Clinical Policy: Ibuprofen/Famotidine (Duexis)

Reference Number: CP.PMN.120
Effective Date: 06.01.18
Last Review Date: 05.25
Line of Business: Commercial, HIM, 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.

It is the policy of health plans affiliated with Centene Corporation® that ibuprofen/famotidine or 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 a H_2RA antagonist (e.g., ranitidine) in combination with a 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 (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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 brand Duexis, member must use generic ibuprofen/famotidine, unless contraindicated or clinically significant adverse effects are experienced;
5. 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: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid 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
H_2RA: histamine H_2-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 for all relevant lines of business 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)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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 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 (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.

†*Off-label indication*

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. Deerfield, IL: Horizon Medicines LLC; November 2024. Available at: https://www.duexis.com/. Accessed January 16, 2025.
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]. Ann Arbor, Michigan: Merative™. Updated periodically. Accessed January 27, 2025.
5. Clinical Pharmacology [database online]. Philadelphia, PA: Elsevier. Updated periodically. Available at: http://www.clinicalkey.com/pharmacology. Accessed January 27, 2025.
6. Laine, L. Approaches to nonsteroidal anti-inflammatory drug use in the high-risk patient. *Gastroenterology*. 2001; 120: 594-606.
7. Fraenkel L, Bathon JM, England BR et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Care & Research. 2021 July; 73(7):924-939.
8. Kolasinski SL, Neogi T, Hochberg MC et al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the management of osteoarthritis of the hand, hip, and knee. Arthritis & Rheumatology. 2020 Feb; 72(2): 220-233.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2021 annual review: revised requirement of medical justification for inability to use individual components to "must use" language; added risk factors for developing NSAID-induced gastric ulcers;	02.12.21	05.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
revised initial and continued approval durations from 12 months (Medicaid/HIM) and length of benefit (Commercial) to 6 months; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.		
2Q 2022 annual review: no significant changes; added redirection to generic product; references reviewed and updated.	01.18.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.03.22	
2Q 2023 annual review: no significant changes; references reviewed and updated.	01.31.23	05.23
2Q 2024 annual review: added redirection to generic product in continued therapy; references reviewed and updated.	01.18.24	05.24
2Q 2025 annual review: clarified generic famotidine-ibuprofen applies to policy; revised continued approval duration to 12 months; references reviewed and updated.	01.16.25	05.25

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan

retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.