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| **Clinical Policy Title:** | dihydroergotamine mesylate |
| **Policy Number:** | RxA.714 |
| **Drug(s) Applied:** | Trudhesa™ |
| **Original Policy Date:** | 12/07/2021 |
| **Last Review Date:** | 12/07/2021 |
| **Line of Business Policy Applies to:** | All lines of business |

## Background

Dihydroergotamine mesylate (Trudhesa™) is an ergotamine derivative indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use: Trudhesa™ is not indicated for the preventive treatment of migraine or for the management of hemiplegic or basilar migraine.

## Dosing Information

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| dihydroergotamine mesylate (Trudhesa™) | Migraine with or without aura | One spray (0.725 mg) into each nostril (total of 2 sprays per dose) may repeat as needed after ≥1 hour (total of 4 sprays in 2 doses). | 2.9 mg/day and 4.35 mg/week intranasal |

## Dosage Forms

- Nasal spray: 0.725 mg dihydroergotamine mesylate per spray.

## 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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

**I. Initial Approval Criteria**

**A. Migraine with or without aura.**

1. Diagnosis of migraine with or without aura;
2. Age ≥ 18 years;
3. Member experiences atleast 4 but not more than 14 headaches per month;
4. Failure of at least two preferred generic 5HT1B/1D-agonist migraine medications (e.g., sumatriptan, rizatriptan, zolmitriptan, etc.) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;

5. Trial and failure of atleast one of these for acute migraine treatment indication- Nurtec ODT, Ubrelvy or Reyvow ;
6. Trudhesa™ is not prescribed concurrently with strong CYP3A4 inhibitors;
7. Requested dose does not exceed 2.9 mg/day and 4.35 mg/week.

**Approval Duration**
**Commercial:** 12 Months
**Medicaid:** 12 Months

## II. Continued Therapy Approval

### A. Migraine with or without aura.

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Requested dose does not exceed 2.9 mg/day and 4.35 mg/week.

**Approval Duration**
**Commercial:** 6 months
**Medicaid:** 6 months

## III. Appendices

**APPENDIX A: Abbreviation/Acronym Key**
FDA: Food and Drug Administration

**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 |
|---|---|---|
| Migranal | 0.5 mg in each nostril, followed by 0.5 mg in each nostril 15 minutes later for a total dose of 2 mg | 3 mg/day and 4 mg/week |
| dihydroergotamine mesylate | 0.5 mg in each nostril, followed by 0.5 mg in each nostril 15 minutes later for a total dose of 2 mg | 3 mg/day and 4 mg/week |

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

**APPENDIX C: Contraindications/Boxed Warnings**

- Contraindication(s):
  - Concomitant use of strong CYP3A4 inhibitors.
  - Patients with ischemic heart disease or coronary artery vasospasm.
  - Patients with uncontrolled hypertension, peripheral arterial diseases, sepsis, following vascular

surgery, or severe hepatic or renal impairment.
    - Patients with hypersensitivity to ergot alkaloids.
    - Recent use (i.e., within 24 hours) of other 5-HT1 agonists (e.g., sumatriptan) or ergotamine-containing or ergot-type medications.
    - Concomitant use of peripheral and central vasoconstrictors because the combination may result in additive or synergistic elevation of blood pressure

- Boxed Warning(s):
    - Serious and/or life-threatening peripheral ischemia has been associated with the coadministration of dihydroergotamine with strong CYP3A4 inhibitors. Because CYP3A4 inhibition elevates the serum levels of dihydroergotamine, the risk for vasospasm leading to cerebral ischemia and/or ischemia of the extremities is increased. Hence, concomitant use of Trudhesa™ with strong CYP3A4 inhibitors is contraindicated.

**APPENDIX D: General Information**

- Peripheral Ischemia Following Coadministration with Strong CYP3A4 Inhibitors: Serious and/or life-threatening peripheral ischemia has been associated with the coadministration of dihydroergotamine with strong CYP3A4 inhibitors, including protease inhibitors, macrolide antibiotics, and antifungals.
- Myocardial Ischemia and/or Infarction, Other Cardiac Adverse Reactions, and Fatalities: In patients with risk factors, consider 1st dose administration under medical supervision with electrocardiogram.
- Cerebrovascular Adverse Reactions and Fatalities: Cerebral hemorrhage, subarachnoid hemorrhage and stroke have been reported; discontinue Trudhesa™ if suspected.
- Other Vasospasm Related Adverse Reactions: Trudhesa™ may cause vasospasm or elevation in blood pressure. Discontinue if signs or symptoms of vasoconstriction develop.
- Increase in Blood Pressure: Significant elevation in blood pressure has been reported on rare occasions in patients with and without a history of hypertension treated with dihydroergotamine mesylate.
- Medication Overuse Headache: Detoxification may be necessary.
- Preterm Labor: Advise pregnant women of the risk.
- Fibrotic Complications: Pleural and retroperitoneal fibrosis have been reported following prolonged daily use of dihydroergotamine mesylate. Administration of Trudhesa™ should not exceed the dosing guidelines or be used for chronic daily administration.
- Local Irritation: If severe local irritation occurs for no other attributable reasons, suspend Trudhesa™ until resolution.

**References**


1. Trudhesa™ prescribing information Seattle, WA: Impel NeuroPharma Inc.; September 2021, Available at: https://www.trudhesa.com/trudhesa-prescribing-information.pdf. Accessed September 28, 2021.
2. Clinical Pharmacology [database online] powered by Clinical Key. Tampa, FL: Elsevier, 2020. Available at: https://www.clinicalkey.com/pharmacology/. Accessed September 28, 2021.
3. Migranal® prescribing information Bridgewater, NJ: Bausch Health US, LLC; July 2019. Available at: https://www.bauschhealth.com/Portals/25/Pdf/PI/Migranal-PI.pdf. Accessed September 27, 2021.
4. Dihydroergotamine Mesylate Nasal Spray prescribing information Bridgewater, NJ: Bausch Health US, LLC; July 2019. Available at: https://www.bauschhealth.com/Portals/25/PDF/PI/Migranal-AG-PI.pdf?ver=2021-05-21-022912-477. Accessed September 27, 2021.
5. IPD Analytics Rx Insights_New Drug Approval Review_ Trudhesa™ _09 2021. Accessed with subscription at: https://secure.ipdanalytics.com/User/Pharma/RxStrategy/Search?q=Trudhesa. Accessed September 27, 2021.

| Review/Revision History | Review/Revision Date | P&T Approval Date |
|---|---|---|
| Policy established. | 9/29/2021 | 12/07/2021 |