Combination NSAID Prior Authorization with Quantity Limit Program Summary

This program applies to Medicaid.

The BCBS MN Step Therapy Supplement also applies to this program for Medicaid.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
07-01-2024	07-01-2019

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Consensi® (amlodipine/ celecoxib) Tablet	Indicated in adult patients for whom treatment with both amlodipine for hypertension and celecoxib for osteoarthritis are appropriate. Amlodipine is indicated for the treatment of hypertension, to lower blood pressure. Lowering blood pressure reduces the risk of fatal and nonfatal CV events, primarily strokes and myocardial infarctions. Celecoxib is indicated for the management of the signs and symptoms of osteoarthritis.		6
Duexis® (ibuprofen/ famotidine) Tablet*	Relief of signs and symptoms of rheumatoid arthritis and osteoarthritis and to decrease the risk of developing upper gastrointestinal ulcers, which in the clinical trials was defined as a gastric and/or duodenal ulcer, in patients who are taking ibuprofen for those indications	* Generic available	4
Vimovo® (naproxen/ esomeprazole) Tablet*	Indicated in adult and adolescent patients 12 years of age and older weighing at least 38 kg, requiring naproxen for symptomatic relief of arthritis and esomeprazole magnesium to decrease the risk of developing naproxen associated gastric ulcers. The naproxen component of Vimovo is indicated for relief of signs and symptoms of: • osteoarthritis, rheumatoid arthritis and ankylosing spondylitis in adults • juvenile idiopathic arthritis (JIA) in adolescent patients The esomeprazole magnesium component of Vimovo is indicated to decrease the risk of developing naproxen-associated gastric ulcers.	* Generic available	1
Yosprala®, Aspirin/ Omeprazole Tablet	Indicated for patients who require aspirin for secondary prevention of cardiovascular and cerebrovascular events and who are at risk of developing aspirin associated gastric ulcers. The aspirin component of Yosprala is indicated for: • Reducing the combined risk of death and nonfatal stroke in patients who have had ischemic stroke or transient ischemia of the brain due to fibrin platelet emboli		5

Agent(s)	FDA Indication(s)	Notes	Ref#
	• Reducing the combined risk of death and nonfatal myocardial infarction (MI) in patients with previous MI or unstable angina pectoris • Reducing the combined risk of MI and sudden death in patients with chronic stable angina pectoris • Use in patients who have undergone revascularization procedures [coronary artery bypass graft (CABG) or percutaneous transluminal coronary angioplasty (PTCA)] when there is a pre-existing condition for which aspirin is already indicated The omeprazole component of Yosprala is indicated for decreasing the risk of developing aspirin associated gastric ulcers in patients at risk for developing aspirin-associated gastric ulcers due to age (greater than or equal to 55) or documented history of gastric ulcers.		

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Clinical Rationale	Nonsteroidal anti-inflammatory drugs (NSAIDs), including aspirin, cause considerable morbidity and mortality related to gastric and duodenal mucosal injury. Thus, prevention of NSAID-induced gastrointestinal (GI) toxicity is an important issue. Strategies for gastroprotection during NSAID therapy include supplementation with a synthetic prostaglandin analog (misoprostol), gastric acid suppression (proton pump inhibitors), or the selective use of those NSAIDs least likely to inhibit gastric prostaglandins.(2,3,8) Per the American College of Gastroenterology (ACG) 2009 practice guidelines on prevention of NSAID-related ulcers, the following are risk factors for developing an NSAID-induced GI ulcer(3): • Age greater than or equal to 65 years • Prior history of peptic, gastric, or duodenal ulcer • History of NSAID-related ulcer • History of clinically significant GI bleeding • Untreated or active *H. pylori* gastritis • Concurrent use of oral corticosteroids • Concurrent use of anticoagulants • Concurrent use of antiplatelets Many hypertensive patients require chronic analgesic therapy with NSAIDs in order to treat chronic pain (e.g., due to osteoarthritis). With the possible exception of calcium channel blockers (CCBs), NSAIDs can inhibit the effectiveness of most antihypertensive drugs. Thus, use of the CCB amlodipine, which is acceptable first-line therapy in the treatment of hypertension, may simplify management of such patients.(7) Consensi, a single-pill combination of amlodipine and celecoxib, has shown similar blood pressure reduction to an equal dose of amlodipine.(6,7)
Efficacy	Although Vimovo, Duexis, and Yosprala showed statistically significant efficacy over placebo or single NSAID agents, no clinical trials were conducted comparing these combination agents against taking both active ingredients separately but at the same time.(1,4,5)
Safety	Consensi is contraindicated in the following:(6) • Known hypersensitivity to amlodipine, celecoxib, or any inactive ingredients of Consensi • History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs • In the setting of coronary artery bypass graft (CABG) surgery

	• History of allergic-type reactions to sulfonamides Consensi also carries the following boxed warnings:(6) • Nonsteroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular (CV) thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in the treatment and may increase with duration of use. • Consensi is contraindicated in the setting of coronary artery bypass graft (CABG) surgery. • NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events. Duexis is contraindicated in the following:(4) • History of asthma, urticaria, or allergic reactions after taking aspirin or other NSAIDs • In the setting of coronary artery bypass graft (CABG) surgery • Known hypersensitivity to ibuprofen or famotidine or any components of Duexis • Known hypersensitivity to other H2-receptor antagonists Duexis also carries the following boxed warnings:(4) • Ibuprofen, a component of Duexis, may increase the risk of serious cardiovascular (CV) thrombotic events, including myocardial infarction, and stroke, which can be fatal. Risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. • Duexis is contraindicated in the setting of coronary artery bypass graft (CABG) surgery. • NSAIDs, including ibuprofen, a component of Duexis, increase the risk of serious gastrointestinal (GI) adverse reactions including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. Reactions can occur at any time without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk. Vimovo is contraindicated in the following:(1) • Known hypersensitivity to naproxen, esomeprazole, magnesium, substituted benzimidazoles or to any components of the drug product including omeprazole • History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs • In the setting of coronary artery bypass graft (CABG) surgery • Patients receiving rilpivirine-containing products Vimovo also carries the following boxed warning:(1) • Naproxen, a component of Vimovo, may cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.

	• Vimovo is contraindicated in the setting of coronary artery bypass graft (CABG) surgery. • NSAIDs, including naproxen, a component of Vimovo, cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients and patient with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious gastrointestinal (GI) events. Yosprala carries the following contraindications:(5) • History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs • In pediatric patients with suspected viral infections, with or without fever, because of the risk of Reye's Syndrome • Known hypersensitivity to aspirin, omeprazole, substituted benzimidazoles, or to any of the excipients of Yosprala • Patients receiving rilpivirine-containing products

REFERENCES

Number	Reference
1	Vimovo prescribing information. Horizon Medicines, LLC. July 2023.
2	Bhatt DL, Scheiman JM, Abraham NS, et al. ACCF/ACG/AHA 2008 Expert Consensus Document on Reducing the Gastrointestinal Risks of Antiplatelet Therapy and NSAID Use. *J Am Coll Cardiol*. 2008;52(18):1502-1519.
3	Lanza FL, Chan FKL, Quigley EMM, et al. American College of Gastroenterology (ACG) Practice Guidelines: Guidelines for Prevention of NSAID-Related Ulcer Complications. *Am J Gastroenterol*. 2009;104:728–738.
4	Duexis prescribing information. Horizon Medicines, LLC. April 2021.
5	Yosprala prescribing information. Pharmaceutika LTD.. January 2020.
6	Consensi prescribing information. Burke Therapeutics, LLC. April 2021.
7	Townsend RR, et al. NSAIDs and Acetaminophen: Effects on Blood Pressure and Hypertension. UpToDate. Last updated March 2022. Literature review current through October 2022.
8	Feldman M, Das S, et al. NSAIDs (Including Aspirin): Primary Prevention of Gastroduodenal Toxicity. UpToDate. Last updated May 2021. Literature review current through November 2022.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Consensi	amlodipine besylate-celecoxib tab	10-200 MG ; 2.5-200 MG ; 5-200 MG	M ; N ; O ; Y	N		
Yosprala	aspirin-omeprazole tab delayed release	325-40 MG ; 81-40 MG	M ; N ; O ; Y	M ; N		
Duexis	ibuprofen-famotidine tab	800-26.6 MG	M ; N ; O ; Y	O ; Y		
Vimovo	naproxen-esomeprazole magnesium tab dr	375-20 MG ; 500-20 MG	M ; N ; O ; Y	O ; Y		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Consensi	amlodipine besylate-celecoxib tab	10-200 MG ; 2.5-200 MG ; 5-200 MG	30	Tablets	30	DAYS			
Duexis	ibuprofen-famotidine tab	800-26.6 MG	90	Tablets	30	DAYS			
Vimovo	naproxen-esomeprazole magnesium tab dr	375-20 MG ; 500-20 MG	60	Tablets	30	DAYS			
Yosprala	aspirin-omeprazole tab delayed release	325-40 MG ; 81-40 MG	30	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Consensi	amlodipine besylate-celecoxib tab	10-200 MG ; 2.5-200 MG ; 5-200 MG	Medicaid
Duexis	ibuprofen-famotidine tab	800-26.6 MG	Medicaid
Vimovo	naproxen-esomeprazole magnesium tab dr	375-20 MG ; 500-20 MG	Medicaid
Yosprala	aspirin-omeprazole tab delayed release	325-40 MG ; 81-40 MG	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Consensi	amlodipine besylate-celecoxib tab	10-200 MG ; 2.5-200 MG ; 5-200 MG	Medicaid
Duexis	ibuprofen-famotidine tab	800-26.6 MG	Medicaid
Vimovo	naproxen-esomeprazole magnesium tab dr	375-20 MG ; 500-20 MG	Medicaid
Yosprala	aspirin-omeprazole tab delayed release	325-40 MG ; 81-40 MG	Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. For Consensi, BOTH of the following: 1. The patient has a diagnosis of hypertension **AND** 2. The patient has a diagnosis of osteoarthritis **OR** B. BOTH of the following: 1. ONE of the following:

Module	Clinical Criteria for Approval
	A. For Duexis or ibuprofen/famotidine requests, the patient has a diagnosis of at least ONE of the following: 1. Rheumatoid arthritis **OR** 2. Osteoarthritis **OR** B. For Vimovo or naproxen/esomeprazole requests, the patient has a diagnosis of at least ONE of the following: 1. Osteoarthritis in adults **OR** 2. Rheumatoid arthritis in adults **OR** 3. Ankylosing spondylitis in adults **OR** 4. Juvenile idiopathic arthritis (JIA) in adolescents weighing greater than or equal to 38 kg **AND** 2. The patient has at least ONE of the following risk factors for developing NSAID-induced gastrointestinal (GI) ulcers: A. Age greater than or equal to 65 years B. Prior history of peptic, gastric, or duodenal ulcer C. History of NSAID-related ulcer D. History of clinically significant GI bleeding E. Untreated or active *H. pylori* gastritis F. Concurrent use of oral corticosteroids G. Concurrent use of anticoagulants H. Concurrent use of antiplatelets **OR** C. For Yosprala or aspirin/omeprazole requests, BOTH of the following: 1. The patient has an indication of use of at least ONE of the following: A. Reducing the combined risk of death and nonfatal stroke in patients who have had ischemic stroke or transient ischemia of the brain due to fibrin platelet emboli **OR** B. Reducing the combined risk of death and nonfatal myocardial infarction (MI) in patients with previous MI or unstable angina pectoris **OR** C. Reducing the combined risk of MI and sudden death in patients with chronic stable angina pectoris **OR** D. Use in patients who have undergone revascularization procedures (coronary artery bypass graft [CABG] or percutaneous transluminal coronary angioplasty [PTCA]) when there is a pre-existing condition for which aspirin is already indicated **AND** 2. The patient has at least ONE of the following risk factors for developing NSAID-induced gastrointestinal (GI) ulcers: A. Age greater than or equal to 55 years B. Prior history of peptic, gastric, or duodenal ulcer C. History of NSAID–related ulcer D. History of clinically significant GI bleeding E. Untreated or active *H. pylori* gastritis F. Concurrent use of oral corticosteroids G. Concurrent use of anticoagulants H. Concurrent use of antiplatelets **AND** 2. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **AND** 3. ONE of the following: A. Information has been provided that use of the individual ingredients within the target combination agent, as separate dosage forms, is not clinically appropriate for the patient **OR** B. BOTH of the following:

Module	Clinical Criteria for Approval
	1. The patient's medication history includes use of the individual ingredients within the target combination agent, as separate dosage forms, as indicated by ONE of the following: A. Evidence of a paid claim(s) **OR** B. The prescriber has stated that the patient has tried the individual ingredients within the target combination agent, as separate dosage forms **AND** 2. ONE of the following: A. The individual ingredients within the target combination agent, as separate dosage forms was discontinued due to lack of effectiveness or an adverse event **OR** B. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over use of the individual ingredients within the target combination agent, as separate dosage forms **OR** C. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currencly receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** D. The prescriber has provided documentation that the individual ingredients within the target combination agent, as separate dosage forms, cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL with PA	**Quantity limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **OR** 3. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** C. There is support for therapy with a higher dose for the requested indication **Length of Approval**: up to 12 months