

Clinical Policy: Ibuprofen/Famotidine (Duexis)

Reference Number: CP.PMN.120

Effective Date: 06.01.18

Last Review Date: 05.21

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 H₂-receptor (H₂RA) 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 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 H₂RA 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 use the individual components (i.e., famotidine and ibuprofen) concurrently, unless contraindicated to the excipients of all commercially available brand and generic products;
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. 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 the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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. Currently receiving medication via Centene benefit 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 Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 12 months (whichever is less); or

- 2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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

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 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)
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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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 CABG surgery; hypersensitivity to other H₂-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 coronary artery bypass graft (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 February 12, 2021.
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 February 12, 2021.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at: <http://www.clinicalpharmacology-ip.com/>. Accessed February 12, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created: replaces CP.CPA.23 Duexis for commercial; Medicaid line of business added	02.27.18	05.18
2Q 2019 annual review: no significant changes. References reviewed and updated.	02.23.19	05.19
2Q 2020 annual review: no significant changes; references reviewed and updated.	02.07.20	05.20
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; 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.	02.12.21	05.21

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.

©2018 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene[®] and Centene Corporation[®] are registered trademarks exclusively owned by Centene Corporation.