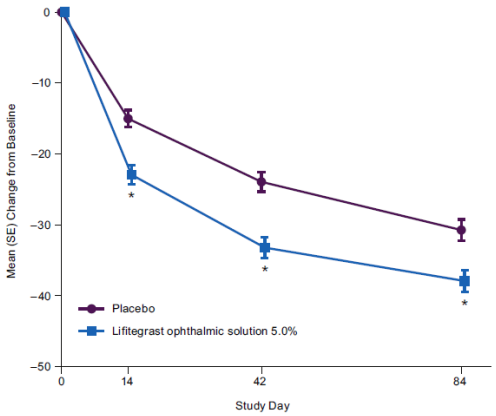
Notable Pharmacokinetics[1]:

- This topical solution is not significantly systemically absorbed.
- 19% of patients tested had plasma trough concentrations of lifitegrast above 0.5 ng/mL (lower limit of assay quantitation). Measureable trough values ranged from 0.55-3.74 ng/mL.

Efficacy[2,3,4]:

Trial Design/ Population	Groups	Outcomes	Results
OPUS-1 12 week, prospective, randomized, double-masked, placebo-controlled, parallel arm, multicenter trial. Adults with dry eye disease with use of or desire to use artificial tears within the past 6 months, presence of conjunctival redness, corneal staining score ≥2 in any field, Schirmer tear test (STT) of ≥1 and ≤10, and best-corrected visual acuity ≥0.7.	N = 588 Placebo: N = 295 Lifitegrast: N = 293 Mean age = 61.1yrs, 73.6% female, 93.6% white	1° outcomes: Mean change from baseline inferior corneal straining score (ICSS) at day 84, mean change form baseline in the visual-related function subscale score of the Ocular Surface Disease Index (VR-OSDI)	Lifitegrast significantly reduced ICSS at day 84 (P=0.0007). Lifitegrast did not demonstrate significant improvement in VR-OSDI (P=0.7894). Although there was no improvement in VR-OSDI, there significant improvements noted in the lifitegrast group for ocular discomfort and eye dryness which were the most common and severe symptoms at baseline.  Figure 1. Corneal fluorescein staining score in a study of lifitegrast compared with placebo for dry eye disease. Results for the inferior, superior, central, and total corneal regions (Ora scale) using mean change from baseline to day 84 analysis (*2-sided t test). LIF = lifitegrast; ODS = ocular discomfort score; SE = standard error.

			
OPUS-2 12-week, multicenter, randomized, prospective, double-blinded, placebo controlled trial Adults who have used artificial tears within 30 days, have an inferior corneal staining score ≥0.5, STT ≥1 and ≤10, and eye dryness score (EDS) ≥40.	N = 718 Placebo: N = 360 Lifitegrast: N = 358 Mean age = 58.9yrs, 73.6% female, 84.7% white	1° outcomes: Change from baseline to day 84 in EDS and ICSS	At day 84, lifitegrast showed significant improvements in EDS; the treatment effect (TE) was 12.61; 95% CI 8.51-16.70; P<0.0001. There was no difference between placebo and lifitegrast in ICSS; the treatment effect was 0.03; 95% CI -0.01-0.17; P=0.6186. 

OPUS-3 12 week, randomized, double-blinded, multicenter, placebo-controlled trial Adult patients with dry eye disease, STT ≥1 and ≤10, corneal fluorescein staining score ≥2, EDS ≥40, and history of artificial tear use within 30 days of study entry	N=711 Placebo: N=356 Lifitegrast: N=355 Mean age=58.7, 75.5% female, 76.5% white	1° outcome: Change in eye dryness score (EDS) from baseline to day 84	At day 84, lifitegrast showed significant improvements in EDS; the treatment effect (TE) was 7.16; 95% CI 3.04-11.28.  Figure 3. Eye dryness score (EDS) (visual analogue scale [VAS]); intention-to-treat population with last observation carried forward. EDS (0- to 100-point VAS; both eyes). Treatment effect, *$P = 0.0007$ (day 84), $P < 0.0001$ (days 42 and 14). SE = standard error.

Conclusion: The studies were sufficiently large, appropriately designed, and presented adequate evidence to demonstrate that lifitegrast relieves dry eye symptoms, but the studies are conflicting regarding its ability to improve ICSS.

Ongoing Clinical Trials: None

Contraindications: No contraindications

Warnings/Precautions[1]:

- If patient wears contact lenses, remove them prior to administration and do not reinsert for 15 minutes.

Drug Interactions[1]: no known significant interactions

Common Adverse Effects[1]:

- Dysgeusia
- Local irritation
- Decreased visual acuity
- Headache
- Blurred vision
- Conjunctival hyperemia
- Eye discharge
- Eye discomfort
- Eye irritation
- Eye pruritis
- Increased lacrimation
- Sinusitis

Safety: No known safety concerns

Dosage/Administration[5]:

- Place 1 drop in each eye from single use applicator every 12 hours
- Remove contact lenses prior to administration and wait 15 minutes before reinserting
- Do not touch the eye, surrounding area, or other surfaces with the dropper tip to avoid contamination
- Discard single use container and unused solution after administration

Special Drug Monitoring: None

Handling and Preparation[5]:

- Store applicators in original foil pouches
- Storage: 20-25°C
- Discard unused product

Financial Impact[6]:

- Xiidra® 5% ophthalmic solution – 60 single use applicators
  - WAC package price = $426.73
  - AWP package price = $512.08
  - AWP unit price = $8.53
- These prices are comparable to Xiidra®'s major competitor, Restasis®.

Product Name	AWP for 1-month supply	Package size	Formulary Status
Xiidra (lifitgrast)	$ 512.08	60 drops	*Proposed: Non-preferred*
Restasis	$ 558.17	60 drops	Non-preferred
Artificial Tears	$ 6.19	225 drops	Preferred

References:

1. LexiComp Online. Lifitegrast. Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc. Updated October 21, 2016.
2. Sheppard J, Torkildsen G, Lonsdale J, et al. Lifitegrast ophthalmic solution 5.0% for treatment of dry eye disease: results of the OPUS-1 phase 3 study. *Ophthalmology*. 2014 Feb; 121(2): 475-83.
3. Tauber J, Karpecki P, and Latkany, et al. Lifitegrast ophthalmic solution 5.0% versus placebo for treatment of dry eye disease: results of the randomized phase III OPUS-2 study. *Ophthalmology*. 2015 Dec; 122(12): 2423-31.
4. Holland E, Luchs J, and Karpecki P et al. Lifitegrast for the treatment of dry eye disease: results of a phase III, randomized, double-masked, placebo-controlled trial (OPUS-3). *Ophthalmology*. 2017 Jan; 124(1): 53-60.
5. Xiidra: lifitegrast ophthalmic solution 5%. *Shire US Inc*. Lexington, MA. 2017. Accessed 11 Feb 2017. Available from http://xiidra.com
6. Red Book Online [database online]. Xiidra. http://www.micromedexsolutions.com/. February 7, 2016

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Cardiovascular: Angiotensin Receptor Blockers and Combinations

Current PDL	Recommended	Rationale	P&T Decision
Preferred Candesartan (Atacand) Candesartan and Hydrochlorothiazide (Atacand HCT) Irbesartan (Avapro) Irbesartan and Hydrochlorothiazide (Avalide) Losartan (Cozaar) Losartan and Hydrochlorothiazide (Hyzaar) Olmesartan (Benicar) Olmesartan and Hydrochlorothiazide (Benicar HCT) Olmesartan and Amlodipine (Azor) Olmesartan, Hydrochlorothiazide, and Amlodipine (Tribenzor) Telmisartan (Micardis) Telmisartan and Hydrochlorothiazide (Micardis HCT) Telmisartan and Amlodipine (Twynsta) Valsartan (Diovan) Valsartan and Hydrochlorothiazide (Diovan HCT) Valsartan and Amlodipine (Exforge) Valsartan, Hydrochlorothiazide, and Amlodipine (Exforge HCT) **Non-Preferred** Azilsartan (Edarbi) - *A 60 day trial of two of the following: Losartan (Cozaar), Irbesartan (Avapro), Candesartan (Atacand), Or Valsartan (Diovan)* Eprosartan (Teveten) - *A 60 day trial of two of the following: Losartan (Cozaar), Irbesartan (Avapro), Candesartan (Atacand), Or Valsartan (Diovan)* Azilsartan and chlorthalidone (Edarbyclor) - *A 60 day trial of two of the following four alternatives: losartan/HCTZ (Hyzaar), candesartan/HCTZ (Atacand HCT), valsartan/HCTZ (Diovan HCT), or irbesartan/HCTZ (Avalide)* Eprosartan and hydrochlorothiazide (Teveten HCT) - *A 60 day trial of two of the following four alternatives: losartan/HCTZ (Hyzaar), candesartan/HCTZ (Atacand HCT), valsartan/HCTZ (Diovan HCT), or irbesartan/HCTZ (Avalide)* Valsartan and sacubitril (Entresto) - *A diagnosis of Chronic Heart Failure (NYHA Class II-IV), reduced ejection fraction 40% or less and a 30 day trial of an ACE inhibitor or ARB*	No recommended changes		Approved

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Cardiovascular: Angiotensin Converting Enzyme (ACE) Inhibitors and Combinations

Current PDL	Recommended	Rationale	P&T Decision
Preferred Benazepril (Lotensin) Benazepril-Amlodipine (Lotrel) Benazepril-Hydrochlorothiazide (Lotensin HCT) Captopril Captopril- Hydrochlorothiazide Enalapril (Vasotec) Enalapril-Hydrochlorothiazide (Vasoteric) Fosinopril Fosinopril-Hydrochlorothiazide (Monopril HCT) Lisinopril (Zestril, Prinivil) Lisinopril-Hydrochlorothiazide (Zestoretic) Moexipril Moexipril-Hydrochlorothiazide (Uniretic) Perindopril (Aceon) Quinapril (Accupril) Quinapril-Hydrochlorothiazide (Accuretic) Ramipril (Altace) Trandolapril (Mavik) **Non-Preferred** Enalapril (Epaned) oral solution - *Age 12 and under or age 12 and older and clinical reason why enalapril tablet cannot be used after 90 day trial in Ohio and Indiana. For KY if age 12 and older, only 30 day trial required.* Lisinopril (Qbrelis) oral solution - *Diagnosis of hypertension and age 6-17. Diagnosis of hypertension, heart failure or post-myocardial infarction if age 18 and older and a 30 day trial in the last 90 days or documented reason why tablets are not an option.* Trandolapril- verapamil (Tarka ER) - *Clinical reason (OH and IN MCD) supported by chart notes why after a 90 day trial (30 day for KY) that trandolapril and verapamil cannot be taken separately and concurrently.* Perindopril-Amlodipine (Prestalia) - *Diagnosis of hypertension and a clinical reason (OH and IN) supported by chart notes why after a 90 day trial (30 day KY) that amlodipine and perindopril cannot be taken separately and concurrently.*	No recommended changes		Approved

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Cardiovascular: Beta Blockers and Combinations

Current PDL	Recommended	Rationale	P&T Decision
Preferred Acebutolol HCl (Sectral) *No PA required for 1200 mg/day* Atenolol (Tenormin) Atenolol and chlorthalidone (Tenoretic) Betaxolol (Kerlone) Bisoprolol (Zebeta) Bisoprolol and Hydrochlorothiazide (Ziac) Carvedilol (Coreg) Propranolol IR (Inderal) tablet and oral solution Propranolol SR (Inderal LA) Propranolol (Hemangeol) oral solution Propranolol and Hydrochlorothiazide Labetalol HCl Metoprolol Tartrate IR tablet (Lopressor) 25 mg, 50 mg, 100 mg Metoprolol (Lopressor) intravenous solution Metoprolol Succinate ER (Toprol XL) Metoprolol and Hydrochlorothiazide (Lopressor HCT) Nadolol (Corgard) Nadolol and Bendroflumethaizide (Corzide) Pindolol *No PA required for 60 mg/day* Sotalol HCl (Betapace, Betapace AF, Sorine) Timolol *No PA required for 60 mg/day* **Non-Preferred** Carvedilol ER (Coreg CR) - *Clinical reason (OH and IN MCD) supported by chart notes why after a 90 day trial (30 days for KY) that carvedilol cannot be used.* Metoprolol succinate ER-hydrochlorothiazide (Dutoprol) - *Clinical reason (OH and IN MCD) supported by chart notes why after a 90 day trial (30 days for KY) that metoprolol tartrate (IR) or succinate (ER) and hydrochlorothiazide cannot be taken separately and concurrently* Metoprolol tartrate 37.5 mg, 75 mg - *A 30 day trial of metoprolol 25 mg, 50 mg, or 100 mg*	No recommended changes		Approved

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Cardiovascular: Beta Blockers and Combinations

Current PDL	Recommended	Rationale	P&T Decision
Non-Preferred (continued) Nebivolol (Bystolic) - *A 90 day trial within the last Year of carvedilol, labetalol, metoprolol, atenolol, nadolol, propranolol, sotalol, or bisoprolol* Nebivolol and Valsartan (Byvalson) - *Diagnosis of hypertension and 30 day trial of an ARB (valsartan, irbesartan, losartan, or candesartan) and a beta-blocker (carvedilol, nadolol, atenolol, metoprolol, propranolol, sotalol, or bisoprolol) taken separately and concurrently.* *Propranolol ER (Inderal XL, Innopran XL)* - *Clinical reason (OH and IN MCD) supported by chart notes why propranolol SR cannot be used.* Sotalol (Sotylize) oral solution - *90 day trial of sotalol (Betapace) tablet*	No recommended changes		Approved

Cardiovascular: Direct Renin Inhibitors / Diuretic Combinations

Current PDL	Recommended	Rationale	P&T Decision
Non-Preferred Aliskiren (Tekturna) - *A 60 day trial of 2 of the following within the last year: losartan (Cozaar), irbesartan (Avapro), candesartan (Atacand), or valsartan (Diovan)* Aliskiren and Hydrochlorothiazide (Tekturna HCT) - *A 60 day trial of 2 of the following within the last year: losartan/HCTZ (Hyzaar), candesartan/HCTZ (Atacand HCT), valsartan/HCTZ (Diovan HCT), or irbesartan/HCTZ (Avalide)*	No recommended changes		Approved

CareSource

Cardiovascular: Nitrates and Combinations

Current PDL	Recommended	Rationale	P&T Decision
Preferred Isosorbide mononitrate, IR and ER (Imdur) Isosorbide dinitrate IR and ER (Isordil) Nitroglycerin transdermal 24hr patch ((Minitran, Nitro-Dur) Nitroglycerin sublingual tablet (Nitrostat) Nitroglycerin CR capsule (Nitro-Time) Nitroglycerin lingual spray (Nitrolingual) Nitroglycerin vial (Nitronal)) Nitroglycerin (Nitro-Bid) ointment **Non-Preferred** Isosorbide dinitrate and hydralazine (Bidil) - *Clinical reason (OH and IN MCD) supported by chart notes why after a 90 day trial (30 day KY) that isosorbide and hydralazine cannot be taken separately and concurrently.* Nitroglycerin (GoNitro packet) - *A 30 day trial of generic nitroglycerin sublingual tablets, translingual solution, or transdermal patches and a clinical reason packet required (OH and IN only).* Nitroglycerin (Nitromist) aerosol solution - *Clinical reason (OH and IN MCD) supported by chart notes why nitroglycerin 0.4mg spray cannot be used.*	No recommended changes		Approved

CareSource

Antilipemics: HMG-CoA Inhibitors and Combinations

Current PDL	Recommended	Rationale	P&T Decision
Preferred Atorvastatin (Lipitor) Lovastatin (Mevacor) Pravastatin (Pravachol) Rosuvastatin (Crestor) Simvastatin (Zocor) **Non-Preferred** Amlodipine-atorvastatin (Caduet) - *Clinical reason (OH and IN) supported by chart notes why after a 90 day trial (30 day KY) that amlodipine and atorvastatin cannot be used taken separately and concurrently.* Fluvastatin (Lescol) capsule - *A 30 day trial within the last year of: simvastatin or atorvastatin* Fluvastatin ER (Lescol XL) tablet - *A 30 day trial within the last year of: simvastatin or atorvastatin* Pitavastatin (Livalo) - *A 30 day trial within the last year of: simvastatin, atorvastatin, or rosuvastatin* Ezetimibe-simvastatin (Vytorin) - *A 90 day trial (30 day KY) of atorvastatin and ezetimibe taken separately and concurrently.*	No recommended changes		Approved

CareSource

Antilipemics: Bile Acid Resins

Current PDL	Recommended	Rationale	P&T Decision
Preferred Cholestyramine Light packet or powder Cholestyramine packet or powder Colestipol tablet **Non-Preferred** Colestipol (Colestid) granules and packet - *Clinical reason (OH and IN) supported by chart notes why after a 90 day trial (30 day KY) that colestipol tablets cannot be used.* Colesevelam (Welchol) tablet or packet - *Diagnosis of hyperlipidemia, a 30 day trial of simvastatin, atorvastatin, or rosuvastatin, and a 30 day trial of cholestyramine or colestipol or an allergy, adverse effect, or intolerance to cholestyramine or colestipol.* - *Diagnosis of liver disease and a 30 day trial of cholestyramine or an allergy, adverse effect, or intolerance to cholestyramine or cholestyramine.* - *Diagnosis of diabetes and a 30 day trial of metformin IR or ER. Not required if allergy, intolerance or adverse effect to metformin, kidney disease or elevated creatinine, or HbA1C greater than 7.5%.*	No recommended changes		Approved

CareSource

Antilipemics: Cholesterol Absorption Inhibitors

Current PDL	Recommended	Rationale	P&T Decision
Preferred Ezetimibe (Zetia) *QL: 30 tablets per 30 days*	No recommended changes		Approved

Antilipemics: Fibrates

Current PDL	Recommended	Rationale	P&T Decision
Preferred Fenofibrate (Antara) capsule 43 mg, 130 mg Fenofibrate (Fenoglide) tablet 40 mg, 120 mg Fenofibrate (Lipofen) capsule Fenofibrate (Lofibra) capsule, tablet Fenofibrate (Tricor) tablet Fenofibric Acid (Fibricor) tablet Fenofibric Acid (Trilipix DR) capsule Gemfibrozil (Lopid) **Non-Preferred** Fenofibrate (Antara) capsule 30 mg, 90 mg - *A 90 day trial (30 day KY) of simvastatin or atorvastatin and a clinical reason (OH and IN) supported by chart notes or provider call why a 90 day trial (30 day KY) of fenofibrate (Lofibra or Tricor) cannot be used.* Fenofibrate (Triglide) - *A 90 day trial (30 day KY) of simvastatin or atorvastatin and a clinical reason (OH and IN) supported by chart notes or provider call why a 90 day trial (30 day KY) of fenofibrate (Lofibra or Tricor) cannot be used.*	No recommended changes		Approved

CareSource

Antilipemics: Niacin

Current PDL	Recommended	Rationale	P&T Decision
Preferred Niacin capsule Niacin CR (Slo-Niacin) Niacin flush free capsule Niacin tablet **Non-Preferred** Niacin (Niaspan ER) - *A 90 day trial (30 day KY) of simvastatin or atorvastatin and a clinical reason (OH and IN MCD) supported by chart notes why a after a 90 day trial (30 day KY) of OTC Niacin cannot be used.*	No recommended changes		Approved

Antilipemics: Omega-3-Fatty Acids

Current PDL	Recommended	Rationale	P&T Decision
Preferred Fish Oil, capsule, EC softgel, softgel Omega-3-acid ethyl esters (Lovaza) capsule **Non-Preferred** Omega-3-fatty acids (Sea-Omega) - *A 90 day trial (30 day KY) of OTC fish oil* Omega-3-fatty acids (Vascepa) - *A 30 day trial of simvastatin or atorvastatin and a clinical reason (OH and IN MCD) supported by chart notes why after a 30 day trial that OTC fish oil or Lovaza cannot be used.*	No recommended changes		Approved

CareSource

Pulmonary Arterial Hypertension: Endothelin Receptor Antagonists

Current PDL	Recommended	Rationale	P&T Decision
Preferred Ambrisentan (Letairis) - *Meets PA criteria:* - *Prescribed by pulmonologist or cardiologist* - *Documented diagnosis of pulmonary arterial hypertension (see Pulmonary Arterial Hypertension policy, SRx-0024)* - *Age 18 years or older* - *WHO Group 1 with NYHA Class II or III* - *Pulmonary arterial pressure not adequately controlled using an oral vasodilator (e.g. calcium channel blocker) at maximal doses OR the member was not vasodilator sensitive as determined by epoprostenol, adenosine, or inhaled nitric oxide challenge* Bosentan (Tracleer) - *Meets PA criteria:* - *Prescribed by pulmonologist or cardiologist* - *Documented diagnosis of pulmonary arterial hypertension (see Pulmonary Arterial Hypertension policy, SRx-0024)* - *Age 12 years or older* - *WHO Group 1 with NYHA Class II, III or IV* - *Pulmonary arterial pressure not adequately controlled using an oral vasodilator (e.g. calcium channel blocker) at maximal doses OR the member was not vasodilator sensitive as determined by epoprostenol, adenosine, or inhaled nitric oxide challenge* Macitentan (Opsumit) - *Meets PA criteria:* - *Prescribed by pulmonologist or cardiologist* - *Documented diagnosis of pulmonary arterial hypertension (see Pulmonary Arterial Hypertension policy, SRx-0024)* - *Age 18 years or older* - *WHO Group 1 with NYHA Class II or III* - *Pulmonary arterial pressure not adequately controlled using an oral vasodilator (e.g. calcium channel blocker) at maximal doses OR the member was not vasodilator sensitive as determined by epoprostenol, adenosine, or inhaled nitric oxide challenge*	No recommended changes		Approved

CareSource

Pulmonary Arterial Hypertension: Phosphodiesterase inhibitors

Current PDL	Recommended	Rationale	P&T Decision
Preferred Sildenafil (Revatio) - *Meets PA criteria:* - *Prescribed by pulmonologist or cardiologist* - *Documented diagnosis of pulmonary arterial hypertension (see Pulmonary Arterial Hypertension policy, SRx-0024)* - *Age 18 years or older* - *WHO Group 1 with NYHA Class II or III symptoms* - *Pulmonary arterial pressure not adequately controlled using an oral vasodilator (e.g. calcium channel blocker) at maximal doses OR the member was not vasodilator sensitive as determined by epoprostenol, adenosine, or inhaled nitric oxide challenge* Tadalafil (Adcirca) - *Meets PA criteria:* - *Prescribed by pulmonologist or cardiologist* - *Documented diagnosis of pulmonary arterial hypertension (see Pulmonary Arterial Hypertension policy, SRx-0024)* - *Age 18 years or older* - *WHO Group 1 with NYHA Class II or III symptoms* - *Pulmonary arterial pressure not adequately controlled using an oral vasodilator (e.g. calcium channel blocker) at maximal doses OR the member was not vasodilator sensitive as determined by epoprostenol, adenosine, or inhaled nitric oxide challenge* Epoprostenol (Flolan, Veletri) - *Meets PA criteria:* - *Prescribed by pulmonologist or cardiologist* - *Documented diagnosis of pulmonary arterial hypertension (see Pulmonary Arterial Hypertension policy, SRx-0024)* - *Age 18 years or older* - *Treatment as indicated by: NYHA or WHO functional class III symptoms and patient has not responded to specific oral therapies for pulmonary hypertension (e.g., bosentan, sildenafil) or NYHA or WHO functional class IV symptoms* - *Pulmonary arterial pressure not adequately controlled using an oral vasodilator (e.g. calcium channel blocker) at maximal doses OR the member was not vasodilator sensitive as determined by epoprostenol, adenosine, or inhaled nitric oxide challenge*	No recommended changes		Approved

CareSource

Pulmonary Arterial Hypertension: Prostaglandin Vasodilators

Current PDL	Recommended	Rationale	P&T Decision
Preferred Illoprost (Ventavis) - *Meets PA criteria:* - *Prescribed by pulmonologist or cardiologist* - *Documented diagnosis of pulmonary arterial hypertension (see Pulmonary Arterial Hypertension policy, SRx-0024)* - *Age 18 years or older* - *NYHA or WHO class III symptoms* - *Patient has received but not adequately responded to conventional treatment or was not a candidate for conventional treatment (e.g., oxygen, anticoagulants, calcium channel blockers, diuretics)* - *Patient is not a candidate for or has failed to respond to tadalafil, sildenafil, or riociguat* Treprostinil (Remodulin) - *Meets PA criteria:* - *Prescribed by pulmonologist or cardiologist* - *Documented diagnosis of pulmonary arterial hypertension (see Pulmonary Arterial Hypertension policy, SRx-0024)* - *Age 18 years or older* - *Pulmonary arterial pressure not adequately controlled using an oral vasodilator (e.g. calcium channel blocker) at maximal doses OR the member was not vasodilator sensitive as determined by epoprostenol, adenosine, or inhaled nitric oxide challenge* - *Transition from another therapy for PAH is needed as indicated by one or more of the following: Patient is not a candidate for or failed to respond to other oral medications (e.g., ambrisentan, bosentan, sildenafil, tadalafil) OR patient requires transition from epoprostenol*	No recommended changes		Approved

CareSource

Pulmonary Arterial Hypertension: Prostaglandin Vasodilators

Current PDL	Recommended	Rationale	P&T Decision
Preferred (continued) Treprostinil (Tyvaso) - *Meets PA criteria:* - *Prescribed by pulmonologist or cardiologist* - *Documented diagnosis of pulmonary arterial hypertension (see Pulmonary Arterial Hypertension policy, SRx-0024)* - *Age 18 years or older* - *NYHA or WHO class III symptoms* - *Patient has received but not adequately responded to conventional treatment or was not a candidate for conventional treatment (e.g., oxygen, anticoagulants, calcium channel blockers, diuretics)* - *Patient is not a candidate for or has failed to respond to tadalafil, sildenafil, or riociguat* Treprostinil (Orenitram) - *Meets PA criteria:* - *Prescribed by pulmonologist or cardiologist* - *Documented diagnosis of pulmonary arterial hypertension (see Pulmonary Arterial Hypertension policy, SRx-0024)* - *Age 18 years or older* - *NYHA or WHO class II or III symptoms* - *Patient has received but not adequately responded to conventional treatment or was not a candidate for conventional treatment (e.g., oxygen, anticoagulants, calcium channel blockers, diuretics)* - *Patient has received but not adequately responded to other oral medications (e.g., ambrisentan, bosentan, sildenafil, tadalafil)* **Non-Preferred** Uptravi (selexipag) - *Prescribed by pulmonologist or cardiologist* - *Documented diagnosis of pulmonary arterial hypertension (see Pulmonary Arterial Hypertension policy, SRx-0024)* - *Age 18 years or older* - *WHO Group 1 with NYHA class II or III symptoms* - *Pulmonary arterial pressure not adequately controlled using an oral vasodilator (e.g. calcium channel blocker) at maximal doses OR the member was not vasodilator sensitive as determined by epoprostenol, adenosine, or inhaled nitric oxide challenge*	No recommended changes		Approved

CareSource

Gastrointestinal: Inflammatory Bowel Disease

Current PDL	Recommended	Rationale	P&T Decision
Preferred Balsalazide (Colazal) capsule Budesonide (Entocort) Hydrocortisone (Cortenema, Cortifoam) Mesalamine (Asacol HD) tablet Mesalamine (Apriso ER) capsule Mesalamine (Canasa) suppository Mesalamine (Delzicol) capsule Mesalamine (Rowasa) Enema Sulfasalazine (Azulfidine, Azulfidine EN) **Non-Preferred (w/ PA)** Budesonide (Uceris) - *A 30 day trial of: Apriso ER, mesalamine (Asacol HD), Delzicol, or balsalazide (*Colazal*)* *Mesalamine (*Lialda DR) tablet - *Clinical reason (OH and IN) supported by chart notes why after a trial of mesalamine (Asacol HD, Apriso ER, Delzicol) cannot be used.* Mesalamine (Pentasa) capsule - *Clinical reason (OH and IN) supported by chart notes why after a trial of mesalamine (Asacol HD, Apriso ER, Delzicol) cannot be used.* Mesalamine (Rowasa) kit - *Clinical reason (OH and IN) supported by chart notes why after a trial of mesalamine (Rowsa) enema cannot be used.* Olsalazine (Dipentum) capsule - *Clinical reason (OH and IN) supported by chart notes why after a trial of sulfasalazine cannot be used.*	No recommended changes		Approved

CareSource

Gastrointestinal: Inflammatory Bowel Syndrome

Current PDL	Recommended	Rationale	P&T Decision
Preferred Alosetron (Lotronex) - *Meets PA criteria: Diagnosis of Severe-Diarrhea OR IBS (Irritable Bowel Syndrome) and a 7 day trial of atropine-diphenoxylate (Lomotil) or dicyclomine (Bentyl).* Lubiprostone (Amitiza) - *Meets PA criteria: A 7 day trial of lactulose or polyethylene glycol in the last 30 days supported by claims history, or currently on Amitza, Linzess, or Movantik for at least the last 30 days.* Linaclotide (Linzess) - *Meets PA criteria: A 7 day trial of lactulose or polyethylene glycol in the last 30 days supported by claims history, or currently on Amitza, Linzess, or Movantik for at least the last 30 days.* Rifaximin (Xifaxin) - *Meets PA criteria: Diagnosis of Irritable Bowel Syndrome-Diarrhea (IBS-D) and a 30 day trial in the last 90 days and inadequate response or intolerance to two of the following loperamide, antispasmodics (hyoscyamine, dicyclomine), or tricyclic antidepressants (amitriptyline, desipramine, doxepin). Or a contraindication to all listed medications.* - *QL: 42 tablets/14 days and at least 10 weeks between courses and maximum of 3 courses in the last 12 months.* **Non-preferred** Naloxegol (Movantik) - *A 7 day trial of lactulose or polyethylene glycol in the last 30 days supported by claims history, or currently on Amitza, Linzess, or Movantik for at least the last 30 days.* Eluxadoline (Viberzi) - *Diagnosis of Severe-Diarrhea OR IBS (Irritable Bowel Syndrome) and a 7 day trial of atropine-diphenoxylate (Lomotil) or dicyclomine (Bentyl).*	Add Linzess 72 mcg as non-preferred agent.	New strength available	Approved

CareSource

Gastrointestinal: Proton Pump Inhibitors

Current PDL	Recommended	Rationale	P&T Decision
Preferred Esomeprazole (Nexium) intravenous solution Esomeprazole (Nexium, Nexium24Hr) *QL: 60 per 30 days* Lansoprazole (Prevacid, Prevacid 24HR) *QL: 60 per 30 days* Lansoprazole (First-Lansoprazole) suspension *QL: 1 bottle per 30 days* Omeprazole (Prilosec, Prilosec OTC) *QL: 60 per 30 days* Omeprazole (Prilosec, Prilosec OTC) *QL: 30 per 30 days* Omeprazole (First-Omeprazole) suspension *QL: 1 bottle per 30 days* Omeprazole-Sodium Bicarbonate (Zegrid OTC) *QL: 60 per 30 days* Pantoprazole (Protonix) tablet *QL: 60 per 30 days* Pantoprazole (Protonix) intravenous solution **Non-Preferred** Dexlansoprazole (Dexilant) - *A 30 day trial of 2 of the following cannot be used: esomeprazole, pantoprazole, lansoprazole, omeprazole. Or, may approve if fax states member is pregnant.* - *QL: 30 capsules/30 days* Esomeprazole (Nexium) packet - A 30 day trial of omeprazole (capsules or First-Omeprazole) and lansoprazole (capsules or First-Lansoprazole) and a clinical reason (OH and IN) supported by chart notes why these formulary options cannot be used. Esomeprazole strontium - *30 day trial of OTC Nexium 20 mg or esomeprazole 20 or 40 mg capsules at maximal dosing and a clinical reason (OH and IN) why the RX version is needed when the OTC version has failed.*	See proposed Medicaid changes. Change to non-preferred: Esomeprazole and Lansoprazole.	No clinically significant differences in efficacy between agents known although no head to head trials. Proton pump inhibitors (PPIs) have only been studied for short duration of use. Recent evidence shows association between long term use of PPIs and increased risk of chronic kidney disease, dementia, and first-time stroke. This is in addition to known risks of acute interstitial nephritis, increased risk of osteoporosis and fractures, decreased magnesium absorption, increased risk of *C. difficile* associated-diarrhea, increased risk of community acquired pneumonia, and rebound hypersecretion.	Approved

CareSource

Gastrointestinal: Proton Pump Inhibitors

Current PDL	Recommended	Rationale	P&T Decision
Non-preferred (continued) Omeprazole-Sodium bicarbonate (Zegrid RX) - *Clinical reason (OH and IN) why after a trial of omeprazole-sodium bicarb 20/1100mg and omeprazole 20mg taken separately and concurrently cannot be taken.* Lansoprazole (Prevacid SoluTab ODT) - *Clinical reason (OH and IN) why after a 30 day trial the following cannot be used: lansoprazole (which can be opened and sprinkled on 1 Tbsp. of applesauce or emptied into 60 mL of apple, orange, or tomato juice) or First-Lansoprazole 3 mg/mL suspension. May approve if diagnosis of Autism or Asperger's or if member has a G-tube or J-tube and is unable to use other agents.* Pantoprazole (Protonix Pak) packet - *A 30 day trial of maximum dosing of omeprazole 40 mg capsules or First-Omeprazole 2 mg/mL suspension AND lansoprazole 30 mg capsules or First-lansoprazole 3 mg/mL suspension.* Rabeprazole (Aciphex) capsule - *Clinical reason (OH and IN) supported by chart notes why after a 30 day trial of 2 of the following cannot be used: esomeprazole, pantoprazole, lansoprazole, omeprazole.* - *QL: 30 capsules/30 days* Rabeprazole (Aciphex) Sprinkle capsule - *Clinical reason (OH and IN) supported by chart notes why after a 30 day trial of 2 of the following cannot be used: esomeprazole, pantoprazole, lansoprazole, omeprazole.* - *QL: 30 capsules/30 days*	No recommended changes for agents on this page.		Approved

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Gastrointestinal: Pancreatic Enzymes

Current PDL	Recommended	Rationale	P&T Decision
Preferred Pancrelipase (Creon DR, Viokace, Zenpep) **Non-Preferred** Pancrelipase (Pancreaze, Pertzye) - *Clinical reason (OH and IN) supported by chart notes why after a 90 day trial of Creon, Viokace, Zenpep cannot be used.*	No recommended changes		Approved

Hematologic: Anticoagulants

Current PDL	Recommended	Rationale	P&T Decision
Preferred Apixaban (Eliquis) Enoxaparin (Lovenox) syringe and vial Heparin Fondaparinux (Arixtra) *No PA required for 30 syringes per 180 days.* Rivaroxaban (Xarelto) Warfarin (Coumadin, Jantoven) *May approve if PA is for DAW request.* **Non-Preferred** Dabigatran (Pradaxa) - *Clinical reason (OH and IN) supported by chart notes why after a 30 day trial of the following cannot be used: Eliquis or Xarelto.* Edoxaban (Savaysa) - *Clinical reason (OH and IN) supported by chart notes why after a 90 day trial (30 day KY) that the following cannot be used: Eliquis, fondaparinux, Xarelto.* Dalteparin (Fragmin) - *Diagnosis of VTE, unstable angina, or non-Q wave MI and unable to take oral warfarin or enoxaparin. Or, a diagnosis of DVT and a one time trial of enoxaparin.*	No recommended changes		Approved

CareSource

Hematologic: Growth Factors

Current PDL	Recommended	Rationale	P&T Decision
Preferred (w/ PA) Darbepoetin (Aranesp) - *Meets PA criteria:* - *Diagnosis of anemia in cancer for members on chemotherapy, anemia in chronic renal failure, anemia in zidovudine-treated, HIV-infection, or anemia associated with myelodysplastic syndrome.* - *Criteria per Hematopoietic Growth Factors policy (SRx-0034)* Epoetin (Epogen, Procrit) - *Meets PA criteria:* - *Diagnosis of anemia in cancer for members on chemotherapy, anemia in chronic renal failure, anemia in zidovudine-treated, HIV-infection, or anemia associated with myelodysplastic syndrome.* - *Criteria per Hematopoietic Growth Factors policy (SRx-0034)* Filgastim (Zarxio) - *Meets PA criteria:* - *Diagnosis of acute myeloid leukemia, myeloid engraftment for bone marrow transplant, severe chronic neutropenia, or severe chronic neutropenia.* - *Criteria per Colony Stimulating Factors (SRx-0047)* **Non-Preferred** Filgastim (Granix) - *Diagnosis of solid tumor/non-myeloid malignancy.* - *Trial of Zarxio (preferred agent if indicated)* - *Criteria per Colony Stimulating Factors (SRx-0047)* Filgastim (Neupogen) - *Diagnosis of acute myeloid leukemia, myeloid engraftment for bone marrow transplant, severe chronic neutropenia, severe chronic neutropenia, and solid tumor/non-myeloid malignancy, or hematopoietic radiation injury syndrome.* - *Trial of Zarxio (preferred agent if indicated)* - *Criteria per Colony Stimulating Factors (SRx-0047)* Pegfilgrastim (Neulasta) - *Diagnosis of hematopoietic radiation injury syndrome or solid tumor/non-myeloid malignancy.* - *Trial of Zarxio (preferred agent if indicated)* - *Criteria per Colony Stimulating Factors (SRx-0047)* Sargramostim (Leukine) - *Diagnosis of acute myeloid leukemia, myeloid engraftment for bone marrow transplant, severe chronic neutropenia, or solid tumor/non-myeloid malignancy.* - *Trial of Zarxio (preferred agent if indicated)* - *Criteria per Colony Stimulating Factors (SRx-0047)*	See proposed Medicaid changes to add Neulasta OnPro to medical benefit as preferred agent.	Neulasta OnPro is applied during appointment for chemotherapy and is delivered the following day. The patient is not required to return to office for an additional appointment for injection of Neulasta. No additional cost for OnPro device vs. prefilled syringe when comparing AWP.	Approved

CareSource

Hematologic: Platelet Aggregation Inhibitors

Current PDL	Recommended	Rationale	P&T Decision
Preferred Anagrelide (Agrylin) Aspirin (chewable tablet, tablet, OTC) Cilostazol (Pletal) Clopidogrel (Plavix) Dipyridamole (Persantine) Prasugrel (Effient) Ticagrelor (Brilinta) - *Meets PA criteria: 30 day trial of clopidogrel or allergy, intolerance or adverse effect with clopidogrel. May approve if started on medication in hospital or if patient has any claim for medication.* **Non-Preferred** Aspirin-Dipyridamole (Aggrenox) - *Diagnosis of TIA or ischemic stroke and trial of aspirin.* Vorapaxar (Zontivity) - *30 day trial of clopidogrel or allergy, intolerance or adverse effect with clopidogrel. May approve if started on medication in hospital or if patient has any claim for medication.*	No recommended changes		Approved

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