

## Clinical Policy: Butorphanol Nasal Spray

Reference Number: HIM.PA.46

Effective Date: 12.01.14

Last Review Date: 05.26

Line of Business: HIM/ICHRA

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### Description

Butorphanol tartrate is a synthetically derived opioid agonist-antagonist analgesic of the phenanthrene series.

### FDA Approved Indication(s)

Butorphanol tartrate nasal spray is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitation(s) of use: Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve butorphanol tartrate nasal spray for use in patients for whom alternative treatment options (e.g., non-opioid analgesics)

- Have not been tolerated, or are not expected to be tolerated,
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

Butorphanol tartrate nasal spray should not be used for an extended period of time unless the pain remains severe enough to require an opioid analgesic and for which alternative treatment options continue to be inadequate.

### 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 butorphanol nasal spray is **medically necessary** when the following criteria are met:

#### I. Initial Approval Criteria

***Please note: for HIM-Arkansas – if a member's covered prescription pain medication requires a prior authorization, then the prior authorization shall not be denied if the member has a terminal illness.***

##### A. Pain Management (must meet all):

1. Prescribed for the management of pain;
2. Age  $\geq$  18 years;
3. Member meets one of the following (a, b, or c):
  - a. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (see *Appendix D*);

- b. Prescribed by or in consultation with a pain management specialist, an oncologist, or for use in palliative or hospice care;
- c. Failure of at least 2 non-opioid ancillary treatments (such as non-steroidal anti-inflammatory drugs [NSAIDs] or acetaminophen-containing products) (*see Appendix B for examples*), unless contraindicated or clinically significant adverse effect are experienced;\*
- \* For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
- 4. For pain related to migraine headache: failure of at least 2 anti-migraine agents (*see Appendix B for examples*), unless contraindicated or clinically significant adverse effect are experienced;\*
- \* For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
- 5. For chronic pain: failure of an antidepressant or anticonvulsant agent (*see Appendix B for examples*), unless contraindicated or clinically significant adverse effect are experienced;\*
- \* For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
- 6. Member is unable to use oral medications for pain relief.

**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/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace/ICHRA; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace/ICHRA; 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: HIM.PA.154 for health insurance marketplace/ICHRA.

**II. Continued Therapy**

***Please note: for HIM-Arkansas – if a member's covered prescription pain medication requires a prior authorization, then the prior authorization shall not be denied if the member has a terminal illness.***

**A. Pain Management (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.
- 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/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace/ICHRA; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace/ICHRA; 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: HIM.PA.154 for health insurance marketplace/ICHRA.

**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 – HIM.PA.154 or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation Key*

FDA: Food and Drug Administration

NSAID: non-steroidal anti-inflammatory disease

REMS: Risk Evaluation and Mitigation Strategy

*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 formulary agents and may require prior authorization.*

| Drug Class | Commonly Used Examples                                                                                                                                                                                                                           | Dose Limit/<br>Maximum Dose        |
|------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|
| NSAIDs     | ibuprofen (Motrin <sup>®</sup> ), naproxen (Naprosyn <sup>®</sup> ), Relafen <sup>®</sup> (nabumetone), Voltaren <sup>®</sup> (diclofenac), Orudis <sup>®</sup> (ketoprofen), Clinoril <sup>®</sup> (sulindac), Toradol <sup>®</sup> (ketorolac) | Varies according to the agent used |

| Drug Class                                    | Commonly Used Examples                                                                                                                                                                                                                                    | Dose Limit/<br>Maximum Dose        |
|-----------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|
| Non-opioid analgesics                         | aspirin, acetaminophen opioid combinations (APAP/codeine, APAP hydrocodone)                                                                                                                                                                               | Varies according to the agent used |
| Anti-migraine agents (non-triptans)           | Cafergot <sup>®</sup> (ergotamine/cafeine), D.H.E.-45 <sup>®</sup> (dihydroergotamine), Midrin <sup>®</sup> (isometheptene/APAP), Fiorinal <sup>®</sup> (butalbital/aspirin), Fioricet <sup>®</sup> (butalbital/APAP)                                     | Varies according to the agent used |
| Anti-migraine agents (triptans)               | almotriptan (Axert <sup>®</sup> ), eletriptan (Relpax <sup>®</sup> ), frovatriptan (Frova <sup>®</sup> ), naratriptan (Amerge <sup>®</sup> ), rizatriptan (Maxalt <sup>®</sup> ), sumatriptan (Imitrex <sup>®</sup> ), zolmitriptan (Zomig <sup>®</sup> ) | Varies according to the agent used |
| Anticonvulsants                               | Carbamazepine (Tegretol <sup>®</sup> ), gabapentin (Neurontin <sup>®</sup> ), divalproex (Depakote <sup>®</sup> ), topiramate (Topamax <sup>®</sup> )                                                                                                     | Varies according to the agent used |
| Antidepressants/<br>tricyclic antidepressants | amitriptyline (Elavil <sup>®</sup> ), desipramine (Norpramin <sup>®</sup> ), imipramine (Tofranil <sup>®</sup> ), nortriptyline (Pamelor <sup>®</sup> ), duloxetine (Cymbalta <sup>®</sup> ), venlafaxine (Effexor <sup>®</sup> )                         | Varies according to the agent used |

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

#### *Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): significant respiratory depression; acute or severe bronchial asthma in an unmonitored setting or in absence of resuscitative equipment; known or suspected gastrointestinal obstruction, including paralytic ileus; hypersensitivity to butorphanol tartrate, the preservative benzethonium chloride, or any of the formulation excipients (e.g., anaphylaxis).
- Boxed warning(s): risks of addiction, abuse, and misuse; opioid analgesic Risk Evaluation and Mitigation Strategy (REMS); life-threatening respiratory depression; accidental exposure; neonatal opioid withdrawal syndrome; cytochrome P450 3A4 interactions; concomitant use with benzodiazepines or other central nervous system depressants.

#### *Appendix D: States with Regulations against Redirections in Cancer*

| State | Step Therapy Prohibited? | Notes                                                                                                                    |
|-------|--------------------------|--------------------------------------------------------------------------------------------------------------------------|
| FL    | Yes                      | For stage 4 metastatic cancer and associated conditions                                                                  |
| GA    | Yes                      | For stage 4 metastatic cancer. Redirection does not refer to review of medical necessity or clinical appropriateness     |
| IA    | Yes                      | For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA |
| IN    | Yes                      | For advanced, metastatic cancer and associated conditions                                                                |

| State | Step Therapy Prohibited? | Notes                                                                                                                                                                                                   |
|-------|--------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| LA    | Yes <sup>‡</sup>         | For stage 4 advanced, metastatic cancer or associated conditions.<br><sup>‡</sup> Exception if clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy |
| MS    | Yes                      | For advanced metastatic cancer and associated conditions                                                                                                                                                |
| NV    | Yes                      | Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person                                                                            |
| OH    | Yes                      | For stage 4 metastatic cancer and associated conditions                                                                                                                                                 |
| OK    | Yes                      | For advanced metastatic cancer and associated conditions                                                                                                                                                |
| PA    | Yes                      | For stage 4 advanced, metastatic cancer                                                                                                                                                                 |
| TN    | Yes <sup>^</sup>         | For cancer and associated conditions<br><sup>^</sup> Exception if step therapy is for AB-rated generic equivalent, interchangeable biologic product, or biosimilar product to the equivalent brand drug |
| TX    | Yes                      | For stage 4 advanced, metastatic cancer and associated conditions                                                                                                                                       |

## V. Dosage and Administration

| Indication | Dosing Regimen                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Maximum Dose   |
|------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|
| Pain       | <p>1 mg (1 spray in one nostril)</p> <p>If adequate pain relief is not achieved within 60 to 90 minutes, an additional 1 mg dose may be given. This initial dose sequence may be repeated in 3 to 4 hours as required after the second dose of the sequence.</p> <p>Depending on the severity of the pain, an initial dose of 2 mg (1 spray in each nostril) may be used in patients who will be able to remain recumbent in the event drowsiness or dizziness occurs. In such patients single additional 2 mg doses should not be given for 3 to 4 hours.</p> | Not applicable |

## VI. Product Availability

Nasal spray solution bottle: 2.5 mL (10 mg/mL)

## VII. References

1. Butorphanol Tartrate Nasal Solution Prescribing Information. Weston, FL: Apotex Corp.; December 2025. Available at: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b8e48063-0b40-ee43-85c1-4ef2de80c404>. Accessed January 23, 2026.
2. Butorphanol Nasal Spray Drug Monograph. Clinical Pharmacology [database online]. Philadelphia, PA: Elsevier. Updated periodically. Available at: <http://www.clinicalkey.com/pharmacology>. Accessed January 30, 2026.
3. Micromedex<sup>®</sup> Healthcare Series [Internet database]. Ann Arbor, Michigan: Merative<sup>™</sup>. Updated periodically. Accessed January 30, 2026.

### **Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| <b>HCPCS Codes</b> | <b>Description</b>                       |
|--------------------|------------------------------------------|
| S0012              | Butorphanol tartrate, nasal spray, 25 mg |

| <b>Reviews, Revisions, and Approvals</b>                                                                                                                                                                                                                                                                                                                                                                                                          | <b>Date</b> | <b>P&amp;T Approval Date</b> |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------|------------------------------|
| 2Q 2022 annual review: no significant changes; references reviewed and updated.                                                                                                                                                                                                                                                                                                                                                                   | 02.27.22    | 05.22                        |
| Template changes applied to other diagnoses/indications and continued therapy section.                                                                                                                                                                                                                                                                                                                                                            | 10.11.22    |                              |
| 2Q 2023 annual review: no significant changes; references reviewed and updated.                                                                                                                                                                                                                                                                                                                                                                   | 02.03.23    | 05.23                        |
| 2Q 2024 annual review: no significant changes; references reviewed and updated.                                                                                                                                                                                                                                                                                                                                                                   | 01.18.24    | 05.24                        |
| 2Q 2025 annual review: added option to bypass redirection if prescribed by or in consultation with a pain management specialist, an oncologist, or for use in palliative care or hospice care; added by-passing of redirection if state regulations do not allow step therapy in certain oncology settings along with Appendix D; added HCPCS code [S0012]; references reviewed and updated. Added step therapy bypass for IL HIM per IL HB 5395. | 04.08.25    | 05.25                        |
| 2Q 2026 annual review: updated Appendix D with revised language and exception for Tennessee; references reviewed and updated.<br>Updated Appendix D to include Indiana. Added ICHRA line of business.                                                                                                                                                                                                                                             | 03.26.26    | 05.26                        |
| Updated Appendix D with revised language for Tennessee.                                                                                                                                                                                                                                                                                                                                                                                           | 06.23.26    |                              |

### **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

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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.

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