Proposed
Preferred Drug List

with

Clinical Criteria

Proposal for TennCare

May 16, 2013
Responsibilities of the TennCare Pharmacy Advisory Committee

Source: Tennessee Code/Title 71 Welfare/Chapter 5 Programs and Services for Poor Persons/Part 24 Tennessee TennCare Pharmacy Advisory Committee/71-5-2401 through 71-5-2404.

- Make recommendations regarding a preferred drug list (PDL) to govern all state expenditures for prescription drugs for the TennCare program.
  - The TennCare Pharmacy Advisory Committee shall submit to the bureau of TennCare both specific and general recommendations for drugs to be included on any state PDL adopted by the bureau. In making its recommendations, the committee shall consider factors including, but not limited to, efficacy, the use of generic drugs and therapeutic equivalent drugs, and cost information related to each drug. The committee shall also submit recommendations to the bureau regarding computerized, voice, and written prior authorization, including prior authorization criteria and step therapy.
  - The state TennCare pharmacy advisory committee shall include evidence-based research in making its recommendations for drugs to be included on the PDL.
  - The TennCare bureau shall consider the recommendations of the state TennCare pharmacy advisory committee in amending or revising any PDL adopted by the bureau to apply to pharmacy expenditures within the TennCare program. The recommendations of the committee are advisory only and the bureau may adopt or amend a PDL regardless of whether it has received any recommendations from the committee. It is the legislative intent that, insofar as practical, the TennCare bureau shall have the benefit of the committee’s recommendations prior to implementing a PDL or portions thereof.

- Keep minutes of all meetings including votes on all recommendations regarding drugs to be included on the state preferred drug list
- The chair may request that other physicians, pharmacists, faculty members of institutions of higher learning, or medical experts who participate in various subspecialties act as consultants to the committee as needed.
The primary clinical decision that needs to be made is determining if the drugs within the therapeutic class of interest can be considered therapeutic alternatives.

A Therapeutic Alternative is defined by the AMA as: “drug products with different chemical structures but which are of the same pharmacological and/or therapeutic class, and usually can be expected to have similar therapeutic effects and adverse reaction profiles when administered to patients in therapeutically equivalent doses”\(^1\).

The Committee should not feel obligated to decide if every drug within the therapeutic class is exactly equal to all other drugs within the class, nor should they feel obligated to decide if every drug within the therapeutic class works equally well in every special patient population or in every disease.

In special situations (e.g., presence of comorbid conditions) and in special populations (e.g., pediatrics) use of a non-preferred drug might be the most appropriate therapy. These cases can be handled through prior authorization (PA). PA serves as a “safety valve” in that it facilitates use of the most appropriate agent regardless of PDL status.

**LENGTH OF AUTHORIZATIONS:** Dependent upon diagnosis and length of therapy needed to treat. (Most medications are used chronically, and thus would be approved for 1 year.)

1. Is there any reason the patient cannot be changed to a medication not requiring prior approval within the same class? 
   **Acceptable reasons include:**
   - Allergy to medications not requiring prior approval
   - Contraindication to or drug-to-drug interaction with medications not requiring prior approval
   - History of unacceptable/toxic side effects to medications not requiring prior approval

2. The requested medication may be approved if both of the following are true:
   - If there has been a therapeutic failure of at least two medications within the same class not requiring prior approval (unless otherwise specified)
   - The requested medication’s corresponding generic (if a generic is available and preferred by the State) has been attempted and failed or is contraindicated

3. The requested medication may be approved if the following is true:
   - An indication which is unique to a non-preferred agent and is supported by peer-reviewed literature or an FDA approved indication exists.

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The information provided for each drug class is organized into the following sections, when applicable:

**BACKGROUND:**
- General overview
- Pharmacology
- Therapeutic effect(s)
- Adverse reactions
- Outcomes data
- Place in therapy according to current Treatment Guidelines

**RECOMMENDATION:**
- General recommendation regarding utility and therapeutic equivalence among the agents in the class, as well as requirements for product availability (PDL placement)

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\(^1\) AMA Policy H-125.991 Drug Formularies and Therapeutic Interchange
BACKGROUND

- Glaucoma is an optic neuropathy that causes gradual degeneration of the cells making up the optic nerve. Glaucoma can be categorized into 4 distinct types which include primary open-angle, acute angle-closure, secondary and congenital. Patients with open-angle glaucoma initially experience peripheral visual field loss, followed by central field loss, which may progress to irreversible blindness if left untreated.

- Intraocular pressure (IOP) is the one major risk factor for glaucoma that is treatable. Clinical evidence suggests that lowering IOP inhibits or reduces the progression of optic nerve damage. Treatment of glaucoma focuses on decreasing IOP by one of three methods: laser therapy, surgery or pharmacological intervention. Pharmacological intervention is generally used as initial therapy prior to laser or surgical treatment. There are five classes of ophthalmic drugs used for the long-term management of glaucoma: alpha-2 adrenergic agonists, β adrenergic antagonists, carbonic anhydrase inhibitors, parasympathomimetics and prostaglandin analogues.

- The ophthalmic alpha-agonists apraclonidine and brimonidine both decrease the amount of aqueous humor formed and increase its outflow. Ophthalmic brimonidine is specifically indicated for the lowering of IOP in patients with open-angle glaucoma or ocular hypertension. Ophthalmic apraclonidine 0.5% is indicated as a short-term adjunct therapy in controlling IOP among patients on maximally tolerated therapy, while ophthalmic apraclonidine 1% is indicated to control or prevent post-surgical elevations in IOP.

- A few common adverse reactions observed with the use of ophthalmic alpha agonists include:

  - **apraclonidine**: xerostomia, allergic conjunctivitis, blurred vision, conjunctivitis, discharge from eye, dry eye, edema of eyelid, foreign body sensation, itching of eye, mydriasis, ocular hyperemia, reduced visual acuity, and visual discomfort.

  - **brimonidine**: hypertension, xerostomia, somnolence, allergic conjunctivitis, burning sensation in eye, conjunctival discoloration, conjunctival hyperemia, follicular conjunctivitis, ocular hypersensitivity reaction, itching of eye, lid retraction, and visual disturbance.

  - **Contraindications**: both apraclonidine and brimonidine should not be co-administered with monamine oxidase inhibitors (MAOIs).

  - Ophthalmic alpha-agonists may be used concomitantly with other ophthalmic drug products. However, if more than one ophthalmic agent is being used, it should be administered at least five minutes apart. Caution is advised when ophthalmic alpha agonists are used in patients with depression. Additionally, patients with severe uncontrolled cardiovascular disease, including hypertension should also use ophthalmic alpha agonists with caution. For further information, a complete list of precautions may be found in the full MedMetrics Class Review under the Warnings/Precaution section, page 16.

  - Clinical trials have not identified any specific drug interactions with the ophthalmic alpha agonists; however, an additive or potentiating effect with CNS (central nervous system) depressants should be considered when these agents are co-administered with ophthalmic alpha agonists.

- For the management of postoperative elevations in intraocular pressure, clinical trials for brimonidine and apraclonidine indicate both agents are effective treatment options with similar efficacy.

  - A double-masked randomized controlled trial by Chen (n=80 patients; duration: 1 week) evaluated brimonidine 0.15% instilled 1 hour before surgery versus apraclonidine 0.5% instilled 1 hour before surgery.
OPHTHALMIC AGENTS

- Thirteen (31.7%) patients in the brimonidine group and 11 (28.2%) patients in the apraclonidine group had postoperative IOP elevations ≥5 mm Hg (p=0.5). Four (9.8%) patients and three (7.7%) patients in the brimonidine and apraclonidine groups had IOP increases ≥10 mm Hg (p=0.5).

- There were no statistically significant changes in mean heart rate or blood pressure in either group except a slight reduction in diastolic blood pressure at one hour in the brimonidine group (-4.7±9.2 mm Hg) compared to that in the apraclonidine group (-0.1±9.1 mm Hg; p=0.01). Additionally, no clinically significant side effects were noted in either group.

- A meta-analysis performed by Cantor et al showed significantly worse allergic conjunctivitis as well as more overall treatment-emergent adverse events were reported with ophthalmic brimonidine containing benzalkonium chloride preservative. In addition, treatment with ophthalmic brimonidine with the Purite® preservative was associated with a significantly lower incidence of treatment discontinuation.

- The American Academy of Ophthalmology, American Optometric Association and National Institute for Clinical Excellence recommend ophthalmic prostaglandin analogues and ophthalmic beta blockers as first-line medication agents in patients with elevated IOP. Ophthalmic alpha agonists are considered second-line therapy agents in patients who have not achieved a target IOP reduction or developed an intolerable adverse event with an ophthalmic beta-blocker or an ophthalmic prostaglandin analogue.

RECOMMENDATION
Brimonidine and apraclonidine are ophthalmic alpha agonists indicated for the management of elevated IOP from glaucoma, ocular hypertension and after surgical treatments. The American Academy of Ophthalmology, American Optometric Association and National Institute for Clinical Excellence recommend ophthalmic prostaglandin analogues and ophthalmic beta blockers as first-line medication agents in patients with elevated IOP. Combination or monotherapy with agents from another class is recommended in patients that experience intolerable side effects or do not achieve goal IOP reductions with first-line agents. Ophthalmic alpha agonists are considered second-line therapy agents and current guidelines do not differentiate between the agents within the class. Additionally, head to head comparisons demonstrate ophthalmic alpha agonists are comparable in efficacy. Therefore it is recommended that at least one ophthalmic alpha agonist be available for use.

COMMITTEE VOTE:
APPROVED  DISAPPROVED  APPROVED with MODIFICATION

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References
6. American Academy of Ophthalmology. Primary open-angle glaucoma, preferred practice
OPHTHALMIC AGENTS


COMMITTEE VOTE:

APPROVED   DISAPPROVED   APPROVED with MODIFICATION

RE-REVIEW: OPHTHALMIC PROSTAGLANDIN ANALOGUES

BACKGROUND

- Treatment of glaucoma focuses on decreasing intraocular pressure (IOP) by one of three methods: laser therapy, surgery or pharmacological intervention. Pharmacological intervention is generally used as initial therapy prior to laser or surgical treatment. There are five classes of ophthalmic drugs used for the long-term management of glaucoma: alpha-2 adrenergic agonists, β adrenergic antagonists, carbonic anhydrase inhibitors, parasympathomimetics and prostaglandin analogues.
- This class review will focus on the ophthalmic prostaglandin analogues which reduces IOP by increasing aqueous humor outflow through both the trabecular meshwork and uveoscleral routes. This class includes bimatoprost, latanoprost, tafluprost and travoprost.
- The ophthalmic prostaglandin analogues are approved by the Food and Drug Administration (FDA) to reduce IOP in patients with open-angle glaucoma or ocular hypertension. All of the ophthalmic prostaglandin analogues are administered once daily. Ophthalmic travoprost contains the preservative sofZia®, an ionic buffered system which may be less irritating/allergenic to the ocular surface compared to benzalkonium chloride, which is used in ophthalmic bimatoprost and latanoprost formulations. Ophthalmic tafluprost is the only agent in the class that is formulated as preservative-free.
- The most frequently reported adverse events associated with these agents are ocular in nature and include burning/stinging, hyperemia, pruritus, iris pigmentation changes and growth and darkening of eyelashes.
  - Bimatoprost and latanoprost both contain benzalkonium chloride; however, latanoprost is the only agent that lists the use of this agent as a contraindication in patients with hypersensitivity to the active ingredient or benzalkonium chloride. Nonetheless, caution should also be utilized with administration of bimatoprost in patients with hypersensitivity to the preservative.
  - Concomitant use of bimatoprost ophthalmic solution (Latisse™) for hypotrichosis may interfere with the intraocular pressure lowering effect of the other ophthalmic prostaglandins. Monitor for changes in intraocular pressure if Latisse™ is coadministered with an ophthalmic prostaglandin.
  - Precautions/Warnings: (See full MedMetrics Class Review, table 8, pg. 36-37)
    - Eye lash changes- gradual changes including increased length, thickness and number of lashes may be reversible upon discontinuation of treatment.
    - Intraocular inflammation- use caution in patients with intraocular inflammation as inflammation may be exacerbated with prostaglandin analogue treatment.
    - Macular edema- use with caution in aphakic patients, patients with a torn posterior lens or in patients with known risk factors for macular edema.
    - Pigmentation- ophthalmic prostaglandin analogues have been reported to cause permanent changes to pigmented tissues.
Faridi et al evaluated (n=122, 6 months) bimatoprost 0.03% one drop in the affected eye(s) nightly vs. latanoprost 0.005% one drop in the affected eye(s) nightly vs. travoprost 0.004% one drop in the affected eye(s) nightly in newly diagnosed patients with ocular hypertension or open-angle glaucoma.

- After two months of treatment, patients receiving bimatoprost experienced a significantly greater reduction in IOP compared to patients receiving latanoprost and travoprost (9.45 vs 6.17 and 7.36 mm Hg, respectively; p=0.013).
- At six months, bimatoprost treatment reduced IOP from baseline compared to latanoprost and travoprost; however, the difference was not statistically significant (9.23 vs 7.57 and 7.81 mm Hg, respectively; p=0.15).

The American Academy of Ophthalmology, American Optometric Association and National Institute for Clinical Excellence support the use of ophthalmic prostaglandin analogues and ophthalmic beta blockers as first-line medication agents in patients with elevated IOP. Latanoprost 0.005% lowers IOP by up to 35% when administered once daily and has additive effects when administered with other agents. Bimatoprost 0.03% and travoprost 0.00004% have a similar effectiveness to latanoprost with reductions in IOP up to 33% for both agents. Clinical trials have shown statistically significant differences in IOP-lowering ability among the agents within the class. However, the differences are small and clinical significance of these differences has not been established.

RECOMMENDATION

The ophthalmic prostaglandin analogues are approved by the Food and Drug Administration (FDA) to reduce IOP in patients with open-angle glaucoma or ocular hypertension. Clinical guidelines by the American Academy of Ophthalmology, American Optometric Association and the National Institute for Clinical Excellence support the use of ophthalmic β adrenergic antagonists or ophthalmic prostaglandin analogues as initial medical therapy to lower IOP and reduce the risk of progression to visual field loss or optic disc changes in patients with elevated IOP. Guidelines do not recommend one ophthalmic prostaglandin analogue over another and differences in IOP-lowering ability among the agents within the class are small and clinical significance has not been established. Therefore it is recommended that at least 2 ophthalmic prostaglandin analogues are available for use.

COMMITTEE VOTE:

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RE-REVIEW: OPHTHALMIC PROSTAGLANDIN ANALOGUES

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COMMITTEE VOTE:

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References

OPHTHALMIC AGENTS


RE-REVIEW: OPHTHALMIC STEROIDS

BACKGROUND

- Ocular inflammation is a manifestation of cellular and vascular response of the host tissue to injury and involves a complex cascade of events. The pharmacological management of ocular inflammation involves administration of anti-inflammatory medications. Ophthalmic steroids are one medication class that is available for control and treatment of ocular inflammation.
- There is no generally accepted explanation for the mechanism of action of ocular steroids; however, they are thought to exert their anti-inflammatory activity by inhibiting phospholipase A_2 and subsequently inhibiting both cyclooxygenase and lipoxygenase pathways.
- With the exception of difluprednate and rimexolone, all of the agents in this class are FDA-approved for the treatment of steroid-responsive inflammatory ocular conditions. Difluprednate is approved for the treatment of post-operative inflammation and pain following ocular surgery. Rimexolone is approved for the treatment of post-operative inflammation as well as the treatment of chronic anterior uveitis. For a complete listing of FDA approved indications, refer to table 2 in the Med Metrics complete therapeutic class review.
- The most common adverse events associated with the ophthalmic steroids include visual impairment, secondary ocular infections and increased intraocular pressure (IOP). Loteprednol is commonly associated with burning & itching upon instillation, and light intolerance. Rimexolone is commonly associated with headache, ocular pain and discharge. Less common, but serious adverse events associated with all ophthalmic steroids include perforation of the scleral globe, glaucoma, optic nerve damage and the formation of cataracts.
  - Ophthalmic steroids are contraindicated in acute, untreated eye infections, in most viral diseases of the cornea and conjunctiva and also in ocular mycobacterial infections and fungal disease of ocular structures. Ophthalmic prednisolone sodium phosphate is contraindicated after uncomplicated removal of a superficial corneal foreign body.
  - Prolonged use of ophthalmic steroids may result in ocular hypertension and/or glaucoma. The ability of a specific ophthalmic steroid to induce elevation of IOP is based on several factors including dosage, anti-inflammatory potency, and duration of treatment. Ophthalmic steroids should be used in caution in patients with glaucoma and intraocular pressure should be monitored routinely with the use of ten or more days. Ocular hypertension is generally reversible 1—3 weeks after steroid discontinuation; however, persistent pressure elevation with glaucoma and vision loss has occurred.
The use of topical steroids may delay healing and increase the incidence of bleb formation after cataract surgery. Ophthalmic steroids may also suppress the host response and increase the hazard of secondary ocular infections when used for extended periods of time.

Because ophthalmic medications have minimal systemic absorption, studies have not been conducted to assess drug interactions with the ophthalmic steroids.

**Clinical Trials**

- Ophthalmic loteprednol etabonate 0.5% when compared to ophthalmic prednisolone acetate 1% in two prospective, randomized-controlled trials (n=245) in patients with acute anterior uveitis, was found to be less effective in resolution of anterior chamber cell inflammation by day 28 (p=0.015). In both trials, an increase in IOP >10 mmHg was observed more frequently in the ophthalmic prednisolone acetate 1% group than the ophthalmic loteprednol etabonate 0.5% group (p value not reported).

- In a multi-study analysis of patients and subjects enrolled in domestic, double-blind, manufacturer-sponsored studies, loteprednol etabonate ophthalmic suspension was less likely than prednisolone acetate to cause clinically significant (10 mmHg or greater) increases in intraocular pressure (IOP) when used long-term. Among 2,210 subjects and patients, 1,648 received either loteprednol etabonate 0.2% or 0.5% (n=901), prednisolone acetate 1% (n=164), or placebo vehicle (n=583) for 28 days or longer. Known corticosteroid responders were excluded from all studies. The incidence of significantly increased IOP was 1.7% in the loteprednol group, 6.7% in the prednisolone group, and 0.5% in the placebo group. After excluding contact-lens wearers, the incidences were 0.6% in the loteprednol group, 6.7% in the prednisolone group, and 1% in the placebo group.

- Ophthalmic steroids have been utilized as first-line therapy in clinical practice since the 1950s for the treatment of ophthalmic inflammatory conditions. They are used in managing postoperative inflammation following various ocular surgeries, anterior uveitis, ocular allergies, external eye inflammatory diseases associated with some infections, corneal injury from chemical, radiation or thermal burns and penetration of foreign bodies. Although consensus guidelines do not recommend one particular ophthalmic steroid over another in the treatment of most ocular conditions, the American Optometric Association does recommend the use of ophthalmic prednisolone acetate 1% to control inflammation associated with anterior uveitis.

**RECOMMENDATION**
The ophthalmic steroids are FDA-approved for the treatment of steroid-responsive inflammatory ocular conditions, with the exception of difluprednate and rimexolone. Difluprednate is approved for the treatment of post-operative inflammation and pain following ocular surgery. Rimexolone is approved for the treatment of post-operative inflammation as well as the treatment of chronic anterior uveitis. Prolonged use of ophthalmic steroids may result in ocular hypertension and/or glaucoma. Results from clinical trials demonstrate that loteprednol is less likely than prednisolone acetate to cause clinically significant increases in intraocular pressure when used long-term. Currently available clinical guidelines do not recommend one particular ophthalmic steroid over another in the treatment of most ocular conditions; however, the American Optometric Association does recommend the use of ophthalmic prednisolone acetate 1% to control inflammation associated with anterior uveitis. Therefore, it is recommended at least three ophthalmic steroids should be available for use, one of which should be prednisolone acetate. Additionally, due to the decreased relative risk of elevated intraocular pressure, loteprednol should be available for patients where a potential increase in intraocular pressure would place the patient at risk.

**COMMITTEE VOTE:**

- APPROVED
- DISAPPROVED
- APPROVED with MODIFICATION
OPHTHALMIC AGENTS

RE-REVIEW: OPHTHALMIC STEROIDS

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References


RE-REVIEW: OPHTHALMIC NSAIDs

BACKGROUND

- Ophthalmic NSAIDs are most commonly used for ophthalmic surgery. These agents have utility to reduce pain and control inflammation during and after surgery as well as to maintain pupillary dilatation during surgery without a significant effect on IOP.
- Ophthalmic NSAIDs exert their anti-inflammatory activity primarily by nonselective inhibition of cyclooxygenase-1 and cyclooxygenase-2 enzymes.
- The ophthalmic NSAIDs are FDA-approved for various non-infectious ocular conditions including management of pain and inflammation following cataract and corneal refractive surgeries, inhibition of intraoperative miosis and relief of ocular itching due to seasonal allergic conjunctivitis. See table 2, page 2 of Therapeutic Class Review for complete listing of FDA-approved indications.
- Common adverse effects associated with the use of ophthalmic NSAIDs include: instillation reactions, corneal edema, and vision changes.
  - Continued use of topical NSAIDs may result in severe corneal adverse events, including: corneal thinning, erosion, ulceration or perforation, which may become sight damaging. Therefore, the use of ophthalmic NSAIDs beyond 14 days is not recommended.
  - Bromfenac contains sodium sulfate and is contraindicated in patients with sulfite hypersensitivity.
  - All agents in this class are Pregnancy Category C.
  - Due to the topical administration of the ophthalmic NSAIDs, systemic absorption is minimal; therefore, clinically significant drug interactions are not well defined.
- The ophthalmic NSAIDs have been shown to be safe and effective in inhibiting intraoperative miosis, reducing postoperative inflammation and pain associated with cataract surgery, relieving pain and photophobia following corneal refractive surgery and relieving seasonal allergic conjunctivitis symptoms in placebo-controlled trials. Although not FDA-approved, there is evidence to support the use of ophthalmic NSAIDs for
OPHTHALMIC AGENTS

preventing or treating cystoid macular edema and for reducing pain associated with various other refractive surgeries. The results of head-to-head trials comparing ophthalmic NSAIDs have not consistently demonstrated any one agent to be more efficacious than another for a given indication. With regard to safety, no one agent was consistently reported to be better tolerated than another across trials, although there is some evidence that the preservative-free products may be associated with less ocular irritation.

- Guidelines from the American Academy of Ophthalmology regarding post-operative management of cataracts state there is no established optimal post-operative regimen of topical antibiotics, corticosteroids, and NSAIDs. Therefore, they recommend that it should be the decision of the operating surgeon to use any or all of these products singly or in combination. Importantly, the guidelines point out that there is evidence that NSAIDs alone or in combination with steroids are more effective than steroids alone at preventing cystoid macular edema (CME), a serious sight-threatening complication of cataract surgery. The guidelines do not recommend one ophthalmic NSAID over another.

- In general, ophthalmic corticosteroids are widely considered first line therapy for the treatment of ophthalmic inflammatory conditions but are commonly associated with increased IOP, which may place some patient populations at risk, including glaucoma patients. Immunosuppressed patients and patients with concerns for wound healing should also avoid the use of corticosteroids. Ophthalmic NSAIDs offer the anti-inflammatory benefits without the risks associated with ophthalmic corticosteroids.

RECOMMENDATION

Ophthalmic NSAIDs are most commonly used for the treatment of inflammation and pain secondary to ophthalmic surgery. Ophthalmic corticosteroids are widely considered first line therapy for the treatment of ophthalmic inflammatory conditions. However, due to adverse effects, certain patient populations should avoid the use of corticosteroids. Ophthalmic NSAIDs offer the anti-inflammatory benefits without the risks associated with ophthalmic corticosteroids in these patient populations. Guidelines from the AAO regarding the post-operative management of cataracts recommend ophthalmic NSAIDs as an alternative to or in combination with ophthalmic corticosteroids for the prevention and treatment of cystoid macular edema associated with cataract surgery. The AAO guidelines do not distinguish between the various NSAIDs. Based on all of this information, it appears that the ophthalmic NSAIDs produce similar anti-inflammatory and pain relieving effects and can thus be considered therapeutic alternatives to one another. In order to maintain costs and ensure appropriate use, it is recommended that ophthalmic NSAIDs be reserved for patients for whom corticosteroid monotherapy is not appropriate.

COMMITTEE VOTE:

APPROVED      DISAPPROVED      APPROVED with MODIFICATION

RE-REVIEW: OPHTHALMIC NSAIDs

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Class Prior Authorization Criteria for Ophthalmic NSAIDs

Will be approved if ANY of the following are true:

- Recipient has a contraindication, intolerance or adverse reaction to an ophthalmic steroid (i.e. prednisolone). Acceptable reasons for not using an ophthalmic steroid (not inclusive):
  - Potential increase in intraocular pressure (IOP) with ophthalmic steroids that would place the patient at risk (i.e. glaucoma, pre/post-cataract surgery)
  - Concerns that the steroid would impair wound healing
  - Concerns that the steroid may cause/induce infection due to immunosuppression.
  - Use of the agent is for pain pre/post-ocular surgery
  - Concomitant use of an ophthalmic steroid and an ophthalmic NSAID is needed to control inflammation

- Approval of non-preferred agents additionally requires trial and failure, contraindication or intolerance of 2 preferred agents

COMMITTEE VOTE:

| APPROVED | DISAPPROVED | APPROVED with MODIFICATION |

References

BACKGROUND

- Short bowel syndrome (SBS) is a disorder related to poor absorption of nutrients that typically occurs in people who have had half or more of their small intestine removed. Individuals with short bowel syndrome cannot absorb enough water, vitamins, and other nutrients to sustain life.
- Teduglutide is an analog of glucagon-like peptide 2 (GLP-2), a naturally occurring hormone that regulates the growth, proliferation, and maintenance of cells lining the gastrointestinal tract. Teduglutide binds to the GLP-2 receptors located in the intestines resulting in increased fluid and nutrient absorption.
- Teduglutide is FDA-approved for the treatment of adult patients with SBS who are dependent on parenteral support.
- The most common adverse reactions (≥ 10%) across all studies were abdominal pain, injection site reactions, nausea, headaches, abdominal distension, upper respiratory tract infection, vomiting and fluid overload. Less common, but serious, adverse reactions included bowel obstruction, cholecystitis, pancreatitis, colorectal polyp, and lung cancer.
  - Teduglutide carries warning and precautions for use due to elevated risks of cancer and polyps in the intestine, intestinal obstructions, gallbladder disease, biliary tract disease, and pancreatic disease. Additionally, due to the potential serious risks of these conditions, teduglutide was approved with a Risk Evaluation and Mitigation Strategy (REMS) that includes required instructions and training for prescribers.
  - Teduglutide has the potential to increase the absorption of concomitant oral medications; therefore, caution should be used with narrow therapeutic index drugs or drugs that require titration. Clinical drug interaction studies were not performed with teduglutide; however, no inhibition or induction of the cytochrome P450 enzyme system has been observed based on in vitro studies.
- The efficacy and safety of teduglutide were evaluated in two randomized, double-blind, placebo-controlled, parallel-group, multi-center trials (Study 004 and 020). Both trials enrolled adult subjects with SBS who were dependent on parenteral nutrition for at least 12 months and required parenteral nutrition (PN) at least 3 times per week. Subjects were randomized to either teduglutide (0.10 mg/kg/day or 0.05 mg/kg/day) or placebo subcutaneously once daily for 24 weeks. The primary endpoint included the percentage of patients who had a reduction of at least 20% in PN volume at weeks 20 and 24.
  - In study 004, the difference between teduglutide 0.10 mg/kg/day and placebo for the primary endpoint was not statistically significant (p=0.161); however, percent responders in the teduglutide 0.05 mg/kg/day group was greater than placebo (45.7% vs 6.3%, p=0.007). Two patients in the teduglutide 0.05 mg/kg/day group were able to be totally weaned off parenteral support by week 24. Treatment with teduglutide resulted in a 2.5 L/week mean reduction in parenteral support requirements versus 0.9 L/week for placebo at week 24.
  - In study 020, a statistically significant difference in the percentage of patients who achieved a reduction of at least 20% in PN volume at weeks 20 and 24 was demonstrated with teduglutide 0.05 mg/kg/day compared to placebo, 62.8% versus 30.2%, respectively (p=0.002). At week 24, the mean reduction of weekly PN/IV volume was 4.4 L/week for teduglutide and 2.3 L/week for placebo (p<0.001).
- The current management strategy in SBS is a combination of specialized diets, anti-diarrheal, anti-secretory agents, and parenteral nutrition/IV fluids to meet the needs of SBS patients. Parenteral nutrition (PN) provides adequate protein, calories, other macronutrients, and micronutrients until the bowel has had time to adapt. The time required for optimal bowel adaptation is controversial. It is suggested that bowel adaptation may not be complete until a year or more after resection. For SBS patients on chronic PN/IV, the goals of intestinal rehabilitation include decreasing the need for PN/IV
and ideally, weaning patients completely off PN/IV therapy while maintaining clinical status. Approximately 50% to 70% of the short bowel patients who initially require total parenteral nutrition (TPN) can be weaned off successfully. Investigators have found that most SBS patients able to wean off TPN do so within 3 to 6 months of initiating therapy; and 95% of the SBS patients who are weaned off TPN, do so within two years. Conversely, 94% of the SBS patients who are on TPN for two years are on indefinitely. Prior to the approval of teduglutide, no targeted long-term treatment aimed at optimizing intestinal absorption of fluids and nutrients and decreasing intestinal fluid and nutrient loss was available. Somatropin [rDNA origin] is approved for the treatment of SBS; however, treatment beyond 4 weeks has not been adequately studied.

RECOMMENDATION

Teduglutide is FDA-approved for the treatment of adult patients with SBS who are dependent on parenteral support. Clinical trial data demonstrates that treatment with teduglutide provides increased absorption of fluids and nutrients and reduces patients’ dependency on parenteral support. However, further evidence is warranted regarding its long term safety. Current evidence indicates that most SBS patients are able to wean off TPN without pharmacologic assistance; however, teduglutide adds to the limited clinical treatment options available for patients with short bowel syndrome. Therefore, it is recommended teduglutide should be subject to prior authorization to ensure appropriate utilization.

COMMITTEE VOTE:

APPROVED    DISAPPROVED    APPROVED with MODIFICATION

NEW: GLP-2 ANALOGS

<table>
<thead>
<tr>
<th>PREFERRED</th>
<th>NON-PREFERRED</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/A</td>
<td>GATTEXľPA (teduglutide)</td>
</tr>
</tbody>
</table>

Prior Authorization Criteria for Gattexľ

Will be approved for patients that meet ALL of the following criteria:
- Diagnosis of short bowel syndrome, AND
- Dependent on parenteral nutrition for at least 12 months (initial approval only), AND
- Receiving parenteral nutrition at least 3 times weekly (initial approval only)

COMMITTEE VOTE:

APPROVED    DISAPPROVED    APPROVED with MODIFICATION

References
RESPIRATORY AGENTS

RE-REVIEW: STEROIDS, ORALLY INHALED

BACKGROUND

- Asthma is a chronic inflammatory disorder of the airways that contributes to airway hyperresponsiveness and airflow limitation. The inhaled corticosteroids (ICSs) include beclomethasone, budesonide, ciclesonide, fluticasone propionate, and mometasone. All of the ICSs are Food and Drug Administration (FDA) approved for the maintenance treatment of asthma as prophylactic therapy. Beclomethasone and fluticasone propionate are also indicated for use in asthma patients who require systemic corticosteroid therapy when the addition of an ICS could reduce or eliminate the need for systemic corticosteroids.
- The ICSs perform a wide range of inhibitory activities against multiple cell types (e.g., mast cells and eosinophils) and mediators (e.g., histamine and cytokines) involved in the asthmatic response. The ICSs exert their anti-inflammatory effects by binding to glucocorticoid receptors with a subsequent activation of genes involved in the anti-inflammatory processes as well as an inhibition of pro-inflammatory genes involved in the asthmatic response. Inflammation is also a component of chronic obstructive pulmonary disease (COPD) pathogenesis. However, no single-entity ICS has been FDA-approved for use in COPD.
- Some common and severe adverse reactions that may occur with these agents include (See MedMetrics Class Review, table 6, pg. 77):
  - **beclomethasone**: headache, nausea, pharyngitis, cataract, upper respiratory infection and glaucoma.
  - **budesonide**: nausea, myalgia, headache, epistaxis, respiratory tract infection, sinusitis, syncope, Cushing’s syndrome, cataract (rare), and glaucoma (rare).
  - **ciclesonide**: abdominal pain, indigestion, nausea, backache, musculoskeletal pain, myalgia, headache, dysmenorrhea, allergic rhinitis, oral candidiasis, epistaxis, pharyngitis, upper respiratory infection, extremity pain, adrenal insufficiency, cataract, and glaucoma.
  - **fluticasone**: oral and esophageal candidiasis, headache, bronchitis, cough, upper respiratory infection, sinusitis, throat irritation, and glaucoma.
  - **mometasone**: abdominal pain, indigestion, nausea, myalgia, headache, dysmenorrhea, allergic rhinitis, oral candidiasis, epistaxis, pharyngitis, and upper respiratory infection.

<table>
<thead>
<tr>
<th>Contraindication</th>
<th>Beclomethasone</th>
<th>Budesonide Powder</th>
<th>Budesonide Suspension</th>
<th>Ciclesonide</th>
<th>Fluticasone Propionate</th>
<th>Mometasone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute episodes of asthma where intensive measures are required</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Hypersensitivity to any components of the product</td>
<td>-</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Hypersensitivity to milk proteins</td>
<td>-</td>
<td>X</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>X</td>
</tr>
<tr>
<td>Primary treatment of status asthmaticus</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>-</td>
</tr>
</tbody>
</table>
**RESPIRATORY AGENTS**

- **Precautions** (See MedMetrics Class Review, table 8, page 81):

<table>
<thead>
<tr>
<th>Warning/Precaution</th>
<th>Beclomethasone</th>
<th>Budesonide Powder</th>
<th>Budesonide Suspension</th>
<th>Ciclesonide</th>
<th>Fluticasone Propionate</th>
<th>Mometasone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candida albicans; infections occur in the mouth and pharynx of some patients</td>
<td>X</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Eosinophilic conditions and Churg-Strauss Syndrome</td>
<td>-</td>
<td>x</td>
<td>x</td>
<td>-</td>
<td>x</td>
<td>-</td>
</tr>
<tr>
<td>Glaucoma, increased intraocular pressure, and cataracts</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Not indicated for relief of acute bronchospasm</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Paradoxical bronchospasm following administration</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Reduction in bone mineral density with long-term use</td>
<td>-</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Reduction in growth velocity in pediatric patients may occur</td>
<td>-</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Systemic absorption at recommended doses may occur</td>
<td>X</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

- **Significant Drug-Drug Interactions:**

  The use of budesonide, fluticasone propionate, and mometasone with strong cytochrome (CYP) 3A4 inhibitors such as the azole antifungals (ketoconazole, fluconazole) may inhibit the metabolism of corticosteroids resulting in enhanced corticosteroid effects and toxicity. Doses of inhaled corticosteroids may need to be adjusted.

  - A multi-center, double-blind trial performed by Nathan et al, evaluated beclomethasone 168 µg BID vs. mometasone 100 µg BID vs. mometasone 200 µg BID vs. placebo. This trial observed 227 patients with moderate persistent asthma over 12 weeks. The primary endpoint assessed was changes in FEV1, which showed:
    - The FEV1 was significantly improved in all three active treatment groups compared to the placebo group (p<0.01).
    - There was no statistically significant difference in FEV1 between the mometasone 200 µg and beclomethasone groups (p=0.07) or the mometasone 200 µg and mometasone 100 µg groups (p=0.08).
  - Von Berg et al performed a multi-center, double blind trial as well that evaluated ciclesonide 160 µg QPM vs. budesonide 400 µg QPM in 621 patients over 12 week duration. The change in FEV1 baseline showed:
    - Significant increases from baseline in FEV1 occurred in both the ciclesonide (0.232 L; p<0.0001) and budesonide (0.250 L; p<0.0001) treatment groups. Ciclesonide proved to be non-inferior to budesonide with no significant differences between treatment groups (p=0.8158).
    - Both treatment groups experienced a statistically significant increase in morning PEF(peak expiratory flow) compared to baseline (ciclesonide, 22.5 L/minute; p=0.0001, budesonide, 26.3 L/minute; p<0.0001).There were no significant differences between treatment groups (p=0.8531).
    - The percentage of days without asthma symptoms and without need for rescue medication was 73% in the ciclesonide treatment group, and 70% in the budesonide treatment group (p value not reported).
  - The 2012 GINA guidelines for Asthma state ICSs are currently the most effective anti-inflammatory medications for the treatment of persistent asthma for patients of all ages.
RESPIRATORY AGENTS

- ICSs differ in potency and bioavailability, but few studies have been able to confirm the clinical relevance of these differences.
- When a medium dose of the ICS fails to achieve control, the addition of a LABA is the preferred treatment.

- The 2013 Global Initiative for Chronic Lung Disease (GOLD) guidelines for COPD recommend inhaled ICSs in patients with an FEV1 <60% of the predicted value.
- The Joint Task Force on Practice Parameters for Allergy and Immunology 2010 guidelines for Exercise-Induced Bronchoconstriction state:
  - Inhaled beta-agonists are the most effective group of agents for short-term protection against exercise-induced bronchoconstriction and for accelerating recovery of airway obstruction after exercise.
  - ICS use may decrease the frequency and severity of exercise-induced bronchoconstriction but does not eliminate the need for acute therapy.

RECOMMENDATION

All of the inhaled corticosteroids (ICSs) are FDA approved for the maintenance treatment of asthma as prophylactic therapy. Beclomethasone and fluticasone propionate are also indicated for use in asthma patients who require systemic corticosteroid therapy when the addition of an ICS could reduce or eliminate the need for systemic corticosteroids. The 2012 GINA guidelines for Asthma state ICSs are currently the most effective anti-inflammatory medications for the treatment of persistent asthma for patients of all ages. Although ICSs may differ in potency and bioavailability, trial data does not indicate the clinical relevance of these differences and clinical guidelines do not give preference to one ICS over another. ICSs are also recommended by the Global Initiative for Chronic Lung Disease (GOLD) guidelines to treat COPD (chronic obstructive pulmonary disease) patients with an FEV1 <60% of the predicted value. Therefore, it is recommended that at least 2 ICS agents are available for use, with budesonide respules available for the pediatric population who are unable to use proper inhaler technique.

COMMITTEE VOTE:

<table>
<thead>
<tr>
<th>APPROVED</th>
<th>DISAPPROVED</th>
<th>APPROVED with MODIFICATION</th>
</tr>
</thead>
</table>

RE-REVIEW: STEROIDS, ORALLY INHALED

<table>
<thead>
<tr>
<th>PREFERRED</th>
<th>NON-PREFERRED</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASMANEX® QL (mometasone)</td>
<td>ALVESCO® QL (ciclesonide)</td>
</tr>
<tr>
<td>FLOVENT HFA® QL (fluticasone propionate aer.)</td>
<td>budesonide respules® PA, QL (Compares to Pulmicort® respules)</td>
</tr>
<tr>
<td>FLOVENT DISKUS® QL (fluticasone propionate pow.)</td>
<td>PULMICORT FLEXHALER® QL (budesonide pow.)</td>
</tr>
<tr>
<td>QVAR® QL (beclomethasone)</td>
<td>Pulmicort Respules® PA, QL (budesonide susp.)</td>
</tr>
</tbody>
</table>

Prior Authorization Criteria for Pulmicort Respules®/budesonide respules:

- PA not required for enrollees ages 6 and under.

COMMITTEE VOTE:

<table>
<thead>
<tr>
<th>APPROVED</th>
<th>DISAPPROVED</th>
<th>APPROVED with MODIFICATION</th>
</tr>
</thead>
</table>
RESPIRATORY AGENTS

<table>
<thead>
<tr>
<th>Quantity Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Asmanex®</strong></td>
</tr>
<tr>
<td><strong>Alvesco®</strong></td>
</tr>
<tr>
<td><strong>Flovent HFA®</strong></td>
</tr>
</tbody>
</table>
| **Flovent Diskus®** | 50mcg: 2 blisters/day  
100mcg: 4 blisters/day  
250mcg: 8 blisters/day |
| **Pulmicort Flexhaler®** | 2 per 30 days |
| **Pulmicort Respules®/budesonide respules** | 0.25mg/2ml & 0.5mg/2ml: 2 vials/day  
1mg/2ml: 1 vial/day |
| **QVAR®**       | 2 per 30 days |

COMMITTEE VOTE:
- APPROVED
- DISAPPROVED
- APPROVED with MODIFICATION

References

RE-REVIEW: LEUKOTRIENE RECEPTOR ANTAGONISTS

BACKGROUND
- The leukotriene modifiers are a class of medications used for long-term symptom control in patients with asthma as well as allergic rhinitis. The leukotriene modifiers may be divided into two categories: leukotriene receptor antagonists and 5-lipoxygenase inhibitors. The leukotriene receptor antagonists, montelukast and zafirlukast, exert their mechanism of action by blocking the leukotriene receptor, thus inhibiting the action of cysteinyl leukotrienes. Blocking the action of cysteinyl leukotrienes has been shown to reduce or prevent airway obstruction and decrease the activation of inflammatory cells. As these agents play an important role in the pathophysiology of asthma and contribute to bronchoconstriction, increased airway responsiveness, mucous secretion and recruitment of inflammatory cells. The 5-lipoxygenase inhibitor, zileuton inhibits the 5-lipoxygenase enzyme, thereby preventing the formation of leukotrienes.
The leukotriene modifiers are Food and Drug Administration (FDA) approved for prophylaxis and chronic treatment of asthma. Montelukast carries additional FDA approvals for the relief of symptoms of seasonal and perennial allergic rhinitis and for the prevention of exercise-induced bronchoconstriction.

The most frequently reported adverse events associated with these agents include headache, nausea, upper respiratory infections, dyspepsia, abdominal pain, influenza and sinusitis.

**Contraindications:**

<table>
<thead>
<tr>
<th>Contraindication</th>
<th>Montelukast</th>
<th>Zafirlukast</th>
<th>Zileuton</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active liver disease or transaminase elevation greater than or equal to three times the upper limit of normal</td>
<td>-</td>
<td>-</td>
<td>X</td>
</tr>
<tr>
<td>Hepatic impairment, including cirrhosis</td>
<td>-</td>
<td>X</td>
<td>-</td>
</tr>
</tbody>
</table>

**Warnings/Precautions** (See MedMetrics Class Review, table 8, pg. 33):

<table>
<thead>
<tr>
<th>Warning/Precaution</th>
<th>Montelukast</th>
<th>Zafirlukast</th>
<th>Zileuton</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute asthma; not indicated for reversal of bronchospasm in acute asthma attacks; treatment may be continued during acute exacerbations</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Concomitant warfarin use; prothrombin time may increase; monitor prothrombin time and adjust anticoagulant dose according</td>
<td>-</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Eosinophilic conditions; monitor for signs and symptoms of systemic eosinophilia</td>
<td>X</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Neuropsychiatric events; evaluate risks the risks and benefits and continuing treatment if such events occur</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Phenylketonuria; the 4- and 5-mg chewable tablets contain phenylalanine</td>
<td>X</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Significant Drug-Drug Interactions** (See MedMetrics Class Review, table 9, pg. 33):

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Interacting Medication or Disease</th>
<th>Potential Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zafirlukast, Zileuton</td>
<td>Pimozide</td>
<td>Zafirlukast and zileuton may inhibit the metabolism of pimozide (possibly via cytochrome P450 3A4 enzyme), potentially causing fatal cardiac arrhythmias. Concurrent use is considered a contraindication.</td>
</tr>
<tr>
<td>Zafirlukast</td>
<td>Erythromycin</td>
<td>Erythromycin may decrease the bioavailability of zafirlukast and thereby decrease the mean plasma levels of zafirlukast.</td>
</tr>
<tr>
<td>Zafirlukast</td>
<td>Theophylline</td>
<td>Concurrent use may result in decreased mean plasma levels of zafirlukast. Zileuton may decrease the metabolism of theophylline and thereby increase theophylline levels. When starting zileuton, it may be necessary to decrease the dose of theophylline by 50%.</td>
</tr>
<tr>
<td>Zileuton</td>
<td>Propranolol</td>
<td>Zileuton may decrease the clearance of propranolol and result in an increase in β-blockade and decrease in heart rate. Close monitoring of blood pressure and heart rate in patients on both medications is recommended.</td>
</tr>
</tbody>
</table>
There are numerous placebo-controlled trials that evaluate the efficacy of the leukotriene modifiers for asthma and allergic rhinitis. There is also clinical data comparing the leukotriene modifiers to inhaled corticosteroids and long-acting beta-agonists. However, currently there is a lack of head-to-head trials that specifically compare the leukotriene modifiers.

The Global Initiative for Asthma (GINA) guidelines recommend that leukotriene modifiers are used as alternative agents to low-dose ICSs. The leukotriene modifiers are considered an appropriate treatment in patients who are unable or experience intolerable adverse events on ICS therapy.

The Joint Task Force on Practice Parameters for Allergy and Immunology recommends intranasal corticosteroids as the most effective medication class for controlling symptoms of allergic rhinitis and all are considered equally efficacious. It is also suggests intranasal antihistamines should be considered as a first-line treatment option for both allergic and non-allergic rhinitis. Additionally, the guidelines state the leukotriene receptor antagonists alone or in combination with antihistamines are useful in the treatment of allergic rhinitis.

The Institute for Clinical Systems Improvement state that leukotriene modifiers may be as effective as second-generation antihistamines for the treatment of allergic rhinitis and less effective than intranasal corticosteroids. Additionally, these agents may be considered as third-line agents in patients whose symptoms are not relieved by an intranasal corticosteroid and an oral antihistamine.

The Joint Task Force on Practice Parameters for Allergy and Immunology recommends inhaled beta-agonists as the most effective agents for the prophylaxis and relief of exercise-induced bronchoconstriction; however, daily use of beta-agonists may lead to tolerance. However, leukotriene receptor antagonists may be used daily or intermittently for the prevention of exercise-induced bronchoconstriction without development of tolerance; but, these agents do not reverse airway obstruction when it occurs.

**RECOMMENDATION**

The leukotriene modifiers are FDA approved for prophylaxis and chronic treatment of asthma. Montelukast is also FDA approved for the relief of symptoms of seasonal and perennial allergic rhinitis and for the prevention of exercise-induced bronchoconstriction. The GINA guidelines list leukotriene modifiers as a treatment alternative to low-dose inhaled corticosteroids (ICSs) in patients with mild persistent asthma. These agents are also considered as adjunctive therapy to reduce the dose of the ICS required by patients with moderate to severe asthma, and in patients not achieving adequate symptom control with an ICS as monotherapy or in combination with a long-acting β₂-agonist (LABA). The allergic rhinitis guidelines consider the leukotriene modifiers either alone or in combination with antihistamines useful. The guidelines for exercise induced bronchoconstriction state leukotriene receptor antagonists may be used daily or intermittently for prevention of exercise-induced bronchoconstriction without the development of beta-agonist tolerance. However these agents do not reverse airway obstruction. Currently, there are no head-to-head trials directly comparing the efficacy and safety of the leukotriene modifiers to each other. However, clinical data shows zafirlukast and zileuton have a higher risk of hepatotoxicity than montelukast. Therefore based on the safety risk profiles and clinical guidelines which view these agents as an alternative treatment option; it is recommended these agents are available for use subject to prior authorization.

**COMMITTEE VOTE:**

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<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>APPROVED</td>
<td>DISAPPROVED</td>
<td>APPROVED with MODIFICATION</td>
</tr>
</tbody>
</table>
RE-REVIEW: LEUKOTRIENE RECEPTOR ANTAGONISTS

<table>
<thead>
<tr>
<th>PREFERRED</th>
<th>NON-PREFERRED</th>
</tr>
</thead>
<tbody>
<tr>
<td>montelukast tabs &amp; chewables PA, QL (Compa\ntes to Singulair®)</td>
<td>ACCOLATE® QL (zafirlukast) montelukast granules PA, QL (compares to Singulair®)</td>
</tr>
<tr>
<td></td>
<td>SINGULAIR® tabs &amp; chewables PA, QL (montelukast) SINGULAIR® granules PA, QL (montelukast) zafirlukast QL (compares to Accolate®) ZYFLO® QL (zileuton) ZYFLO CR® QL (zileuton ER)</td>
</tr>
</tbody>
</table>

Prior Authorization Criteria for montelukast/Singulair® tabs & chewables:

- Unrestricted for recipients 17 years and younger.
- Recipients > 17 years old:
  - Unrestricted for asthma documented with concomitant use of at least one other asthma medications
  - For treatment of seasonal allergic rhinitis, patient must have failed trial of a non-sedating antihistamine.

COMMITTEE VOTE:
APPROVED DISAPPROVED APPROVED with MODIFICATION

Prior Authorization Criteria for montelukast granules:

- Recipients less than 3 years of age: no prior authorization required.
- Recipients 3-17 years and younger:
  - Will be approved ONLY for patients who have clinically valid reason not to use chewable tablets
- Recipients > 17 years old:
  - Diagnosis of asthma documented with concomitant use of at least one other asthma medications
  - For treatment of seasonal allergic rhinitis, patient must have failed trial of a non-sedating antihistamine.
  - Will be approved for patient meeting the above criteria ONLY for patients who have clinically valid reason not to use chewable tablets

COMMITTEE VOTE:
APPROVED DISAPPROVED APPROVED with MODIFICATION

Prior Authorization Criteria for Singulair® granules:

- Recipients 17 years and younger:
  - Will be approved ONLY for patients who have clinically valid reason not to use chewable tablets.
- Recipients > 17 years old:
  - Diagnosis of asthma documented with concomitant use of at least one other asthma medication.
  - For treatment of seasonal allergic rhinitis, patient must have failed trial of a non-sedating antihistamine.
  - Will be approved for patient meeting the above criteria ONLY for patients who have clinically valid reason not to use chewable tablets

COMMITTEE VOTE:
APPROVED DISAPPROVED APPROVED with MODIFICATION
**RESPIRATORY AGENTS**

<table>
<thead>
<tr>
<th>Quantity Limits</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>montelukast/ Singulair® tabs &amp; chewables</td>
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</tr>
<tr>
<td>montelukast/ Singulair® granules</td>
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<tr>
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<tr>
<td>Zyflo®</td>
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<tr>
<td>Zyflo CR®</td>
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**COMMITTEE VOTE:**

APPROVED | DISAPPROVED | APPROVED with MODIFICATION

**References**


**RE-REVIEW: BETA-AGONISTS: COMBO PRODUCTS**

**BACKGROUND**

- Inhaled bronchodilators and corticosteroids are the mainstay of chronic obstructive pulmonary disease (COPD) and Asthma treatment. The use of combination products that contain agents with different mechanisms of action allows targeting of more than one pathophysiologic pathway. There are 3 products available which combine an inhaled corticosteroid (ICS) and a long acting beta-2 agonist (LABA): fluticasone propionate/salmeterol (Advair®), budesonide/formoterol (Symbicort®), and mometasone/formoterol (Dulera®).
- Corticosteroids have a large range of inhibitory activities against multiple cell types (e.g., mast cells, eosinophils) and mediators (e.g., histamine, cytokines) which are involved in the asthmatic response. The ICSs exert their anti-inflammatory effect by binding to the glucocorticoid receptors with a subsequent activation of genes involved in anti-inflammatory processes, as well as via the inhibition of pro-inflammatory genes involved in the asthmatic response. Inflammation also plays a role in COPD pathogenesis. The LABAs are also useful for long-term control of persistent asthma and COPD, and have been proven to help control nocturnal symptoms. These agents have selective action on beta-2 receptors which stimulate adenyl cyclase, resulting in an increased intracellular cyclic adenosine monophosphate level, which subsequently triggers bronchial smooth
muscles relaxation. The LABA medications also inhibit the release of mediators that are involved in immediate hypersensitivity.

- All of the beta-agonist combination products are Food and Drug Administration (FDA) approved for the treatment of asthma, with budesonide/formoterol and fluticasone propionate/salmeterol being FDA-approved for the treatment of COPD.
- The most common adverse events associated with these agents include cough, headache, nausea, oral candidiasis, nasopharyngitis, pharyngitis and upper respiratory infection.
  - All LABA-containing medications contain a Black Box Warning regarding an increased risk of asthma-related deaths. In February 2010, results from a meta-analysis demonstrated that LABAs were associated with an increased risk of asthma exacerbations and hospitalizations in pediatric and adult patients, as well as death in some patients.
  - Caution should be used in patients with hepatic impairment who take fluticasone/salmeterol due to possible accumulation of both active ingredients. The combination ICS/LABA products should be used with caution in patients with convulsive disorders thyrotoxicosis and in those who are unusually responsive to sympathomimetic amines. Physicians should monitor for the development of pneumonia in patients with COPD who are receiving a combination ICS/LABA product as the clinical features of pneumonia and exacerbations frequently overlap. The steroid components may cause an inadequate adrenal response, bone mineral density loss or a small growth velocity reduction in children and adolescents. Lastly, the beta agonist component may cause cardiovascular disorders such as palpitations or tachycardia due to stimulation of beta receptors in the heart.
  - The combination ICS/LABA products are contraindicated for the primary treatment of status asthmaticus or in any other acute asthma or chronic obstructive pulmonary disease (COPD) episodes where intensive measures might be required. Fluticasone propionate/salmeterol is further contraindicated in patients with severe milk protein hypersensitivities, as the salmeterol component contains milk proteins.
- An open label, non-inferiority study by Bernstein et al, evaluated 722 patients 12 years of age and older with persistent asthma received mometasone/formoterol or fluticasone propionate/salmeterol for 12 weeks following a two week run in period with mometasone. The primary endpoint was the change in forced expiratory volume in 1 second (FEV1) area under the curve from 0 to 12 hours (AUC 0 to 12h) after 12 weeks. At the end of treatment, the change in FEV1 AUC 0 to 12h associated with mometasone/formoterol was non inferior to improvements observed with fluticasone propionate/salmeterol (3.43 vs 3.24 L/h, respectively; 95% Confidence Interval, -0.40 to 0.76). Mometasone/formoterol was associated with a significantly quicker onset of action (P<0.001) and a greater least squares mean change in FEV1 (200 vs 90 mL; P≤0.001) compared to fluticasone propionate/salmeterol. Additionally, there were no differences between the two treatment groups in regard to 24-hour asthma symptom scores, the number of symptom-free days and nights or asthma deterioration over 12 weeks (P values not reported).
- In another randomized, double-blind, double-dummy study, FitzGerald et al, compared the efficacy of fluticasone/salmeterol (250/50 [1 inhalation] mcg BID) to budesonide/formoterol (200/6 mcg [2 inhalations] BID) in 706 adults, with a documented clinical history of asthma and an FEV1 between 60 to 90% of projected normal. The percentage of symptom-free days was higher with fluticasone/salmeterol compared to budesonide/formoterol (58.8 vs 52.1%; P=0.034). The percentage of symptom-free days was significantly higher with fluticasone/salmeterol compared to budesonide/formoterol during weeks five through 52 (73.8 vs 64.9%; P=0.030). The median value for the percentage of days free of rescue medication over weeks five through 52 was 94.5% in the fluticasone/salmeterol group compared to 90.7% in the budesonide/formoterol group (P=0.008). Over the 52-week treatment period the mean morning PEF was significantly
higher in the fluticasone/salmeterol group compared to the budesonide/formoterol group (400.1 vs 390.6 L/minute; \( P=0.006 \)).

- The current guidelines for the treatment of Asthma support the use of combination ICS/LABA products for long term control and prevention of symptoms in patients who do not achieve sufficient symptom control with an ICS (low to medium dose) as monotherapy, as LABA medications are the preferred add on therapy in these patients. According to the Global Initiative for Asthma (GINA) guidelines, clinical trials have demonstrated that delivering a LABA and an ICS in a combination inhaler is as effective as giving the two individual agents concomitantly. They also state that fixed combination inhalers are more convenient, may increase compliance and ensure that the LABA is always accompanied by an ICS.

- In the treatment of COPD, consensus guidelines from both the Global Initiative for Chronic Obstructive Lung Disease and the National Institute for Health and Clinical Excellence recommend the use of combination ICS/LABA products as second-line, when a patient remains symptomatic and has repeated exacerbations while on an initial short- and long-acting bronchodilator. The GOLD guidelines also states that an ICS combined with a LABA is more effective than either component alone in reducing exacerbations or improving lung function and health status, but that this combination increases the risk of pneumonia in COPD patients. Lastly, currently available asthma and COPD treatment guidelines do not specifically recommend the use of one combination ICS/LABA product over another.

**RECOMMENDATION**

Inhaled bronchodilators and corticosteroids are the mainstay of chronic obstructive pulmonary disease (COPD) and Asthma treatment. The \( \beta_2 \)-agonist combination agents, fluticasone propionate/salmeterol, budesonide/formoterol, and mometasone/formoterol are all FDA approved for the treatment of asthma, with only budesonide/formoterol and fluticasone propionate/salmeterol being FDA-approved for the treatment of COPD. Consensus guidelines from both the Global Initiative for Chronic Obstructive Lung Disease and the National Institute for Health and Clinical Excellence recommend the use of combination ICS/LABA products as second-line, when a patient remains symptomatic and has repeated exacerbations while on an initial short- and long-acting bronchodilator. The current guidelines for the treatment of Asthma support the use of combination ICS/LABA products for long term control and prevention of symptoms in patients who do not achieve sufficient symptom control with an ICS (low to medium dose) as monotherapy, as LABA medications are the preferred add on therapy in these patients. Based on current guidelines that place \( \beta_2 \)-agonist combination agents as second-line therapy, it is recommended that the combination LABA/ICS agents be reserved for asthma patients who require frequent use of an inhaled short-acting bronchodilator while maintained on an optimal dose of an inhaled steroid, and for COPD patients who have symptoms despite optimal doses of a LABA.

**COMMITTEE VOTE:**

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<th>APPROVED</th>
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**RE-REVIEW: BETA-AGONISTS: COMBO PRODUCTS**

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<tr>
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<tbody>
<tr>
<td>ADVAIR DISKUS® PA, QL (fluticasone/salmeterol)</td>
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<td>ADVAIR HFA® PA, QL (fluticasone/salmeterol aer)</td>
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<tr>
<td>DULERA® PA, QL (mometasone/formoterol)</td>
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</tr>
<tr>
<td>SYMBICORT® PA, QL (budesonide/formoterol)</td>
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Prior Authorization Criteria for Advair Diskus®, Advair HFA®, Dulera®, & Symbicort®

Will be approved if ONE of the following is met:

- For the treatment of asthma or the treatment of other reversible airway disease(s) where optimal doses of inhaled steroids are being used and breakthrough symptoms require frequent use of inhaled short-acting bronchodilators.
- For the treatment of COPD where optimal doses of a long-acting beta agonist are being used and symptoms are still uncontrolled.

COMMITTEE VOTE:

APPROVED  DISAPPROVED  APPROVED with MODIFICATION

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<tr>
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<td>Advair HFA®</td>
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<td>Dulera®</td>
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<td>Symbicort®</td>
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COMMITTEE VOTE:

APPROVED  DISAPPROVED  APPROVED with MODIFICATION

References

RESPIRATORY AGENTS

RE-REVIEW: INHALED ANTICHOLINERGICS

BACKGROUND

- Chronic obstructive pulmonary disease (COPD) is a medical condition characterized by progressive airflow restrictions that are not fully reversible. Symptoms associated with COPD include dyspnea, cough, sputum production, wheezing, and chest tightness.
- The inhaled anticholinergics work by inhibiting acetylcholine at parasympathetic sites in bronchial smooth muscle thus causing bronchodilation.
- Aclidinium, ipratropium and tiotropium are Food and Drug Administration (FDA) approved for the maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema. Tiotropium is the only inhaled anticholinergic that is FDA-approved for reducing exacerbations associated with COPD. The combination agent, ipratropium/albuterol is indicated for treatment of bronchospasms associated with COPD in patients who require more than one bronchodilator. Ipratropium/albuterol is currently available as an aerosol metered dose inhaler until July 2013 and as a propellant-free inhaler that uses a slow moving mist to deliver the same amount of the two agents. It should be noted that the two formulations differ in their dosing and administration schedules.
- Common and Severe Adverse Reactions (See MedMetrics Class Review, Table 6, pg. 40):
  - **aclidinium**- headache, cough, and nasopharyngitis.
    - **serious**: first degree atrioventricular block (less than 1%), and heart failure (less than 1%).
  - **ipratropium**- abnormal bitter taste in mouth, xerostomia, and sinusitis.
    - **serious**: bronchospasm
  - **tiotropium**- constipation, xerostomia, pharyngitis, sinusitis, and upper respiratory infection.
    - **serious**: bowel obstruction, immediate hypersensitivity reaction, and cerebrovascular accident
  - **ipratropium/albuterol**- abnormal bitter taste in mouth, xerostomia, bronchitis, and sinusitis
    - **serious**: bronchospasm

<table>
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<th>Contraindication</th>
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<tr>
<td>Ipratropium</td>
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<td>Tiotropium</td>
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<th>Warning/Precaution</th>
<th>Single Entity Agents</th>
<th>Combination Products</th>
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<tr>
<td>Hypersensitivity reactions may occur following administration as demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm and anaphylaxis</td>
<td>X</td>
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</table>
Warning/Precaution
Narrow-angle glaucoma; use anticholinergics with caution in this patient population as clinical worsening of the condition has been reported

<table>
<thead>
<tr>
<th>Single Entity Agents</th>
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<tr>
<td>Aclidinium</td>
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<tr>
<td>Ipratropium</td>
<td>Tiotropium</td>
</tr>
<tr>
<td></td>
<td>Ipratropium/Albuterol</td>
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</table>

- In a 12-week study by Kerwin et al, patients randomized to receive aclidinium 200 or 400 µg twice daily experienced a statistically significant increase from baseline in trough FEV1 compared to patients in the placebo group (86 and 124 mL, respectively; p<0.0001 for both).
- A few head-to-head trials have noted significant differences as it relates to improvements in lung function favoring tiotropium over ipratropium. However, there is inconsistent data regarding a clinical advantage of tiotropium over other long-acting bronchodilators. Although in one trial, tiotropium significantly increased the time to first exacerbation by 42 days compared to salmeterol (187 vs 145 days; p<0.001). In a meta-analysis, tiotropium significantly reduced the odds of a COPD exacerbation compared to placebo (p=0.004) and ipratropium (p=0.020) but not compared to salmeterol (p=0.25).
- The 2013 Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines state inhaled bronchodilators are preferred for the management of COPD. The principle bronchodilators include β2-agonists, anticholinergics and theophylline used as monotherapy or in combination therapy. The guidelines state that regular use of long-acting β2-agonists or short- or long-acting anticholinergics improve health status and long-acting anticholinergics reduce the rate of COPD exacerbations and improve the effectiveness of pulmonary rehabilitation.
- The GOLD guidelines emphasize that the use of long-acting bronchodilators is more effective and convenient than the use of short-acting bronchodilators. However, according to the 2010 National Institute for Clinical Excellence (NICE), short-acting bronchodilators should be the initial empiric treatment for the relief of breathlessness and exercise limitation while long-acting bronchodilators should be used in patients who remain symptomatic with use of short-acting agents.

RECOMMENDATION
Aclidinium, ipratropium and tiotropium are Food and Drug Administration (FDA) approved for the maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema. The combination agent, ipratropium/albuterol is indicated for treatment of bronchospasms associated with COPD in patients who require more than one bronchodilator. The guidelines state that regular use of long-acting β2-agonists or short- or long-acting anticholinergics improve health status and long-acting anticholinergics reduce the rate of COPD exacerbations and improve the effectiveness of pulmonary rehabilitation. Treatment with aclidinium has demonstrated statistically significant improvements in pulmonary function in patients with COPD compared to placebo. However, there are currently no head-to-head studies with other anticholinergics available. Tiotropium is the only inhaled anticholinergic that is FDA-approved for reducing exacerbations associated with COPD. Therefore it is recommended that at least 2 inhaled anticholinergics are available for use, which should include tiotropium.

COMMITTEE VOTE:
APPROVED   DISAPPROVED   APPROVED with MODIFICATION
REVIEW: INHALED ANTICHOLINERGICS

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<tr>
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Quantity Limits

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COMMITTEE VOTE:

APPROVED  DISAPPROVED  APPROVED with MODIFICATION

References

NEW: ANTI-RHEUMATIC: KINASE INHIBITORS

BACKGROUND

- Rheumatoid arthritis is a chronic systemic autoimmune disease that affects roughly 1.3 million Americans. Tofacitinib (Xeljanz®) is currently the only Food and Drug Administration (FDA)-approved Janus kinase (JAK) inhibitor on the market.
- Tofacitinib is a selective inhibitor of JAK1 and JAK3 which modulate a signaling pathway that influences the cellular processes of hematopoiesis and immune cell function. Inhibition of JAK prevents the phosphorylation and activation of signal transducers and activators of transcription, which modulate intracellular activities, including gene expression. Through its broad effect on multiple cytokine pathways, tofacitinib may reduce tissue inflammation and joint damages in rheumatoid arthritis.
- Tofacitinib is FDA-approved for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate.
- The most common adverse reactions associated with the use of tofacitinib occurring at a frequency ≥ 2% include: upper respiratory tract infections, headache, diarrhea and inflammation of the nasal passage and the upper part of the pharynx.
  - Tofacitinib carries a black box warning regarding the increased risk for developing serious infections that may lead to hospitalization or death. Tuberculosis, bacterial, invasive fungal, viral, and other opportunistic infections have occurred in patients receiving tofacitinib. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. Additionally, tofacitinib carries a black box warning regarding lymphoma and other malignancies that have been observed in patients treated with tofacitinib. Epstein Barr Virus-associated post-transplant lymphoproliferative disorder has been observed at an increased rate in renal transplant patients treated with concomitant immunosuppressive medications.
  - No contraindications to tofacitinib have been reported.
  - Warnings and precautions associated with tofacitinib include gastrointestinal perforation and laboratory abnormalities (low lymphocytes, neutrophils, hemoglobin, and an increase in liver enzymes and lipids). Live vaccines should not be administered while receiving treatment with tofacitanib.
  - Tofacitanib is Pregnancy Category C.
  - Drug interactions include an increased exposure to tofacitanib when administered with moderate and potent inhibitors of cytochrome P450 (CYP) 3A4 and potent inhibitors of CYP2C19. Dosage should be reduced to 5 mg once daily when administered with medications that inhibit these enzymes. Tofacitanib exposure is decreased when administered with drugs that induce CYP3A4 which may result in loss or reduced clinical response.
- The FDA approval of tofacitinib was based on the results of seven clinical trials in adult patients with moderately to severely active rheumatoid arthritis. In all of the trials, treatment with tofacitinib resulted in improved clinical response and physical functioning compared to treatment with placebo. While both 5 and 10 mg twice-daily dosing regimens were investigated, the FDA has only approved the 5 mg twice-daily dosing regimen. In its press release, the manufacturer noted that further data are required to assess the benefit-risk profile of the 10 mg twice-daily dose regimen, which the manufacturer plans to generate and provide to the FDA.
- The 2012 American College of Rheumatology (ACR) guidelines recommend traditional disease-modifying antirheumatic drugs (DMARDs) as first-line treatment in rheumatoid arthritis patients. In patients with inadequate response to DMARDs, adding or switching to another traditional or biologic DMARD is appropriate. The guideline was published prior to the FDA-approval of tofacitinib and does not address its place in therapy.
Tofacitinib is the first FDA-approved oral JAK inhibitor, which is indicated for the treatment of patients with moderately to severely active RA who have had an inadequate response or intolerance to methotrexate. In clinical trials involving adult patients with moderately to severely active rheumatoid arthritis, treatment with tofacitinib resulted in improved clinical response and physical functioning compared to treatment with placebo. Tofacitinib carries a boxed warning highlighting the risks of serious infections and malignancy. Additionally, the agent was approved with a Risk Evaluation and Mitigation Strategy program to inform healthcare providers and patients about the serious risks associated with treatment. The ACR guidelines recommend traditional DMARDs as first-line treatment in rheumatoid arthritis patients. In patients with inadequate response to DMARDs, adding or switching to another traditional or biologic DMARD is appropriate. Therefore, due to the fact that tofacitinib is not considered first line therapy, as well as the risk of significant adverse events, it is recommended that tofacitinib should be subject to prior authorization.

COMMITTEE VOTE:
APPROVED  DISAPPROVED  APPROVED with MODIFICATION

NEW: ANTI-RHEUMATIC: KINASE INHIBITORS

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<tr>
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</table>

Prior Authorization Criteria for XelJanz®
XelJanz will be approved, if ALL of the following have been met:
- Diagnosis of rheumatoid arthritis
- Patient must have tried and failed or been intolerant to at least methotrexate (unless there is a documented absolute contraindication such as alcohol abuse, cirrhosis, chronic liver disease) AND one preferred immunomodulator.
- Patient is not currently taking biologic agents (i.e. adalimumab, anakinra, etanercept, rituximab, tocilizumab, infliximab and abatacept), OR potent immunosuppressants (i.e. azathioprine, or cyclosporine)

COMMITTEE VOTE:
APPROVED  DISAPPROVED  APPROVED with MODIFICATION

Quantity Limits
XelJanz®  2/day

COMMITTEE VOTE:
APPROVED  DISAPPROVED  APPROVED with MODIFICATION

References
Prior Authorization Criteria for Eliquis®

Eliquis will be approved for recipients meeting the following criteria:

- Diagnosis of non-valvular atrial fibrillation, AND
  - Failure of warfarin therapy due to inability to maintain therapeutic INR, OR
  - Recipient does not have access to adequate monitoring services for warfarin therapy, OR
  - Non-bleeding related contraindication to warfarin therapy

Committee Vote:

APPROVED  DISAPPROVED  APPROVED with MODIFICATION

Quantity Limits

Eliquis®  2/day

Committee Vote:

APPROVED  DISAPPROVED  APPROVED with MODIFICATION

Prior Authorization Criteria for Oseni®

Will be approved for recipients who meet the following criteria:

- Diagnosis of type 2 diabetes AND
  - Hemoglobin A1c ≥6.5, AND
  - Trial and failure of metformin AND either a GLP-1, DPP-4, TZD, SU, or glinide agent (unless, recipient has an adverse reaction, intolerance or contraindication to metformin)

Committee Vote:

APPROVED  DISAPPROVED  APPROVED with MODIFICATION

Quantity Limits

Kazano®  2/day
Nesina®  1/day
Oseni®  1/day

Committee Vote:

APPROVED  DISAPPROVED  APPROVED with MODIFICATION

Prior Authorization Criteria for Fulyzaq®

Fulyzaq® will be approved for recipients meeting ALL of the following criteria:

- Patient has non-infectious diarrhea AND
- Diagnosis of HIV or AIDS AND
- Currently receiving anti-retroviral therapy

Committee Vote:

APPROVED  DISAPPROVED  APPROVED with MODIFICATION
### Prior Authorization Criteria for Abilify Maintena™

Atypical Antipsychotics will be approved for the following:

- Aggression: disorder, in autism, in mental retardation
- Agitation: in autism, in mental retardation, of dementia
- Bipolar and manic disorders
- Bipolar depression, bipolar maintenance, bipolar mania-acute, bipolar mixed states
- Brief psychiatric disorder
- Delusional disorder
- Depression with psychotic symptoms
- Drug-induced psychotic disorder with hallucinations
- Impulse control disorders, including Oppositional Defiant Disorder and Intermittent Explosive Disorder
- Organic psychotic condition
- Psychosis secondary to a medical condition, psychotic depression, psychotic disorders
- Schizoaffective disorder, schizoid/schizotypal personality disorder, schizophrenia, schizophrenic disorders
- Substance-induced psychotic disorder, Substance-induced withdrawal psychotic disorder
- Severe refractory OCD or PTSD
- Tourette's/Severe tic disorder
- For a diagnosis of major depressive disorder (MDD):
  - Atypicals will be approved only as adjunctive treatment for MDD. Recipients must have undergone an adequate trial of at least one agent in three of the following classes of antidepressants (unless contraindicated or intolerant to):
    - SSRIs
    - SNRIs
    - TCAs
    - New generation antidepressants (including bupropion, mirtazapine, etc.)
- For patients without one of the above diagnoses: May be approved if the physician can provide documented clinical evidence supporting the use of the requested medication for the requested indication.

### COMMITTEE VOTE:

- **APPROVED**
- **DISAPPROVED**
- **APPROVED with MODIFICATION**
### Prior Authorization Criteria for Preferred ARB CCBs

Will be approved for patients with a diagnosis of hypertension requiring combination therapy with an ARB and a calcium channel blocker who meet ONE of the following criteria:

- Diagnosis of diabetic nephropathy, heart failure, left ventricular hypertrophy, or renal insufficiency. ARB/CCBs will be reserved for those patients who have a contraindication to an ACEI (history of ACEI-induced angioedema, hypersensitivity to an ACEI, pregnancy) or are unable to tolerate an ACEI due to cough.
- History of ACEI-induced angioedema, hypersensitivity to an ACEI, or inability to tolerate ACEI due to cough. ARB-CCBs will be approved, without contraindication or intolerance to an ACEI, for patients with diabetes.

### Prior Authorization Criteria for Non-preferred ARB-CCBs

Will be approved for patients with a diagnosis of hypertension requiring combination therapy with an ARB and a calcium channel blocker who meet ONE of the following criteria:

- Diagnosis of diabetic nephropathy, heart failure, left ventricular hypertrophy, or renal insufficiency. ARB/CCBs will be reserved for those patients who have a contraindication to an ACEI (history of ACEI-induced angioedema, hypersensitivity to an ACEI, pregnancy) or are unable to tolerate an ACEI due to cough AND are unable to take the products individually.
- History of ACEI-induced angioedema, hypersensitivity to an ACEI, or inability to tolerate ACEI due to cough. ARB-CCBs will be approved, without contraindication or intolerance to an ACEI, for patients with diabetes AND are unable to take the products individually.

### Prior Authorization Criteria for TOBI Podhaler®

TOBI Podhaler® will be approved for patients meeting ALL of the following criteria:

- Diagnosis of cystic fibrosis, AND
- A clinically valid reason not to use TOBI® nebulizer solution

### Quantity Limits

| TOBI Podhaler® | 8/day |

### Committee Vote:

- **APPROVED**
- **DISAPPROVED**
- **APPROVED with MODIFICATION**