# Ergotamine Quantity Limit Program Summary

This program applies to Medicaid.

## POLICY REVIEW CYCLE

| Effective Date | Date of Origin |
|---|---|
| 8/1/2023 | 10/1/2022 |

## FDA APPROVED INDICATIONS AND DOSAGE

| Agent(s) | FDA Indication(s) | Notes | Ref# |
|---|---|---|---|
| Cafergot® (ergotamine/caffeine)*<br><br>Tablet | Therapy to abort or prevent vascular headache, e.g., migraine, migraine variants, or so-called "histaminic cephalalgia" | *generic available | 1 |
| D.H.E. 45® (dihydroergotamine mesylate)*<br><br>Injection | Acute treatment of migraine headaches with or without aura<br><br>Acute treatment of cluster headache episodes | *generic available | 2 |
| Ergomar® (ergotamine tartrate)<br><br>Sublingual tablet | Therapy to abort or prevent vascular headache, e.g., migraine, migraine variants, or so-called "histaminic cephalalgia" | | 3 |
| Migergot® (ergotamine/caffeine)<br><br>Suppository | Therapy to abort or prevent vascular headache, e.g., migraine, migraine variants, or so-called "histaminic cephalalgia" | | 4 |

*See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm*

## CLINICAL RATIONALE

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| Acute Migraine | The American Headache Society 2015 guideline for The Acute Treatment of Migraine in Adults state that specific medications – triptans (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan [oral, nasal spray, injectable, transcutaneous patch], zolmitriptan [oral and nasal spray]) are effective (Level A). The evidence base for medication efficacy should be considered along with potential medication side effects, potential adverse events, patient-specific contraindications to use of a particular medication, and drug-to-drug interactions when deciding which medication to prescribe for acute therapy of a migraine attack.(5) Dihydroergotamine is recommended for use as second- or third-line therapy for select patients or for those with refractory migraine. Intranasal dihydroergotamine has strong evidence of effectiveness but more adverse effects than triptans because of its decreased receptor specificity. Ergotamine use is not noted in guidelines.(6)<br><br>Ergotamine has been used in clinical practice for the acute treatment of migraine for over 50 years, but there has been little agreement on its place in clinical practice. In a review of pre-clinical and clinical data on ergotamine as it relates to the treatment of migraine, specific suggestions for the patient groups and appropriate use of ergotamine have been agreed. In essence, ergotamine, from a medical perspective, is the drug of choice in a |

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| | limited number of migraine sufferers who have infrequent or long duration headaches and are likely to comply with dosing restrictions. For most migraine sufferers requiring a specific anti-migraine treatment, a triptan is generally a better option from both an efficacy and side-effect perspective.(7) |
| Safety (1-4) | D.H.E. 45 carries the following boxed warning:<br><br>Serious and/or life-threatening peripheral ischemia has been associated with the coadministration of dihydroergotamine with potent CYP 3A4 inhibitors including protease inhibitors and macrolide antibiotics. Because CYP 3A4 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 these medications is contraindicated.<br><br>Ergotamine agents carry the following boxed warning:<br><br>Serious and/or life-threatening peripheral ischemia has been associated with the coadministration of ergotamine tartrate/ergotamine tartrate and caffeine with potent CYP 3A4 inhibitors including protease inhibitors and macrolide antibiotics. Because CYP 3A4 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 these medications is contraindicated.<br><br>D.H.E. 45 is contraindicated in the following:<br><br>• Patients with ischemic heart disease (angina pectoris, history of myocardial infarction, or documented silent ischemia) or patients who have clinical symptoms or findings consistent with coronary artery vasospasm including Prinzmetal's variant angina<br>• Patients with uncontrolled hypertension<br>• Use within 24 hours of 5-HT1 agonists (e.g., sumatriptan), ergotamine-containing or ergot-type medications, or methysergide<br>• Patients with hemiplegic or basilar migraine<br>• Patients with known peripheral arterial disease, sepsis, following vascular surgery, and severely impaired hepatic or renal function<br>• Pregnant women<br>• Patients who have previously shown hypersensitivity to ergot alkaloids<br>• Nursing mothers<br>• Use with peripheral and central vasoconstrictors<br><br>Ergotamine agents are contraindicated in the following:<br><br>• Coadministration of ergotamine with potent CYP 3A4 inhibitors (ritonavir, nelfinavir, indinavir, erythromycin, clarithromycin and troleandomycin) has been associated with acute ergot toxicity (ergotism) characterized by vasospasm and ischemia of the extremities, with some cases resulting in amputation. There have been rare reports of cerebral ischemia in patients on protease inhibitor therapy when ergotamine was coadministered, at least one resulting in death. Because of the increased risk for ergotism and other serious vasospastic adverse events, ergotamine use is contraindicated with these drugs and other potent inhibitors of CYP 3A4 (e.g., ketoconazole, itraconazole)<br>• Ergotamine may cause fetal harm when administered to pregnant women. Ergotamine is contraindicated in women who are or may become pregnant. If this drug is used during pregnancy or if the patient becomes pregnant while |

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| | taking this product, the patient should be apprised of the potential hazard to the fetus.<br>• Peripheral vascular disease, coronary heart disease, hypertension, impaired hepatic or renal function and sepsis<br>• Hypersensitivity to any of the components |

## REFERENCES


| Number | Reference |
|---|---|
| 1 | Cafergot prescribing information. Sandoz Inc. December 2019. |
| 2 | D.H.E. 45 prescribing information. Bausch Health U.S. LLC. November 2019. |
| 3 | Ergomar prescribing information. Rosedale Therapeutics. September 2012. |
| 4 | Migergot prescribing information. Cosette Pharmaceuticals, Inc. November 2022. |
| 5 | Marmura M, Silberstein SD, Schwedt TJ. The acute treatment of migraine in adults: the American Headache Society evidence assessment of migraine pharmacotherapies. Headache. 2015;55:3–20. |
| 6 | Mayans L, Walling A. Acute Migraine Headache: Treatment Strategies. Am Fam Physician. 2018;97(4):243-251. |
| 7 | P. Tfelt-Hansen, P. R. Saxena, C. Dahlöf, J. Pascual, M. Láinez, P. Henry, H.-C. Diener, J. Schoenen, M. D. Ferrari, P. J. Goadsby, Ergotamine in the acute treatment of migraine: A review and European consensus, *Brain*. 2000;123(1):9-18. https://doi.org/10.1093/brain/123.1.9 |


## POLICY AGENT SUMMARY QUANTITY LIMIT

| Target Brand Agent Name(s) | Target Generic Agent Name(s) | Strength | QL Amount | Dose Form | Day Supply | Duration | Addtl QL Info | Allowed Exceptions | Targeted NDCs When Exclusions Exist |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | |
| Cafergot | Ergotamine w/ Caffeine Tab 1-100 MG | 1-100 MG | 40 | Tablets | 28 | DAYS | | | |
| Cafergot | Ergotamine w/ Caffeine Tab 1-100 MG | 1-100 MG | 40 | Tablets | 28 | DAYS | | | |
| D.h.e. 45 | Dihydroergotamine Mesylate Inj 1 MG/ML | 1 MG/ML | 24 | Ampules | 28 | DAYS | | | |
| D.h.e. 45 | Dihydroergotamine Mesylate Inj 1 MG/ML | 1 MG/ML | 24 | Ampules | 28 | DAYS | | | |
| Ergomar | Ergotamine Tartrate SL Tab 2 MG | 2 MG | 20 | Tablets | 28 | DAYS | | | |
| Migergot | Ergotamine w/ Caffeine Suppos 2-100 MG | 2-100 MG | 20 | Suppositories | 28 | DAYS | | | |

## CLIENT SUMMARY – QUANTITY LIMITS

| Target Brand Agent Name(s) | Target Generic Agent Name(s) | Strength | Client Formulary |
|---|---|---|---|
| Cafergot | Ergotamine w/ Caffeine Tab 1-100 MG | 1-100 MG | Medicaid |
| Cafergot | Ergotamine w/ Caffeine Tab 1-100 MG | 1-100 MG | Medicaid |
| D.h.e. 45 | Dihydroergotamine Mesylate Inj 1 MG/ML | 1 MG/ML | Medicaid |

| Target Brand Agent Name(s) | Target Generic Agent Name(s) | Strength | Client Formulary |
|---|---|---|---|
| D.h.e. 45 | Dihydroergotamine Mesylate Inj 1 MG/ML | 1 MG/ML | Medicaid |
| Ergomar | Ergotamine Tartrate SL Tab 2 MG | 2 MG | Medicaid |
| Migergot | Ergotamine w/ Caffeine Suppos 2-100 MG | 2-100 MG | Medicaid |

## QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

| Module | Clinical Criteria for Approval |
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| | **Target Agent(s)** will be approved when ONE of the following is met:<br><br>1. The requested quantity (dose) does NOT exceed the program quantity limit **OR**<br>2. The requested quantity (dose) is greater than the program quantity limit AND ONE of the following:<br>A. BOTH of the following:<br>1. The requested agent does not have a maximum FDA labeled dose for the requested indication **AND**<br>2. Information has been provided to support therapy with a higher dose for the requested indication **OR**<br>B. BOTH of the following:<br>1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND**<br>2. Information has been provided to support why the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **OR**<br>C. BOTH of the following:<br>1. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication **AND**<br>2. Information has been provided to support therapy with a higher dose for the requested indication<br><br>**Length of Approval**: up to 12 months |