Clinical Policy: Ibuprofen/Famotidine (Duexis)

Reference Number: ERX.NPA.154
Effective Date: 06.01.21
Last Review Date: 05.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

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

FDA Approved Indication(s)

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.

Policy/Criteria

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

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Duexis is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Prescribed to decrease the risk of developing NSAID-induced gastric ulcers in patients with rheumatoid arthritis or osteoarthritis;
2. Age ≥ 18 years;
3. Failure of an H_2RA antagonist (e.g., ranitidine) 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 clinically significant adverse effects are experienced or all are contraindicated;
5. Member must instead use the individual components (i.e., famotidine and ibuprofen) concurrently, unless contraindicated or clinically significant adverse effects are experienced;
6. Member has at least one of the following risk factors for developing NSAID-induced gastric ulcers (a, b, or c):
   a. Age > 65 years;
   b. Member has a history of peptic ulcer disease;
   c. Concurrent use of antiplatelets, corticosteroids, or anticoagulants;
7. If request is for brand Duexis, member must use generic ibuprofen/famotidine, unless contraindicated or clinically significant adverse effects are experienced;
8. Dose does not exceed 2,400 mg ibuprofen/79.8 mg famotidine (3 tablets) per day.

Approval duration: 6 months

B. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Rheumatoid Arthritis or Osteoarthritis (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Member continues to have at least one of the following risk factors for developing NSAID-induced gastric ulcers (a, b, or c):
   a. Age > 65 years;
   b. Member has a history of peptic ulcer disease;
   c. Concurrent use of antiplatelets, corticosteroids, or anticoagulants;
4. If request is for a dose increase, new dose does not exceed 2,400 mg ibuprofen/79.8 mg famotidine (3 tablets) per day.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CABG: coronary artery bypass graft
FDA: Food and Drug Administration
GI: gastrointestinal
H2RA: histamine H2-receptor antagonist
NSAID: nonsteroidal anti-inflammatory drug
PPI: proton pump inhibitor

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
PPIs		
lansoprazole (Prevacid®)	NSAID-induced ulcer prophylaxis: 15 mg PO QD NSAID-associated gastric ulcer (healing): 30 mg PO QD	30 mg/day (for most indications)
omeprazole (Prilosec®)	NSAID-induced ulcer prophylaxis†: 20 mg PO QD	40 mg/day (for most indications)
pantoprazole (Protonix®)	NSAID-induced ulcer prophylaxis†: 40 mg PO QD	80 mg/day (for most GERD indications)
NSAIDs		
diclofenac (Voltaren®)	Osteoarthritis: 50 mg PO BID-TID or 75 mg PO BID	Osteoarthritis: 150 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	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	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 (Indocin SR®)	75 mg PO QD-BID	150 mg/day
ketoprofen (Orudis®)	50 mg PO QID or 75 mg PO TID	300 mg/day
meloxicam (Mobic®)	7.5 mg – 15 mg PO QD	15 mg/day
naproxen (Naprosyn®)	250 – 500 mg PO BID	1,500 mg/day
naproxen sodium (Anaprox®, Anaprox DS®)	275 – 550 mg PO BID	1,650 mg/day
oxaprozin (Daypro®)	600 – 1200 mg PO QD	1,800 mg/day
piroxicam (Feldene®)	10 – 20 mg PO QD	20 mg/day
salsalate (Disalcid®)	1,500 mg PO BID or 1,000 mg PO TID	3,000 mg/day
sulindac (Clinoril®)	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
ranitidine (Zantac®)	150 mg PO BID	300 mg/day (for most indications)
cimetidine (Tagamet®)	NSAID induced ulcer prophylaxis†: 200-400 mg PO QD	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.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity to ibuprofen or famotidine; history of asthma, urticaria, or allergic-type reactions to aspirin or other NSAIDs; in the setting of coronary artery bypass graft (CABG) surgery; hypersensitivity to other H_2-receptor antagonists
- Boxed Warning(s): NSAIDs cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke; NSAIDs cause an increased risk of serious GI adverse events including bleeding, ulceration, and perforation of the stomach or intestines; Duexis is contraindicated in the setting of CABG surgery

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Rheumatoid arthritis or osteoarthritis	One tablet PO TID	2,400 mg ibuprofen/79.8 mg famotidine per day

VI. Product Availability

Tablet: 800 mg ibuprofen/26.6 mg famotidine

VII. References

1. Duexis Prescribing Information. Lake Forest, IL: Horizon Pharma; July 2019. Available at: https://www.duexis.com/. Accessed January 18, 2022.
2. Castellsague J, Riera-Guardia N, Calingaert B, et al. Individual NSAIDs and Upper Gastrointestinal Complications: A systematic review and meta-analysis of observational studies (the SOS Project). Drug Saf 2012; 35(12):1127-1146.
3. Momeni M and Katz J. Mitigating GI risks associated with the use of NSAIDs. Pain Medicine 2013; 14:S18-S22.
4. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed January 18, 2022.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at: http://www.clinicalpharmacology-ip.com/. Accessed January 18, 2022.
6. Laine, L. Approaches to nonsteroidal anti-inflammatory drug use in the high-risk patient. Gastroenterology. 2001; 120: 594-606.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	02.12.21	05.21
2Q 2022 annual review: no significant changes; added redirection to generic formulation; references reviewed and updated.	01.18.22	05.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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