Dihydroergotamine (DHE) Guidance Document

What is it and how does it work?

Dihydroergotamine (DHE) is an ergot alkaloid that vasoconstricts vessels and inhibits the trigeminal release of inflammatory peptides. It also binds to serotonin receptors. DHE may be used for the treatment of migraines, cluster headache episodes, cyclic vomiting and other migraine variants or atypical migraines.

Which patients may benefit from it?

DHE can be used for patients who have had an acute migraine, usually lasting longer than 72 hours, that was unresponsive to home treatment. Typically, patients will initially receive an IV migraine cocktail and if the patient does not respond to these medications, they may be admitted for DHE treatment.

DHE may also be used for cyclic vomiting, which is often considered to be a variant of migraines such as abdominal migraines. If a patient is unable to stop the cycle of vomiting at home, DHE is an option to provide relief and break the cycle.

Which patients should NOT use DHE?

DHE is contraindicated in patients < 6 years of age and in the following situations:

Disease States	Medications
• Patients with ischemic cardiac disease (angina pectoris, history of myocardial infarction, or documented silent ischemia), coronary artery vasospasm, or history of Kawasaki disease • Uncontrolled hypertension • Hemiplegic or basilar migraines • Peripheral artery disease (i.e., Reynaud's Syndrome) • Sepsis • Renal or hepatic failure • Following vascular surgery • Patients with known hypersensitivity to ergot alkaloids • Pregnancy or breastfeeding • Coronary/cerebral/peripheral vascular disease (i.e., sickle cell disease)	• Concomitantly with strong CYP3A4 inhibitors including: – Macrolide antibiotics (i.e., erythromycin, clarithromycin) – Protease inhibitors (i.e., ritonavir, nelfinavir, indinavir) – Azole antifungals (i.e., voriconazole, itraconazole) • Triptan medications (i.e., sumatriptan, zolmitriptan) within 24 hours

What medications should be discontinued prior to initiation of DHE?

- Midodrine or alpha-agonists due to risk for hypertension
- Peripheral or central vasoconstrictor should be used with caution and concomitant use should be discussed with initial prescribing provider and approved by the admitting provider
  - Beta blockers should be discontinued in patient's with Reynaud's syndrome

Which patients should be monitoring closely?

- Patients taking serotonin-modulating medications due to risk for serotonin syndrome – manifesting as confusion/agitation, tachycardia, hypertension, hyperthermia, skin flushing, hyperreflexia, clonus, and muscle rigidity

What monitoring should be completed prior to initiating treatment?

- Pain assessment
- 12-lead electrocardiogram
  - Preferably prior to initiation, but should have one documented within the past 6 months
- Vital signs (blood pressure, heart rate, respiratory rate, pulse oximetry, temperature)
- Basic metabolic panel (if the patient has not had one within the past 6 months)
- Pregnancy test in females > 10 years of age

What routine monitoring is required with DHE administration?

- May be caustic to veins, if patient requires multiple IVs, a PICC line may be considered
- With each administration, vital signs (blood pressure, heart rate, respiratory rate, pulse oximetry, temperature)
- Should be monitored every 15 minutes for the first hour, then every 8 hours until completion of DHE treatment course for every dose

Supportive care medications to be given prior to DHE:

- 0.9% sodium chloride 20 mL/kg bolus (maximum dose= 1000 mL) over 1 hour prior to the **first dose** of DHE
- Diphenhydramine 0.5 mg/kg (maximum dose= 50 mg) IV and prochlorperazine 0.15 mg/kg (maximum dose=10 mg) IV 30 minutes prior to **each dose** of DHE excluding when DHE dose is given 1 hour apart
  - Metoclopramide 0.2 mg/kg (maximum dose=10 mg) may be used in the presence of an allergy to prochlorperazine
- Additional antiemetics may be ordered for increased nausea and vomiting

DHE administration:

- Must be administered using Equashield
- Does not require PICU admission or stepdown level of care for administration if clinical presentation is appropriate
- Infused over 15 minutes.
- If patient is experiencing intolerable side effects:
  - The infusion may be run over 30 minutes
  - The dose may be decreased or consider returning to last tolerated dose

Dosing:

Weight	Cyclic Vomiting	Migraines	Minimum Dose	Maximum Dose
< 25 kg	• 0.25 mg x 1 dose • 8 hours later, 0.5 mg every 8 hours	• 0.25 mg x 2 doses every 1 hour, then 0.5 mg IV every 8 hours	2.5 mg TOTAL	6 mg TOTAL
≥ 25kg	• 0.25 mg x 1 dose • 8 hours later, 0.5 mg x 1 dose • 8 hours later, 0.75 mg x 1 dose • 8 hours later, 1 mg every 8 hours	• 0.5 mg x 2 doses every 1 hour, then 1 mg IV every 8 hours	5 mg TOTAL	12 mg TOTAL

- Continue treatment until patient is headache-free
- DHE will be discontinued when either of the following occur:
  - Patient reaches maximum recommended dose with or without complete resolution of the headache
  - One additional dose may be given after resolution/improvement of headache/vomiting and/or improvement in function (even if not at the maximum dose), at the discretion of the attending physician

Expected response rate:

- 40% of patients reported to be headache free after completion of the 5th dose
- Of the remaining 60%, 67% were headache free after completion of the 12th dose
- Overall, 97% of patients showed improvement and 77% were headache free upon discharge from the hospital

Common side effects:

Side Effect	Response
Central Nervous System: initial worsening of headache, dizziness, paresthesia, leg cramps	-Ketorolac may be added for additional pain control -Patient should be considered a fall risk and have these safety measures in place
Cardiovascular: hypertension, tachycardia, vasospasms, chest tightness	-Elevated blood pressure may occur within the first 30-60 minutes of infusion -Notify provider if patient complains of chest tightness, provider may reduce the dose or prolong the infusion time
Gastrointestinal: Nausea/vomiting and diarrhea (most common side effect), abdominal cramping	-Add ondansetron 0.15 mg/kg (maximum dose=4 mg) as needed or consider additional antiemetics ordered

- **Notify the provider and stop the infusion if the following side effects occur:**
  - Chest pain
  - Severe nausea/vomiting
  - Shortness of breath
  - Systolic and diastolic blood pressure increases or decreases outside the parameters ordered by the provider for more than 60 minutes
  - Changes in mental status or neurological deficits
  - Peripheral ischemia (painful cramping and/or numbness and/or tingling)

References:

-Taketomo CK, Hodding JH, Kraus DM, eds. Pediatric and Neonatal Dosage Handbook. 23rd ed. Lexi-Comp. 2022.

-Kabbouche MA, et al. Inpatient treatment of status migraine with dihydroergotamine in children and adolescents. Headache 2009;49:106-9.

- Dihydroergotamine mesylate injection prescribing information. Valeant. August 2008. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/005929s044lbl.pdf