

**P&T Committee Meeting Minutes**  
**GHP Family**  
**September 17, 2019**

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<p><b>Present:</b> Bret Yarczower, MD, MBA – Chair Kristen Bender, PharmD – via phone Kim Castelnovo – via phone Rajneel Farley Pharm.D. Dean Christian, MD – via phone Kimberly Clark, Pharm.D. Tricia Heitzman, Pharm.D. Jason Howay, Pharm.D. – via phone Keith Hunsicker, Pharm.D. Kelli Hunsicker, Pharm.D. – via phone Steven Kheloussi, Pharm.D. – via phone Phillip Krebs, R.EEG T. – via phone Aubrielle Prater Pharm.D. Kimberly Reichard Pharm.D. Angela Scarantino – via phone Kristen Scheib, Pharm.D. – via phone Richard Silbert, MD – via phone Michael Spishock, RPh – via phone Todd Sponenberg, Pharm.D. Jill Stone, Pharm.D. – via phone Kevin Szczecina, RPh Kelly Yelenic Pharm.D.</p>	<p><b>Absent:</b> Kenneth Bertka, MD Beverly Blaisure, MD Holly Bones, Pharm.D. Alyssa Cilia, RPh Michael Evans, RPh Perry Meadows, MD Jamie Miller, RPh Steven Moscola, RPh Jonas Pearson, RPh William Seavey, Pharm.D.</p>
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**Call to Order:**

Dr. Bret Yarczower called the meeting to order at 1:03 p.m., Tuesday, September 17, 2019.

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**Review and Approval of Minutes:**

Dr. Bret Yarczower asked for a motion or approval to accept the July 16, 2019 minutes as written. Keith Hunsicker accepted the motion and Kimberly Clark seconded the motion. None were opposed.

## Ophthalmic Corticosteroid/NSAIDs Update

<b>Corticosteroid Eye Drops<sup>1-16</sup></b>			
<b>Brand Name</b>	<b>Generic Name</b>	<b>Generic Available?</b>	<b>Manufacturer</b>
Maxidex 0.1%	Dexamethasone	No	Novartis
-	Dexamethasone Sodium Phosphate 0.1%	Yes	Multiple
Durezol 0.05%	Difluprednate	No	Novartis
Flarex 0.1%	Fluorometholone	No	Novartis
FML Liquifilm 0.1%	Fluorometholone	Yes	Multiple
FML Forte 0.25%	Fluorometholone	No	Allergan
FML ointment 0.1%	Fluorometholone	No	Allergan
Inveltys 1%	Loteprednol	No	Kala Pharms Inc
Alrex 0.2%	Loteprednol Etabonate	No	Bausch & Lomb
Lotemax 0.5% suspension	Loteprednol Etabonate	Yes	Multiple
Lotemax 0.5% ointment	Loteprednol Etabonate	No	Bausch & Lomb
Lotemax 0.5% gel	Loteprednol Etabonate	No	Bausch & Lomb
Lotemax SM 0.38%	Loteprednol Etabonate	No	Bausch & Lomb
Pred Forte, Prednisolone Acetate P-F 1%	Prednisolone Acetate	Yes	Multiple
Pred Mild 0.12%	Prednisolone Acetate	No	Allergan
-	Prednisolone Sodium Phosphate 1%	Yes	Multiple

<b>NSAID Eye Drops<sup>17-25</sup></b>			
<b>Brand Name</b>	<b>Generic Name</b>	<b>Generic Available?</b>	<b>Manufacturer</b>
Prolensa 0.07%	Bromfenac	No	Bausch & Lomb
BromSite 0.075%	Bromfenac	No	Sun Pharma Global FZE
-	Bromfenac 0.09%	Yes	Multiple
-	Diclofenac Sodium 0.1%	Yes	Multiple
Acular 0.5%	Ketorolac Tromethamine	Yes	Multiple
Acular LS 0.4%	Ketorolac Tromethamine	Yes	Multiple
Acuvail 0.45%	Ketorolac Tromethamine	No	Allergan
Ilevro 0.3%,	Nepafenac	No	Novartis
Nevanac 0.1%	Nepafenac	No	Novartis

### **Corticosteroid indications**

<b>Medication</b>	<b>Steroid responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe*</b>	<b>Corneal injury from chemical, radiation, or thermal burns, or penetration of foreign bodies</b>	<b>Treatment of endogenous anterior uveitis</b>	<b>Post-operative inflammation and pain following ocular surgery</b>	<b>Temporary relief of the signs and symptoms of seasonal allergic conjunctivitis</b>
<b>Maxidex 0.1%</b>	<b>X</b>	<b>X</b>			
<b>Dexamethasone Sodium Phosphate 0.1%</b>	<b>X</b>	<b>X</b>			
<b>Durezol 0.05%</b>			<b>X</b>	<b>X</b>	
<b>Flarex 0.1%</b>	<b>X</b>				
<b>FML 0.1%</b>	<b>X</b>				
<b>FML Forte 0.25%</b>	<b>X</b>				
<b>FML S.O.P ointment 0.1%</b>	<b>X</b>				
<b>Inveltys 1%</b>				<b>X</b>	
<b>Alrex 0.2%</b>					<b>X</b>
<b>Lotemax 0.5% suspension, ointment, gel</b>	<b>X (Suspension Only)</b>			<b>X</b>	
<b>Lotemax SM 0.38%</b>				<b>X</b>	
<b>Pred Forte, Prednisolone Acetate P-F 1%</b>	<b>X</b>	<b>X (P-F 1% Only)</b>			
<b>Pred Mild 0.12%</b>	<b>X<sup>^</sup></b>	<b>X<sup>^</sup></b>			
<b>Prednisolone Sodium Phosphate 1%</b>	<b>X</b>				

\*Steroid responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe such as allergic conjunctivitis, acne rosacea, superficial punctate keratitis, herpes zoster keratitis, iritis, cyclitis, selected infective conjunctivitis when the inherent hazard of steroid use is accepted to obtain an advisable diminution in edema and inflammation

<sup>^</sup> Indication is similar to other listed topical corticosteroids, but language differs in a slight, non-clinically significant way. Pred Mild 0.12% is indicated for “mild to moderate noninfectious allergic and inflammatory disorders of the lid, conjunctiva, cornea, and sclera (including chemical and thermal burns)”

<b>Corticosteroid Eye Drops Dosing<sup>1-16</sup></b>			
<b>Brand Name</b>	<b>Generic Name</b>	<b>Dosing</b>	<b>Notes</b>
Maxidex 0.1%	Dexamethasone	1-2 drops 4-6 times daily	Used up to hourly in severe disease
-	Dexamethasone Sod Phosphate 0.1%	1-2 drops 4-6 times daily	Used up to hourly in severe disease
Durezol 0.05%	Difluprednate	<b><u>Inflammation &amp; pain post-ocular surgery:</u></b> 1 drop 4 times daily <b><u>Endogenous anterior uveitis:</u></b> 1 drop 4 times daily	Dose is tapered after 2 weeks
Flarex 0.1%	Fluorometholone	1-2 drops 4 times daily	During initial 24-48 hours, dose can be increased to 2 drops every 2 hours
FML Liquifilm 0.1%	Fluorometholone	1-2 drops 4 times daily	During initial 24-48 hours, dose can be increased to 2 drops every 2 hours or 1 drop every 4 hours
FML Forte 0.25%	Fluorometholone	1 drop 2-4 times daily	During initial 24-48 hours, frequency can increase to 1 drop every 4 hours
FML ointment 0.1%	Fluorometholone	1/2" ribbon 1-3 times daily	During initial 24-48 hours, frequency can be 1 application every 4 hours
Inveltys 1%	Loteprednol	1-2 drops twice daily	Begin 24 hours after surgery and continue for 2 weeks
Alrex 0.2%	Loteprednol Etabonate	1 drop 4 times daily	
Lotemax 0.5% suspension	Loteprednol Etabonate	1-2 drops 4 times daily	Begin 24 hours after surgery and continue for 2 weeks
Lotemax 0.5% ointment	Loteprednol Etabonate	1/2" ribbon 4 times daily	Begin 24 hours after surgery and continue for 2 weeks
Lotemax 0.5% gel	Loteprednol Etabonate	1-2 drops 4 times daily	Begin day after surgery and continue for 2 weeks
Lotemax SM 0.38%	Loteprednol Etabonate	1 drop 3 times daily	Begin day after surgery and continue for 2 weeks
Pred Forte, Prednisolone Acetate P-F 1%	Prednisolone Acetate	1-2 drops 4 times daily	During initial 24-48 hours, dose can be increased if necessary
Pred Mild 0.12%	Prednisolone Acetate	1-2 drops 4 times daily	During initial 24-48 hours, dose can be increased if necessary
-	Prednisolone Sodium Phosphate 1%	<b><u>Ophthalmic inflammatory injury:</u></b> 1-2 drops every hour during the day and every 2 hours at night; then 1 drop every 4 hours; then 1 drop 3-4 times daily <b><u>Off-label for anterior uveitis:</u></b> 1 drop up to 8 times daily	

**Current Formulary Status (Corticosteroids):**

	<b>GHP Family</b>
<b>Preferred Generic</b>	
<b>Generic</b>	dexamethasone sodium phosphate drops 0.1%, fluorometholone drops, prednisolone acetate 1%, prednisolone sodium phosphate drops 1%
<b>Brand Preferred</b>	FML S.O.P. 0.1%
<b>Brand Non-Preferred</b>	
<b>Specialty</b>	

**NSAID Indications**

<b>Medication</b>	<b>Postoperative inflammation and reduction of ocular pain in patients who have undergone cataract surgery</b>	<b>Postoperative inflammation and reduction of ocular pain in patients following cataract extraction</b>	<b>Temporary relief of pain, burning/stinging in patients following corneal refractive surgery</b>	<b>Temporary relief of ocular itching due to seasonal allergic rhinitis</b>
<b>Prolensa 0.07%</b>	<b>X</b>			
<b>BromSite 0.075%</b>	<b>X</b>			
<b>Bromfenac 0.09%</b>	<b>X</b>			
<b>Diclofenac Sodium 0.1%</b>	<b>X</b>		<b>X*</b>	
<b>Acular 0.5%</b>		<b>X</b>		<b>X</b>
<b>Acular LS 0.4%</b>			<b>X</b>	
<b>Acuvail 0.45%</b>	<b>X</b>			
<b>Ilevro 0.3%</b>	<b>X</b>			
<b>Nevanac 0.1%</b>	<b>X</b>			

\*Diclofenac is also indicated for use in photophobia post-refractive corneal surgery but is not indicated for burning/stinging following surgery. However, data supports its use for this indication.

**Current formulary status (NSAIDs)**

	<b>GHP Family</b>
<b>Preferred Generic</b>	

<b>Generic</b>	ketorolac drops 0.4% and 0.5%, diclofenac sodium 0.1%
<b>Brand Preferred</b>	
<b>Brand Non-Preferred</b>	
<b>Specialty</b>	

NSAID Eye Drops Dosing <sup>17-25</sup>			
Brand Name	Generic Name	Dosing	Notes
Prolensa 0.07%	Bromfenac	1 drop once daily	Begin 1 day prior to surgery, day of surgery, and 14 days post-surgery
BromSite 0.075%	Bromfenac	1 drop twice daily	Begin 1 day prior to surgery, day of surgery, and 14 days post-surgery
-	Bromfenac 0.09%	1 drop once daily	Begin 1 day prior to surgery, day of surgery, and 14 days post-surgery
-	Diclofenac Sodium 0.1%	<b>Ocular pain/photophobia:</b> 1-2 drops 4 times daily for 3 days <b>Post-op ocular inflammation:</b> 1 drop 4 times daily for 2 weeks	<b>Ocular pain/photophobia:</b> Begin with 1-2 drops within 1 hour prior to surgery; within 15 minutes after surgery <b>Post-op ocular inflammation:</b> Begin 24 hours after surgery for up to 2 weeks
Acular 0.5%	Ketorolac Tromethamine	<b>Allergic conjunctivitis:</b> 1 drop 4 times daily <b>Post-op ocular inflammation:</b> 1 drop 4 times daily for 2 weeks	<b>Post-op ocular inflammation:</b> Begin 24 hours after surgery for up to 2 weeks
Acular LS 0.4%	Ketorolac Tromethamine	1 drop 4 times daily as needed	Continue for up to 4 days after surgery
Acuvail 0.45%	Ketorolac Tromethamine	1 drop twice daily	Begin 1 day prior to surgery, day of surgery, and 14 days post-surgery
Ilevro 0.3%,	Nepafenac	1 drop once daily	Begin 1 day prior to surgery, day of surgery, and 14 days post-surgery. 1 additional drop 30-120 minutes prior to surgery
Nevanac 0.1%	Nepafenac	1 drop three times daily	Begin 1 day prior to surgery, day of surgery, and 14 days post-surgery

#### Review:

**Allergic Conjunctivitis:** There are five types of ocular allergy: seasonal allergic conjunctivitis (SAC), perennial allergic conjunctivitis (PAC), vernal keratoconjunctivitis (VKC), atopic keratoconjunctivitis (AKC), and giant papillary conjunctivitis (GPC).<sup>26</sup> The majority of cases (90-95%) are attributed to SAC and PAC.<sup>27</sup> For SAC and PAC, topical antihistamines, mast cell stabilizers, and topical NSAIDs are helpful for reducing itching.

Antihistamines work quickly, mast cell stabilizers work for both acute and late-phase responses, and NSAIDs work for late-phase responses.<sup>27</sup> Vasoconstrictors (decongestants) aid in relieving redness, while topical corticosteroids are effective for multiple allergic conjunctivitis symptoms and work for both early- and late-phase responses.<sup>27</sup> Recommended first line treatment for SAC and PAC involves a dual-acting antihistamine-mast cell stabilizer agent (ketotifen [Alaway, Zaditor], olopatadine [Patanol, Pataday, Pazeo], alcaftadine [Lastacaft], epinastine, and bepotastine [Bepreve], azelastine). This is due to their ability to target multiple targets within the allergic response cascade, allowing for immediate and long-lasting relief. Additionally, several of these agents (Pataday, Pazeo, and Lastacaft) allow for once daily administration.<sup>27</sup> Mild symptoms can also be treated with an OTC antihistamine/vasoconstrictor or second-generation topical histamine H<sub>1</sub>-receptor antagonist with no preference of one product over another.<sup>28</sup> If symptoms are not adequately controlled, a brief, 1-2 week course of a topical corticosteroid may be added to the regimen.<sup>28</sup> Patients who experience moderate-to-severe symptoms that interfere with daily life may require longer-term treatment.<sup>27</sup> Long-term use of topical corticosteroids can lead to unwanted side effects such as increased intraocular pressure, corneal abnormalities, and cataract formation.<sup>27</sup> Most cases of SAC or PAC do not often require corticosteroid intervention.<sup>27</sup>

Vernal keratoconjunctivitis (VKC) and atopic keratoconjunctivitis (AKC) are chronic, bilateral, and severe forms of allergic inflammation affecting the ocular surface and can lead to severe damage to the ocular surface.<sup>26</sup> VKC is treated similarly, with dual-acting antihistamine-mast cell stabilizer agents as first line therapies.<sup>26</sup> If these agents aren't available the use of single agent antihistamines (cetirizine ophth) or mast cell stabilizers (cromolyn, nedocromil (Alocril), and lodoxamide (Alomide)) in combination or as monotherapy can be used. For refractory disease, those not responding after 2-3 weeks of initial therapy, topical corticosteroids may be used short-term and the addition of cyclosporine 0.2% (Restasis) can be considered. While prednisolone acetate 1% and dexamethasone 0.1% have the greatest efficacy for this indication, they also carry the largest risk of raising IOP. Others, including prednisolone acetate 0.12%, fluorometholone, and loteprednol etabonate 0.5 or 0.2%, are expected to raise IOP to a lesser extent.<sup>26</sup>

Atopic keratoconjunctivitis (AKC) is a chronic, allergic disorder that occurs most often in patients with a history of atopic dermatitis.<sup>29</sup> While differing opinions on the optimal first-line therapy exist (dual-acting antihistamine-mast cell stabilizer agents versus mast-cell stabilizers alone as first line options), sources agree that steroids should be used only short-term for refractory disease.<sup>29,30</sup> Cyclosporine 0.2% can also be used as a steroid-sparing option.<sup>29</sup>

Giant papillary conjunctivitis (GPC) is a noninfectious inflammatory disorder that represents a reaction to lid movement over a foreign substance, such as contact lenses.<sup>31</sup> Treatment, again, involves topical antihistamines, mast cell stabilizers, and dual-acting agents with topical corticosteroids being reserved for severe, acute cases of GPC.<sup>31</sup>

No data could be found comparing the efficacy of corticosteroids for any of the types of allergic conjunctivitis.

**Temporary relief of pain, burning/stinging in patients following corneal refractive surgery<sup>32</sup>:** Diclofenac sodium 0.1% was found to be significantly superior ( $p < 0.001$ ) to placebo in reducing ocular pain, photophobia, foreign-body sensation, and burning/stinging at all intervals (6, 24, and 48 hours post-surgery) after bilateral radial keratotomy. Acular LS is also indicated for burning/stinging, but this is the only agent indicated for post-surgery photophobia.

**NSAIDs for post-operative inflammation and reduction of ocular pain in patients who have undergone cataract surgery:** Diclofenac sodium 0.1% was found to have similar high tolerability with no significant differences to nepafenac for discomfort, itching, burning, and pain in patients treated for inflammation and pain following cataract surgery.<sup>33</sup> A review of NSAID efficacy studies for this indication concluded that all NSAIDs studied for this indication are comparable and that limited data exists to support the efficacy of one over another for post-surgery inflammation and pain.<sup>34</sup> The American Academy of Ophthalmology also mentions that there is no optimal regimen for post-surgical eyedrops; it is determined by physician choice.<sup>35</sup> Additionally, a systematic

review of 48 RCTs comparing NSAIDs +/- corticosteroids to corticosteroids alone found no superiority of one treatment group over another for postoperative inflammation treatment.<sup>36</sup>

**Comparative efficacy of steroids for post-operative inflammation:** Generically available forms of steroidal eyedrops have been found to demonstrate efficacy in relieving inflammation and pain post-operatively. In a prospective randomized controlled trial, prednisolone acetate, ketorolac tromethamine and fluorometholone acetate were compared in reduction of inflammation after phacoemulsification.<sup>37</sup> All agents were found to effectively reduce post-op inflammation, with prednisolone showing comparable efficacy to fluorometholone and ketorolac showing statistically significantly less efficacy.<sup>37</sup> IOP was significantly higher in the prednisolone acetate group compared with the fluorometholone group.<sup>37</sup>

A comparative case series of bromfenac 0.09% plus either loteprednol etabonate 0.5% or prednisolone acetate 1% found that both corticosteroids reduced inflammation similarly after cataract surgery, with loteprednol causing less fluctuation in IOP.<sup>38</sup> In a separate randomized, double-blind study, 20 patients were assigned to loteprednol etabonate 0.5% or prednisolone acetate 1% for inflammation following cataract surgery.<sup>39</sup> Patients from both groups achieved a similar resolution of postoperative inflammation (conjunctival hyperemia, corneal edema, aqueous cells, flare), with 60% of patients in the loteprednol etabonate group and 50% of patients in the prednisolone group achieving significant resolution of inflammation by the final visit.<sup>39</sup> Though there were only 20 patients included in this study, loteprednol etabonate had a numerically smaller effect on IOP compared to prednisolone acetate.<sup>5</sup> No statistical analyses were completed.

A separate 30-patient RCT compared fluorometholone acetate 0.1% to loteprednol etabonate 0.5% after phacoemulsification. The study found no statistically significant differences in flare, anterior segment cell, conjunctival hyperemia scores, or adverse events between groups.<sup>40</sup> An additional comparison of loteprednol 0.5% and fluorometholone 0.1% found no significant differences in uncorrected distance visual acuity, corrected visual distance acuity, manifest refraction, corneal haze, IOP, and ocular discomfort and redness between groups.<sup>41</sup>

Finally, difluprednate (Durezol) 0.05% was compared to prednisolone acetate 1% in a multicenter RCT in patients undergoing bilateral phacoemulsification. Patients received difluprednate 0.05% for one eye and prednisolone 1% for the other eye.<sup>42</sup> Difluprednate reduced inflammation more effectively than prednisolone acetate, resulting in more rapid return of vision. Difluprednate vs prednisolone was superior at protecting the cornea [62% vs 38% of patients without corneal edema, respectively, at day 1 (p=0.019)] and reducing macular thickening after cataract surgery (p=0.011).<sup>42</sup>

**Endogenous, Non-infectious, Anterior and Intermediate Uveitis:** Uveitis is a disease of sight-threatening intraocular inflammation that typically involves the uveal tract. There are four types of uveitis including anterior (occurring at the front of the eye), posterior (inflammation of the retina, optic nerve, and choroid), intermediate (inflammation of the ciliary body and iris), and panuveitis (inflammation that affects the entire eye). Anterior uveitis is the most common form of uveitis.<sup>43</sup>

Topical corticosteroids are used to treat anterior uveitis determined to be of noninfectious origin.<sup>43</sup> Prednisolone acetate 1% may be used off-label, with the dosage based on the severity of inflammation (up to 8 doses daily).<sup>44</sup> If patients have uveitis that is caused by an infection, anti-infective agents are needed to treat the patient (more commonly seen with intermediate or posterior uveitis).<sup>43</sup> Ophthalmic corticosteroids may be used for intermediate or posterior uveitis, but more appropriate treatment involves targeting the underlying cause. Durezol is currently FDA approved for the treatment of exogenous anterior uveitis. A phase 3, randomized, double-blinded, non-inferiority study was conducted to investigate the comparative efficacy of Durezol 0.05% four times daily vs prednisolone acetate 1% eight times daily for the treatment of uveitis. The results showed that the Durezol was just as well tolerated and non-inferior to prednisolone acetate for the treatment of uveitis symptoms in patients at 14 days. Durezol also increased IOP significantly more than prednisolone acetate 1% (2.5 mmHg for Durezol vs.



0.1 mmHg for Prednisolone Acetate) at 3 days, but not at any other timepoint. Results support Durezol as a reasonable alternative to prednisolone acetate for the treatment of anterior uveitis.<sup>45</sup>

Currently, Durezol (difluprednate) is the only FDA approved drug for the treatment of anterior uveitis. In two parallel, randomized, double-masked, active-controlled comparison studies, loteprednol 0.5% ophthalmic suspension was less effective than prednisolone acetate 1% for acute anterior uveitis.<sup>46</sup>

**Steroid responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe:**

- **Superficial punctate keratitis<sup>47</sup>:** An observational case series of 35 patients from 1992-2001 evaluated the treatment, presentation, and course of disease for superficial punctate keratitis (coarse, bilateral opacities on the epithelium of the cornea). Fluorometholone 0.1% & 0.25%, loteprednol 0.2% and 0.5%, prednisolone acetate 1% and 0.12%, and prednisolone sodium phosphate 0.125% were all used in initial treatment of symptoms. No significant differences in efficacy were reported, and there were no complications recorded in relation to any of the corticosteroid treatments.
- **Herpes zoster keratitis<sup>48</sup>:** A 2018 clinical review of acute keratitis associated with herpes zoster evaluated the role of corticosteroids in the treatment of this condition. There is currently a lack of consensus for treatment of this condition. Corticosteroid use is controversial as patients with this condition would likely need them chronically, therefore increasing the risk of cataract development and steroid-induced glaucoma.

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

**Clinical Discussion:** Concern raised about time to complete coverage determinations for post-operative medications; formulary placement did not change, only the creation of NF guidelines for review. For corticosteroids: Todd Sponenberg made a motion to accept the recommendations as presented. Kelly Yelenic seconded the motion. For NSAIDS: Tricia Heitzman made a motion to accept the recommendations as presented. Aubrielle Prater seconded the motion None were opposed.

**Financial Discussion:** No questions or comments. For corticosteroids: Todd Sponenberg made a motion to accept the recommendations as presented. Keith Hunsicker seconded the motion. For NSAIDS, Kevin Szczecina made a motion to accept the recommendations as presented. Rajneel Farley seconded the motion None were opposed.

Medication	Recommendations
Maxidex 0.1%	<p><b>Recommendation:</b> No changes to formulary status. Add PA criterion.</p> <p><b>Recommended Formulary Status:</b> No changes recommended</p> <p><b>Policy Update:</b> The following criterion should apply:  <b>Requests should be approved if patients meet the following criteria:</b></p> <p><u>For Diagnosis of Steroid Responsive Inflammatory Condition:</u></p> <ul style="list-style-type: none"> <li>• Medical record documentation of therapeutic failure, contraindication, or intolerance to three (3) formulary alternatives</li> </ul> <p><b>Note –</b> Formulary alternatives should include only the formulary steroids as NSAIDs are not indicated.</p> <p><u>For Diagnosis of Chemical or Thermal Burns:</u></p> <ul style="list-style-type: none"> <li>• Medical record documentation of therapeutic failure, contraindication, or intolerance to prednisolone acetate 1% or prednisolone acetate 1% (P-F) <b>AND</b> dexamethasone sodium phosphate 0.1%</li> </ul>

	<p><i>Rationale: This branded agent is more expensive than other generically available formulary alternatives. As the brand tier copay on GHP Family will not offset the cost heavily, it is recommended that this agent stays nonformulary. For steroid responsive inflammatory conditions, any of the preferred formulary corticosteroid alternatives are appropriate. However, for the diagnosis of chemical or thermal burns, only prednisolone acetate 1% (p-f) and dexamethasone sodium phosphate 0.1% are indicated.</i></p>
<b>Dexamethasone Sodium Phosphate 0.1%</b>	<p>No changes recommended based on cost review at this time</p> <p><i>Rationale: This agent is a low cost, generic option. No prior authorization should be added based on cost.</i></p>
<b>Durezol 0.05%</b>	<p><b>Recommendation:</b> No changes to formulary status. Additional PA criteria.</p> <p><b>Recommended Formulary Status:</b> No changes recommended</p> <p>The following additional criteria should apply:</p> <p><u>Diagnosis of Uveitis:</u></p> <ul style="list-style-type: none"> <li>• If being used for uveitis, medical record documentation of therapeutic failure, contraindication, or intolerance to prednisolone acetate 1%</li> </ul> <p><u>Diagnosis of Post-Operative Inflammation:</u></p> <ul style="list-style-type: none"> <li>• If being used for post-operative inflammation, medical record documentation of therapeutic failure on, intolerance to, or contraindication to three formulary alternatives.</li> </ul> <p><i>Rationale: For uveitis, prednisolone acetate specifically has been shown to be effective. While it is dosed up to 8 times daily, it may be dosed less based on the severity of the disorder and is a less costly option. As for the other indication, other generically available steroids are effective though they are not FDA-approved for this indication. In addition, diclofenac 0.1% is also indicated for this condition. All of these agents are significantly less expensive.</i></p>
<b>Flarex 0.1% susp</b>	<p><b>Recommendation:</b> No changes to formulary status. Add PA criterion.</p> <p><b>Recommended Formulary Status:</b> No changes recommended</p> <p><b>Policy Update:</b> The following criterion should apply:</p> <ul style="list-style-type: none"> <li>• Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three (3) formulary alternatives</li> </ul> <p><i>Rationale: This branded agent is more expensive than other generically available formulary alternatives. As the brand tier copay on GHP Family will not offset the cost heavily, it is recommended that this agent stays nonformulary and requires failure on three alternatives prior to approval.</i></p>
<b>Fluorometholone 0.1% Liquifilm</b>	<p>No changes recommended based on cost review at this time</p> <p><i>Rationale: This agent is a low cost, generic option. No prior authorization should be added based on cost.</i></p>
<b>FML Forte 0.25%</b>	<p><b>Recommendation:</b> No changes to formulary status. Add PA criterion.</p> <p><b>Recommended Formulary Status:</b> No changes recommended</p> <p><b>Policy Update:</b> The following criterion should apply:</p>

	<ul style="list-style-type: none"> <li>Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three (3) formulary alternatives</li> </ul> <p><i>Rationale: This branded agent is more expensive than other generically available formulary alternatives. As the brand tier copay on GHP Family will not offset the cost heavily, it is recommended that this agent stays nonformulary and requires failure on three alternatives prior to approval.</i></p>
<b>FML S.O.P. ointment 0.1%</b>	<p>No changes recommended based on cost review at this time</p> <p><i>Rationale: This agent is one of the two options available as an ointment. It is less expensive than the Lotemax ointment.</i></p>
<b>Inveltys 0.1%</b>	<p>No changes recommended based on cost review at this time</p> <p><i>Rationale: The current policy is consistent with treatment recommendations and the cost analysis.</i></p>
<b>Alrex 0.2%</b>	<p><b>Recommendation:</b> No changes to formulary status. Additional PA criteria.</p> <p><b>Recommended Formulary Status:</b> No changes recommended</p> <p>The following additional prior authorization criterion should apply:</p> <ul style="list-style-type: none"> <li>Medical record documentation of therapeutic failure on, intolerance to, or contraindication to two (2) formulary steroid or NSAID eye drop alternatives</li> </ul> <p><b>Note</b> – Formulary alternatives should include only the formulary steroids and ketorolac 0.5% drops as the other NSAIDs are not indicated.</p> <p><i>Rationale: All of the generic corticosteroids are indicated for seasonal allergic conjunctivitis and are less costly alternatives. Requiring a trial of only two (rather than 3 as normal) as the patient is also required to try an ophthalmic antihistamine-mast cell stabilizer agent (per the clinical criteria above).</i></p>
<b>Loteprednol Etabonate 0.5% (generic for Lotemax 0.5% susp) AND the branded product</b>	<p>No changes recommended based on cost review at this time</p> <p><i>Rationale: The current policy is consistent with treatment recommendations and the cost analysis.</i></p>
<b>Lotemax 0.5% ointment</b>	<p>No changes recommended based on cost review at this time</p>
<b>Lotemax 0.5% gel</b>	<p><i>Rationale: The current policy is consistent with treatment recommendations and the cost analysis.</i></p>
<b>Lotemax SM 0.38%</b>	
<b>Prednisolone Acetate 1% (Pred Forte)</b>	<p>No changes recommended based on cost review at this time</p> <p><i>Rationale: This agent is a low cost, generic option. No prior authorization should be added based on cost.</i></p>
<b>Prednisolone acetate P-F 1%</b>	<p><b>Recommendation:</b> Update tiering.</p> <p><b>Recommended Formulary Status:</b> Generic</p> <p><i>Rationale: This agent is a low cost, generic option. No prior authorization should be added based on cost.</i></p>
<b>Pred Mild 0.12%</b>	<p><b>Recommendation:</b> No changes to formulary status. Add PA criteria.</p> <p><b>Recommended Formulary Status:</b> No changes recommended</p> <p>The following prior authorization criteria should apply:</p>

	<p><u>For Diagnosis of Steroid Responsive Inflammatory Condition:</u></p> <ul style="list-style-type: none"> <li>• Medical record documentation of therapeutic failure, contraindication, or intolerance to three (3) formulary alternatives</li> </ul> <p><b>Note</b> – Formulary alternatives should include only the formulary steroids as NSAIDs are not indicated.</p> <p><u>For Diagnosis of Chemical or Thermal Burns:</u></p> <ul style="list-style-type: none"> <li>• Medical record documentation of therapeutic failure, contraindication, or intolerance to prednisolone acetate 1% or prednisolone acetate 1% (P-F) <b>AND</b> dexamethasone sodium phosphate 0.1%</li> </ul> <p><i>Rationale: Pred Mild is a less cost-effective option for the treatment of the conditions for which it is FDA-approved. For steroid responsive inflammatory conditions, any of the preferred formulary corticosteroid alternatives are appropriate. However, for the diagnosis of chemical or thermal burns, only prednisolone acetate 1% (p-f) and dexamethasone sodium phosphate 0.1% are indicated.</i></p>
<b>Prednisolone Sodium Phosphate 1%</b>	<p>No changes recommended based on cost review at this time</p> <p><i>Rationale: This agent is a low cost, generic option. No prior authorization should be added based on cost.</i></p>

<b>Medication</b>	<b>Recommendations</b>
<b>Prolensa 0.07%</b>	<p><b>Recommendation:</b> No changes to formulary status. Add PA criterion.</p> <p><b>Recommended Formulary Status:</b> No changes recommended</p> <p><b>Policy Update:</b> The following additional criterion should apply:</p> <ul style="list-style-type: none"> <li>• Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three (3) formulary alternatives</li> </ul> <p><i>Rationale: Two generically available formulary NSAIDs (diclofenac and ketorolac) are available and are effective for the treatment of the indication for which this agent is FDA-approved. Generically available bromfenac is also available and is less costly. Though there is PA on the generically available bromfenac, it is more cost-effective than this agent.</i></p>
<b>BromSite 0.075%</b>	<p><b>Recommendation:</b> No changes to formulary status. Add PA criterion.</p> <p><b>Recommended Formulary Status:</b> No changes recommended</p> <p><b>Policy Update:</b> The following additional criterion should apply:</p> <ul style="list-style-type: none"> <li>• Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three (3) formulary alternatives</li> </ul> <p><i>Rationale: See rationale from Prolensa above.</i></p>
<b>Bromfenac 0.09%</b>	<p><b>Recommendation:</b> Update formulary status. Alter PA criterion.</p> <p><b>Recommended Formulary Status:</b> Generic with PA</p> <p><b>Policy Update:</b> The following prior authorization criterion should apply to requests for bromfenac:</p> <ul style="list-style-type: none"> <li>• Medical record documentation of therapeutic failure on, intolerance to, or contraindication to diclofenac sodium 0.1% <b>AND</b> ketorolac 0.4% or 0.5%</li> </ul>

	<p><i>Rationale: Bromfenac is the most expensive generically available option.</i></p>
<b>Diclofenac Sodium 0.1%</b>	<p>No changes recommended based on cost review at this time</p> <p><i>Rationale: This agent is a low cost, generic option. No prior authorization should be added based on cost.</i></p>
<b>Ketorolac Tromethamine 0.5%</b>	<p>No changes recommended based on cost review at this time</p> <p><i>Rationale: This agent is a low cost, generic option. No prior authorization should be added based on cost.</i></p>
<b>Ketorolac Tromethamine 0.4%</b>	<p>No changes recommended based on cost review at this time</p> <p><i>Rationale: This agent is a low cost, generic option. No prior authorization should be added based on cost.</i></p>
<b>Acuvail 0.45%</b>	<p><b>Recommendation:</b> No changes to formulary status. Add PA criterion.</p> <p><b>Recommended Formulary Status:</b> No changes recommended.</p> <p><b>Policy Update:</b> The following additional criterion should apply:</p> <ul style="list-style-type: none"> <li>• Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three (3) formulary alternatives</li> </ul> <p><i>Rationale: See rationale from Prolensa above.</i></p>
<b>Ilevro 0.3%</b>	<p><b>Recommendation:</b> No changes to formulary status. Add PA criterion.</p> <p><b>Recommended Formulary Status:</b> No changes recommended.</p> <p><b>Policy Update:</b> The following additional criterion should apply:</p> <ul style="list-style-type: none"> <li>• Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three (3) formulary alternatives</li> </ul> <p><i>Rationale: See rationale from Prolensa above.</i></p>
<b>Nevanac 0.1%</b>	<p><b>Recommendation:</b> No changes to formulary status. Add PA criterion.</p> <p><b>Recommended Formulary Status:</b> No changes recommended.</p> <p><b>Policy Update:</b> The following additional criterion should apply:</p> <ul style="list-style-type: none"> <li>• Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three (3) formulary alternatives</li> </ul> <p><i>Rationale: See rationale from Prolensa above.</i></p>

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## DRUG REVIEWS

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### ZULRESSO (brexanolone)

**Review:** Zulresso (brexanolone) is the first and only treatment indicated for the treatment of postpartum depression (PPD) in adults. The exact mechanism of action is unknown; however, Zulresso is thought to function via positive allosteric modulation of GABAA receptors, increasing neuronal inhibition and restoring function to the GABA system and reducing overactivity within the HPA axis and other neuronal networks. The dosing of Zulresso is complicated, requiring a continuous 60-hour infusion and at least 5 IV bag preparations.

In three clinical trials evaluating the safety, efficacy, and pharmacokinetics of Zulresso versus placebo in patients with moderate to severe PPD, Zulresso outperformed placebo in the least squared mean reduction in the HAM-D (Hamilton Depression Rating Scale) total score from baseline. Zulresso also showed better outcomes in terms of HAM-D response, HAM-D remission, CGI-I (Clinical Global Impression – Improvement) response, MADRS (Montgomery-Asberg Depression Rating Scale), Bech-6 subscale, and EPDS (Edinburgh postnatal depression scale).

Zulresso maintains a black box warning due to the risk of excessive sedation or sudden loss of consciousness during Zulresso administration. Because of the risk of harm, patients must be monitored for the above and have continuous pulse oximetry monitoring. Zulresso is only available through a restricted program called the Zulresso REMS. The most common adverse reactions included tachycardia, dizziness/presyncope/vertigo, loss of consciousness, sedation/somnolence, and flushing. Aside from the black box warning, Zulresso has a warning and precaution significant for suicidal thoughts and behaviors.

Due to the unique administration requirements of Zulresso, Zulresso will likely be provided while a patient is admitted in an inpatient facility. There are reports that Zulresso may be transitioned to outpatient administration in the future. There is one ongoing clinical trial evaluating Zulresso in female patients ages 15 to 17 years diagnosed with PPD. Geisinger Health System opted to make Zulresso non-formulary due to lack of robust data, REMS implementation challenges, and high cost. Geisinger Psychiatry believes Zulresso will be prescribed mainly by the psychiatry specialty but will have OB/GYN input. For now, Zulresso may be accessed by Geisinger prescribers on a case-by-case basis through Geisinger Health System's non-formulary process.

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

**Clinical Discussion:** Dr. Silbert questioned if a person with bipolar depression disorder could be considered for this medication. Keith stated that the use in bipolar was not studied, but its use for this indication could be considered depending on the circumstances. Tricia asked if the REMS program limits the use to 6 months after delivery, Keith stated that this is the current REMS criteria, since it refers back to the product labeling. Kevin Szczecina made a motion to accept the recommendations as presented. Aubrielle Prater seconded the motion. None were opposed.

**Financial Discussion:** No comments or questions. Kimberly Clark made a motion to accept the recommendations as amended. Aubrielle Prater seconded the motion. None were opposed.

**Outcome:** Zulresso will be a medical benefit. Prior authorization with the following criteria will apply:

- Prescribed by (or in consultation with) a psychiatrist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis postpartum depression (PPD) as defined by ALL of the following:
  - Patient experiencing a major depressive episode **AND**
  - Patient experienced onset of symptoms within the third trimester or within 4 weeks of delivery

**AND**

- Medical record documentation that patient is less than or equal to 6 months postpartum **AND**
- Medical record documentation that current depressive episode is moderate to severe based on a standardized and validated questionnaire/scale (e.g. a score of greater than 10 on the Patient Health Questionnaire (PHQ-9), a score of greater than 20 on the Hamilton Depression Rating Scale (HAM-D), etc.)

**AUTHORIZATION DURATION:** One-time authorization of one 60-hour infusion of Zulresso

Note: The safety and efficacy of repeated Zulresso infusions have not been studied. Additional infusion(s) of Zulresso for future cases of PPD associated with additional pregnancies will be reviewed for medical necessity based on the above criteria. More than one administration of Zulresso per pregnancy/birth is considered investigational and not covered.

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

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**MAYZENT (siponimod)**

**Review:** Mayzent, an agonist of the sphingosine-1-phosphate receptor, is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing remitting disease, and active secondary progressive disease in adults. It works by selectively binding S1P subtype-1 expressed on lymphocytes, resulting in their retention in lymphoid tissues. Although Mayzent was the first agent approved specifically for active secondary progressive multiple sclerosis, with its approval the FDA clarified that all drugs approved for “relapsing forms of MS” includes the treatment of clinically isolated syndrome, relapsing-remitting MS, and active secondary progressive MS.

The efficacy of Mayzent was shown in the BOLD trial, a phase 2 study investigating Mayzent in the treatment of relapsing-remitting multiple sclerosis, and the EXAND trial, a phase 3 study investigating Mayzent in the treatment of secondary progressive multiple sclerosis. In the BOLD trial, 292 patients with relapsing-remitting multiple sclerosis were randomized to receive Mayzent 10 mg, 2 mg, 0.5 mg, 1.25 mg, or 0.25 mg in two cohorts. The primary endpoint, the number of combined unique active lesions (CUALs), showed a significant dose-related reduction in all five doses of Mayzent compared to placebo. It was concluded from this study that doses greater than 2 mg per day had the highest rate of adverse events leading to study drug discontinuation and only showed a small gain in efficacy in clinical and MRI outcomes.

The EXPAND trial, a randomized, double-blind, placebo-controlled, phase 3 study, investigated the efficacy of Mayzent in 1651 patients with a diagnosis of active secondary progressive multiple sclerosis. Patients were randomly assigned treatment 2:1 with Mayzent or placebo. The primary endpoint was time to 3-month confirmed disease progression (an increase in Expanded Disability Status Scale score confirmed at a scheduled visit 3 months later). The Mayzent treatment group met the primary endpoint with a lower proportion of patients with 3-month confirmed disease progression in a time-to-event analysis. Key secondary endpoints investigating lesion volume and mobility showed there was a significantly lower increase in T2 lesion volume from baseline in the Mayzent treatment group, but there were no significant differences between the two groups in the timed 25-foot walk test. Other endpoints investigated showed that brain volume decreased at a lower rate and more patients were free from gadolinium-enhancing lesions and new or enlarging T2 lesions in the patients treated with Mayzent.

The safety profile of Mayzent was found to be comparable to other medications used in the treatment of multiple sclerosis. Adverse events reported more frequently than placebo during clinical trials were elevated liver enzymes,

bradycardia at treatment initiation, macular edema, hypertension, varicella zoster virus reactivation, and convulsions, all of which have been described with S1P receptor agonists in the treatment of multiple sclerosis.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, 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 presented. Kimberly Clark seconded the motion. None were opposed.

**Financial Discussion:** No comments or questions. Todd Sponenberg made a motion to accept the recommendations as presented. Kelly Yelenic seconded the motion. None were opposed.

**Outcome:** Mayzent will be covered as a pharmacy benefit and will be added to the GHP Family formulary at the Brand tier. No prior authorization will apply. The following quantity limits will apply:

**QUANTITY LIMIT:** Mayzent 0.25 mg tablets: 5 tablets per day; Mayzent 2 mg tablets: 1 tablet per day

**Other Recommendations:** With the approval of Mayzent, and the FDA clarification that “relapsing forms of MS” includes the treatment of clinically isolated syndrome, relapsing-remitting MS, and active secondary progressive MS, several disease-modifying treatments have expanded their indications on labeling to include these subtypes of MS. It is recommended to update the following policies for relapsing multiple sclerosis to include the expanded indication as outlined below. No changes are recommended for the current authorization duration or quantity limits.

#### Medical Benefit Policy 57.0 Tysabri

##### **1. Relapsing Multiple Sclerosis**

Tysabri is considered medically necessary for the treatment of relapsing forms of multiple sclerosis, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, when the following criteria are met:

- Medical record documentation of member being established on and responding to Tysabri for at least 60 days prior to their effective date with the plan

**OR**

- Medical record documentation of a diagnosis of a relapsing form of multiple sclerosis, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease **AND**
- Medical record documentation that the patient 18 years or older **AND**
- Medical record documentation that Tysabri is being prescribed by a neurologist **AND**
- Patient is enrolled in a risk-minimization program, called the TOUCH™ Prescribing Program, **AND**
- Physician documentation that Tysabri is being used as monotherapy is provided. **AND**
- Medical record documentation that the member has been tested for anti-JCV antibody prior to start of Tysabri therapy.
  - If patient is anti-JCV antibody positive, medical record documentation that benefits of drug outweigh the risks of progressive multifocal leukoencephalopathy (PML) and patient is aware of increased PML risk

**AND**

- Medical record documentation of therapeutic failure on, contraindication to, or intolerance to two formulary alternatives.

#### Medical Benefit Policy 155.0 Ocrevus



Ocrevus (ocrelizumab) will be considered medically necessary when ALL of the following criteria are met:

- Medical record documentation of age > 18 years **AND**
- Medical record documentation Ocrevus is prescribed by a neurologist **AND**
- Medical record documentation of a diagnosis of primary progressive MS (PPMS) **OR**
- Medical record documentation of a diagnosis of a relapsing form of multiple sclerosis, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease **AND**
- For members with a diagnosis of a relapsing form of multiple sclerosis, medical record documentation of therapeutic failure on, intolerance to, or contraindication to two formulary alternatives.

**Discussion:** No comments or questions. Rajneel Farley made a motion to accept the recommendations as presented. Kelly Yelenic 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.

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### **MAVENCLAD (cladribine)**

**Review:** Mavenclad, an immunosuppressive purine antimetabolite, selectively depletes lymphocytes through DNA synthesis impairment and is indicated for the treatment of adults with relapsing forms of multiple sclerosis including relapsing-remitting disease and active secondary progressive disease. Because of safety concerns, Mavenclad should be reserved for patients who have had an inadequate response to alternative treatments. It is not recommended for use in patients with clinically isolated syndrome where it is uncertain if the patients will develop multiple sclerosis and there are no clear benefits to treatment with Mavenclad.

The efficacy of Mavenclad were investigated in the double-blind, placebo-controlled CLARITY trial where patients with relapsing-remitting multiple sclerosis were randomized to receive one of two doses of Mavenclad or placebo over 96 weeks. The primary endpoint measuring rate of relapse at 96 weeks was significantly lower in the patients treated with Mavenclad compared to placebo. The Mavenclad treatment groups also had a longer time to first relapse, a relative reduction in risk of 3-month sustained disability, and a reduction in MRI activity with fewer lesions per patient per scan when compared to placebo.

A long-term safety, tolerability and clinical benefit trial, the CLARITY Extension, compared efficacy of 2 years treatment with Mavenclad followed by 2 years of placebo to 2 years of Mavenclad followed by 2 additional years of treatment. Results from the Extension showed that there was little clinical benefit to treating patients with Mavenclad beyond two years in terms of annualized relapse rate, proportion of patients remaining relapse free, time to relapse and time to confirmed EDSS progression.

Mavenclad has a black box warning for risk of malignancy and teratogenicity. During clinical trials, neoplasms, both benign and malignant, were reported in 1.4% of the study population. Other serious adverse reactions including lymphopenia, increased risk of infection, elevation of liver enzymes, and cardiac failure have been reported. The most common adverse events reported during clinical trials were upper respiratory tract infection, headache, and lymphopenia.

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:** Kimberly Clark recommended adding a note to the policy clarifying that 2 years of therapy is 4 cycles. Bret questioned the study/use beyond 2 years. Kimberly Reichard explained that use beyond 2 years was not any more effective than 2 years of treatment plus 2 years of placebo, and patients were at risk for adverse

events. Keith Hunsicker made a motion to accept the recommendations as presented. Kim Clark seconded the motion. None were opposed

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

**Outcome:** Mavenclad will be covered as a pharmacy benefit and will be added to the GHP Family formulary at the Brand tier. The following prior authorization criteria will apply:

- Medical record documentation of member age 18 years or older AND
- Medical record documentation Mavenclad is prescribed by a neurologist AND
- Medical record documentation of diagnosis of relapsing form of multiple sclerosis including relapsing-remitting disease and active secondary progressive disease AND  
*Note: Mavenclad is not indicated for the clinically isolated syndrome subtype of multiple sclerosis.*
- Medical record documentation that Mavenclad will be used as monotherapy AND
- Medical record documentation that the prescribed dosing is appropriate for patient’s weight AND
- Medical record documentation that patient has not been treated with more than three previous treatment cycles of Mavenclad for relapsing forms of multiple sclerosis. AND
- Medical Record documentation of therapeutic failure on, intolerance to, or contraindication to two formulary alternatives for the treatment of MS.

NOTE: Dose of Mavenclad per Cycle by Patient Weight in Each Treatment Course

Weight Range (kg)	First Cycle	Second Cycle
40* to less than 50	40 mg (4 tablets)	40 mg (4 tablets)
50 to less than 60	50 mg (5 tablets)	50 mg (5 tablets)
60 to less than 70	60 mg (6 tablets)	60 mg (6 tablets)
70 to less than 80	70 mg (7 tablets)	70 mg (7 tablets)
80 to less than 90	80 mg (8 tablets)	70 mg (7 tablets)
90 to less than 100	90 mg (9 tablets)	80 mg (8 tablets)
100 to less than 110	100 mg (10 tablets)	90 mg (9 tablets)
110 and above	100 mg (10 tablets)	100 mg (10 tablets)

**QUANTITY LIMIT:** Pharmacist note to CSR: *Authorization should be entered by HICL and only checking the Formulary PA required box (no QLs need to be entered within the authorization).*

Dosage	Quantity Limit
40 mg	4 tablets per 27 days
50 mg	5 tablets per 28 days
60 mg	6 tablets per 28 days
70 mg	7 tablets per 28 days
80 mg	8 tablets per 28 days
90 mg	9 tablets per 28 days
100 mg	10 tablets per 28 days

**AUTHORIZATION DURATION:** The initial authorization will be for 48 weeks with an RX Count 2. One subsequent authorization will be for 48 weeks with an RX Count 2 and will require the following:

- Medical record documentation that patient has not received more than three previous cycles of Mavenclad treatment for relapsing forms of multiple sclerosis.

The medication will no longer be covered if the member experiences unacceptable toxicity or worsening of disease.

**NOTE:** Cumulative use of Mavenclad for more than two years (4 cycles) of treatment during a patient's lifetime has not been evaluated.

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

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### **SKYRIZI (risankizumab-rzaa)**

**Review:** Skyrizi is a humanized immunoglobulin G1 (IgG1) monoclonal antibody indicated for the treatment of moderate-to-severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. It comes in a pack of two prefilled syringes each containing 75 mg/0.83 mL. It is dosed as 150 mg (2 syringes) subcutaneously at weeks 0 and 4, followed by a dose of 150 mg subcutaneously every 12 weeks thereafter. In comparison to other biologics, Skyrizi is less frequently dosed than all of the TNF- $\alpha$  inhibitors, but is similar to other IL-23 inhibitors, Stelara (every 12 weeks) and Ilumya (every 12 weeks). In clinical trials, Skyrizi has compared well to other current biologic therapies including Humira and Stelara. Skyrizi nearly doubled the percentage of patients reaching the primary endpoints of PASI 90 and achievement of an sPGA score of 0-1 when compared to both Humira and Stelara. When compared to placebo, Skyrizi consistently showed more than 70% of patients achieved PASI 90 and sPGA scores of 0 or 1. Patients also showed significant improvement when switching to Skyrizi after an inadequate response or failure to respond to Humira. The side effect profile was very similar between all biologics, but Skyrizi was shown to have a slightly higher risk of tinea or upper respiratory tract infections and should not be given to patients with acute or chronic infections or those with latent or active TB. Skyrizi should not be given to those receiving live vaccines or vice versa as Skyrizi can compromise the immune system, increasing the risk of infection or reactivation of latent infections

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 presented. Aubrielle Prater seconded the motion. None were opposed

**Financial Discussion:** No comments or questions. Todd Sponenberg made a motion to accept the recommendations as presented. Rajneel Farley seconded the motion. None were opposed

**Outcome:** Skyrizi will be covered as a pharmacy benefit and will be added to the GHP Family formulary at the Brand tier. The following prior authorization criteria will apply:

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

**QUANTITY LIMIT:** Initial: One-time, one-week authorization: QL 1 kit per 28 days; Max quantity supply: 1 kit; Min and Max day supply: 28

Remainder/Subsequent: QL 1 kit per 84 days; Max quantity supply: 1 kit; Min and Max day supply: 84

**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 signs and symptoms of psoriasis on six (6) months of Skyrizi therapy is required.

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

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

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### **CUTAQUIG (immune globulin subcutaneous (human) -hipp)**

**Review:** Cutaquig is one of 17 immune globulin therapies FDA-approved for the treatment of primary humoral immunodeficiencies, and one of seven subcutaneous immune globulin therapies on the market. Cutaquig provides replacement of IgG antibodies, which fight against bacteria, viral, parasitic and mycoplasma antigens. Cutaquig should be started one week after discontinuation of IGIV/IGSQ therapy, with doses of Cutaquig being individualized based on each patient's IgG goal. Therefore, constant monitoring of each patient's clinical response and serum IgG is needed for guidance on subsequent doses. Cutaquig is indicated to treat primary humoral immunodeficiencies, namely common variable immunodeficiency (CVID), congenital agammaglobulinemia, severe combined immunodeficiency syndrome (SCIDS), common variable immunodeficiency, X-linked agammaglobulinemia, and Wiskott-Aldrich syndrome.

In the phase 3 trial involving Cutaquig, none of the 61 patients treated experienced a serious bacterial infection (SBI). Of the 61 patients participating, 85.2% experienced a viral and/or non-serious bacterial infection during the observation period. Although it is hard to compare efficacy to other IGSQ products, the published results do state the rates seen in the Cutaquig trial were similar to other IGSQ results. The rate of days missed from school/work per patient-year was 2.63 days. During the observation period, 67.2% of patients were treated with systemic or topical antibiotics, with an average of 2.1 treatment episodes per patient-year.

Cutaquig maintains a black box warning for thrombosis, a warning all immune globulin products carry. During the phase 3 study, no indications of thrombosis were observed. A total of 14 adverse events related to Cutaquig were observed, with none of these AE being classified as serious. In addition to the black box warning, the package insert describes warnings and precautions including Aseptic Meningitis Syndrome (AMS), hemolysis, renal dysfunction/failure and Transfusion-Related Acute Lung Injury (TRALI).

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. Aubrielle Prater made a motion to accept the recommendations as presented. Kevin Szczecina seconded the motion. None were opposed

**Financial Discussion:** No comments or questions. Todd Sponenberg made a motion to accept the recommendations as presented. Kelly Yelenic seconded the motion. None were opposed

**Outcome:** Cutaquig will be covered as a medical benefit and should not be added to the GHP Family formulary. It will require a prior authorization and will be added to the existing medical IVIG policy (MBP 4.0) below.

**Primary Humoral Immunodeficiencies, including combined immunodeficiencies**  
Congenital Agammaglobulinemia (X-linked agammaglobulinemia)

Autosomal recessive agammaglobulinemia  
 Common Variable Immunodeficiency (CVID)  
 Wiskott-Aldrich Syndrome  
 X-linked or autosomal recessive immunodeficiency with hyperimmunoglobulin M  
 Severe Combined Immunodeficiency (SCID)  
 Ataxia-telangiectasia  
 DiGeorge syndrome  
 Nijmegen breakage syndrome  
 Griscelli syndrome  
 NEMO deficiency  
 WHIM (warts, hypogammaglobulinemia, immunodeficiency, and myelokathexis) syndrome  
 X-linked lymphoproliferative disease (in patients with hypogammaglobulinemia or dysgammaglobulinemia and infections)  
 Hypogammaglobulinemia provided the appropriate work up is performed to determine extent (ex. flow cytometry and anamnestic response to recall antigens)

Patients with primary immunodeficiencies must meet the following criteria:

1. Medical record documentation/laboratory results of immunoglobulin deficiency; **AND**
2. Medical record documentation of an inability to mount an adequate immunologic response to inciting antigens; **AND**
3. Medical record documentation of persistent and severe infections

#### **Idiopathic Thrombocytopenia Purpura (ITP)**

1. Acute ITP when either of the following are present:
  - Active bleeding and a platelet count of less than 30,000/mm<sup>3</sup>; **AND**
  - Medical record documentation of use in conjunction with a corticosteroid or a contraindication to or failure on corticosteroid therapy; **OR**
  - As a preoperative treatment prior to major invasive surgical procedures **AND**
  - IVIG be used with corticosteroids when a more rapid increase in platelet count is required
2. Chronic ITP when the following criteria are met:
  - Platelet count less than 30,000/mm<sup>3</sup> in children or less than 20,000/mm<sup>3</sup> in adults; **AND**
  - No concurrent illness or disease explaining thrombocytopenia; **AND**
  - Medical documentation of prior treatment with a long course or high dose of corticosteroids (ex, prednisone 1 mg/kg orally for 21 days then tapered off), a splenectomy;  
**OR**
  - Active bleeding and a platelet count of less than 30,000/mm<sup>3</sup>; **OR**
  - As a preoperative treatment prior to major invasive surgical procedures
3. ITP in pregnancy with medical documentation of any of the following:
  - Platelet counts less than 10,000/mm<sup>3</sup> during the third trimester
  - Platelet count of 10,000/mm<sup>3</sup> to 30,000/mm<sup>3</sup> and active bleeding
  - Platelet counts less than 10,000/mm<sup>3</sup> after steroid failure
  - Platelet count of 10,000/mm<sup>3</sup> to 30,000/mm<sup>3</sup> and active bleeding after steroid failure
  - Platelet count of 10,000/mm<sup>3</sup> to 30,000/mm<sup>3</sup> during third trimester and asymptomatic after steroid failure
4. Secondary ITP
  - a. *H-pylori*-associated
    - i. Eradication of H-pylori in patients testing positive

#### **Acquired Hypogammaglobulinemia Secondary to Chronic B-cell Lymphocytic Leukemia or Multiple Myeloma**

The following criteria must be met:

1. IgG less than 500 mg/dl, **AND**
2. a documented history of repeated bacterial infection two times in one year or a severe bacterial infection within the last 6 months

**Post-transfusion purpura**

The following criteria must be met:

1. Medical documentation of failure, intolerance, or contraindication to corticosteroids and plasmapheresis; **OR**
2. Platelet count less than 10,000/mm<sup>3</sup> with bleeding

**Kawasaki Disease**

The following criteria must be met:

1. Documentation of a diagnosis of Kawasaki disease.
2. Treatment with IVIG is begun within 10 days of the onset of fever.

**Pediatric HIV infection – Bacterial infection prevention**

The following criteria must be met:

1. Indicated in HIV positive children with humoral immunodeficiency AND
2. Entry CD4+ lymphocyte count of 200/mm<sup>3</sup> or greater AND
3. Hypogammaglobulinemia AND one or more of the following:
4. Recurrent serious bacterial infections OR
5. Failure to form antibodies to common antigens OR
6. There is a high risk for measles OR
7. There is a documented bronchiectasis that has not adequately responded to antimicrobial and pulmonary therapy.

**Bone Marrow Transplantation (for lines of business not covered by the transplant vendor only)**

The following criteria must be met:

1. The transplant recipient is within the first 100 days after transplant from a matched unrelated donor; OR
2. Documentation of treatment of Graft vs. Host Disease in a transplant recipient receiving allogenic matched bone marrow transplant with chronic repeated infections or hypogammaglobulinemia (IgG levels less than 400 mg/dL); OR
3. Documentation of autologous transplant with hypogammaglobulinemia (IgG level less than 400 mg/dL) or repeated infections.

**Myasthenia Gravis (Acute use)**

The following criteria must be met:

1. Must be prescribed by a neurologist; AND
2. Documentation of therapeutic failure on, intolerance to, or contraindication to at least two standard treatments (e.g. cholinesterase inhibitors, azathioprine, corticosteroids) and /or a combination of these treatments for a minimum of 3 months; AND

Medical documentation of one of the following indications:

3. Diagnosis of acute myasthenic crisis with decompensation; OR
4. Use during postoperative period following a thymectomy; OR
5. Use prior to planned thymectomy

**Refractory Chronic Debilitating Myasthenia Gravis**

1. Medical record documentation of refractory Chronic Debilitating Myasthenia Gravis AND
2. Prescribed by or in consultation with a neuromuscular specialist AND
3. Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least one corticosteroid AND
4. Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least one cholinesterase inhibitor AND
5. Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least one non-steroidal immunosuppressive therapy

**Dermatomyositis and Polymyositis**

All of the following criteria must be met:

1. Diagnosis of dermatomyositis or polymyositis confirmed by biopsy AND
2. Documented evidence of active disease AND

3. Must be prescribed by a neurologist AND
4. Documented evidence that the condition is refractory to both of the following therapies
  - A) First line therapy: corticosteroids (at least 4 months of therapy)
  - B) Second line therapy: at least two immunosuppressants (e.g. cyclosporine, azathioprine, methotrexate, cyclophosphamide)

### **Guillain-Barre Syndrome/Ascending Paralysis**

The following criteria must be met:

1. Adults with a diagnosis of either acute or chronic Guillain-Barre syndrome; AND
2. Must be prescribed by a neurologist AND
3. IVIG will be initiated within 2 weeks but no longer than 4 weeks of neuropathic symptom onset if acute onset; AND.
4. No plan for combining IVIG with plasma exchange or sequential plasma exchange and IVIG.

### **Chronic Inflammatory Demyelinating Polyneuropathy**

All of the following criteria must be met:

1. Must be prescribed by a neurologist; AND
2. Documented evidence of focal or symmetric neurologic deficits that are slowly progressive or relapsing over 12 weeks or longer AND
3. Physician provided documentation of EMG abnormalities consistent with the diagnosis of Chronic Inflammatory Demyelinating Polyneuropathy (a minimum of 3 of the following must be documented):
  - a. Partial conduction block of one or more motor nerves
  - b. Decreased conduction velocity of two or more motor nerves
  - c. Prolongation of distal latency of two or more motor nerves
  - d. Prolongation or absence of F-wave latencies in two or more motor nerves

Improvement should be apparent after 8 weeks of treatment; otherwise, requests for further treatment will require Medical Director review.

Relapses may require periodic isolated treatments with a single dose of IVIG.

### **Fetal or Neonatal Alloimmune Thrombocytopenia (FAIT)**

The following criteria must be met:

1. There has been a history of a previous pregnancy affected by FAIT and the father is homozygous for HPA-1a; OR
2. At 20 weeks, cordocentesis reveals fetal platelets less than 100,000/uL; OR
3. Neonate with severe thrombocytopenia, who is at high risk of developing intracranial hemorrhage and washed irradiated maternal platelets are not available, have not been successful, have become intolerable, or are contraindicated

### **Multifocal Motor Neuropathy**

The following criteria must be met:

1. Must be prescribed by a neurologist; AND
2. Medical documentation of progressive symptoms for a minimum of 2 months; AND
3. Documentation of a diagnosis of multifocal motor neuropathy with conduction block as shown on electrophysiologic study as evidenced by:
  - Conduction block on a single nerve or probable conduction block in two or more nerves
  - Normal sensory nerve conduction in upper limb segments and normal sensory nerve action potential (SNAP) amplitude

Treatment is limited to one course of therapy defined as 3 months if approved. Requests for further treatment will require Medical Director review.

### **CMV Interstitial Pneumonia in Allogenic Bone Marrow Transplant or HSCT patients <sup>(1b/A)</sup>**

The following criteria must be met:

1. Medical record documentation of CMV pneumonia
2. Medical record documentation that IVIG is being used in combination with or patient has a contraindication to ganciclovir

**Toxic shock syndrome (III/C)**

The following criteria must be met:

1. Used in conjunction with conventional therapy
2. Caused by staphylococcal or streptococcal organisms

**Neonatal sepsis (Ia/A)**

The following criteria must be met:

1. Used in conjunction with conventional therapy

**Graves' Ophthalmopathy (Ib/A)**

The following criteria must be met:

1. Medical record documentation of failure on, contraindication to, or intolerance to conventional treatment (corticosteroids)
2. Prescription must be written by an ophthalmologist

**Autoimmune Mucocutaneous Blistering Diseases (pemphigus, pemphigoid, pemphigus vulgaris, pemphigus foliaceus, Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis (III/C))**

The following criteria must be met:

1. Diagnosis must be substantiated by biopsy; AND
2. Failure or contraindication to two or more conventional therapies (corticosteroids, azathioprine, cyclophosphamide, etc.);  
OR
3. Have rapidly progressive disease in which a clinical response could not be quickly achieved utilizing conventional therapy. IVIG would be given in conjunction with conventional therapy and only until such time as conventional therapy could take effect

Note: IVIG for the treatment of autoimmune mucocutaneous blistering disease must be used only for short-term therapy and not as maintenance therapy.

**Solid Organ Transplant**

The following criteria must be met:

Prevention of acute humoral rejection

- Medical record documentation that patient is at high risk for antibody-mediated rejection, including highly sensitized patients or receiving ABO incompatible organ

OR

Treatment of acute humoral rejection

- Medical record documentation of antibody-mediated rejection

**Rasmussen's Encephalitis (III/B)**

The following criteria must be met:

1. Medical record documentation that short term amelioration of encephalitis is needed prior to definitive surgical therapy
2. Medical record documentation of intractable focal motor seizures and progressive neurologic deterioration

**Stiff-Person Syndrome (Ib/A)**

The following criteria must be met:

1. Prescription written by a neurologist
2. Medical record documentation of failure on, intolerance to, or contraindication to all standard therapies (muscle relaxants, benzodiazepines, and gabapentin-related medications)

**Eaton-Lambert myasthenic syndrome (Ib/A)**

All of the following criteria must be met:



1. Prescription written by a neurologist
2. Medical record documentation of failure on, contraindication to, or intolerance to other treatments including corticosteroids or other immunosuppressants, cholinesterase inhibitors, and 3,4-diaminopyridine.

#### **Multiple Sclerosis (relapsing/remitting type)**

All of the following criteria must be met:

1. Must be prescribed by a neurologist; AND
2. Medical record documentation of RRMS AND
3. Medical record documentation of current MS exacerbation AND
4. Medical record documentation of therapeutic failure on, contraindication to, or intolerance to an appropriate trial of high dose corticosteroids

Improvement should be apparent after 2 courses of monthly treatment, otherwise, requests for further treatment will require Medical Director review of supporting documentation of expected outcome.

Note: IVIG is considered investigational for primary or progressive multiple sclerosis and will not be covered.

#### **Warm Antibody Autoimmune hemolytic anemia (III/D)**

The following criteria must be met:

1. Refractory to or contraindicated to corticosteroids and immunosuppressive agents
2. Refractory to splenectomy

#### **Parvovirus B19 Infection**

All of the following criteria must be met

1. Prescribed by or in consultation with an infectious disease specialist, immunologist, hematologist, or transplant specialist
2. Medical record documentation of chronic immunodeficient condition (HIV, solid organ transplant etc)
3. Medical record documentation of chronic parvovirus B19 infection
4. Medical record documentation of severe anemia as defined by hemoglobin < 8 g/dL

#### **Catastrophic Antiphospholipid Syndrome (CAPS) (III/C)**

All of the following criteria must be met:

1. Documentation of a life-threatening condition
2. Documentation of severe thrombocytopenia and microangiopathic hemolytic anemia
3. Documentation of failure on, contraindication to, or intolerance to conventional treatment with anticoagulation and steroids
4. Should be used in combination with plasma exchange

**AUTHORIZATION DURATION:** Each treatment period will be defined as 6 months or less, unless otherwise stated (e.g. Chronic Inflammatory Demyelinating Polyneuropathy, Multiple Sclerosis, and Multifocal Motor Neuropathy). Re-review will occur every 6 months or less, dependent on the indication. Documentation of clinical response to therapy is required after initiation of therapy. If initial benefit is seen and continued therapy is deemed necessary, documentation of objective monitoring must be seen. Clinical improvement is superior to laboratory monitoring. IVIG will no longer be covered if there is a medical record documentation of disease progression.

**LIMITATIONS:** When approved, IVIG will be administered in a setting determined by the Plan, in consultation with the requesting physician to be the most clinically appropriate and/or medically necessary.

**Initial Dosing:** Dosing should be calculated using adjusted body weight (ABW) if one or more of the following criteria are met:

- Patient's body mass index (BMI) is 30 kg/m<sup>2</sup> or more
- Patient's actual body weight is 20% higher than his or her ideal body weight (IBW)

Dosing formulas:

- BMI = weight in kg / height in meters<sup>2</sup>
- IBW (kg) for males = 50 + [2.3 (height in inches – 60)]
- IBW (kg) for females = 45.5 + [2.3 \* (height in inches – 60)]
- ABW = IBW + 0.5 (actual body weight – IBW)

Geisinger Health Plan considers some conditions other than those listed under Indications to be **Experimental, Investigational or Unproven** and **NOT Medically Necessary**. These conditions include:

- Alzheimer's disease
- amyotrophic lateral sclerosis
- atopic dermatitis
- autism
- chronic fatigue syndrome
- chronic mucocutaneous candidiasis (CMCC)
- complex regional pain syndrome (CRPS)
- epilepsy
- inclusion body myositis
- Lyme disease
- neuromyelitis optica (NMO) (Devic's Disease)
- optic neuritis
- paraproteinemic demyelinating neuropathy (PDN)
- post-polio syndrome
- recurrent spontaneous miscarriage
- rheumatic fever
- secondary progressive multiple sclerosis (SPMS)
- systemic lupus erythematosus

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

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### **ROCKLATAN (netarsudil/latanoprost)**

**Review:** Glaucoma is a chronic, progressive ocular disease characterized by irreversible damage to the optic nerve resulting in visual field loss and, ultimately, blindness if left untreated. There are six topical ophthalmic drug classes approved to reduce IOP that ultimately work by either increasing the outflow of aqueous humor or decreasing the production of aqueous humor. The AAO strongly recommends prostaglandin analogs as initial therapy because they are the most efficacious and well-tolerated agents, and they require only once-daily instillations (whereas other drug classes require dosing two to four times daily). Approximately half of all patients with glaucoma will go on to require more than one drug. If a single medication is effective in lowering IOP but the target pressure is not reached, combination therapy or switching to an alternative therapy may be appropriate. Adequate treatment of glaucoma requires a high level of adherence to therapy. Besides prostaglandins, the AAO guidelines do not mention a preference for a specific agent or a therapeutic drug class to be tried after failing to reach target IOP.

Rocklatan offers a new combination ophthalmic product for the glaucoma treatment space, joining Combigan, Cosopt/Cosopt PF, and Simbrinza. Compared to these existing combination medications, Rocklatan is unique in that it includes a first-line therapy prostaglandin analog (in the form of the latanoprost) with a first-in-class ROCK inhibitor (netarsudil). While both latanoprost and netarsudil increase the outflow of aqueous humor, latanoprost does so via the uveoscleral pathway and netarsudil by the trabecular meshwork route (the eye's main fluid drainage pathway). Rocklatan is recommended to be given as one drop into the affected eye(s) once daily in the evening. If a dose is missed, treatment should continue with the next evening dose. The dosage of Rocklatan should not exceed once daily.

In the two phase 3 clinical trials, Mercury 1 and Mercury 2, subjects with IOP<36 mmHg were enrolled and randomized in a 1:1:1 ratio between three treatment groups. The treatment groups consisted of Rocklatan dosed once daily, latanoprost 0.005% dosed once daily or netarsudil 0.02% dosed once daily. The treatment duration was 12 months for Mercury 1 and 3 months for Mercury 2. In these studies, Rocklatan achieved its primary 90-day efficacy endpoint as well as positive 12-month safety and efficacy results, demonstrating statistically superior IOP reduction over latanoprost and netarsudil at every measured timepoint.

Rocklatan does not carry any contraindications, but, consistent with the ophthalmic prostaglandin class, it has notable warnings and precautions for ocular pigmentation and eyelash changes due to its latanoprost component. Additionally, Rocklatan should be used with caution in patients with a history of/active intraocular inflammation, those with known risk factors for macular edema, and those with a history of herpetic keratitis. Conjunctival hyperemia, reported in 59% of patients in clinical studies, was the most common adverse reaction to Rocklatan and caused discontinuation of therapy in 5% of patients. Regarding drug interactions, the combined use of two or more prostaglandins or prostaglandin analogs, including latanoprost ophthalmic solution 0.005%, is not recommended. It has been shown that administration of these prostaglandin products more than once daily may decrease the IOP lowering effect or cause paradoxical elevations in IOP.

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

**Financial Discussion:** No comments or questions. Kevin Szczecina made a motion to accept the recommendations as presented. Kelly Yelenic seconded the motion. None were opposed.

**Outcome:** Rocklatan is a pharmacy benefit that will not be added to the GHP Family formulary. It will be added to the current Rhopressa policy and requests for coverage will require the following:

- Medical record documentation of an intolerance to, contraindication to, or therapeutic failure on three (3) formulary alternatives, one of which must be a prostaglandin analog eye drop

**QUANTITY LIMIT:** Pharmacist note to CSR: Authorization should be entered by HICL and only checking the Formulary box (no QLs need to be entered within the authorization). **0.17 mL per day** (max dose)

**NOTE:** There are certain ocular inflammatory conditions including iritis and uveitis which do not warrant the use of Prostaglandin eye drops as first line therapy.

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

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## **VYNDAQEL/VYNDAMAX (tafamidis meglumine)**

**Review:** Tafamidis is the first medication in the class transthyretin stabilizers and first drug to be approved specifically for treatment of cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis. Transthyretin amyloid cardiomyopathy is caused by misfolded transthyretin protein accumulating in the heart, causing symptoms of heart failure and dysrhythmias. The overwhelming patient population is males above the age of 60, where, if left untreated, survival is expected to be 2.5-3.6 years after diagnosis. Tafamidis is shown to stabilize transthyretin tetramers, inhibiting dissociation of the tetramers into soluble oligomers, protofilaments, and amyloid fibrils. Before the approval of tafamidis for the treatment of ATTR cardiomyopathy, treatment of ATTR

cardiomyopathy included only supportive care for heart failure symptoms or heart or liver transplant in an attempt to treat the cause, depending on the type of ATTR.

The ATTR-ACT was conducted to investigate the safety and efficacy of tafamidis. The phase 3 trial conducted found that tafamidis significantly reduced all-cause mortality and cardiovascular-related hospitalization compared to placebo. Tafamidis also significantly decreased the decline in distance walked during the 6-minute walk test and the decline in the KCCQ-OS score for quality of life.

The ATTR-ACT also determined the safety profiles of tafamidis and placebo were similar, with adverse events observed being mild to moderate in severity. More patients discontinued therapy due to adverse events in the placebo group than either of the tafamidis groups. There is no listed contraindications or warnings/precautions in the package insert of Vyndaqel and Vyndamax.

Vyndaqel is supplied as 20mg capsules in a blister pack (120 capsules), directing to take 4 capsules by mouth once daily. Vyndamax is supplied as 61mg capsules in a blister pack (30 capsules), directing to take 1 capsule by mouth once daily. Vyndaqel and Vyndamax are not substitutable on a per mg basis.

Dr. Brendan Carry (MD, GMC Cardiology) and Dr. Nate Sauers (PharmD, Cardiology MTDM) indicated that a cardiac biopsy is not necessary for the diagnosis of ATTR cardiomyopathy and that the diagnosis can be confirmed via a Nuclear Pyrophosphate Scan (PYP). They indicated that it is appropriate to exclude patients with NYHA Class IV heart failure from treatment with tafamidis based on the ATTR-ACT study and mechanism of the drug. Dr. Carry indicated that a liver or heart transplant may not exclude patients from treatment with tafamidis and that depending on patient specific factors tafamidis may be used in these patients. To his experience, Dr. Carry indicated that tafamidis is well tolerated by patients. Dr. Sauers noted that it may be difficult to determine efficacy of the treatment due to the lack of a biomarker to monitor.

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. Kelly Yelenic made a motion to accept the recommendations as presented. Tricia Heitzman seconded the motion. None were opposed.

**Financial Discussion:** No comments or questions. Kevin Szczecina made a motion to accept the recommendations as presented. Todd Sponenberg seconded the motion. None were opposed.

**Outcome:** Vyndaqel and Vyndamax will be covered as pharmacy benefits and will be added to the Brand tier of the GHP Family formulary. Prior authorization will apply with the following criteria:

- Prescription written by or in consultation with a cardiologist **AND**
- Medical record documentation of 18 years of age or older **AND**
- Medical record documentation of cardiomyopathy resulting from wild type transthyretin-mediated amyloidosis OR hereditary transthyretin-mediated amyloidosis as confirmed by ONE of the following:
  - Bone scan (scintigraphy) strongly positive for myocardial uptake of 99mTcPYP/DPD (*Note: Strongly positive defined as heart to contralateral lung [H/CL] ratio of at least 1.5 or Grade 2 or greater localization to the heart using the Perugini Grade 1-3 scoring system*) **OR**
  - Biopsy of tissue of the affected organ to confirm amyloid presence AND chemical typing to confirm presence of transthyretin (TTR) protein

**AND**

- Medical record documentation that the patient has New York Heart Association (NYHA) Class I, II, or III heart failure

**QUANTITY LIMIT:** Vyndaqel: 4 tablets per day; maximum 30-day supply per fill; Vyndamax: 1 tablet per day; maximum 30-day supply per fill

**AUTHORIZATION DURATION:** Initial approval will be for **12 months**. Subsequent approvals will be for an additional **12 months**, requiring prescriber attestation that the patient continues to benefit from tafamidis therapy. The medication will no longer be covered if the member experiences toxicity or progresses to NYHA class IV heart failure.

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

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### **EVENTITY (romosozumab-aqqg)**

**Review:** Eventity is a first-in-class sclerostin inhibitor indicated in postmenopausal women with osteoporosis at a high risk for a fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy. Eventity increases bone formation and, to a lesser extent, decreases bone resorption. It is given as a subcutaneous injection once a month for up to 12 months in 2 prefilled syringes and must be administered by a healthcare professional. The therapy duration limit is due to waning of the anabolic effect after 12 months. As with other osteoporosis therapies, it is recommended to supplement with calcium and vitamin D. There is a black box warning for increased risk of MI, stroke, and cardiovascular-related death. Patients with a recent history (within 12 months) of cardiovascular events should avoid this drug, and those who experience events should stop taking it. Other warnings and precautions include hypocalcemia, hypersensitivity reactions, osteonecrosis of the jaw, and atypical femoral fractures. It should be used with caution in patients with a CrCl < 30 ml/min due to the risk of hypocalcemia, and use is contraindicated in patients with hypocalcemia or hypersensitivity. Guidelines currently recommend bisphosphonates, denosumab, teriparatide, or abaloparatide as appropriate first- and second-line options. Eventity is not currently included in the guidelines.

Eventity decreased the incidence of new vertebral fracture at 12 months by 72% compared to placebo in one clinical trial (incidence, 0.5% versus 1.8%, respectively). In a study comparing alendronate vs Eventity initially before switching all patients to alendronate, Eventity → alendronate lowered the risk of nonvertebral fractures by 19% compared with alendronate → alendronate. In another trial, vertebral strength increased by 27.3% with Eventity, compared to an 18.5% increase with teriparatide and the 3.9% decrease with placebo. Eventity also significantly increased femoral strength by 3.6% compared with baseline, which was statistically greater than the -0.7% change from baseline with teriparatide, but not statistically significantly greater than the change of -0.1% with placebo. Though it is not currently FDA approved for use in men, one study found that romosozumab statistically significantly increased the lumbar spine and total hip bone mineral density compared to placebo in male patients.

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 presented. Kim Clark seconded the motion. None were opposed.

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

**Outcome:** Eventity will be a medical benefit and will not be added to the formulary this time. The following criteria will apply:

- Medical record documentation that Evenity is prescribed by a rheumatologist or endocrinologist **AND**
- Medical record documentation that the patient has not had a myocardial infarction or stroke within the past 12 months **AND**
- Medical record documentation of a diagnosis of postmenopausal osteoporosis **AND**
- Medical record documentation that the member has not previously received greater than or equal to 12 monthly doses of Evenity **AND**
- Medical record documentation that the patient is at high-risk of a fracture, determined by the presence of **ONE** or more of the following:
  - Previous osteoporotic fracture **OR**
  - Spine or hip DXA T-Score of -2.5 or below **OR**
  - FRAX calculation of the 10-year hip fracture risk of 3% or greater **OR**
  - FRAX calculation of the 10-year risk of major osteoporotic fractures of 20% or greater **OR**
  - Medical record documentation that the patient has failed or is intolerant to at least one prior osteoporosis therapy

**QUANTITY LIMITS:** 12 visits over 12 months

**AUTHORIZATION DURATION:** Approval will be for 12 months, or less if there is medical record documentation of a previous incomplete course of therapy with Evenity.

**NOTE:** The anabolic effect of Evenity wanes after 12 monthly doses of therapy. Therefore, the duration of Evenity use should be limited to 12 monthly doses. If osteoporosis therapy remains warranted, continued therapy with an anti-resorptive agent should be considered.

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

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### **DUOBRII (halobetasol propionate and tazarotene)**

**Review:** Duobrii is a topical combination product of halobetasol propionate (0.01%) and tazarotene (0.045%) indicated for the treatment of plaque psoriasis in adults. Duobrii is applied to the affected area(s) once daily until the patient achieves control, at which time Duobrii should be discontinued. The maximum recommended weekly dose of Duobrii is 50 grams. Mild or limited plaque psoriasis can be treated with topical therapy alone, while moderate to severe plaque psoriasis is usually treated with a combination of topical therapy and either phototherapy or systemic therapy. Response to treatment should be continually monitored, and topical corticosteroids particularly, should be discontinued once control is achieved due to long-term safety concerns and limited data available on long-term efficacy.

In two phase 3 trials assessing the safety and efficacy of Duobrii, 35.8% and 45.3% (study 1 and study 2, respectively) of 418 patients studied achieved the primary efficacy outcome of reducing IGA by at least 2 grades at week 8 of treatment. This was compared to a vehicle only group, where only 7% and 12.5% of the patients in this group achieved the primary efficacy outcome ( $P < 0.001$ ). Duobrii also significantly reduced symptoms of psoriasis such as erythema, plaque elevation and scaling along with significantly increasing quality of life based on DLQI score.

Duobrii does carry a contraindication in pregnancy as low birthweight was seen in observational studies and increased malformations was seen in animal reproduction studies. HPA axis suppression is a precaution of both use and abrupt discontinuation of Duobrii. Periodic monitoring for evidence of HPA axis suppression should be conducted.

When compared to halobetasol propionate and tazarotene individually in a phase 2 trial, Duobrii was shown to be significantly more efficacious than either therapy alone. Duobrii was not however, studied with any other topical standards of care for plaque psoriasis. These standards include treatment with other topical corticosteroids, vitamin D analogues, tacrolimus and pimecrolimus (for sensitive areas), coal tar or anthralin. Duobrii potentially offers an increased length of remission compared to each product individually, due to synergistic effects of the products. In addition, the tolerability of tazarotene may be improved when combined with halobetasol propionate. Less concern over the adverse effects associated with ultra-high potency halobetasol 0.05% is another benefit of Duobrii, since a lower-potency form, halobetasol 0.01%, can be used with tazarotene while maintaining efficacy.

Duobrii is the first lotion that combines a topical corticosteroid with a topical retinoid for the treatment of plaque psoriasis. Another combination product used for treatment of plaque psoriasis combines a topical corticosteroid and a vitamin D derivative, available now as a generic. Besides these two combination products, all other topical treatments for plaque psoriasis are provided as individual entities.

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. Todd Sponenberg made a motion to accept the recommendations as presented. Kelly Yelenic seconded the motion. None were opposed.

**Financial Discussion:** No comments or questions. Todd Sponenberg made a motion to accept the recommendations as presented. Kelly Yelenic seconded the motion. None were opposed.

**Outcome:** Duobrii will be a pharmacy benefit and will not be added to the GHP Family formulary. Prior authorization will apply with the following criteria:

- Medical record documentation that patient is 18 years of age or older **AND**
- Medical record documentation of a diagnosis of plaque psoriasis **AND**
- Prescribed by or in consultation with a dermatologist **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to tazarotene used in combination with 3 different topical corticosteroids.

**Additional Recommendation:** halobetasol propionate cream and tazarotene cream will be added to the GHP Family pharmacy formulary at the generic tier

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

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### **APADAZ (benzhydrocodone/acetaminophen)**

**Review:** Apadaz, a combination of benzhydrocodone and acetaminophen, is an immediate release opioid analgesic indicated for the short term (no more than 14 days) management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Benzhydrocodone, a prodrug which is converted to hydrocodone by esterases in the gastrointestinal system or blood, was designed to reduce the abuse potential of hydrocodone.

The efficacy of Apadaz was investigated in five pharmacokinetic studies and two clinical studies comparing the abuse deterrent potential of Apadaz to hydrocodone/acetaminophen and placebo. The pharmacokinetic studies showed that exposure to both hydrocodone and acetaminophen in patients taking Apadaz tablets were bioequivalent to Norco tablets. In both abuse deterrent studies, it was found that there were no significant differences for the primary endpoint of Drug Liking on a visual analogue scale between Apadaz and hydrocodone acetaminophen

administered through oral and intranasal routes. The results of these studies did not support the conclusion that Apadaz would be expected to deter abuse from either the oral or intranasal route of administration.

There were no new safety concerns identified in any of the clinical trials of Apadaz and the safety data was similar to the existing hydrocodone/acetaminophen formulations. The prodrug benzhydrocodone was quickly converted to hydrocodone and was not present in the blood long enough for detection. The most commonly reported adverse events were constipation, nausea, somnolence, fatigue, headache, and dizziness.

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

**Financial Discussion:** No comments or questions. Kelly Yelenic made a motion to accept the recommendations as presented. Tricia Heitzman seconded the motion. None were opposed.

**Outcome:** Apadaz and Benzhydrocodone/Acetaminophen are pharmacy benefits that will not be added to the GHP Family formulary. Apadaz and Benzhydrocodone/Acetaminophen will be added to the existing GHP Family Opioid Use policy 1382.0F.

Apadaz	4.08-325mg	Tablet	Oral	10 tab
Apadaz	6.12-325 mg	Tablet	Oral	6 tab
Apadaz	8.16-325 mg	Tablet	Oral	5 tab
Benzhydrocodone/Acetaminophen	4.08-325mg	Tablet	Oral	10 tab
Benzhydrocodone/Acetaminophen	6.12-325 mg	Tablet	Oral	6 tab
Benzhydrocodone/Acetaminophen	8.16-325 mg	Tablet	Oral	5 tab

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

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## **KANJINTI (trastuzumab-anns)**

**Review:** Kanjinti is a biosimilar to Herceptin. Kanjinti shares all the same indications as Herceptin. Kanjinti is indicated as adjuvant treatment of HER2 overexpressing node positive or node negative (ER/PR negative or with one high risk feature) breast cancer: as part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel, as part of a treatment regimen with docetaxel and carboplatin, or as a single agent following multi-modality anthracycline based therapy. Kanjinti is also indicated in combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer or as a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease. Kanjinti is indicated in combination with cisplatin and capecitabine or 5-fluorouracil, for the treatment of patients with HER2 overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma who have not received prior treatment for metastatic disease. The same dosage recommendations for Herceptin apply to Kanjinti (see the full drug review for details). Kanjinti is supplied as 420 mg/vial in a multiple-dose vial. Herceptin is supplied as 150 mg single-dose vial.

The clinical program for trastuzumab-anns consisted of 2 key studies. The comparative clinical study was a randomized double-blind comparative study that included 715 adult women with HER2+ early breast cancer who were planning to undergo surgery. In the neoadjuvant phase, patients were randomized 1:1 to receive either



trastuzumab-anns or trastuzumab plus paclitaxel once every 3 weeks for 4 cycles. In the adjuvant phase, patients that initially were on trastuzumab-anns continued it. Patients who initially received trastuzumab, either continued on it or transitioned to trastuzumab-anns. The clinical equivalence was demonstrated based on the risk difference and risk ratio of the incidence of pathological complete response in breast tissue and axillary lymph nodes. The results demonstrated that trastuzumab-anns is non-inferior to trastuzumab but did not conclude non-superiority.

Trastuzumab-anns was similar to trastuzumab in terms of clinical safety. The clinical pharmacology study was a randomized, single-blind, single-dose, 3-arm parallel-group pharmacokinetic trial of 157 healthy adult male patients. Patients received a single dose of IV trastuzumab-anns, trastuzumab (from US), or trastuzumab (from EU). Trastuzumab-anns was found to be bioequivalent to both trastuzumab (US) and trastuzumab (EU), and the US and EU trastuzumab products were found to be bioequivalent to each other. There were no new safety signals identified and the safety profiles were similar across treatment groups. There were no pre-existing binding ADAs detected at baseline and no subjects had a positive binding ADA test at the end of the study. A comprehensive analytical similarity assessment demonstrated that trastuzumab-anns is analytically highly similar to trastuzumab. Some minor differences in structural and purity attributes were observed, but have no effect on pharmacokinetics, efficacy, safety, or immunogenicity in trastuzumab-anns clinical studies. The only direct evidence is for adjuvant breast cancer. Kanjinti's use in metastatic breast cancer and metastatic gastric cancer is through extrapolated evidence.

Kanjinti shares all the same safety concerns as Herceptin. Kanjinti has a boxed warning for cardiomyopathy, infusion reactions/pulmonary toxicity, and embryo-fetal toxicity.

The NCCN guidelines have been updated to include Kanjinti for invasive breast cancer.

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 presented. Todd Sponenberg seconded the motion. None were opposed.

**Financial Discussion:** No comments or questions. Kevin Szcecina made a motion to accept the recommendations as presented. Tricia Heitzman seconded the motion.

**Outcome:** Kanjinti will be covered as a medical benefit for GHP Family. Kanjinti will not require a prior authorization.

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

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## **XPOVIO (selinexor)**

**Review:** Xpovio is a selective exportin-1 (XPO-1) inhibitor indicated for the treatment of relapsed or refractory multiple myeloma in combination with dexamethasone in adult patients who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents and an anti-CD38 monoclonal antibody. Exportin-1 which mediates the transport of tumor suppressor proteins, growth regulators, and oncogenic proteins can be overexpressed in solid tumors and hematologic malignancies and typically correlates with drug resistance and poor survival.

The safety and efficacy of Xpovio were investigated in a single-arm, open-label study in patients with refractory or relapsed multiple myeloma who had previously received three or more anti-myeloma treatment regimens. FDA approval was based on Part 2 of the study in a prespecified subgroup of 83 patients whose disease was refractory to bortezomib, carfilzomib, lenalidomide, pomalidomide, and daratumumab because the benefit-risk ratio appeared

greater in this population. The primary endpoint was overall response rate to treatment with Xpovio and dexamethasone. The overall response rate for this subgroup was 25.3 % (21 patients) with only one patient achieving a stringent complete response, no patients achieving a complete response, and 20 patients achieving a partial or very good partial response. The median time to first response was 4 weeks and the median duration of response was 3.8 months. Since this was a single arm trial and Xpovio was used in combination with dexamethasone, there is no way to isolate the treatment effect of Xpovio, which showed no response in clinical trials investigating Xpovio as monotherapy.

In clinical trials, one or more adverse events were experienced in 100% of patients with nearly two-thirds of patients experiencing a serious adverse event. The most frequently reported adverse events during clinical trial were thrombocytopenia, anemia, neutropenia, leukopenia, nausea, diarrhea, vomiting, constipation, fatigue, weight loss, decreased appetite, hyponatremia, and dyspnea. Adverse events led to dose modifications in a majority of patients and discontinuation in one-quarter of the patients treated with Xpovio. Of 202 patients receiving Xpovio during clinical trials, 18 of 42 deaths which occurred during or within 30 days of treatment with Xpovio were attributed to treatment emergent adverse events.

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 presented. Kevin Szczecina seconded the motion. None were opposed.

**Financial Discussion:** No comments or questions. Aubrielle Prater made a motion to accept the recommendations as presented. Kelly Yelenic seconded the motion. None were opposed.

**Outcome:** Xpovio is a pharmacy benefit that will be added to the Brand Tier on the GHP Family formulary. The following prior authorization criteria will apply:

- Medical record documentation that Xpovio is prescribed by a hematologist or oncologist AND
- Medical record documentation of age 18 years or older AND
- Medical record documentation that Xpovio will be used in combination with dexamethasone AND
- Medical record documentation of a diagnosis of relapsed or refractory multiple myeloma and the member has received at least four prior complete regimens which include at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody.

**AUTHORIZATION DURATION:** Initial approval will be for 6 months. Subsequent approvals will be for an additional 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.

**QUANTITY LIMIT:** Pharmacist note to CSR: *Authorization should be entered by HICL and only checking the Formulary PA required box (no QLS need to be entered within the authorization).*

80 mg twice weekly	32 tablets / 28 days
100 mg once weekly	20 tablets / 28 days
80 mg once weekly	16 tablets / 28 days
60 mg once weekly	12 tablets / 28 days

**Note: Currently Approved Agents for the treatment of Multiple Myeloma<sup>2</sup>**

Class	Single-agent (+/- steroids)	Combination therapy
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<b>Immunomodulatory agents (IMiD)</b>	Revlimid (lenalidomide) Pomalyst (pomalidomide)	--
<b>Proteasome inhibitors (PI)</b>	Velcade (bortezomib) Kyprolis (carfilzomib)	Ninlaro (ixazomib) (with lenalidomide)
<b>anti-CD38</b>	Darzalex (daratumumab)	--
<b>Anti-SLAM F7</b>	--	Empliciti (elotuzumab) (with IMiD)
<b>Histone deacetylase inhibitor (HDAC)</b>	--	Farydak (panobinostat) (with bortezomib)

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

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### **MVASI (bevacizumab-awwb)**

**Review:** Mvasi is a biosimilar to Avastin indicated for the treatment of: metastatic colorectal cancer, in combination with intravenous fluorouracil-based chemotherapy for first- or second-line treatment; metastatic colorectal cancer, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line bevacizumab product-containing regimen; unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer (NSCLC), in combination with carboplatin and paclitaxel for first-line treatment; recurrent glioblastoma in adults; metastatic renal cell carcinoma in combination with interferon-alfa; and persistent, recurrent, or metastatic cervical cancer, in combination with paclitaxel and cisplatin, or paclitaxel and topotecan. Mvasi shares the same indications as Avastin, except it did not gain approval for ovarian, fallopian tube and primary peritoneal cancer because these indications are protected by the Orphan Drug Exclusivity.

Similar to Avastin, Mvasi is supplied as single-dose vials in available as 100 mg/4mL and 400 mg/16mL (25 mg/mL). Mvasi shares the same dosage recommendations as Avastin (see drug review for details).

The FDA's approval of Mvasi is based on review of evidence that included structural and functional characterization, animal study data, human pharmacokinetic and pharmacodynamics data, clinical immunogenicity data and other clinical safety and effectiveness data. The clinical equivalence of bevacizumab-awwb to bevacizumab was demonstrated in a randomized, double-blind, active controlled comparative clinical trial in 642 patients with advanced non-squamous NSCLC receiving first-line chemotherapy with carboplatin and paclitaxel. Both treatment groups experienced similar response duration and progression-free survival (PFS). Bevacizumab-awwb and bevacizumab was similar in terms of clinical safety as well. There was also a pharmacology study in healthy adult males, and it was concluded that bevacizumab-awwb was bioequivalent to both bevacizumab (US) and bevacizumab (EU), and the US and EU bevacizumab products were found to be bioequivalent to each other. Also, there was no new safety signals identified and the safety profiles were similar across treatment groups. There was also a pharmacology study evaluating bevacizumab-awwb and bevacizumab in Japanese male subjects. The pharmacokinetics were consistent with the study previously described. A comprehensive analytical similarity assessment demonstrated that bevacizumab-awwb is analytically highly similar to bevacizumab. The only direct evidence for Mvasi was in NSCLC. The data support the extrapolation to 4 other approved bevacizumab indications that were not studied in the bevacizumab-awwb clinical program.

In terms of warnings/precautions, Mvasi shares the same safety concerns as Avastin.

Per NCCN, Mvasi is recommended for use in kidney cancer and NSCLC (as a substitute for bevacizumab). For relapsed or stage IV disease kidney cancer, Mvasi is recommended as single-agent subsequent therapy for clear cell histology, as single-agent systemic therapy for non-clear cell histology, in combination with erlotinib for non-clear cell histology in selected patients with advanced papillary renal cell carcinoma including hereditary leiomyomatosis and renal cell carcinoma (HLRCC), and in combination with everolimus as systemic therapy for non-clear cell histology.

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 presented. Kevin Szczecina seconded the motion. None were opposed.

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

**Outcome:** Mvasi will be covered as a medical benefit for GHP Family. Mvasi will not require a prior authorization.

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

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## **NUBEQA (darolutamide)**

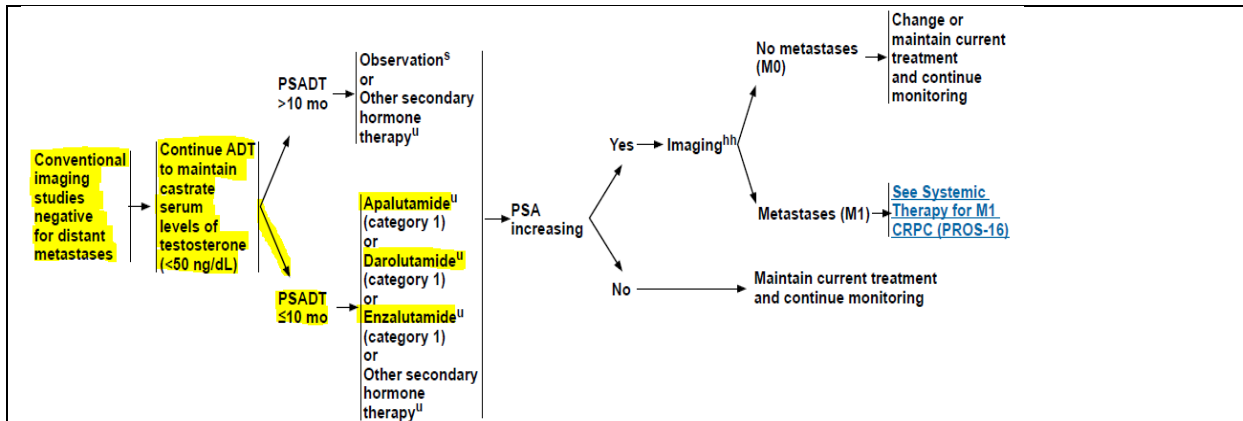
**Review:** Nubeqa is an androgen receptor (AR) inhibitor indicated for the treatment of non-metastatic castration-resistant prostate cancer. Nubeqa is dosed as two (300 mg) tablets orally twice a day. Treatment with Nubeqa should be considered once the prostate-specific antigen doubling time (PSADT) is  $\leq 10$  months. Nubeqa should be used concomitantly with GnRH analogs unless patients have had a bilateral orchiectomy.

The efficacy and safety of Nubeqa was evaluated by the ARAMIS trial. Nubeqa proved to be superior to placebo in metastasis free survival (MFS) improvement. Time to pain progression also supported the MFS result. Although overall survival was not concluded in the study, it was an additional endpoint. At interim analysis, 3-year overall survival rates were 83% in the darolutamide group and 73% in the placebo group. Safety concerns of Nubeqa include embryo-fetal toxicity, fatigue, pain in extremities, rash, urinary retention, pneumonia, hematuria, as well as neutropenia and elevated AST/bilirubin.

Other agents in the nonsteroidal anti-androgen (NSAA) class that share similar efficacy as Nubeqa, include apalutamide and enzalutamide. NCCN's recommendation in therapy (Figure 3), does not imply superiority between agents.

Apalutamide shares the same indication as Nubeqa, whereas enzalutamide does not differentiate between non-metastatic or metastatic disease. While generally having the same side effects as Nubeqa, apalutamide has a direct contraindication in pregnancy. However, all three agents propose safety precautions in this setting. Overall, Dr. Fizazi and Dr. Dahut associate Nubeqa with a preferred safety profile. Dr. Fizazi supports the safety profile by explaining that Nubeqa does not cross the blood-brain barrier, whereas the other agents do.

*Figure 3: Systemic Therapy for M0 Castration-Resistant Prostate Cancer (CRPC)<sup>7</sup>*



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. Aubrielle Prater made a motion to accept the recommendations as presented. Kevin Szczecina seconded the motion. None were opposed.

**Financial Discussion:** No comments or questions. Todd Spenberg made a motion to accept the recommendations as written. Aubrielle Prater seconded the motion. None were opposed.

**Outcome:** Nubeqa will be a pharmacy benefit that will be added to the GHP Family formulary on the Brand tier requiring prior authorization. The following prior authorization criteria should apply:

- Prescription written by or in consultation with an oncologist, hematologist or urologist **AND**
- Medical record documentation of age 18 years or older **AND**
- Medical record documentation of a diagnosis of non-metastatic, castration-resistant prostate cancer **AND**
- Medical record documentation that patient is receiving GnRH analog(s) concurrently OR that patient has had a bilateral orchiectomy

**QUANTITY LIMIT:** 4 tablets per day, 30-day supply per fill

**AUTHORIZATION DURATION:** Initial approval will be for **12 months**. Subsequent approvals will be for an additional **12 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.

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

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## TURALIO (Pexidartinib)

**Review:** Turalio, the first FDA-approved systemic treatment for tenosynovial giant cell tumor (TGCT), selectively inhibits the receptor for colony-stimulating factor-1 (CSF1), a hematopoietic growth factor overexpressed in many cancers, as well as KIT and FLT3 which regulate cell proliferation. It should be reserved for patients with functional limitations and severe mobility in patients who are not candidates for surgery. Turalio is a category 1 NCCN recommendation for single-agent treatment of pigmented villonodular synovitis/tenosynovial giant cell tumor.

The efficacy of Turalio was investigated in the ENLIVEN trial, a randomized, double-blind, two-part study comparing Turalio to placebo in the treatment of symptomatic, advanced TGCT in whom surgery was not recommended. In part one, patients were randomized 1:1 to receive placebo or a loading dose of 1000 mg of Turalio for the first two weeks followed by the recommended FDA dosage of 800 mg per day for 22 weeks. The primary endpoint measuring overall response rate at week 25 using Response Evaluation Criteria in Solid Tumors (RECIST) was significantly higher in the Turalio treatment group (38%) compared to placebo (0%). Secondary endpoints showed the Turalio group achieved a significantly greater overall response rate by tumor volume score at week 25 as well as improvements in range of motion, physical function scale (PROMIS), and pain and stiffness scales compared to placebo. At data cutoff with a median follow up of 22 months, the overall response rate for the Turalio treatment group increased to 53% and median duration of response by RECIST or tumor volume score in the Turalio group was not reached since very few patients had disease progression. Part two was an open-label study of 30 patients who had received placebo during the first part of the trial. At data cut off, 16/30 patients had a RECIST response and 20/30 had a tumor volume score response.

Turalio has a black box warning for serious and potentially fatal liver injury. Severe and fatal hepatotoxicity with ductopenia and cholestasis occurred in patients treated with Turalio. During the ENLIVEN clinical trial, the most common serious adverse events and the most frequent adverse events requiring permanent discontinuation were abnormal liver tests and hepatotoxicity. Liver tests should be monitored at specific intervals during treatment with Turalio to determine if dose reduction or discontinuation is required. Other common adverse events reported in more than 20% of patients were hair color changes, increased LDH, laboratory abnormalities including decreased neutrophils, lymphocytes, phosphate and hemoglobin, eye edema, rash, and dysgeusia. Dose reductions or interruptions occurred in 38% of patients and permanent discontinuation was required in 13% of patients. The most common adverse events leading to dosage modification were elevated liver enzymes, nausea, vomiting, dizziness, and abdominal pain.

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 presented. Keith Hunsicker seconded the motion. None were opposed.

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

**Outcome:** Turalio is a pharmacy benefit that will be added to the Brand tier. The following prior authorization criteria will apply:

- Medical record documentation that Turalio is prescribed by an oncologist AND
- Medical record documentation of age 18 years or older AND
- Medical record documentation of diagnosis of tenosynovial giant cell tumor that meets both of the following criteria:
  - Associated with functional limitations or severe morbidity AND
  - Not amenable to improvement with surgery

**AUTHORIZATION DURATION:** Initial approval will be for 12 months. Subsequent approvals will be for an additional 12 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.

**QUANTITY LIMIT:** 4 capsules per day, 30-day supply per fill

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

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## **FAST FACTS**

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### **GATTEX (teduglutide)**

**Updated Indication:** Gattex is a glucagon-like peptide-2 (GLP-2) analog indicated for the treatment of pediatric patients 1 year of age and older with Short Bowel Syndrome (SBS) who are dependent on parenteral support.

Previously, Gattex did not maintain any indications for pediatric patients.

Gattex maintains its FDA-approved indication for treatment of adult patients with SBS who are dependent on parenteral support.

**Current formulary Status:** Specialty Tier requiring PA

**Recommendations:** No changes are recommended to the formulary status of Gattex at this time. The current policy will be updated to account for the pediatric indication as outlined below.

#### GHP Family Policy 1210.0F

- Medical record documentation that Gattex is prescribed by a gastroenterologist **AND**
- Medical record documentation of age greater than or equal to 1 year **AND**
- Medical record documentation of a diagnosis of short bowel syndrome **AND**
- Medical record documentation that the member has been dependent on parenteral nutrition/intravenous support for a minimum of 12 consecutive months continuously **AND**
- Medical record documentation that the member requires parenteral nutrition at least 3 times per week

**Discussion:** No comments or questions

**Outcome:** Todd Sponenberg made a motion to accept the recommendations as presented. Kelly Yelenic 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.

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### **PRALUENT (alirocumab)**

**Updated Indication:** Praluent is a PCSK9 (proprotein convertase subtilisin kexin type 9) inhibitor antibody indicated:

- to reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established cardiovascular disease.
- as adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe), for the treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia) to reduce low-density lipoprotein cholesterol LDL-C.

Previously Praluent was indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL-C.

**Current Formulary Status/Prior Authorization Criteria:** Brand Preferred tier requiring PA

**Recommendations:** No changes are recommended to the formulary placement or prior authorization criteria of Praluent at this time. The following changes will be made to authorization duration:

**Praluent GHP Family Policy 1316.0F**

**AUTHORIZATION DURATION:** Initial authorizations will be approved for 12 months.

Reauthorizations will be for a period of 12 months each provided the following criteria are met:

- Medical record documentation of an up to date low density lipoprotein (LDL) cholesterol level since the date of the previous review showing the patient has had a clinically significant response to treatment with a PCSK9 inhibitor **AND**
- Medical record documentation that the patient is not experiencing any significant adverse events related to therapy **AND**
- Claims history and attestation from the provider showing the patient is adherent to PCSK9 therapy **AND**
- Claims history or attestation from the provider that the patient is staying adherent to (filling at least 90% of doses) statin therapy (if statin tolerant) **AND**
- Medical record documentation that Praluent continues to not be used in combination with another PCSK9 inhibitor, Juxtapid, or Kynamro

**Other Recommendations:** The authorization duration for Repatha will be updated as follows:

**Repatha GHP Family Policy 1326.0F**

**AUTHORIZATION DURATION:** Initial authorizations for Repatha will be approved for a period of 12 months. Reauthorizations will be for a period of 12 months each provided the following criteria are met:

- Medical record documentation of an up to date LDL cholesterol level since the date of the previous review showing the patient has had a clinically significant response to treatment with a PCSK9 inhibitor **AND**
- Medical record documentation that the patient is not experiencing any significant adverse events related to therapy **AND**
- Claims history and attestation from the provider showing the patient is adherent to PCSK9 therapy **AND**
- Claims history or attestation from the provider that the patient is staying adherent to (filling at least 90% of doses) statin therapy (if statin tolerant) **AND**
- Medical record documentation that Repatha continues to not be used in combination with another PCSK9 inhibitor, Juxtapid or Kynamro

**Discussion:** No comments or questions.

**Outcome:** No comments or questions. Kelly Yelenic 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.

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**KALYDECO (ivacaftor)**

**Updated Indication:** Kalydeco is now indicated for the treatment of CF in patients age 6 months and older who have one mutation in the *CFTR* gene that is responsive to ivacaftor based on clinical and/or in vitro assay data.



If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use.

Note: Previously, Kalydeco was indicated in patients 12 months and older.

**Current formulary status:** Specialty tier or the Brand Non-Preferred tier for members with a three tier benefit, requiring PA

**Recommendation:** There are no recommended changes to formulary status at this time. However, it is recommended to update the age restriction to the following:

- "...Medical record documentation of member age  $\geq$  6 months AND"

There will be no changes to quantity limits or authorization durations at this time.

**Discussion:** No comments or questions.

**Outcome:** Kim Clark 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.

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### **MAVYRET (glecaprevir-pibrentasvir)**

**Updated Indication:** Mavyret is indicated for the treatment of adult and pediatric patients 12 years and older or weighing at least 45 kg with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5 or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A).

Mavyret is indicated for the treatment of adult and pediatric patients 12 years and older or weighing at least 45 kg with HCV genotype 1 infection, who previously have been treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor (PI), but not both.

Mavyret was previously only approved in adults age 18 and older.

**Current Formulary Status/Prior Authorization Criteria:** Mavyret is a pharmacy benefit on the Brand tier requiring prior authorization.

**Recommendations:** There are no changes recommended to formulary placement, quantity limits, and authorization duration at this time. However, the prior authorization criteria will be updated to the following.

- Medical record documentation of age greater than or equal to 12 years **OR** weight greater than 45 kg **AND**

**Discussion:** No comments or questions.

**Outcome:** Kevin Szczecina 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.

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**SORILUX (calcipotriene)**

**Updated Indication:** Sorilux Foam is now indicated as a topical treatment for plaque psoriasis of the scalp and body for patients 12 years and older. Previously, Sorilux was only approved for those 18 years and older.

**Current Formulary Status/Prior Authorization Criteria:** Non-Formulary

**Recommendations:** Due to the availability of three other generic calcipotriene alternatives with a more favorable pricing profile and the lack of evidence to support superiority of the foam formulation compared to the alternatives, it is recommended that Sorilux remains as a non-formulary medication for all lines of business. Currently there is not a drug policy in place for Sorilux for any line of business. It is not recommended to develop a policy at this time due to low utility of the drug (GHP has not received a Sorilux prior authorization request for Sorilux in greater than one year). Requests for Sorilux should be reviewed utilizing the respective administrative policies as a guide.

**Discussion:** No comments or questions.

**Outcome:** Aubrielle Prater made a motion to accept the recommendations as presented. Rajneel Farley 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.

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**FRAGMIN (dalteparin sodium)**

**Updated Indication:** Fragmin is now indicated for the treatment of symptomatic venous thromboembolism (VTE) to reduce the recurrence in pediatric patients 1 month of age and older.

Note: Fragmin is also indicated for:

- Prophylaxis of ischemic complications of unstable angina and non-Q-wave myocardial infarction, when concurrently administered with aspirin therapy
- Prophylaxis of deep vein thrombosis (DVT) in abdominal surgery, hip replacement surgery or medical patients with severely restricted mobility during acute illness
- Extended treatment of symptomatic VTE to reduce the recurrence in adult patients with cancer. In these patients, the Fragmin therapy begins with the initial VTE treatment and continues for six months

Fragmin is not indicated for the acute treatment of VTE.

**Current Formulary Status/Prior Authorization Criteria:** Fragmin is a pharmacy benefit and is non-formulary for GHP Family. Fragmin is at the Specialty tier for Exchange requiring a prior authorization.

**Recommendations:** The utilization of Fragmin is low and is not expected to increase since the current guideline also recommends the use of enoxaparin in pediatric patients. Therefore, it is not recommended to add a policy at this time and requests will be reviewed for medical necessity utilizing the administrative policy as a guide.

**Recommendation:** There is no change to formulary status at this time

**Discussion:** No comments or questions.

**Outcome:** Todd Sponenberg made a motion to accept the recommendations as presented. Rajneel Farley 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.

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### **LIVALO (pitavastatin)**

**Updated Indication:** Livalo is a HMG-CoA reductase inhibitor indicated as an adjunctive therapy to diet in pediatric patients aged 8 years and older with heterozygous familial hypercholesterolemia (HeFH) to reduce elevated TC, LDL-C, and Apo B.

Previously, Livalo did not maintain any indications for pediatric patients.

Previously, Livalo was only indicated as an adjunctive therapy to diet in adult patients with primary hyperlipidemia or mixed dyslipidemia to reduce elevated total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (Apo B), triglycerides (TG), and to increase high-density lipoprotein cholesterol (HDL-C).

**Current Formulary Status:** NF

**Recommendations:** Not all of the currently listed formulary alternatives are indicated for patients 8 years and older (atorvastatin & simvastatin – 10 years and older; rosuvastatin – 7 years and older). To ensure that formulary alternatives are being applied to appropriate ages the criteria will be changed as outlined below.

#### GHP Family Policy 1167.0F

- Medical record documentation that patient is  $\geq 8$  years of age  
**AND**  
*For patient age  $\geq 10$  years:*
- Medical record documentation of intolerance to, contraindication to, or therapeutic failure (including up-to-date laboratory values) to reach goal low-density lipoprotein (LDL) (per NCEP guidelines) after titration to tolerated doses of simvastatin AND atorvastatin AND rosuvastatin  
**OR**  
*For patient age  $\geq 8$  to  $< 10$  years:*
- Medical record documentation of intolerance to, contraindication to, or therapeutic failure (including up-to-date laboratory values) to reach goal low-density lipoprotein (LDL) (per NCEP guidelines) after titration to tolerated doses of rosuvastatin.

**Discussion:** No comments or questions.

**Outcome:** Kim Clark 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.

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**ZELNORM (tegaserod maleate)**

**Updated Indication:** Zelnorm is a serotonin-4 (5-HT<sub>4</sub>) receptor agonist indicated for the treatment of adult women less than 65 years of age with irritable bowel syndrome with constipation (IBS-C).

Limitations of Use: The safety and effectiveness of Zelnorm in men with IBS-C have not been established.

**Note:** Zelnorm is not indicated in patients 65 years of age and older.

**Current Formulary Status/Prior Authorization Criteria:** Nonformulary

**Recommendation:** There is no change to formulary status at this time. Zelnorm is a pharmacy benefit that will not be added to the GHP Family formulary. The following prior authorization criteria will apply:

Prior Authorization Criteria:

- Medical record documentation of a diagnosis of irritable bowel syndrome with constipation (IBS-C) AND
- Medical record documentation that patient is a female between the ages of 18 and 65 years AND
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Amitiza and Linzess.

**QUANTITY LIMIT:** 2 tablets per day

**Discussion:** Aubrielle questioned having a gender in the policy. Since indicated as such, will leave in for now. No further comments or questions.

**Outcome:** Kim Clark 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.

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**DARZALEX (daratumumab)**

**Updated Indication:** Darzalex is now indicated in combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant.

Previously, Darzalex did not maintain an indication for newly diagnosed multiple myeloma in combination with lenalidomide and dexamethasone.

Darzalex maintains its other FDA approved indications for adult patients with multiple myeloma:

- in combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant
- in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
- in combination with pomalidomide and dexamethasone in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor
- as monotherapy, in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent

- indicated in combination with lenalidomide and dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have at least one prior therapy.

**Current Formulary Status/Prior Authorization Criteria:** Non-formulary – Medical Benefit requiring PA

**Recommendation:** No changes will be made to the formulary status of Darzalex at this time. The current policies will be updated to account for the new indication as outlined below.

#### MBP 139.0

##### **Multiple Myeloma**

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation a diagnosis of multiple myeloma **AND**

If newly diagnosed multiple myeloma:

- Medical record documentation that the member is not eligible for stem-cell transplantation (e.g. coexisting conditions, age greater than 65, etc.) **AND**
- Medical record documentation that Darzalex will be given in combination with one of the following options:
  - Bortezomib (Velcade), melphalan, AND prednisone [VMP] **OR**
  - Lenalidomide (Revlimid) AND dexamethasone **OR**

If relapsed/refractory multiple myeloma: One of the following:

- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least three prior lines of therapy including a proteasome inhibitor (including but not limited to Velcade\*, Kyprolis\*, or Ninlaro\*) and an immunomodulatory agent (including but not limited to Pomalyst\*, Revlimid\*, Thalomid\*) **OR**
- Medical record documentation that the patient is double-refractory to a proteasome inhibitor (including but not limited to Velcade\*, Kyprolis\*, or Ninlaro\*) and an immunomodulatory agent (including but not limited to Pomalyst\*, Revlimid\*, Thalomid\*) **OR**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least 1 prior therapy including a proteasome inhibitor (including but not limited to Velcade\*, Kyprolis\*, or Ninlaro\*) or an immunomodulatory agent (including but not limited to Pomalyst\*, Revlimid\*, Thalomid\*) **AND** one of the following:
- Medical record documentation that Darzalex will be prescribed in combination with lenalidomide and dexamethasone **OR**
- Medical record documentation that Darzalex will be prescribed in combination with bortezomib and dexamethasone

**Discussion:** No comments or questions.

**Outcome:** Aubrielle Prater 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.

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## LYRICA (pregabalin)

**Updated Indication:** Lyrica is now indicated as adjunctive therapy for the treatment of partial-onset seizures in patients 1 month of age and older.

Previously, Lyrica was indicated as adjunctive therapy for the treatment of partial-onset seizures in patients 4 years of age and older.

**Current Formulary Status/Prior Authorization Criteria:** Pregabalin is currently on the Generic Tier requiring a prior authorization and Lyrica is currently on the Brand Tier requiring a prior authorization.

**Recommendation:** No changes are recommended to the current formulary placement and current quantity limits. The following changes are recommended to the policy to incorporate the new indication.

Partial seizures:

- Medical record documentation that patient is  $\geq 1$  month of age **AND**
- Medical record documentation of partial seizures **AND**
- Medical record documentation of Lyrica being used as adjunctive therapy **AND**  
*For patient age  $\geq 3$  years:*
- Medical record documentation of failure on, intolerance to or contraindication to gabapentin.

**Discussion:** No comments or questions.

**Outcome:** Kevin Szczecina made a motion to accept the recommendations as presented. Rajneel Farley 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.

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## KEYTRUDA (pembrolizumab)

**Updated Indication:** Keytruda is now indicated for the treatment of patients with recurrent locally advanced or metastatic squamous cell carcinoma of the esophagus (ESCC) whose tumors express PD-L1 (CPS $\geq$ 10) as determined by an FDA approved test, with disease progression after one or more prior lines of systemic therapy.

Keytruda was not previously indicated for esophageal cancer. Keytruda maintains its previously approved indications for melanoma, non-small cell lung cancer, small cell lung cancer, head and neck squamous cell cancer, classical Hodgkin lymphoma, primary mediastinal large B-cell lymphoma, urothelial carcinoma, microsatellite instability-high cancers, gastric cancer, cervical cancer, hepatocellular carcinoma, Merkel cell carcinoma, and renal cell carcinoma.

**Current Formulary Status/Prior Authorization Criteria:** medical benefit requiring PA

**Recommendation:** There are no changes to the formulary placement of Keytruda at this time. The following prior authorization criteria will be added to account for the new indication. No changes will be made to the authorization duration criteria at this time.

### Esophageal Cancer

- Prescription written by a hematologist/oncologist **AND**

- Medical record documentation that patient is  $\geq 18$  years of age **AND**
- Medical record documentation of a diagnosis of locally advanced or metastatic squamous cell carcinoma of the esophagus **AND**
- Medical record documentation that tumors express PD-L1 (CPS  $\geq 10$ ) as determined by an FDA-approved test **AND**
- Medical record documentation of disease progression after one or more prior lines of systemic therapy for advanced disease.

**Discussion:** No comments or questions

**Outcome:** Aubrielle Prater 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.

### **CIMZIA (certolizumab pegol)**

**Updated Indication:** Cimzia, a tumor necrosis factor (TNF) blocker is now indicated in adult patients for the treatment of non-radiographic axial spondylarthritis with objective signs of inflammation.

**Current Formulary Status/Prior Authorization Criteria:** Medical or Pharmacy Benefit on Specialty tier (or Brand Non-preferred tier for a members with a three tier benefit) requiring a prior authorization

**Recommendation:** There are no changes to the formulary placement or authorization duration at this time. The prior authorization criteria outlined below will be added to GHP Family Policy 903.0F (for self-administered).

Medical: The prior authorization criteria outlined below be added to Medical Policy 74.0.

#### **Non-radiographic Axial Spondylarthritis**

- Medical record documentation that Cimzia is written by a rheumatologist **AND**
- Medical record documentation of age 18 years or older **AND**
- Medical record documentation of non-radiographic axial spondylarthritis **AND**
- Medical record documentation of at least one of the following:
  - C-reactive protein (CRP) level above the upper limit of normal (10 mg/dL) **OR**
  - Sacroiliitis on magnetic resonance imaging (MRI)

**AND**

- Medical record documentation of an intolerance to, contraindication to, or therapeutic failure on at least two (2) nonsteroidal anti-inflammatory drugs (NSAIDs) **AND**
- Medical record documentation that Cimzia is not being used concurrently with a TNF blocker or other biologic agent.

**QUANTITY LIMIT:** One-week authorization for QL of 3 kits per 28 days; Remainder of the 6-month authorization duration: QL of 1 kit per 28 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 signs and symptoms of non-radiographic axial spondylarthritis on six (6) months of Cimzia 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 non-radiographic axial spondylarthritis while on Cimzia therapy.

**Discussion:** No comments or questions.

**Outcome:** Kevin Szczecina 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.

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### **ARRANON (nelarabine)**

**Updated Indication:** Arranon is now indicated for the treatment of patients with T-cell acute lymphoblastic leukemia and T-cell lymphoblastic lymphoma in adult and pediatric patients age 1 year and older whose disease has not responded to or has relapsed following treatment with at least two chemotherapy regimens.

Prior labeling did not have an age restriction and included dosing recommendations for both adult and pediatric patients. Previously, Arranon was indicated for the treatment of patients with T-cell acute lymphoblastic leukemia and T-cell lymphoblastic lymphoma whose disease has not responded to or has relapsed following treatment with at least two chemotherapy regimens. This use is based on the induction of complete responses. Randomized trials demonstrating increased survival or clinical benefit have not been conducted.

**Current Formulary Status/Prior Authorization Criteria:** Arranon is a medical benefit and requires a prior authorization.

**Recommendation:** There is no change to formulary status at this time.

**Discussion:** No comments or questions.

**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.

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## **UPDATES**

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### **SEPTEMBER 2019 DUR/ADHERENCE UPDATE**

#### **GHP Family**

#### **Drug Use Evaluations (DUEs)**

- Asthma DUE
  - This is the 2019 3<sup>rd</sup> quarter MedImpact DUE for all LOBs



- From this report, we identified **90 members** who received 4 or more prescriptions for an asthma medication over a 12-month period but did not receive an asthma controller medication in that same 12-month period.
- Brandy P. completed the mail merge and sent out the letters to the member's providers on 8/26/2019.
- We will have Adam re-run this data in December 2019 to show us the effectiveness of the letter.
- Congestive Heart Failure DUE
  - This is the 2019 2<sup>nd</sup> quarter MedImpact DUE for GHP Family
  - From this report, we identified **90 members** who have a presumed diagnosis of heart failure taking metoprolol succinate, carvedilol, or bisoprolol, and who were not taking an angiotensin-converting enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARB) drug therapy in a 3-month timeframe.
  - We will have Adam re-run this data in October 2019 to show us the effectiveness of the letter.
- Coronary Artery Disease DUE
  - This is the 2019 1<sup>st</sup> quarter MedImpact DUE for all LOBs
  - From this report, we identified **100 members** age 40-75 years who are not on a statin drug therapy in a 3-month timeframe and who have at least one of the following cardiovascular disease (CVD) risk factors: diabetes, hypertension, or smoking.
  - Brandy P. completed the mail merge and sent out the letters to the member's providers on 2/19/2019
  - Adam K. was able to re-run the data on this population and of the original 100 members that we sent letters to 94 members are still active. Of those 94 members 13 now have a claim for a statin medication. This equates to 13.8% of the members.
- Polypharmacy DUE
  - This is the 2018 4<sup>th</sup> quarter MedImpact DUE for all LOBs
  - From this report, we identified **95 members** who were receiving more than 10 unique, chronic medications from 3 or more prescribers over a 3-month timeframe
  - Brandy P. completed the mail merge and sent out the letters to their providers on 12/17/2018.
  - Adam K. was able to re-run the data on this population vs. a control population on 4/30/19. The population we sent letters to had an 8.9% decrease in total claims after the letters were sent compared to the control population which had an 8.6% decrease in total claims.
- Statin Use in Persons with Diabetes (SUPD)
  - This is the 2018 3<sup>rd</sup> quarter MedImpact DUE for GHP Family
  - From this report, we identified **99 members** whose medication history was suggestive of the presence of diabetes and who were not receiving a statin drug during the previous three-month period.
  - Brandy P. completed the mail merge and sent out the letters to their providers on 09/13/2018.
  - Adam K. was able to re-run the data on this population on 4/19/19 and of the of original 99 members that we sent letters to 81 members are still active. Of those 81 members 27 members now have a claim for a statin medication. This equates to 33.3% of the members.

## In Progress

- Nothing in progress at this time

## Ongoing

- DUR Duplicate Anticoagulant Report
  - We get this report **weekly** for **all LOBs** flagging members filling duplicate anticoagulant medications. We personally reach out to the providers/pharmacy of the flagged members to confirm proper medication therapy.
    - For GHS30 in 2019 we have reviewed **95 members** and have made interventions for **4 members**
- Duplicate Specialty Therapy
  - We run an in-house retrospective report **quarterly** for **all LOBs** with help from Adam Kelchner and Aubrielle Prater. These members are identified and written up and sent to a medical director if follow up is needed.
    - For Family 2019-we have reviewed both the Q1 and Q2 reports, but have not made any interventions for GHS30 so far
- Duplicate Buprenorphine Therapy
  - We are getting this report **quarterly** with help from Adam Kelchner. The report works to identify members who have at least a 7 day overlap period of generic Buprenorphine and generic Buprenorphine/naloxone products. Members identified as being on both products are being forwarded to Dr. Meadows for further outreach.
    - For GHS30 in 2019 we have reviewed **8 members** and no outreach is needed at this time.
- Suboxone with an Opioid Report
  - We are getting this report **weekly** for **all LOBs** from Adam Kelchner and we are writing up each member that flags on the report. These members are being forwarded to Dr. Meadows, and he is looking into whether it is appropriate to end the opioid authorizations still in place
  - For GHS30 in 2019, we have reviewed **93 new members**, and **28 members** were referred to Dr. Meadows
- Ending Opioid Authorizations
  - We are working on identifying members who have active opioid authorizations in place but have since started Buprenorphine therapy. The letter is sent to the members notifying them the opioid authorization has been ended due to the start of buprenorphine therapy.
  - For GHS30 in 2019, we have sent **27 members** letters notifying them of the end of their opioid authorization
- Medicaid Opioid Overutilization Report
  - We are getting this report **monthly** from MedImpact and we are writing up each member that flags on the report. We have been monitoring the members that are continuously showing up on the report by any change in their MED. For those members we deem appropriate we will send a letter to their PCP.
  - For GHS30 in 2019, we have reviewed **12 cases** so far, referred **2 patients** to Dr. Meadows, and did not send any prescriber letters
- FWA Reports
  - We are getting this report **weekly** for **all LOBs** from Marie Strausser. We prepare this report by determining which claims need to be verified, and the Wilkes pharmacy students/GHP technicians have been making the calls to pharmacies.
  - We review claims for anti-hypertensives, statins, 1-day supply, and inhalers

- For GHS30 in 2019, we have reviewed **316 cases** so far and **corrected 227 claims**, resulting in a **cost savings of \$16,809.57**
- Stent Antiplatelet Adherence Program
  - We continue to identify new stent patients for **all LOBs** at GMC/GWV/CMC/Susq and follow these members for 1 year after discharge to ensure adherence to their aspirin, beta blocker, antiplatelet, and statin therapy regimens.
  - For GHS30 in 2019, we have identified and outreached to **71 new stent patients**
- Severity Report
  - This is a **monthly** report for **all LOBs** on members who have filled a medication that has a level one interaction with another medication they have a claim for
  - For GHS30 in 2019, we have sent letters to providers on **154 GHP Family members**
- Duplicate Antipsychotics
  - Adam Kelchner runs this report **quarterly**, and we send letters to the PCPs to address potential duplicate therapy issues.
  - For GHS30 in 2019, we have sent letters to **293 providers** so far concerning patients on multiple antipsychotics.
- Adherence to Antipsychotics for Individuals with Schizophrenia (SAA)
  - Kayla Stanishefski runs this report **monthly**, and we send letters to the flagged members who appear non-adherent to their antipsychotic medications.
  - HEDIS Specifications: The percentage of members 19-64 years of age during the measurement year with schizophrenia or schizoaffective disorder who were dispensed and remained on an antipsychotic medication for at least 80% of their treatment period.
  - For GHS30 in 2019, we have sent letters to **7 members** so far to encourage adherence.
- Enbrel Overutilization for Treating Plaque Psoriasis
  - A **monthly** report was created to determine members who have been overutilizing Enbrel twice weekly dosing as outlined by the FDA approved dose. One (1) member flagged on the February 2019 report, and the case was written up and sent to Dr. Yarczower on 2/13/19. The member has since switched to once weekly dosing.
    - We put in place QLs for Enbrel, so we should not be seeing these cases moving forward for new starts and at re-authorization periods for members currently on therapy
    - Working on follow up to ensure members are on proper therapy.
- Tobacco Cessation Program
  - Quarterly meeting with Wellness/MTDM RPhs to create a program that identifies GHP members who may benefit from tobacco cessation interventions/medications.
  - We gathered drug utilization data to determine which medications are being commonly prescribed and assessed proper utilization. We also informed the group of the Chantix updates approved at the March 2018 P&T meeting: Chantix was added to the Brand Tier for GHP Family without prior authorization.
  - We send a letter and resource pamphlet to members on prolonged tobacco cessation treatment to provide additional behavioral health support through Geisinger Health and Wellness.
    - For GHS30 in 2019 we have sent letters to **69 members** so far.
- Antidepressant Medication Management

- Kayla Stanishefski runs this proactive HEDIS report **monthly**, and we send letters to the flagged members who appear non-adherent to their antidepressant medications.
  - For GHS30 in 2019, we have sent letters to **115 members** so far to encourage compliance.
- Asthma Medication Ratio
  - Kayla Stanishefski runs this proactive HEDIS report **monthly**, and we send letters to the flagged members who have a ratio of controller to total asthma medications of < 0.5.
    - For GHS30 in 2019, we have sent letters to **20 members** so far to encourage compliance.
- Medication Management for People with Asthma
  - Kayla Stanishefski runs this proactive HEDIS report **monthly**, and we send letters to the flagged members who appear non-adherent to their asthma controller medications.
    - For GHS30 in 2019, we have sent letters to **97 members** so far to encourage compliance.
- Antipsychotic with Opioid Report
  - This is a **quarterly** report to identify **Medicaid** members with an overlap of 8 or more days between an opioid and antipsychotic medication.
  - We send a letter with claims data to both the opioid prescriber and the antipsychotic prescriber to encourage collaboration in medication management.
    - For GHS30 in 2019, we have identified **209 patients** and sent letters to **201 opioid prescribers** and **184 antipsychotic prescribers**.

## Completed

- Medicaid DUR/FWA Program Fliers
  - Last updated 06/2019 next update December 2019
- Current Provider Letters
  - Congestive Heart Failure DUE
  - Coronary Artery Disease DUE
  - Polypharmacy DUE
  - Statin Use in Persons with Diabetes DUE
  - Adherence to Antidepressants DUE
  - Asthma Med Ratio DUE
  - Opioid Overutilization
  - Duplicate Antipsychotics
  - Severity Report
  - Duplicate Anticoagulant Report
  - Antipsychotic with Opioid Report
- Current Member Letters
  - Ending opioid Authorizations
  - Stent Antiplatelet Adherence Program
  - Adherence to Antipsychotics-SAA
  - Antidepressant Medication Management-AMM
  - Asthma Medication Ratio-AMR
  - Medication Management for People with Asthma-MMA

**Recommendation:** Information only

**Discussion:** No comments or questions.

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

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## ADAPALENE/BENZOYL PEROXIDE

**Background:** Adapalene/benzoyl peroxide 0.1%-2.5% gel pump is available as a generic. Current policies require failure on the separate agents used in combination prior to receiving the combination product. The cost of the combination product has recently dropped to match that of the generic adapalene.

### Formulary Alternatives:

	<b>GHP Family</b>
<b>Preferred Generic</b>	
<b>Generic</b>	adapalene 0.1% gel, cream, benzoyl peroxide (some formulations OTC)
<b>Brand Preferred</b>	
<b>Brand Non-Preferred</b>	
<b>Specialty</b>	

**Recommendations:** It is recommended that the combination adapalene/benzoyl peroxide 0.1%-2.5% gel pump be added to the GHP Family formulary on the generic tier, no PA.

**Discussion:** No comments or questions.

**Outcome:** Aubrielle Prater 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.

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## ENBREL – quantity limit

**Summary:** Some formulations of Enbrel had a change to their packaging, resulting in a need to update our quantity limits.

**Recommendations:** The quantity limits will be updated to the following:

### **RA, AS, PsA, Pediatric PP, JIA**

*25 mg vial*

- Max Qty Supply: 8
- Max Day Supply: 28
- Min Day Supply: 28

*25 mg syringe*

- Max Qty Supply: 4 mL
- Max Day Supply: 28

- Min Day Supply: 28

*50 mg syringe/pen*

- Max Qty Supply: 4 mL
- Max Day Supply: 28
- Min Day Supply: 28

### **Plaque Psoriasis**

#### Initial 6 month auth:

*25 mg vial*

One-time 3-month auth

- Max Qty Supply: 16
- Max Day Supply: 28
- Min Day Supply: 28

For the remainder of the 6 month auth duration:

- Max Qty Supply: 8
- Max Day Supply: 28
- Min Day Supply: 28

#### Subsequent:

- Max Qty: 8
- Max Day Supply: 28
- Min Day Supply: 28

*25 mg syringe*

One-time 3-month auth

- Max Qty Supply: 8 mL
- Max Day Supply: 28
- Min Day Supply: 28

For the remainder of the 6 month auth duration:

- Max Qty Supply: 4 mL
- Max Day Supply: 28
- Min Day Supply: 28

#### Subsequent:

- Max Qty: 4 mL
- Max Day Supply: 28
- Min Day Supply: 28

*50 mg syringe/pen*

One-time 3-month auth

- Max Qty Supply: 8 mL
- Max Day Supply: 28
- Min Day Supply: 28

For the remainder of the 6 month auth duration:

- Max Qty Supply: 4 mL
- Max Day Supply: 28
- Min Day Supply: 28

Subsequent:

- Max Qty: 4 mL
- Max Day Supply: 28
- Min Day Supply: 28

**Discussion:** No comments or questions.

**Outcome:** Kim Clark 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.

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**FORMULARY UPDATE**

**Recommendations:** It is recommended that Mesalamine 1.2 g tablet be added to the GHP Family formulary on the Generic tier

**Discussion:** No comments or questions.

**Outcome:** Kim Clark made a motion to accept the recommendations as presented. Kelly Yelenic 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

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**QUARTERLY CASE AUDIT RESULTS**

The Quarterly Case Audit was held on September 5, 2019. A class review of eye products was reviewed as a result of the case audit as the non-preferred eye products appear frequently as medication requests associated with the administrative policies. Will continue to look for opportunities to create more drug specific policies at future quarterly case audit meetings.

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Meeting adjourned at 4:40 pm.

**Future Scheduled Meetings**

The next bi-monthly scheduled meeting will be held on Tuesday, November 19, 2019 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.