Clinical Policy Title:	ibuprofen and famotidine
Policy Number:	RxA.273
Drug(s) Applied:	Duexis®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All Line of Business

Background

Duexis® is a combination of a non-steroidal anti-inflammatory drug (NSAID) ibuprofen and the histamine H_2-receptor (H_2RA) antagonist famotidine.
Duexis® is indicated for the 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.

Limitation(s) of use: The clinical trials primarily enrolled patients less than 65 years of age without a prior history of gastrointestinal ulcer. Controlled trials do not extend beyond 6 months.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Ibuprofen and famotidine (Duexis®)	Rheumatoid arthritis or osteoarthritis	One tablet PO TID	2,400 mg ibuprofen/79.8 mg famotidine per day

Dosage Forms

- Tablets: 800 mg ibuprofen/26.6 mg famotidine.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Rheumatoid Arthritis or Osteoarthritis (must meet all)**:**

1. Prescribed to decrease the risk of developing gastric ulcers in patients with rheumatoid arthritis or osteoarthritis;
2. Age ≥ 18 years;
3. Failure of an H_2RA antagonist (e.g., famotidine) in combination with an NSAID (e.g., ibuprofen) unless contraindicated or clinically significant adverse effects are experienced;
4. Failure of three proton pump inhibitors (PPIs) (e.g., omeprazole, pantoprazole, lansoprazole) in combination with three different NSAIDs, unless contraindicated or clinically significant adverse effects are experienced;
5. Medical justification supports inability to use the individual components (i.e., famotidine and ibuprofen) concurrently (e.g., contraindications to the excipients of all brand and generic products);
6. Dose does not exceed 2,400 mg ibuprofen/79.8 mg famotidine per day (3 tablets per day).

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. Rheumatoid Arthritis or Osteoarthritis (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 2,400 mg ibuprofen/79.8 mg famotidine per day (3 tablets per day).

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendix

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
GI: gastrointestinal
H_2RA: Histamine H_2-receptor antagonist
NSAID: Nonsteroidal anti-inflammatory drug
PPI: Proton pump inhibitor

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/Maximum Dose
PPIs		
lansoprazole (Prevacid®)	NSAID-induced ulcer prophylaxis: 15 mg PO once daily NSAID-associated gastric ulcer (healing): 30 mg PO once daily	30 mg/day (for most indications)
omeprazole (Prilosec®)	NSAID-induced ulcer prophylaxis†: 20 mg PO once daily	40 mg/day (for most indications)
pantoprazole (Protonix®)	NSAID-induced ulcer prophylaxis†: 40 mg PO once daily	40 mg/day (for most GERD indications)

Drug Name	Dosing Regimen	Dose Limit/Maximum Dose
NSAIDs		
diclofenac (Voltaren®)	Osteoarthritis: 50 mg PO BID-TID or 75 mg PO BID Rheumatoid arthritis: 50 mg PO TID-QID, or 75 mg PO BID Ankylosing spondylitis: 25 mg PO QID with an additional 25 mg dose at bedtime	Osteoarthritis: 150 mg/day Rheumatoid arthritis: 200 mg/day PO Ankylosing spondylitis 125 mg/day
etodolac (Lodine®)	Osteoarthritis or rheumatoid arthritis: 400 – 500 mg PO BID	1,200 mg/day
fenoprofen (Nalfon®)	400 – 600 mg PO TID-QID	3,200 mg/day
ibuprofen (Motrin®)	400 – 800 mg PO TID-QID	3,200 mg/day
indomethacin (Indocin®)	25 PO BID-TID	200 mg/day
indomethacin SR	75 mg PO once daily-BID	150 mg/day
ketoprofen	50 mg PO QID or 75 mg PO TID	300 mg/day
meloxicam (Mobic®)	7.5 mg – 15 mg PO once daily	15 mg/day
naproxen (Naprosyn®)	250 – 500 mg PO BID	1,500 mg/day
naproxen sodium (Anaprox DS®)	275 – 550 mg PO BID	1,650 mg/day
oxaprozin (Daypro®)	600 – 1200 mg PO once daily	1,800 mg/day
piroxicam (Feldene®)	10 – 20 mg PO once daily	20 mg/day
salsalate (Disalcid®)	1,500 mg PO BID or 1,000 mg PO TID	3,000 mg/day
sulindac	150 mg – 200 mg PO BID	400 mg/day
tolmetin	400 – 600 mg PO TID	1,800 mg/day
meclofenamate	50 – 100 mg PO Q4-6hr	400 mg/day
H2RA antagonists		
famotidine (Pepcid®)	20 mg-40 mg BID	Varies based on indication
cimetidine	NSAID induced ulcer prophylaxis†: 200-400 mg PO once daily	1,200 mg/day (for most indications)

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic. †Off-label indication

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Hypersensitivity to ibuprofen or famotidine or any components of the drug product.
  - History of asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs.
  - In the setting of CABG surgery.
  - Hypersensitivity to other H_2-receptor antagonists.

- Boxed Warning(s):
  - Nonsteroidal anti-inflammatory drugs (NSAIDs) 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.
  - Duexis® is contraindicated in the setting of coronary artery bypass graft (CABG) surgery.
  - NSAIDs cause an increased risk of serious 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 evets.

References

1. Duexis® Prescribing Information. Lake Forest, IL: Horizon Pharma; July 22, 2019. Available at: https://www.Duexis.com/. Accessed February 4, 2021.
2. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed February 4, 2021.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2016. Available at: http://www.clinicalpharmacology-ip.com/. Accessed February 4, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy was established	01/2020	02/07/2020
Appendix B: Therapeutic Alternatives - removed ranitidine (Zantac) Boxed Warning – added Duexis® is contraindicated in the setting of coronary artery bypass graft (CABG) surgery Updated References	05/01/2020	05/20/2020
Policy was reviewed: 1. Clinical policy title table was updated. 2. Drug(s) applied was updated. 3. Line of Business Policy Applies to was update to all lines of business.	02/04/2021	03/09/2021

4. Dosing information was updated for indication. 5. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 6. Drug names Indocin SR, Orudis, Anaprox, Clinoril, Tagamet removed from Appendix C for therapeutic alternative. 7. References were reviewed and updated. 8. Updated and reformatted contraindications: Hypersensitivity to ibuprofen or famotidine or any components of the drug product, History of asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs, In the setting of CABG surgery, Hypersensitivity to other H2-receptor antagonists. 9. Updated Box Warning: • Nonsteroidal anti-inflammatory drugs (NSAIDs) 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. • Duexis® is contraindicated in the setting of coronary artery bypass graft (CABG) surgery. • NSAIDs cause an increased risk of serious 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.		