Antidote Use Guideline

New Jersey Poison Information and Education System [NJPIES] should be contacted for ALL toxin exposures at 1-800-222-1222.

The recommendations below are not meant to substitute for consultation with NJPIES. Table 1 outlines the appropriate dosing and primary indications for antidotes used at University Hospital. The antidote guidance starting on page 6 provides more detail on antidotes including pediatric dosing, additional indications, monitoring details, and additional guidance for antidote use.

Table 1: Antidote Basic Indications and Adult Dosing

Antidote	Indication	Standard Dose
N-Acetylcysteine (NAC) IV	Single, acute Acetaminophen overdose	• 150 mg/kg IV over 1 hour followed by • 50 mg/kg IV over 4 hours (12.5 mg/kg/hr) followed by • 100 mg/kg IV over 16 hours (6.25 mg/kg/hr) • **Dose adjustments and extended treatment may be needed (see in-depth antidote section below)**
Atropine	Cholinergic toxidromes	• 1-2 mg IV bolus for mild to moderate poisoning • 3-5 mg IV bolus for severe poisoning with unconsciousness • Double dose every 3-5 min until resolution of bronchorrhea (no maximum dose)
	Drug-induced symptomatic bradycardia	• 1 mg IV every 3 to 5 min; maximum total dose 3 mg
Calcium chloride	Calcium channel blocker or beta blocker	• 1 g IV over 10 mins (unless in extremis then infuse over 1 min) ○ May repeat every 10-20 minutes for 3-4 additional doses
Calcium gluconate	Calcium channel blocker or beta blocker	• 3 g IV over 10 mins ○ May repeat every 10-20 minutes for 3-4 additional doses
Calcium disodium edetate (EDTA)	Lead	• Encephalopathy: 1500 mg/m^2/day IV continuous infusion or 2-4 divided IV doses for 5 days (start 4 hours after dimercaprol) • Acutely ill with blood lead level (BLL) >100 mcg/dL (45 mcg/dL in pediatric patients): 1500 mg/m^2/day as continuous infusion or 2-4 divided IV doses for 5 days (start 4 hours after dimercaprol) • Specific indication and dosing should be discussed with medical toxicology

L-Carnitine	Valproic acid hyperammonemia and hepatotoxicity	• 100 mg/kg IV as a bolus over 30 mins (maximum bolus dose: 6 grams) followed by 15 mg/kg intermittent infusions over 10-30 minutes every 8 hours • Oral 50-100 mg/kg/day (max daily dose: 3 grams) **should not be used for acutely ill patients**. ○ If IV formulation is unavailable for acutely ill patients, giving the oral formulation via PO/NGT is acceptable
Crotalidae Polyvalent Immune Fab (CroFab)	Crotalidae envenomation	• Initial dose: 4-6 vials IV to be given as soon as possible (preferably within 6 hours of envenomation); continue to treat with 4-6 vial doses until patient is controlled (maximum initial dose is 12 vials) • Maintenance dose: 2 vials IV to be given every 6 hours for up to 18 hours; treatment may be continued if deemed necessary
Cyproheptadine	Serotonin syndrome	• 12 mg orally or via nasogastric (NG) tube followed by 2 mg every 2 hours or 4-8 mg every 6 hours as needed for symptom control
Dantrolene	Malignant hyperthermia	• Crisis: 2.5 mg/kg IV initially; give repeat doses of 2.5 mg IV every 15 mins until symptoms subside or a cumulative dose of 10 mg/kg is reached • Post-crisis follow-up and to prevent recurrence: 1 mg/kg IV every 4-6 hours for at least 24 hours

Deferoxamine	Iron	• 5 mg/kg/h IV starting dose, increase after 15 minutes if tolerated to 15 mg/kg/h
		  ○ After first 1 g is infused and symptoms improve, the dose may be reduced to infuse remainder of 6-8 g over next 23 hours
		  ○ Duration of therapy should be limited to 24 hours to maximize effectiveness while minimizing risk of pulmonary toxicity

	Aluminum	• 5-15 mg/kg/hr IV infused over several hours followed 6-8 hrs later by hemodialysis (occurs almost exclusively in patients with severe renal insufficiency) • Repeat infusions until symptoms of acute toxicity resolve
Digoxin immune fab	Cardiac glycoside (e.g. digoxin)	• Empiric acute toxicity: 10 vials • Empiric chronic toxicity: 3 vials • Known dose ingested: number of vials = (amount ingested, mg/0.5 mg/vial) x 0.8 ○ Fractioned vials should always be rounded up • Known digoxin level: Number of vials = (serum digoxin level, ng/mL x patient weight, kg)/100; fractions rounded up

Dimercaprol (BAL)	Lead	• Severe lead poisoning (defined as encephalopathy, acutely ill, and/or BLL >70 mcg/dL): 75 mg/m^2 IM every 4 hours for 5 days (give 4 hours before CaNa2EDTA)
	Arsenic	• 3 mg/kg IM every 4 hours for 48 hours followed by every 12 hours for 10 days or until complete recovery of severe poisoning
	Mercury	• 5 mg/kg IM once followed by 2.5 mg/kg every 12 to 24 hours until patient appears clinically stable, up to a total of 10 days
Fomepizole	Methanol/ ethylene glycol	• 15mg/kg IV loading dose followed in 12 hours by 10 mg/kg IV every 12 hours for 4 doses ○ HD dosing and dosing beyond 48 hours can be found within the in-depth antidote section below
Flumazenil	Benzodiazepine	• 0.1 mg IV over 1 minute; if the desired level of consciousness is not obtained 1 min after the dose, 0.2-0.3 IV mg can be given over 1 minute. Maximum cumulative total dose: 1 mg • **Not routinely recommend, see in-depth antidote section below**
Glucagon	Beta blocker	• 3-5 mg IV infusion over 3-10 minutes. If initial dose inadequate, a higher dose (up to 10 mg) is recommended ○ If patient improves, can repeat dose of 3-5 mg as needed or a continuous infusion of 2-5 mg/h tapered as patient improves and in conjunction with high dose insulin. Infusions up to 10mg/hr have been used
Glucarpidase	Methotrexate	• 50 units/kg as a single dose infused over 5 mins within 48-60 hours of the high dose MTX infusion
Hydroxocobalamin	Cyanide	• 5g IV over 15 minutes; may repeat an additional 5g IV over 15 minutes to 2 hours as needed, for a total dose of 10g
Insulin	Beta blocker or calcium channel blocker	• 1 unit/kg bolus IV followed by a continuous infusion at 1 unit/kg/hour titrated to clinical response • Doses up to 10 units/kg/hour
Leucovorin	Methotrexate	• 10 mg/m^2 Oral, IM, IV every 6 hours until MTX level is <0.01 umol. Increased dose may be indicated based on 24-hour creatinine and 24 and 48-hour MTX levels • For MTX overexposure (high dose) use leucovorin nomogram and dosing outlined below

Lipid Emulsion	Local anesthetic or impending cardiac arrest due to lipid soluble agent	20% lipid emulsion BOLUS • ≥ 70 kg: 100 mL over 2 min • < 70 kg: 1.5 mL/kg over 2 min Followed by: 20% lipid emulsion INFUSION • ≥ 70 kg: 250 mL over 15 min • < 70 kg: 0.25 mL/kg/min (continue until 10 mL/kg or 250 mL is infused, whichever value is less) • If circulatory stability is not attained, consider re-bolus
Methylene Blue	Methemoglobinemia	• 1 - 2 mg/kg IV over 5 minutes followed immediately by fluid flush of 15-30 mL to minimize local pain. • Dose can be repeated in 30-60 minutes, if necessary
Naloxone	Opioid	• Initial dose 0.02 - 0.04 mg IV; may need to repeat doses doubling dose every 2 to 3 minutes until sufficient respiratory drive is reestablished. • Intranasal spray: 1 spray (4mg) into one nostril as a single dose; may repeat every 2 to 3 minutes in alternating nostrils • Pediatric dosing: 0.1 mg/kg IV (if not opioid dependent)
Octreotide	Oral hypoglycemic (e.g. sulfonylurea)	• 50 mcg to 75 mcg SC/IV; repeat every 6 hours as needed based upon glucose concentrations
Physostigmine	Anticholinergic	• 0.5 mg to 2 mg IM/IV given no faster than 1 mg/min; may repeat every 10 to 30 minutes until response occurs

Pralidoxime chloride	Organophosphate	• Intravenous (IV)
		  ○ Loading dose: 30 mg/kg IV (maximum: 2000 mg) or 2000 mg given over 15-30 mins
		  ○ Maintenance dose: 8-10 mg/kg/hour (maximum: 650 mg/hour) or 500 mg/hour; duration of therapy should reflect the patient's clinical state
		• Intramuscular (IM)
		  ○ Mild symptoms: 600 mg; repeat as needed for persistent mild symptoms every 15 minutes to a maximum total dose of 1800 mg; may administer doses in rapid succession if severe symptoms develop
		  ○ Severe symptoms: 600 mg; repeat twice in rapid succession to deliver a total dose of 1800 mg
		  ○ Persistent symptoms: may repeat entire series (1800 mg) starting 1 hour after administration of the last injection

	Anticholinesterase overdose	• 1000-2000 mg IV; followed by increments of 250 mg every 5 minutes as neede

Pyridoxine HCl	Isoniazid (INH)	• Acute ingestion of KNOWN amount: Give pyridoxine dose equal to the amount of isoniazid ingested (maximum dose: 5 g IV) • Acute ingestion of UNKNOWN amount: initially 5 g (peds 70 mg/kg max 5g) IV • May repeat dose every 5-10 minutes as needed to control persistent seizure activity and/or CNS toxicity • **Oral pyridoxine should be used if IV pyridoxine is unavailable**
Sodium thiosulfate	Cyanide	• 12.5 g (50 mL) IV. Repeat administration at ½ the initial dose if toxicity persists or recurs • Sodium thiosulfate may be given after hydroxocobalamin (adjunct agent)
Sodium bicarbonate	Drug-induced wide complex dysrhythmia due to sodium channel blockade	• 1-2 mEq/kg IV (50-100 ml of sodium bicarbonate 8.4%) bolus over 1-2 minutes • Repeat boluses until improvement of ECG and hemodynamics, then begin an infusion of 150 mEq/L at 150-250 mL/h
	Urine alkalinization	• 150 mEq/L IV infused at 150-200 mL/h for a goal urine pH 7.5-7.55
Succimer	Lead, arsenic, or mercury	• 10 mg/kg oral every 8 hours for 5 days ○ Followed by 10 mg/kg/dose orally every 12 hours for 14 days
Thiamine	Wernicke encephalopathy treatment and prevention	• 500 mg IV every 8 hours until improvement in mental status or neurologic abnormality and tolerating a normal diet
Uridine Triacetate	Fluorouracil	• 1 packet (10 g) orally every 6 hours for 20 doses; mix with soft food and follow with water

Antidotes

N-Acetylcysteine (NAC)

Indication

- Acute acetaminophen (APAP) overdose
- Repeated supratherapeutic acetaminophen ingestion (RSTI)
- Fulminant hepatic failure due to acetaminophen overdose or other hepatotoxic toxins
- Ingestion of toxic amanita species of mushrooms

Mechanism of Action

- Replenishes glutathione stores by providing cysteine residues, increases hepatic perfusion, and acts directly as an antioxidant and free radical scavenger

Dosage Forms

- IV solution (Acetadote®)
- Oral solution (Mucomyst®)

Dose

- Standard dose / Serum [APAP] < 300 mcg/mL
    - IV: 150 mg/kg over 1 hour, followed by 50 mg/kg over 4 hours (12.5 mg/kg/hr), and then 100 mg/kg over 16 hours (6.25 mg/kg/hr)
    - Oral: 140 mg/kg load followed by 70 mg/kg x 6 doses every 4 hours
- Serum [APAP] 300-600 mcg/mL (High dose)
    - IV: 150 mg/kg over 1 hour, followed by 12.5 mg/kg/hr over at least 20 hours OR
    - Give standard infusion rate PLUS oral NAC (140mg/kg initial dose, followed by 70mg/kg every 4 hours)
- Serum [APAP] > 600 mcg/mL (High dose)
    - IV: 150 mg/kg over 1 hour, followed by 25 mg/kg/hr over at least 20 hours
    - Give standard infusion rates PLUS oral NAC (140mg/kg initial dose, followed by 70mg/kg every 4 hours)

Monitoring and Adverse Effects

- IV: anaphylactoid reactions can occur, especially during the first hour of drug administration. This is usually related to the rate of infusion. Symptoms can include flushing, vomiting, erythema, urticaria, wheezing, shortness of breath, angioedema, and very rarely hypotension and death. In the event of a reaction, slowing the rate of infusion is usually helpful. Treatment of anaphylactoid reactions may need to be initiated (diphenhydramine). In serious reactions, NAC infusions may be temporarily held and carefully restarted after treatment. Contact NJ Poison Control Center if assistance is needed.
- Oral: nausea, vomiting

Other important considerations

- The IV and oral routes of NAC are equally efficacious in prevention and treating APAP toxicity.
- The Rumack-Matthew nomogram is only validated in acute ingestions when EXACT time of ingestion is confirmed with a reasonable degree of certainty and the product is not an extended release or combination formulation.
- Nomogram cannot be used for levels obtained within 4 hrs of ingestion.
- NAC therapy should be continued beyond the prescribed course if there is evidence of hepatic injury (AST >1,000 IU/L or >50% of peak, PT/INR >2x normal or encephalopathy is present) or APAP metabolism is incomplete (APAP detectable).

- Discontinuation based on the patient's condition: for patients who develop hepatic failure, continue NAC until PT/INR <2x normal and encephalopathy, if present, is resolved; for patients without hepatic failure but with elevated AST, continue until AST decreasing and <50% of peak, or AST/ALT ratio < 0.4.

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. Wolters Kluwer Clinical Drug Information, Inc. (Lexi-Drugs). Wolters Kluwer Clinical Drug Information, Inc.; Accessed November 8, 2019
3. IWK Regional Poison Centre (2015). Antidote Acetylcysteine. Retrieved from https://iwkpoisoncentre.ca/acetylcysteine-pediatric.html
4. Bailey B, McGuigan MA: Management of anaphylactoid reactions to intravenous N-acetylcysteine. Ann Emerg Med June 1998;31: 710-715
5. Chiew AL, Isbister GK, Kirby KA, Page CB, Chan BSH, Buckley NA. Massive paracetamol overdose: an observational study of the effect of activated charcoal and increased acetylcysteine dose (ATOM-2). Clin Toxicol (Phila). 2017;55(10):1055-1065a

Atropine Sulfate

Indication

- Reversal of cholinergic toxidromes due to organophosphates, carbamate insecticide, nerve agent poisoning or muscarine-containing mushroom poisoning
- Drug-induced symptomatic bradycardia

Mechanism of Action

- Competitive antagonist of the muscarinic acetylcholine receptor

Dosage Forms

- IV solution

Dose

- Reversal of cholinergic toxidromes due to organophosphates, carbamate insecticide, nerve agent poisoning, or muscarine-containing mushroom poisoning
    - Adults: Initial dose of 1-2 mg IV bolus for mild to moderate poisoning and 3 to 5 mg IV bolus for severe poisoning with unconsciousness. Double dose every 3-5 min until resolution of bronchorrhea
        - In severe poisonings requiring a large dose of atropine, administer 10-20% of total loading dose required to induce the desired response diluted in 0.9% sodium chloride as a continuous IV infusion per hour. Adjust as needed to maintain adequate response without atropine toxicity.
    - Pediatrics: Initial dose of 0.02-0.1 mg/kg mg IV bolus for mild to moderate poisoning and 3 to 5 mg IV bolus for severe poisoning with unconsciousness. Double dose every 5-10 min until atropinization (decreased secretions and/or wheezing, dry flushed skin, tachycardia, mydriasis, fever)
        - In severe poisonings requiring a large dose of atropine, administer 10-20% of total loading dose required to induce the desired response as a continuous IV infusion per hour; adjust as needed to maintain adequate response without atropine toxicity.
- Drug-induced symptomatic bradycardia
    - Adults: 1 mg IV every 3 to 5 min; maximum total dose 3 mg

- Pediatrics: 0.02 mg/kg up to adult doses (depending on age) every 3-5 mins; maximum total dose of 0.5 mg in young children and 3 mg in older children

Monitoring and Adverse Effects

- Dry mouth, decreased sweat, tachycardia, respiratory depression, delirium, and hyperthermia (typically do not appear in treatment of cholinergic toxidromes until many milligrams are administered)
- Paradoxical bradycardia with slow or low dose injections (<0.5 mg)

Other important considerations

- IV boluses of atropine may also be given IO, IM, or ET
  - AtroPen Auto-Injector is a prefilled syringe designed for IM injection by an autoinjector into the outer thigh available in 4 strengths: 0.25 mg, 0.5 mg, 1 mg and 2 mg
  - Also available as an IM injection in a kit packaged with a pralidoxime injector for nerve agent exposures.
- Atropine is only effective for the treatment of muscarinic effect of poisoning and will not reverse nicotinic poisoning (muscular weakness, diaphragmatic weakness, etc.).
- In organophosphate insecticide and nerve agent toxicity, atropine should be administered in conjunction with pralidoxime.

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. Wolters Kluwer Clinical Drug Information, Inc. (Lexi-Drugs). Wolters Kluwer Clinical Drug Information, Inc.; Accessed November 12, 2019
3. IWK Regional Poison Centre (2015). Antidote Atropine. Retrieved from https://iwkpoisoncentre.ca/atropine-pediatric.html

Calcium Disodium Edetate (EDTA)

Indication

- Chelator used for the management of patients with severe lead poisoning (acutely ill and/or blood lead concentrations >70 mcg/dL) in conjunction with dimercaprol (British anti-Lewisite {BAL}).

Mechanism of Action

- Direct chelator of heavy metal ions inactivating them and allowing increased urinary excretion

Dosage Forms

- IV solution

Dose

- Adults:
  - Encephalopathy: 1500 mg/m^2/d in D5%W or 0.9% NaCl as continuous infusion or 2-4 divided IV doses for 5 days (start 4 hours after dimercaprol)
  - Acutely ill with BLL >100 mcg/dL: 1500 mg/m^2/d as continuous infusion or 2-4 divided IV doses for 5 days (start 4 hours after dimercaprol)
  - Mild symptoms or BLL 45-70 mcg/dL: Treatment with succimer monotherapy is recommended

- Pediatrics:
    - Encephalopathy: 1500 mg/m^2/d as continuous infusion or 2-4 divided IV doses for 5 days (start 4 hours after dimercaprol)
    - Symptomatic (without encephalopathy) or >69 mcg/dL: 1000-1500 mg/m^2/d as continuous infusion or 2-4 divided IV doses for 5 days (start 4 hours after dimercaprol)
    - Asymptomatic and 45-69 mcg/dL: Treatment with succimer monotherapy is recommended

Monitoring and Adverse Effects

- Major nephrotoxicity, including renal tubular necrosis, can occur, possibly due to the release of lead in the kidneys during excretion.
    - Ensure urine flow prior to administration and adequate ongoing hydration during treatment
    - Monitor urine output, proteinuria, serum creatinine and BUN during administration
    - Nephrotoxicity is minimized by decreasing the dose (limit totally daily dose to 1 g in children or 2 g in adults in non-encephalopathic cases) or maintaining good hydration
- Mild increases in AST/ALT, decreases in alkaline phosphatase, and extravasation resulting in development of painful calcinosis at injection site.
- Supplementation with multivitamin containing zinc is recommended
- Other adverse events (uncommon): malaise, fatigue, thirst, chills, fever, myalgia, headache, anorexia, urinary frequency and urgency, sneezing, nasal congestion, lacrimation, glycosuria, anemia, transient hypotension, increased prothrombin time and inverted T waves on ECG.

Other important considerations

- Substitution with sodium EDTA (Na2EDTA) for lead chelation is NOT recommended due to the potential for life-threatening hypocalcemia.

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. Wolters Kluwer Clinical Drug Information, Inc. (Lexi-Drugs). Wolters Kluwer Clinical Drug Information, Inc.; Accessed November 12, 2019

Calcium (Gluconate/Chloride)

Indication

- Hypotension and bradycardia due to calcium channel blocker or beta blocker overdose
- Hypocalcemia secondary to ethylene glycol, hydrofluoric acid and fluoride-releasing exposures, phosphate exposures and citrate toxicity
- Pain due to hydrofluoric acid dermal exposures

Mechanism of Action

- Overwhelms calcium channel receptor blockade and provides additional calcium for muscle fiber contraction in cardiac and vascular myocytes

Dosage Forms

- IV calcium chloride (contains 27.3 mg [1.36 mEq) of elemental calcium per mL)
- IV calcium gluconate (contains 9.5 mg [0.464 mEq] or elemental calcium per mL)

- Calcium gluconate 2.5% jelly (commercially available or can be prepared by combining 35 mL of 10% calcium gluconate solution, 3.5 g of calcium gluconate powder, or 10 g calcium carbonate powder with 5 oz of water-based lubricating jelly)

Dose

- Hypotension and bradycardia due to calcium channel blocker or beta blocker overdose
    - Adults:
        - Calcium gluconate: 3 g/dose administered IV over 10 mins (unless in extremis then administer over 1 min). May repeat every 10-20 minutes for 3-4 additional doses or initiate a continuous infusion of 60-120 mg/kg/hour titrated to improve hemodynamics in conjunction with other therapies
        - Calcium chloride: 1 g/dose administered IV over 10 mins (unless in extremis then infuse over 1 min). May repeat every 10-20 minutes for 3-4 additional doses.
    - Pediatrics:
        - Calcium gluconate: 60 mg/kg (0.6 mL/kg) of 10% solution infused over 5-10 mins (unless in extremis then infuse over 1 minute). May repeat every 10-20 mins for 3-4 additional doses.
        - Calcium chloride: 20 mg/kg (0.2 mL/kg) infused over 5-10 mins (unless in extremis then infuse over 1 min). May repeat every 10-20 mins for 3-4 additional doses.

- Hydrofluoric acid burns
    - Topical: Massage 2.5% calcium gluconate jelly into affected area until pain has subsided. If pain persists after 15 to 30 minutes, consider other routes of administration
        - Calcium gluconate 2.5% jelly (commercially available or can be prepared by combining 35 mL of 10% calcium gluconate solution, 3.5 g of calcium gluconate powder, or 10 g calcium carbonate powder with 5 oz of water-based lubricating jelly)
    - Subcutaneous: 5 to 10% solution; 0.5 mL/cm2 of burned tissue
    - Bier block: Add 10 mL of 10% calcium gluconate in a total volume of 40 mL and infuse into a vein distal to a blood pressure cuff inflated to 100 mmHg above systolic pressure. Maintain ischemia for 20-25 mins then slowly deflate the cuff over 5 mins.
    - Intra-arterial: Add 10mL of 10% solution to 50 mL D5W. Infused over 4 hours into artery that provides vascular supply to affected area. Extreme care should be taken and should only be performed by experienced practitioners in order to avoid extravasation.
    - Inhalation: Mix 1.5 mL of 10% calcium gluconate solution with 4.5 mL NS to make a 2.5% solution and administered via nebulization.

Monitoring and Adverse Effects

- Rapid administration can lead to vasodilation, hypotension, bradycardia, dysrhythmias, syncope and cardiac arrest
- Infusion rates of 200 mg/min is not recommended except in the case of life-threatening hypocalcemia, a slow IV push is reasonable

Other important considerations

- Calcium gluconate is preferred for peripheral administration because extravasation of calcium chloride causes higher incidences of tissue necrosis
    - Extravasation management: if extravasation occurs, stop infusion immediately and disconnect (leaving needle/cannula in place): gently aspirate extravasated solution (do NOT flush line)
        - In some cases, hyaluronidase may be needed
- Neither calcium chloride or calcium gluconate should be combined and administered IV with sodium bicarbonate because calcium carbonate, a precipitate will form

    - If using the same line, flush line twice after calcium before administering bicarbonate and vice versa
- Calcium gluconate is not compatible with fluids containing phosphate and will result in precipitation if mixed

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. Wolters Kluwer Clinical Drug Information, Inc. (Lexi-Drugs). Wolters Kluwer Clinical Drug Information, Inc.; Accessed November 12, 2019
3. Graudins A, Burns MJ, Aaron CK. Regional intravenous infusion of calcium gluconate for hydrofluoric acid burns of the upper extremity. Ann Emerg Med. 1997 Nov;30(5):604-7. doi: 10.1016/s0196-0644(97)70076-3. PMID: 9360569.

L-Carnitine

Indication

- Valproic acid-induced hyperammonemia and hepatotoxicity

Mechanism of Action

- Replenishes carnitine in valproic acid poisoned cells, thereby shunting VPA metabolism away from the production of the toxic metabolites causing disruption of the urea cycle and hepatic injury

Dosage Forms

- [Carnitor®, Carnitor SF®, G-levOCARNitine S/F® (OTC), McCarnitine® (OTC)]
- Generic available for all forms except intravenous
    - Oral capsules
    - Oral solution
    - Oral tablet
    - Intravenous solution

Dose

- Adults
    - IV: 100 mg/kg as an IV bolus over 30 mins (maximum bolus dose: 6 grams) followed by 15 mg/kg intermittent infusions over 10-30 minutes every 8 hours
    - Oral 50-100 mg/kg/day (max daily dose: 3 grams) **should not be used for acutely ill patients**.
        - If IV formulation is unavailable for acutely ill patients, giving the oral formulation via PO/NGT is acceptable
- Pediatrics
    - IV: 100 mg/kg as an IV bolus over 30 mins (max bolus dose: 6 grams) followed by 15 mg/kg intermittent infusions over 10-30 every 4 hours

Monitoring and Adverse Effects

- Obtain valproic acid concentrations every 4-6 hours until a decreasing trend is observed
- Monitor blood ammonia concentration, platelets, serum lactate, electrolytes, hepatic function
- PO: serious hypersensitivity reactions (rash, urticaria, facial edema) were reported - discontinue drug, supportive care
- IV: hypertension, nausea, vomiting, diarrhea, dizziness, and headaches are common. Seizures - serious, but uncommon

- Serious hypersensitivity reactions (anaphylaxis, laryngeal edema, bronchospasm) were reported - discontinue drug, supportive care

References

1. Howland M. Vitamin K1. In: Nelson LS, Howland M, Lewin NA, Smith SW, Goldfrank LR, Hoffman RS. eds. Goldfrank's Toxicologic Emergencies, 11e New York, NY: McGraw-Hill
2. Levocarnitine [monograph]. In: Lexicomp Online [online database]. Hudson, OH: Lexi-Comp.
3. Levocarnitine [monograph]. In: Micromedex [online database]. Greenwood Village, CO: Truven Health Analytics.

Crotalidae polyvalent immune fab (CroFab)

Indication

- Crotalid (pit viper) envenomation resulting in:
    - Severe or progressing swelling beyond a major joint and/or coagulopathy and/or hypotension

Mechanism of Action

- Antibody fragment that binds and inactivates crotalid venoms

Dosage Forms

- IV solution (CroFab®)

Dose

- Adult and Pediatric
    - Initial dose: 4-6 vials IV to be given as soon as possible (preferably within 6 hours of envenomation); continue to treat with 4-6 vial doses until patient is controlled (maximum initial dose is 12 vials)
    - Maintenance dose: 2 vials IV to be given every 6 hours for up to 18 hours; treatment may be continued if deemed necessary

CONTRAINDICATIONS

- Hypersensitivity to any component of the formulation (including papaya or papain), unless benefits outweigh the risks and anaphylaxis management is readily available

Monitoring and Adverse Effects

- Adverse effects
    - Dermatologic: pruritis, rash, and urticaria
    - Gastrointestinal: nausea
    - Hematologic: recurrent blood coagulation disorder
    - Immunologic: anaphylaxis and acute/delayed hypersensitivity reaction
    - Musculoskeletal: backache
    - Other: infusion reaction
- Monitoring
    - Monitor for up to 1 hour following infusion to determine if initial control has been achieved (arrest of local signs of envenomation, improvement of fibrinogen, platelets, PT/INR)
    - Monitor CBC, platelet count, PT, aPTT, fibrinogen levels, fibrin split products, clot retraction, bleeding and coagulation times, BUN, electrolytes, bilirubin; swelling of bite area (every 15-30 minutes); intake and output; signs and symptoms of anaphylaxis/allergy; signs and symptoms of delayed allergic reactions or serum sickness

Other Important Considerations

- Antivenom dosage is based on venom load and symptom severity, not on patient size
- Adults: administer over 60 minutes at 10 mL/hour for the first 5 minutes. If no allergic reaction observed, double the rate every few mins increasing to goal rate of 250 mL/hour. Subsequent doses may be given at the rate of 250 mL/hr if well-tolerated.
- Pediatrics: administer over 60 minutes at 10 mL/hour for the first 5 minutes. If no allergic reaction observed, double the rate every few mins increasing to goal rate of 250 mL/hour. Subsequent doses may be given at the rate of 250 mL/hr if well-tolerated.
- Vials should be refrigerated (do NOT freeze)
- Vials should used within 4 hours of reconstitution
- Each vial is reconstituted with 18 mL NS and mixed with continuous manual inversion until no solid material is visible (do NOT shake); contents of the reconstituted vials are further diluted to a total volume of 250 mL with NS (swirl gently to mix)
    - Lower infusion volumes (total volume of 125 mL with NS) can be used in pediatrics and fluid sensitive populations (congestive heart failure, chronic lung disease, or renal insufficiency)
    - Reconstitution with 25 mL SWFI and hand rolling/inverting may result in shorter dissolution times and allow for more rapid administration

References

1. Crotalidae polyvalent immune FAB [monograph]. In: Lexicomp Online [online database]. Hudson, OH: Lexi-Comp.
2. Crotalidae polyvalent immune FAB [monograph]. In: Micromedex [online database]. Greenwood Village, CO: Truven Health Analytics.
3. Pizon AF, Ruha A. Antivenom for North American Venomous Snakes (Crotaline and Elapid). In: Nelson LS, Howland M, Lewin NA, Smith SW, Goldfrank LR, Hoffman RS. eds. Goldfrank's Toxicologic Emergencies, 11e New York, NY: McGraw-Hill.

Cyproheptadine

Indication

- Serotonin syndrome (off-label)

Mechanism of Action

- Potent competitive antagonist of 5-HT_2 serotonin receptors as well as H_1 histamine receptors

Dosage Forms

- Oral syrup, oral tablet

Dose

- Adults
    - Initially 12 mg orally followed by 2 mg every 2 hours or 4-8 mg every 6 hours as needed for symptom control

CONTRAINDICATIONS

- Use in newborn/premature infants/breast-feeding mothers; hypersensitivity to cyproheptadine or any component of the formulation; monoamine oxidase inhibitor therapy; angle-closure glaucoma; stenosing peptic ulcer; symptomatic prostatic hypertrophy; bladder neck obstruction; pyloroduodenal obstruction; elderly, debilitated patients

Monitoring and Adverse Effects

- Adverse effects
    - Endocrine-metabolic: increased appetite and weight gain
    - Gastrointestinal: abdominal discomfort, diarrhea, nausea, vomiting, and xerostomia
    - Hepatic: hepatitis
    - Neurologic: central nervous system depression and somnolence
    - Respiratory: thick bronchial sputum
- Monitoring
    - Monitor for excess anticholinergic effects at beginning and periodically throughout; monitor for drowsiness, fatigue, dry mouth, nausea, and GI upset

Other Important Considerations

- Please discuss use with Medical Toxicology Service as evidence is insufficient for routine use. Benzodiazepines are first line treatment
- Avoid use in the elderly; significant confusion, constipation, and urinary retention
- No renal dose adjustments, but elimination is diminished in renal insufficiency
- Oral syrup needs to be protected from light

References

1. Cyproheptadine [monograph]. In: Lexicomp Online [online database]. Hudson, OH: Lexi-Comp.
2. Cyproheptadine [monograph]. In: Micromedex [online database]. Greenwood Village, CO: Truven Health Analytics.
3. Stork CM. Serotonin Reuptake Inhibitors and Atypical Antidepressants. In: Nelson LS, Howland M, Lewin NA, Smith SW, Goldfrank LR, Hoffman RS. eds. Goldfrank's Toxicologic Emergencies, 11e New York, NY: McGraw-Hill.

Dantrolene

Indication

- Malignant hyperthermia

Mechanism of Action

- Antagonist of the ryanodine receptor decreasing calcium release from the sarcoplasmic reticulum, thereby inhibiting calcium-mediated muscle contraction

Dosage Forms

- IV suspension (Ryanodex®)
- IV solution (Dantrium® intravenous/Revonto®) **(NOT ON UH FORMULARY)**

Dose

- Adult
    - Malignant hyperthermia
        - Crisis (MHAUS recommendation): 2.5 mg/kg IV initially; monitor and give repeat doses of 2.5 mg/ every 15 mins until symptoms subside or a cumulative dose of 10 mg/kg is reached
        - Post-crisis follow-up and to prevent recurrence (MHAUS recommendation): 1 mg/kg every 4-6 hours for at least 24 hours.

- Pediatric
    - Malignant hyperthermia
        - Crisis (MHAUS recommendation): 2.5 mg/kg IV initially; monitor and give repeat doses of 2.5 mg/ every 15 mins until symptoms subside or a cumulative dose of 10 mg/kg is reached
        - Post-crisis follow-up and to prevent recurrence (MHAUS recommendation): 1 mg/kg every 4-6 hours for at least 24 hours.

CONTRAINDICATIONS

- IV: no contraindications listed in manufacturer's labeling
- Oral: active hepatic disease (e.g., cirrhosis, hepatitis)

Monitoring and Adverse Effects

- **Black Box Warning**
    - Oral formulation has potential for hepatotoxicity; symptomatic hepatitis has been reported; risk is greater in females, patients >35 years, and in those taking concurrent medications
- Adverse effects
    - Cardiovascular: heart failure and tachycardia
    - Dermatologic: flushing
    - Gastrointestinal: diarrhea, nausea, dysphagia, and gastrointestinal hemorrhage
    - Hematologic: aplastic anemia, leukopenia, small lymphocytic lymphoma, and thrombocytopenia
    - Immunologic: anaphylaxis
    - Musculoskeletal: muscle weakness
    - Neurologic: somnolence
    - Other: fatigue and malaise
    - Respiratory: dyspnea, respiratory muscle weakness, and reduced inspiratory vital capacity
- Monitoring
    - Patient should be observed in an ICU for at least 24 hours for recrudescence
    - Monitor for arrhythmias, vital signs (including core temperature), electrolytes, ABG, CK, end tidal CO_2 ($EtCO_2$)/capnography, urine output, and urine myoglobin

Other Important Considerations

- Discontinue all malignant hyperthermia-triggering agents (e.g., volatile anesthetics, succinylcholine) once crisis is recognized and administer supportive care
- Vesicant; ensure proper needle or catheter placement prior to and during infusion; avoid extravasation
- Injection powder for reconstitution should be protected from light; reconstituted solution should be used within 6 hours of preparation
- Do NOT reconstitute with non-bacteriostatic water for injection
- Discuss use with Medical Toxicology Service if considering use for severe, life-threatening neuroleptic malignant syndrome

References

1. Dantrolene [monograph]. In: Lexicomp Online [online database]. Hudson, OH: Lexi-Comp.
2. Dantrolene [monograph]. In: Micromedex [online database]. Greenwood Village, CO: Truven Health Analytics.
3. Guo CJ, Sutin KM. Dantrolene Sodium. In: Nelson LS, Howland M, Lewin NA, Smith SW, Goldfrank LR, Hoffman RS. eds. Goldfrank's Toxicologic Emergencies, 11e New York, NY: McGraw-Hill.

Deferoxamine

Indication

- Chelation of iron in patients with any of the following findings due to iron toxicity:
    - Repetitive vomiting
    - Toxic appearance
    - Lethargy
    - Hypotension accompanied by metabolic acidosis or signs of shock
    - Any patients with serum iron concentrations above 500 mcg/dL
- Chelation of aluminum in patients with acute or chronic aluminum toxicity based on symptoms or significantly elevated aluminum concentrations

Mechanism of Action

- Direct binding of heavy metal ions inactivating them and allowing increased urinary excretion

Dosage Forms

- IV solution

Dose

- Iron Toxicity
    - Adults: 5 mg/kg/h starting dose, increase after 15 minutes if tolerated to 15 mg/kg/h
        - After first 1 g is infused and symptoms improve, the dose may be reduced to infuse remainder of 6-8 g over next 23 hours
        - Duration of therapy should be limited to 24 hours to maximize effectiveness while minimizing risk of pulmonary toxicity
    - Pediatrics: 20 mg/kg (maximum dose: 1,000 mg) administered no faster than 15 mg/kg/hour followed by 10 mg/kg (maximum dose: 500 mg) over 4-hour intervals for 2 doses; subsequent doses of 10 mg/kg (maximum dose: 500 mg) over 4 to 12 hours may be repeated depending upon the clinical response; maximum daily dose: 6 g/day
    - Renal impairment: For CrCl 10-30 mL/min or CRRT, administer 25 to 50% of normal dose
- Aluminum Toxicity
    - Occurs almost exclusively in patients with severe renal insufficiency
    - 5-15 mg/kg/hr infused over several hours followed 6-8 hrs later by hemodialysis
    - Repeat infusions until symptoms of acute toxicity resolve

Monitoring and Adverse Effects

- Rate-related systemic hypersensitivity, including flushing of skin, urticarial, hypotension and shock
    - Deferoxamine should be administered by slow intravenous infusion
- Ocular and auditory disturbances; including blurring of vision, visual loss, optic neuritis, cataracts, retinal pigmentary abnormalities, tinnitus and hearing loss; have been reported with administration over prolonged periods of time, at high doses or in patients with low ferritin levels.
    - Serial ophthalmological and audiological testing should be performed if symptoms noted and then as necessary
        - In most cases, disturbances are reversible upon immediate detection and cessation of treatment.
- Pulmonary toxicity, including acute respiratory distress syndrome (ARDS) have been reported.
- Increases in serum creatinine (possible dose-related), acute renal failure and renal tubular disorders have been reported.

    - Monitor for changes in renal function.
    - Adequate urine output is required to excrete the deferoxamine-iron complex. If oliguria or anuria develop, dialysis may be required
- Infections, including Yersinia spp. and Mucormycosis (with long-term dosing for iron overload)
- Local irritation, pain, burning, swelling, infiltration; arthralgia, fever, headache, myalgia, nausea, vomiting, abdominal pain, asthma, hypotension from rapid infusion
- Monitor urine for vinrose appearance, can be diagnostic if an iron level is not available

Other important considerations

- Because of the limited amount of iron that can be chelated by deferoxamine, aggressive GI decontamination should accompany its use in iron overdose
- Duration of therapy for iron toxicity should be limited to 24 hours to maximize effectiveness while minimizing risk of pulmonary toxicity
- Reddish discoloration of the urine will occur as chelated iron is being excreted.

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. Wolters Kluwer Clinical Drug Information, Inc. (Lexi-Drugs). Wolters Kluwer Clinical Drug Information, Inc.; Accessed November 12, 2019
3. IWK Regional Poison Centre (2015). Antidote Deferoxamine. Retrieved from https://iwkpoisoncentre.ca/deferoxamine-adult.html

Digoxin-specific Fab (DigiFab)

Indication

- Life-threatening, or potentially life-threatening acute or chronic toxicity from any cardioactive steroids (CASs) including digoxin, digitoxin, ouabain, and those derived from dogbane, oleander, squill, Bufo toad, and Birgus crab species
    - Evidence of cardiotoxicity
    - Acute ingestion with a potassium concentration >5.5 mEq/L in adults or >6 mEq/L in children

Mechanism of Action

- Antibody fragment that binds and inactivates digoxin and related molecules

Dosage Forms

- IV solution for reconstitution (DigiFab©)

Dose

- Empiric dosing:

	Acute Ingestion	Chronic Toxicity
Adult	10 vials	3 vials
Children	10 vials	2 vials

- Known dose ingested: Number of vials = (amount ingested, mg/0.5 mg/vial) x 0.8
    - Fractioned vials should always be rounded up

- Known digoxin level: Number of vials = (serum digoxin level, ng/mL x patient weight, kg)/100
    - Fractioned vials should always be rounded up

Monitoring and Adverse Effects

- Administration of exogenous calcium for hyperkalemia as a direct result of digoxin toxicity IS NOT RECOMMENDED
- Atrial fibrillation (with rapid ventricular rate) or worsening congestive heart failure (due to digoxin withdrawal); hypokalemia; phlebitis, postural hypotension related to infusion; hypersensitivity reactions
- Vital signs, EKG and serum potassium should be monitored before and after DSFab administration
    - Improvement in signs and symptoms of digoxin toxicity usually begin within ≤30 minutes following DSFab administration with maximum effect in 4 hours
    - Digoxin levels should ONLY be drawn before DSFab administration
        - It is not recommended to check digoxin levels after DSFab administration as most laboratories are not equipped to determine free serum concentrations.
        - Serum concentrations may be misleading until digoxin-bound Fab fragments are eliminated from the body
        - Elimination is variable depending on renal function
    - Additional administration of DSFab should be guided by clinical response (EKG, vital signs)

Other important considerations

- Serum digoxin concentrations do not correlate with myocardial concentrations until 4-6 hours after ingestion, when an equilibrium from the serum to the myocardium is achieved
    - However, serum concentrations ≥10 ng/mL sooner after an acute ingestion may predict need for treatment with DSFab
- Older adults are at greatest risk of lethality with digoxin poisoning and treatment threshold for patients >60 years old recommended to be lower

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. Wolters Kluwer Clinical Drug Information, Inc. (Lexi-Drugs). Wolters Kluwer Clinical Drug Information, Inc.; Accessed November 18, 2019
3. IWK Regional Poison Centre (2015). Antidote Digoxin Immune Fab. Retrieved from https://iwkpoisoncentre.ca/digoxin-immune-fab-adult.html

Dimercaprol (British Anti-Lewisite or BAL)

Indication

- Treatment of lead encephalopathy and severe lead poisoning in conjunction with edetate calcium disodium
- Treatment of arsenic and mercury poisoning with compromised GI tract (in place of oral succimer)

Mechanism of Action

- Direct chelator of heavy metal ions inactivating them and allowing increased urinary excretion

Dosage Forms

- Solution for IM injection only: unintentional IV administration can theoretically produce fat embolism, lipoid pneumonia, chylothorax, and associated hypoxia

Dose

- Severe lead poisoning (defined as encephalopathy, acutely ill, and/or BLL >70 mcg/dL): 75 mg/m^2 IM every 4 hours for 5 days (give 4 hours before CaNa2EDTA)
- Arsenic poisoning: 3 mg/kg IM every 4 hours for 48 hours followed by every 12 hours for 10 days or until complete recovery of severe poisoning
- Mercury poisoning: 5 mg/kg IM once followed by 2.5 mg/kg every 12 to 24 hours until patient appears clinically stable, up to a total of 10 days

Monitoring and Adverse Effects

- Dimercaprol is formulated in peanut oil; determine peanut allergy and conduct risk-benefit analysis before administration.
- Pain at injection site
- With higher doses: fever; hypertension; tachycardia; nausea; vomiting; headache; burning sensation of lips, mouth, throat and eyes; lacrimation; rhinorrhea; salivation; muscle aches; burning and tingling of extremities; tooth pain; diaphoresis; chest pain; anxiety; and agitation
- Patients at risk of G6PD deficiency syndromes should be monitored carefully for hemolysis
- Dimercaprol is a relatively nonspecific chelator and can bind metals other than those desired, thus, causing essential metal deficiencies

Other important considerations

- Patients receiving dimercaprol should be alkalinized with sodium bicarbonate to a urinary pH 7.5-8.0 to prevent dissociation of the dimercaprol-metal chelate which occurs in acidic urine
- Doses above 5 mg/kg not recommended because of high risk of adverse reactions
    - Doses above 25 mg/kg often result in hypertensive encephalopathy with convulsions and coma
- Use is contraindicated in hepatotoxicity (unless hepatotoxicity is arsenic induced)
- Iron supplementation during dimercaprol administration should be avoided because limited evidence suggestions dimercaprol-iron complex causes severe vomiting and decreases metal chelation

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. Wolters Kluwer Clinical Drug Information, Inc. (Lexi-Drugs). Wolters Kluwer Clinical Drug Information, Inc.; Accessed November 18, 2019

Flumazenil

Indication

- Reversal for pure benzodiazepine overdose in a nontolerant individual who has CNS depression, normal vital signs (including SaO2), normal ECG findings and otherwise normal neurologic examination
    - Also effective for the overdoses of zolpidem and zaleplon
- Generally not necessary unless there is a question regarding prognosis or for diagnostic certainty and prognostication

Mechanism of Action

- Competitively inhibits the activity at the benzodiazepine receptor site on the GABA/benzodiazepine receptor complex

Dosage Forms

- IV solution

Dose

- Adults: initial dose of 0.1 mg over 1 minute; if the desired level of consciousness is not obtained 1 min after the dose, 0.2-0.3 mg can be given over 1 minute. Maximum cumulative total dose: 1 mg
    - In the event of resedation consider infusion of 0.1 mg-1 mg/hr titrated to effect
- Pediatrics: 0.01 mg/kg (maximum dose: 0.2 mg) with repeat doses of 0.01 mg/kg (maximum dose: 0.2 mg) given every minute to a maximum total cumulative dose of 1 mg
    - As an alternative to repeat bolus doses, continuous infusions of 0.005-0.01 mg/kg/hour may be considered

CONTRAINDICATIONS

- Seizure history or current treatment of seizures; ingestion of a xenobiotic capable of provoking seizures or cardiac dysrhythmias; long-term use of benzodiazepines; potential ECG evidence of cyclic antidepressants use: terminal rightward 40-ms axis; QRS or QT prolongation; head trauma
- Hypotension and hypoxia should be corrected prior to flumazenil use
    - Do not rely on flumazenil to reverse benzodiazepine-induced respiratory depression

Monitoring and Adverse Effects

- Due to short duration of flumazenil, resedation from benzodiazepine may occur
- Pay precipitate benzodiazepine withdrawal symptoms in patients on long-term benzodiazepines (anxiety, agitation, tachycardia, dizziness, diaphoresis, seizures)
- Nausea; vomiting; flushing; hypertension and tachycardia (transient); may cause agitation, anxiety and fear; pain at injection site

Other important considerations

- Risks of flumazenil administration rarely outweigh the benefits in patients with overdoses. Risks are limited in only non-benzodiazepine-dependent patients with sole ingestion of benzodiazepines in overdoses
- Resedation following flumazenil is expected to occur between 20 and 120 minutes. Readministration may be necessary

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. Wolters Kluwer Clinical Drug Information, Inc. (Lexi-Drugs). Wolters Kluwer Clinical Drug Information, Inc.; Accessed November 18, 2019
3. IWK Regional Poison Centre (2015). Antidote Flumazenil. Retrieved from https://iwkpoisoncentre.ca/flumazenil-pediatric.htm

Fomepizole

Indication

- Treatment of toxic ingestions of methanol and ethylene glycol. Indications for treatment include:
    - Serum methanol or ethylene glycol concentration >20 mg/dL (methanol >6 mmol/L; ethylene glycol >3 mmol/L)
    - Documented history of ingestion and osmol gap >20 mOsm or osmol gap >50 mosm without other explanation
    - Strong clinical suspicion of ingestion and anion gap metabolic acidosis with/without acute kidney injury, hypocalcemia, oxalate crystalluria, or vision changes
- May potentially also be used for the treatment of: terminating adverse reactions resulting from co-administration of disulfiram and ethanol; limiting toxicity of exposure to other substances metabolized by alcohol dehydrogenase including diethylene glycol and glycol ethers)
- **OFF LABEL USE**: adjunct treatment with N-acetylcysteine for massive acetaminophen overdose. Fomepizole inhibits the CYP2E1 pathway of APAP metabolism, thus preventing conversion of APAP into NAPQI (the hepatotoxic metabolite of APAP). Contact NJPIES prior to use for this indication

Mechanism of Action

- Potent competitive antagonist of the alcohol dehydrogenase enzyme, thereby preventing conversion of alcohols to their toxic metabolites

Dosage Forms

- IV solution

Dose

- 15mg/kg IV loading dose followed in 12 hours by 10 mg/kg every 12 hours for 4 doses
    - If therapy is necessary beyond 48 hours, dose is then increased to 15 mg/kg every 12 hours for as long as necessary because fomepizole stimulates its own metabolism
    - Continue therapy until serum toxic alcohol concentration is predicted or measured ≤35 mg/dL in the absence of any acid-base disturbances
- The following dose adjustments are recommended during hemodialysis:

○ Fomepizole is dosed every 4 hours

    - At time of hemodialysis initiation:
        - If last fomepizole dose <6 hours earlier, do not administer another dose prior to initiating hemodialysis
        - If last dose ≥6 hours, administer fomepizole at the beginning of hemodialysis
    - At time of hemodialysis completion:
        - If >3 hours have passed since last dose, administer next scheduled dose
        - If 1-3 hours have passed, administer ½ of dose
        - Following hemodialysis, resume every 12 hours dosing schedule

Monitoring and Adverse Effects

- Headache, nausea, dizziness, increased drowsiness, dysgeusia or metallic taste, phlebitis, rash, fever and eosinophilia

Other important considerations

- Fomepizole is a potent inhibitor of alcohol dehydrogenase (ADH) and should be preferred over ethanol. However, ethanol may be easier to deploy, particularly in prehospital settings, mass poisonings or resource-poor settings.
    - Fomepizole will inhibit the metabolism of ethanol, and vice versa

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. Barceloux DG, Bond GR, Krenzelok EP, Cooper H, Vale JA. American Academy of Clinical Toxicology practice guidelines on the treatment of methanol poisoning. J Toxicol Clin Toxicol 2002;40(4):415-446.
3. Barceloux DG, Krenzelok EP, Olson K, Watson W. American academy of clinical toxicology practice guidelines on the treatment of ethylene glycol poisoning. Jf Toxicol Clin Toxicol 1999;37(5):537-560.
4. IWK Regional Poison Centre (2015). Antidote Fomepizole. Retrieved from https://iwkpoisoncentre.ca/fomepizole-adult.html

Glucagon

Indication

- Treatment of hypotension, bradycardia or conduction defects due to beta-blocker or calcium channel blocker toxicity in conjunction with other agents (i.e. IV fluids, vasopressors, high-dose insulin)

Mechanism of Action

- Stimulates β adrenergic activity while bypassing the β receptor itself by directly affecting adenylate cyclase

Dosage Forms

- IV solution

Dose

- Adults: 3-5 mg IV infusion over 3-10 minutes. If initial dose inadequate, a higher dose (up to 10 mg) is recommended.
    - If patient improves, can repeat dose of 3-5 mg as needed or a continuous infusion of 2-5 mg/h tapered as patient improves and in conjunction with high dose insulin. Infusions up to 10mg/hr have been used
- Pediatrics: 0.05 mg/kg IV over 1-2 minutes (not to exceed 1 mg/min). If vomiting is a concern, consider administering over 10-20 minutes.
    - Continuous infusion: 0.05-0.1 mg/kg/hour

Monitoring and Adverse Effects

- Nausea and vomiting (high incidence with rapid administration of large doses), hyperglycemia, hypoglycemia, hypokalemia. Rarely urticaria, respiratory distress and hypotension.

Other important considerations

- Nausea and vomiting can be limited by diminishing the initial dose, rate of infusion or both
- Tachyphylaxis (loss of drug effect) is common with repeated doses and infusions

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.

2. Wolters Kluwer Clinical Drug Information, Inc. (Lexi-Drugs). Wolters Kluwer Clinical Drug Information, Inc.; Accessed November 25, 2019
3. IWK Regional Poison Centre (2015). Antidote Glucagon. Retrieved from https://iwkpoisoncentre.ca/glucagon-pediatric.html

Glucarpidase

Indication

- MTX toxicity in adults & children, defined as concentrations >1 umol/L in the presence of impaired kidney function induced by MTX and delayed drug clearance (concentration >2 SD above the excretion curve)
- Intrathecal MTX overdose (limited data)

Ordering

- If considering use, please contact central pharmacy as soon as possible to facilitate ordering as these medications are not kept in stock. If both oncology and toxicology agree that medication is needed, please contact the Main Pharmacy at 2-5120. If emergent ordering in needed during nights, holidays, or weekends please contact the Main Pharmacy and have them reach out to the Pharmacy Supervisor.

Mechanism of Action

- Enzymatically hydrolyzes circulating MTX to less toxic glutamate and DAMPA metabolites

Dosage Forms

- Intravenous, reconstituted solution: 1000 units per each vial; no generic available (Voraxaze®)

Dose

- Always flush IV line before and after administration
- 50 units/kg as a single dose infused over 5 mins within 48-60 hours of the high dose MTX infusion
- A second dose within 48 hours is not recommended
- Continue IV hydration and urinary alkalization as appropriate
- Intrathecal MTX overdose:
- 2000 units administered intrathecally over 5 mins as soon as possible after MTX overdose
- Give within 3-9 hours of intrathecal MTX overdose along with lumbar drainage or ventriculolumbar perfusion

Monitoring and Adverse Effects

- Monitor serum MTX levels using chromatographic method for the first 48 hours from glucarpidase administration
    - Because DAMPA metabolite interferes with immunoassay results until >48 hours
- Rebound increase in MTX levels may occur 48 hours post glucarpidase treatment
- Continue to monitor methotrexate levels
- Hypotension, flushing, headache, paresthesia, nausea, and vomiting are common
    - Hypersensitivity reaction is not common

Other important Information

- Leucovorin calcium is a potential substrate for glucarpidase and must be administered at least 2 hours before or after glucarpidase administration
- IV administration: each vial is to be reconstituted in 1 mL of NS with gentle mixing, no shaking
- Intrathecal: each 2000 units is to be reconstituted in 12mL of NS with gentle mixing

References
1. Howland M. Vitamin K1. In: Nelson LS, Howland M, Lewin NA, Smith SW, Goldfrank LR, Hoffman RS. eds. Goldfrank's Toxicologic Emergencies, 11e New York, NY: McGraw-Hill
2. Glucarpidase [monograph]. In: Lexicomp Online [online database]. Hudson, OH: Lexi-Comp.
3. Glucarpidase [monograph]. In: Micromedex [online database]. Greenwood Village, CO: Truven Health Analytics.

Hydroxocobalamin

Indication
- Cyanide poisoning from hydrogen cyanide gas, ingestion of cyanide salts, or high dose nitroprusside infusion
- Cardiac arrest or hypotension in a fire victim
- Lactate >10 in a fire victim or >9 in a person who reports ingestion of a cyanide containing agent

Dosage Forms
- IV powder for reconstitution

Mechanism of Action
- Rapidly combines with cyanide to form nontoxic cyanocobalamin (B_{12})

Dose
- Cyanide poisoning:
    - Adults
        - 5g IV over 15 minutes; may repeat an additional 5g IV over 15 minutes to 2 hours as needed, for a total dose of 10g
    - Pediatrics (limited data available)
        - IV/Intraosseous: 70mg/kg (maximum 5g/dose) as a single infusion; a second dose of 70mg/kg (maximum 5g/dose) may be repeated depending on severity of poisoning and clinical response

Monitoring and Adverse Effects
- Blood pressure and heart rate should be monitored during and after the infusion. Serum lactate levels, venous-arterial PO2 gradients should be monitored. Renal function (BUN and SCr) should be monitored for at least 7 days following therapy.
- Erythema, rash, nausea, headache, dizziness, urine discoloration, hypertension (transient), infusion site reactions
- Lab interference
- Colorimetric assays may be adversely affected; some clinical chemistry laboratory tests are falsely elevated, decreased, or unpredictable. Hemoglobin, MCH, MCHC, and basophils may be falsely increased. Coagulation tests are unpredictable. False increases in COHb may be seen; draw bloods prior to administration whenever possible . Hemodialysis machines may sound a false “blood leak” alarm.

Other important considerations
- 5 g vial of hydroxocobalamin must be reconstituted with 200mL NS, D5W, or LR
- Drug should be protected from light during storage
- Can cause skin and mucous membrane redness persisting up to 2 weeks - advise patient to avoid sunlight as drug may cause photosensitivity
- Rash can develop anytime between 7 and 28 days after drug administration but is self-limited.

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. IWK Regional Poison Centre (2015). Antidote Hydroxycobalamin. Retrieved from https://iwkpoisoncentre.ca/hydroxocobalamin-adult.html
3. Hydroxycobalamin. DrugPoints Summary. Micromedex 2.0. Truven Health Analytics, Inc. Greenwood Village, CO. Available at: http://www.micromedexsolutions.com. Accessed December 4, 2019

Insulin

Indication

- Non-dihydropyridine calcium channel blocker toxicity, dihydropyridine calcium channel blocker toxicity with evidence of cardiotoxicity, or beta-blocker overdose/toxicity (off-label use)

Mechanism of Action

- Stimulates release of calcium from the sarcoplasmic reticulum with or without functional calcium channels; provides cardiac myocytes enhanced access to glucose; increases coronary microcirculation

Dosage Forms

- Solution for injection (100 units/mL)
- High dose infusion (2500 units/ 250 ml)

Dose

- IV: 1 unit/kg bolus followed by a continuous infusion at 1 unit/kg/hour titrated to clinical response
    - Titrate 1 unit/kg/h every 15 min to max of 10 units/kg/hr until shock improves
    - *Some sources suggest an absolute max of 22 units/kg/hr*
- Start a dextrose infusion when insulin therapy is initiated to maintain euglycemia
    - 0.5 g/kg dextrose bolus if blood glucose (BG) ≤300 mg/dL + 0.5 g/kg/hr continuous dextrose infusion
    - **Initiate prior to insulin to avoid hypoglycemia**

Monitoring and Adverse Effects

- Monitor blood glucose every 15 minutes until unchanged and then hourly
- Monitor potassium every 1 hour until unchanged and then every 4-6 hours
- Correct hypokalemia prior to initiation of insulin therapy
- Hypokalemia should be treated based on severity, max rate of repletion with peripheral line 10 meq/hr
- Monitor magnesium and phosphorous 1 hour after starting insulin and then every 4-6 hours
- Volume overload may occur in long-term infusions or with multiple additional drug infusions
- Hypersensitivity reaction

Other important considerations

- Insulin may require additional concentration to avoid volume overload
- Refer to the calcium chloride and calcium gluconate sections for dosing and monitoring instructions for use in calcium channel blocker and beta block overdose

References

1. Howland M. Vitamin K1. In: Nelson LS, Howland M, Lewin NA, Smith SW, Goldfrank LR, Hoffman RS. eds. Goldfrank's Toxicologic Emergencies, 11e New York, NY: McGraw-Hill
2. Insulin Regular [monograph]. In: Lexicomp Online [online database]. Hudson, OH: Lexi-Comp.
3. Insulin Regular [monograph]. In: Micromedex [online database]. Greenwood Village, CO: Truven Health Analytics.

Leucovorin

Indication

- IV and oral methotrexate toxicity
- Adjunctive cofactor therapy for methanol toxicity (off-label)

Dosage Forms

- Solution for injection, reconstituted solution, oral tablets; generics available

Mechanism of Action

- Directly provides reduced form of folate to cells, thereby bypassing the inhibited dihydrofolate reductase step of DNA synthesis
- Enhances the oxidation of the toxic methanol metabolite formic acid to CO_2 and H_20

Dose

- MTX overdose
    - Oral, IM, IV: 10 mg/m^2 every 6 hours until MTX level is <0.01 µmol. Increased dose may be indicated based on 24-hour creatinine and 24 and 48-hour MTX levels
- MTX overexposure (high dose) using leucovorin nomogram
    - At 24 hours, if levels are:
        - >/= 100 µmol give 1000 mg/m^2 IV every 6 hours
        - >/= 10 to <100 µmol give 100mg/m^2 IV every 3 hours or 6 hours
        - >/=1 to 10 µmol give 10 mg/m^2 IV or PO every 3 or 6 hours
    - At 48 hours, if levels are:
        - >/= 100 µmol give 1000 mg/m^2 IV every 6 hours
        - >/= 10 to <100 µmol give 100mg/m^2 IV every 3 hours
        - >/=1 to 10 µmol give 100mg/m^2 IV every 6 hours OR 10 mg/m^2 IV or PO to 100 mg/m^2 IV every 3 hours
    - At 72 hours, if levels are:
        - >/= 10 µmol give 100 to 1000 mg/m^2 IV every 3 to 6 hours
        - >/=1 to 10 µmol give 10 mg/m^2 IV or orally to 100 mg/m^2 IV every 3 hours
        - ~0.1 to 1 µmol give 10 mg/m^2 IV or orally every 3 to 6 hours
- Methanol toxicity, adjunctive cofactor therapy
    - IV: 1 mg/kg over 30 to 60 minutes every 4 to 6 hours. Therapy should continue until methanol and formic acid have been eliminated .

CONTRAINDICATIONS

- Pernicious or megaloblastic anemias due to vitamin B12 deficiency

Monitoring and Adverse Effects

- Measure MTX levels as needed based on leucovorin dosing; discontinue leucovorin when MTX levels are < 0.01 µmol
- GI symptoms (diarrhea, nausea, vomiting, stomatitis) and fatigue are common
- An allergic reaction is not common

Other important considerations

- Leucovorin calcium is a potential substrate for glucarpidase and must be administered at least 2 hours before or after glucarpidase administration
- If SCr is increased by 50%, increase standard dose to 100 mg/m^2 IV every 4 hours, then adjust leucovorin dosing according to MTX level
- For adjunctive treatment of methanol poisoning folic acid can be used in place of leucovorin

References

1. Howland M. Vitamin K1. In: Nelson LS, Howland M, Lewin NA, Smith SW, Goldfrank LR, Hoffman RS. eds. Goldfrank's Toxicologic Emergencies, 11e New York, NY: McGraw-Hill
2. Leucovorin Calcium [monograph]. In: Lexicomp Online [online database]. Hudson, OH: Lexi-Comp.
3. Leucovorin Calcium [monograph]. In: Micromedex [online database]. Greenwood Village, CO: Truven Health Analytics.

Lipid Emulsion

Indication

- Local anesthetic toxicity
- Serious hemodynamic instability secondary to highly lipid soluble substances; for patients not responsive to fluids, vasopressors, inotropes (Off-label)

Dosage Forms

- Intravenous emulsion

Mechanism of Action

- Provides a lipid sink for the adsorption of circulating lipid-soluble xenobiotics; provides a lipid shuttle pulling lipid-soluble xenobiotics out of vascular tissues and moving them into muscle and liver for storage and metabolism; provides a source of fatty acid-based energy directly to cardiac myocytes

Dose

20% lipid emulsion BOLUS

- ≥ 70 kg: 100 mL over 2 min
- < 70 kg: 1.5 mL/kg over 2 min

Followed by:

20% lipid emulsion INFUSION

- > 70 kg: 250 mL over 15 min
- < 70 kg: 0.25 mL/kg/min (continue until 10 mL/kg or 250 mL is infused, whichever value is less)

If circulatory stability is not attained, consider rebolus

CONTRAINDICATIONS

- Hypersensitivity to fish, egg, soybean proteins, peanut proteins or any components of the product
- Severe hemorrhagic disorders
- Severe hyperlipidemia (serum triglyceride greater than 1000 mg/dL), or severe disorders of lipid metabolism characterized by hypertriglyceridemia
- Abnormal fat metabolism, including pathological hyperlipidemia, lipid nephrosis, or acute pancreatitis with hyperlipidemia

Monitoring and Adverse effects

- Acute pancreatitis, fat emboli, Hypertriglyceridemia, hypersensitivity reaction, elevated triglycerides, hyperglycemia, bradyarrhythmia, nausea, vomiting, flatulence, viral infection, apnea, and agitation. Pulmonary edema, hepatic impairment, hemorrhage, sepsis, fat overload syndrome are serious but not common
- Monitor serum triglycerides, metabolic, hepatic, and renal function

References

1. Neal, Joseph M et al. "The Third American Society of Regional Anesthesia and Pain Medicine Practice Advisory on Local Anesthetic Systemic Toxicity: Executive Summary 2017." Regional anesthesia and pain medicine vol. 43,2 (2018): 113-123. doi:10.1097/AAP.0000000000000720
2. Howland M. Vitamin K1. In: Nelson LS, Howland M, Lewin NA, Smith SW, Goldfrank LR, Hoffman RS. eds. Goldfrank's Toxicologic Emergencies, 11e New York, NY: McGraw-Hill
3. Lipid Emulsion [monograph]. In: Lexicomp Online [online database]. Hudson, OH: Lexi-Comp.
4. Lipid Emulsion [monograph]. In: Micromedex [online database]. Greenwood Village, CO: Truven Health Analytics.

Methylene Blue

Indication

- Treatment of patients with symptomatic methemoglobinemia (typically methemoglobin levels >20%)
- Drug-related vasoplegia (off-label)

Mechanism of Action

- Enhances reduction of Fe^{3+} back to functional Fe^{2+}; reduces oxidant stressInhibits guanylate cyclase decreasing cGMP, thereby preventing vascular relaxation

Dosage Forms

- IV solution

Dose

- Methemoglobinemia: 1 – 2 mg/kg IV over 5 minutes followed immediately by fluid flush of 15-30mL to minimize local pain. Dose can be repeated in 30-60 minutes, if necessary, based on clinical signs and symptoms and a consequential methemoglobin level
    - If no effect after 2 sequential doses of 1 mg/kg, then subsequent dosing should be halted and diagnosis should be reexamined or the possibility of severe G6PH deficiency considered.
- The dose of methylene blue for refractory hypotension is not established. Doses of 1-3 mg/kg increase systemic vascular resistance and mean arterial pressure and improve tissue oxygenation.
    - Although doses of 7 mg/kg may produce further increases in mean arterial pressure, this result is associated with a decrease in splanchnic blood flow

CONTRAINDICATIONS

- Hypersensitivity to methylene blue, patients with glucose-6-phosphate dehydrogenase deficiency (G6PD) due to the risk of hemolytic anemia

Monitoring and Adverse Effects

- **BBW**: Methylene blue may cause serious or fatal serotonergic syndrome when used in combination with serotonergic drugs. Avoid concomitant use of methylene blue with selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs) and monoamine oxidase inhibitors. If drugs with serotonin reuptake inhibition properties are being taken, careful consideration needs to be given to stop them before methylene blue injectable use, to allow a washout period equivalent to at least 4-5 half-lives. **In acute methemoglobinemia the risk of not treating the patient must be weighed against the possibility of the development of serotonin syndrome. Consult NJ Poison Control Center as necessary.**
- Extremity pain, chromaturia, dysgeusia, dizziness, feeling hot, dizziness, diaphoresis, nausea, skin discoloration, headache, back pain, shortness of breath, tachypnea, chest discomfort, burning sensation of the mouth and stomach, initial bluish tinged skin and mucous membranes, paresthesias, restlessness, apprehension, tremors, dysuria, and excitation.
- IV methylene blue is irritating and painful. It may cause local tissue damage even in the absence of extravasation. Subcutaneous and intrathecal administrations are contraindicated.
- Patients with G6PD deficiency may not reduce methylene blue to its active form and may not be effective in these cases.
- Methylene blue is also contraindicated for use in patients with G6PD deficiency due to concerns of severe hemolysis and anemia. There are reports of the development of body hemolytic anemia in young infants without G6PD deficiency who received doses of methylene blue as low as 4mg/kg
- Methylene blue will transiently alter pulse oximeter readings. Large doses often interfere with the ability to detect a clinical decrease in cyanosis; therefore, repeat cooximetery measurements and arterial or venous blood gas analysis should be used in conjunction with clinical findings to evaluate improvement
- Methylene blue interferes with photometric lab tests including blood gas analysis. Repeat testing should be delayed until 1 hour after administration
- Reports of paradoxical induction of methemoglobinemia have occurred with excessively large or inappropriate doses

Other important considerations

- Methylene blue can be diluted in 50 mL of 5% dextrose in water to decrease the risk of local pain
- Sodium chloride should not be used for dilution because the chloride may decrease the solubility of methylene blue

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. Wolters Kluwer Clinical Drug Information, Inc. (Lexi-Drugs). Wolters Kluwer Clinical Drug Information, Inc.; Accessed November 25, 2019
3. IWK Regional Poison Centre (2015). Antidote Methylene Blue. Retrieved from https://iwkpoisoncentre.ca/glucagon-pediatric.html
4. PROVAYBLUE (Methylene Blue) [package insert]. Fontenay sous Bois, France; PROVEPHARM SAS; Revised 04/30/2016

Naloxone

Indication

- Reversal of opioid-induced respiratory depression

Dosage Forms

- Injection solution
- Intranasal spray

Mechanism of Action

- Potent competitive antagonist of the μ opioid receptor

Dose

- Opioid overdose:
    - IV solution: initial dose 0.02 - 0.04 mg; may need to repeat doses doubling dose every 2 to 3 minutes until sufficient respiratory drive is reestablished.
    - Intranasal spray: 1 spray (4mg) into one nostril as a single dose; may repeat every 2 to 3 minutes in alternating nostrils
- Reversal of respiratory depression with therapeutic opioid doses:
    - IV solution: initial 0.02mg to 0.2mg; titrate to avoid profound withdrawal, seizures, arrhythmias, or severe pain

Monitoring and Adverse Effects

- Monitor efficacy by checking for reduction in respiratory depression utilizing end-tidal CO2 capnometry.
- Monitor patient for recurrence of symptoms 1 hour after last dose of naloxone or after infusion is stopped. Monitor for recurrence of symptoms during the weaning process for infusions.
- Monitor patient for delayed effects of opioid reversal (pulmonary edema, aspiration) for 4-6 hours after administration
- Erythema at injection site, dizziness, headache, nausea, vomiting

Other important considerations

- Use of naloxone in opioid dependent patients poses a risk of precipitating acute withdrawal
- If more than 4 doses of naloxone (doubling each dose) are given without satisfactory effect, diagnosis should be reexamined, or mixed overdose suspected
- Naloxone infusions are rarely necessary. Please discuss with medical toxicology service if considering use.

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. IWK Regional Poison Centre (2015). Antidote Naloxone Hydrochloride. Retrieved from https://iwkpoisoncentre.ca/naloxone-hydrochloride-adult.html
3. Naloxone. DrugPoints Summary. Micromedex 2.0. Truven Health Analytics, Inc. Greenwood Village, CO. Available at: http://www.micromedexsolutions.com. Accessed December 6, 2019

Octreotide

Indication

- Hypoglycemia due to acute or chronic sulfonylurea toxicity refractory to dextrose and PO intake

Dosage Forms

- IV solution

Mechanism of Action

- Decreases insulin release from pancreatic β-islet cells by reducing intracellular calcium flow via the somatostatin receptor

Dose

- Adults:
    - SubQ/IV: initial 50 mcg to 100 mcg; repeat every 6 hours as needed based upon glucose concentrations for a total of 24 hours
    - IV: Doses of up to 125 mcg/hr have been used successfully
- Pediatrics:
    - SubQ: 1 mcg/kg/dose to 1.25 mcg/kg/dose every 6 hours; repeat as needed based upon blood glucose concentrations
- Indications and dosing for octreotide have not firmly been established. Subcutaneous administration is the preferred route; however, IV bolus and IV infusions have been described in the literature. Repeat dosing, dose escalations, and initiation of continuous infusions may be necessary for patients experiencing recurrent hypoglycemia. Treatment duration may exceed 24 hours

Monitoring and Adverse Effects

- Sinus bradycardia, hypertension, fatigue, headache, dizziness, pain, hyperglycemia, abdominal distress, diarrhea, loose stools, nausea, constipation, injection site irritation, hypokalemia, hyperkalemia, anaphylactoid reactions, hypertension, apnea.
- Monitor blood glucose frequently during treatment

Other important considerations

- Administer in conjunction with adequate dextrose infusion or oral intake (superior if/when possible) to maintain euglycemia
- Avoid boluses of high concentration dextrose unless altered mental status or seizures
- Stored in the refrigerator
- Protect ampules from light

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. IWK Regional Poison Centre (2015). Antidote Octreotide. Retrieved from https://iwkpoisoncentre.ca/octreotide-adult.html
3. Octreotide. DrugPoints Summary. Micromedex 2.0. Truven Health Analytics, Inc. Greenwood Village, CO. Available at: http://www.micromedexsolutions.com. Accessed December 6, 2019

Physostigmine

Indication

- Reversal of toxic anticholinergic effects

Dosage Forms

- IM, IV solution

Mechanism of Action

- Reversibly inhibits acetylcholinesterase, thereby increasing the amount of acetylcholine in the neuronal synaptic clefts

Dose

- Adults: IM, IV initial: 0.5 mg to 2 mg given no faster than 1 mg/min; may repeat every 10 to 30 minutes until response occurs
- Pediatric: IM, IV initial: 0.02 mg/kg given no faster than 0.5 mg/min; may repeat every 5 to 10 minutes until response occurs; maximum total dose: 2 mg/dose

CONTRAINDICATIONS

- Do not administer in patients with hemodynamic instability, pathologically widened QRS, seizures, or anticholinergic syndrome resulting from TCA overdose
- Gastrointestinal or genitourinary obstructions; asthma; gangrene; diabetes; cardiovascular disease; co-administration of choline esters and depolarizing neuromuscular-blocking agents
- Physostigmine should not be used in the absence of an anticholinergic agent toxicity

Monitoring and Adverse Effects

- Monitor ECG
- May induce cholinergic effects such as bradycardia, salivation, urinary incontinence, diarrhea, diaphoresis, vomiting. May also cause ataxia, dizziness, tremors, anxiety, arrhythmias, coma, and seizures

Other important considerations

- Atropine should be readily available to reverse effects of physostigmine if necessary

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. Physostigmine. DrugPoints Summary. Micromedex 2.0. Truven Health Analytics, Inc. Greenwood Village, CO. Available at: http://www.micromedexsolutions.com. Accessed December 11, 2019

Potassium Iodide

Indication

- Thyroid block following nuclear radiation emergency including pregnant/lactating women

Dosage Forms

- Oral solution and tablet

Mechanism of Action

- Provides a source of non-radioactive iodine for thyroid hormone synthesis, thereby reducing the risk of thyroid cancer in those exposed to radiation

Dose

- Antidote for nuclear radiation emergency
    - Adults: 130 mg once daily
    - Infants and Children ≤3 years: 32.5 mg once daily
    - Children >3 to 12 years: 65 mg once daily
    - Adolescents:
        - Weight <68 kg: 65 mg once daily
        - Weight ≥68 kg: 130 mg once daily
    - Continue treatment for 10 to 14 days or as directed by public officials (until risk of exposure has passed or other measures are implemented)

CONTRAINDICATIONS

- Dermatitis herpetiformis; hypocomplementemic vasculitis, nodular thyroid condition with heart disease

Monitoring and Adverse Effects

- Thyroid function tests, EKG, potassium levels especially in renally impaired patients
- Metallic taste or burning in the mouth and throat, or sore teeth and gums, cardiac arrhythmias, muscle weakness, rhinitis, fatigue

Other important considerations

- Pediatric Administration
    - SSKI: Dilute with a large quantity of water, fruit juice, milk, or broth; take with food or milk to decrease gastric irritation
    - Iosat, Thyrosafe, Thyroshield: Take as soon as possible after instructed to do so by public officials
    - Take every 24 hours; do not take more than 1 dose in 24 hours
    - Tablets may be crushed and mixed with water, low fat milk (white or chocolate), orange juice, soda (flat), raspberry syrup, or infant formula

References

1. Howland M. Vitamin K1. In: Nelson LS, Howland M, Lewin NA, Smith SW, Goldfrank LR, Hoffman RS. eds. Goldfrank's Toxicologic Emergencies, 11e New York, NY: McGraw-Hill
2. Potassium Iodide [monograph]. In: Lexicomp Online [online database]. Hudson, OH: Lexi-Comp.
3. Potassium Iodide [monograph]. In: Micromedex [online database]. Greenwood Village, CO: Truven Health Analytics.

Pralidoxime (2-PAM)

Indication

- Organophosphate poisoning (e.g., pesticides and nerve agents)
- Anticholinesterase overdose (e.g., neostigmine, pyridostigmine)

Dosage Forms

- Pralidoxime chloride
    - IM solution
    - IV solution

Mechanism of Action

- Reactivates acetylcholinesterase enzymes by accepting phosphorylation by the organophosphate in place of the enzyme, thereby preventing permanent acetylcholinesterase inactivation

Dose

- Adult
    - Organophosphate poisoning (e.g., pesticides and nerve agents)
        - Intravenous (IV)
            - Loading dose: 30 mg/kg (maximum: 2000 mg) or 2000 mg given over 15-30 mins
            - Maintenance dose: 8-10 mg/kg/hour (maximum: 650 mg/hour) or 500 mg/hour; duration of therapy should reflect the patient's clinical state
        - Intramuscular (IM)
            - Mild symptoms: 600 mg; repeat as needed for persistent mild symptoms every 15 minutes to a maximum total dose of 1800 mg; may administer doses in rapid succession if severe symptoms develop
            - Severe symptoms: 600 mg; repeat twice in rapid succession to deliver a total dose of 1800 mg
            - Persistent symptoms: may repeat entire series (1800 mg) starting 1 hour after administration of the last injection
    - Anticholinesterase overdose (e.g., neostigmine, pyridostigmine)
        - 1000-2000 mg IV; followed by increments of 250 mg every 5 minutes as needed
- Pediatric
    - Organophosphate poisoning
        - Intravenous (IV)
            - Loading dose of 20-50 mg/kg (maximum dose: 2,000 mg/dose)
            - Maintenance dose 10-20 mg/kg/hour (maximum dose 650 mg/hr)
        - Intramuscular (IM)
            - Infants, children, and adolescents <40 kg:
                - Mild symptoms: 15 mg/kg/dose IM; repeat as needed for persistent mild symptoms every 15 minutes (maximum total dose: 45 mg/kg); may administer doses in rapid succession if severe symptoms develop
                - Severe symptoms: 15 mg/kg/dose IM; repeat twice in rapid succession to deliver a total dose of 45 mg/kg
                - Persistent symptoms: may repeat the entire series (45 mg/kg IM in 3 divided doses) beginning 1 hour after administration of the last injection

- Children and adolescents ≥40 kg:
    - Mild symptoms: 600 mg IM; repeat as needed for persistent mild symptoms every 15 minutes (maximum total dose: 1800 mg); may administer doses in rapid succession if severe symptoms develop
    - Severe symptoms: 600 mg IM; repeat twice in rapid succession to deliver a total dose of 1800 mg
    - Persistent symptoms: may repeat the entire series (1800 mg IM in 3 divided doses) beginning 1 hour after administration of the last injection

CONTRAINDICATIONS

- No absolute contraindications

Monitoring and Adverse Effects

- Adverse effects: cardiac arrest, increased creatine kinase level, seizure, apnea and laryngeal spasm

- Monitoring: Heart rate, respiratory rate, muscle fasciculations and strength, pulse oximetry; cardiac monitor and blood pressure monitor required for IV administration

Other Important Considerations

- Pralidoxime not indicated for poisoning by carbamates
- There is a relative contraindication for hypersensitivity to pralidoxime or any component of the formulation

References

1. Pralidoxime [monograph]. In: Lexicomp Online [online database]. Hudson, OH: Lexi-Comp.
2. Pralidoxime [monograph]. In: Micromedex [online database]. Greenwood Village, CO: Truven Health Analytics.
3. Howland M. Pralidoxime. In: Nelson LS, Howland M, Lewin NA, Smith SW, Goldfrank LR, Hoffman RS. eds. Goldfrank's Toxicologic Emergencies, 11e New York, NY: McGraw-Hill.

Prussian Blue

Indication

- Enhance elimination of cesium and thallium in the gastrointestinal tract

Dosage Forms

- 0.5 g oral powder in gelatin capsule

Mechanism of Action

- Binds cesium and thallium in the gastrointestinal tract, thereby preventing systemic absorption

Dose

- Adults and adolescents:
    - 3 g orally 3 times daily for a minimum of 30 days
- Pediatrics 2-12 years old:
    - 1 g orally 3 times daily for a minimum of 30 days
- Alternative dosing:
    - 150-250 mg/kg/day for all groups due to low concern for toxicity

Monitoring and Adverse Effects

- Decreased motility, constipation , bluing of mucosa, teeth, sweat, tears, and stool may occur
- Monitor for hypokalemia, especially in patients with arrhythmias or electrolyte abnormalities
- Obtain cesium/thallium concentrations prior to initiation and radioactivity in urine and fecal samples weekly throughout therapy
- Monitor CBC and electrolytes weekly

Other important considerations

- For cesium poisoning, base duration on weekly measurement of urine and fecal radioactivity
- For thallium poisoning, continue therapy until a normal 24-hour urine thallium test results and the radiation level is acceptable
- Administer with food, may open capsule and mix with bland food
- Activated charcoal may be effective for thallium, but not cesium poisoning

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. Prussian Blue. Micromedex 2.0. Truven Health Analytics, Inc. Greenwood Village, CO. Available at: http://www.micromedexsolutions.com. Accessed January 9, 2020

Pyridoxine (Vitamin B6)

Indication

- Adjunctive therapy for ethylene glycol poisoning (off-label)
- Gyromitrin-containing mushroom poisoning (and other hydrazine poisoning) (off-label)
- Neurological toxicities (i.e., seizures, coma) associated with isoniazid toxicity (off-label)

Dosage Forms

- Injection solution
- Oral capsule
- Oral tablet
    - **Oral pyridoxine should be used if IV pyridoxine is unavailable**

Mechanism of Action

- Replenishes pyridoxine in poisoned cells, thereby restoring the ability to convert glutamate to GABA and halting seizure activity
- Increases conversion of the toxic ethylene glycol metabolite glyoxylic acid to nontoxic glycine

Dose

- <u>Adult</u>
    - Adjunctive therapy for ethylene glycol poisoning (off-label)
        - 100 mg/day IV (oral*) until resolution of intoxication
    - Gyromitrin-containing mushroom poisoning (and other hydrazine poisoning) (off-label)
        - 25 mg/kg IV (oral*) over 15-30 minutes; repeat dose as needed to control seizures
    - Neurological toxicities (i.e., seizures, coma) associated with isoniazid overdose (prevention/treatment) (off-label)

        - Prevention: Asymptomatic patients who present within 2 hours of ingesting a potentially toxic amount of isoniazid should receive a prophylactic dose of pyridoxine IV equal to the amount of INH ingested; administer at a rate of 0.5-1 g/minute
        - Acute ingestion of KNOWN amount: Give pyridoxine dose equal to the amount of isoniazid ingested (maximum dose: 5 g IV); administer at a rate of 0.5-1 g/minute IV until seizures stop or the maximum initial dose has been administered; may repeat every 5-10 minutes as needed to control persistent seizure activity and/or CNS toxicity; if seizures stop prior to the administration of the calculated initial dose, infuse the remaining pyridoxine over 4-6 hours
        - Acute ingestion of UNKNOWN amount: initially 5 g IV; may repeat every 5-10 minutes as needed to control persistent seizure activity and/or CNS toxicity
- <u>Pediatric</u>
    - Drug-induced deficiency/toxicity (cycloserine, isoniazid, penicillamine) from chronic use
        - Isoniazid/cycloserine
            - Prevention
                - Non-HIV-exposed/positive
                    - Infants/children: 1 mg/kg/day orally*/IM/IV; usually 10-50 mg/day
                    - Adolescents: 30 mg/day orally/IM/IV
                - HIV-exposed/positive
                    - Infants/children: 1-2 mg/kg orally*/IM/IV once daily (maximum daily dose: 50 mg/day)
                    - Adolescents: 25 mg/day orally/IM/IV
            - Treatment
                - Infants/children: usually 100 mg/day orally/IM/IV; higher doses may be needed to alleviate signs/symptoms
                - Adolescents: initially 100 mg/day orally for 3 weeks followed by 30 mg/day
        - Penicillamine: 25-50 mg/day orally
    - Acute isoniazid ingestion
        - Treatment of seizures and/or coma
            - Prevention: Asymptomatic patients who present within 2 hours of ingesting a potentially toxic amount of isoniazid should receive a prophylactic dose of pyridoxine IV equal to the amount of INH ingested; administer at a rate of 0.5-1 g/minute IV (maximum dose: 5 g)
            - Acute ingestion of KNOWN amount: total dose of pyridoxine is equal to the amount of isoniazid ingested (maximum dose: 70 mg/kg IV up to 5 g); administer at a rate of 0.5-1 g/minute until seizures stop or the maximum initial dose has been administered; may repeat every 5-10 minutes as needed to control persistent seizure activity and/or CNS toxicity; if seizures stop prior to the administration of the calculated initial dose, infuse the remaining pyridoxine over 4-6 hours
            - Acute ingestion of UNKNOWN amount: initially 70 mg/kg IV (maximum dose: 5 g); may repeat every 5-10 minutes as needed to control persistent seizure activity and/or CNS toxicity
    - Acute intoxication from mushroom ingestion (genus *Gyromitra*)
        - 25 mg/kg/dose IV; repeat as necessary (maximum total dose: 15-20 g)
    - ***Oral pyridoxine should be used if IV pyridoxine is unavailable**

CONTRAINDICATIONS

- Hypersensitivity to pyridoxine or any component of the formulation

Monitoring and Adverse Effects

- Adverse Effects
    - Hematologic: decreased folic acid
    - Neurologic: paresthesia and somnolence
- Monitoring
    - For treatment of isoniazid or gyromitrin-containing mushroom toxicity: anion gap, ABG, electrolytes, neurological exam, seizure activity

Other Important Considerations

- Injection solution should be protected from light
- A 1 mg/mL oral solution may be made using pyridoxine injection; withdraw 100 mg (1 mL of 100 mg/mL injection) from a vial with a needle and syringe, add to 99 mL simple syrup in an amber bottle; stable for 30 days refrigerated

References

1. Howland M. Pyridoxine. In: Nelson LS, Howland M, Lewin NA, Smith SW, Goldfrank LR, Hoffman RS. eds. Goldfrank's Toxicologic Emergencies, 11e New York, NY: McGraw-Hill.
2. Pyridoxine [monograph]. In: Lexicomp Online [online database]. Hudson, OH: Lexi-Comp.
3. Phytonadione [monograph]. In: Micromedex [online database]. Greenwood Village, CO: Truven Health Analytics.

Sodium Bicarbonate

Indication

- Treatment of drug-induced wide complex dysrhythmia due to sodium channel blockade
- Treatment of toxin-induced metabolic acidosis from methanol, ethylene glycol, metformin until definitive treatment (dialysis) can be arranged
- Alkalinization of urine to enhance excretion of salicylates, chlorophenoxy herbicides, phenobarbital, and methotrexate
- Adjunctive therapy for chlorine gas inhalation with respiratory symptoms

Mechanism of Action

- Competes directly with sodium channel blockers; increases local pH at sodium channels, thereby increasing dissociation of TCAs
- Serum (and urinary alkalinization) facilitates movement of salicylate anion away from sensitive CNS tissues
- Urinary alkalinization enhances elimination of some xenobiotics (salicylates, chlorophenoxy herbicides, phenobarbital, methotrexate); prevents nephrotoxic precipitation of MTX and metabolites in the renal tubules
- Supports normal physiology in patients with severe (pH <7.0) drug-related acidemia while definitive treatment (often dialysis) is arranged
- Neutralizes hydrochloric acid in the respiratory tract created by the inhalation of chlorine gas (not routinely used)

Dosage forms

- IV solution: 4.2%, 8.4%
- Oral tablet: 325mg, 650mg

Dose

- Adults:
    - Drug-induced wide complex dysrhythmia:
        - 1-2 mEq/kg IV (50-100 ml of sodium bicarbonate 8.4%) bolused over 1-2 minutes
        - Repeat boluses until improvement of ECG and hemodynamics, then begin an infusion of 150 mEq/L at 150-250 mL/h
    - Toxin-induced metabolic acidosis:
        - 50-150 mEq/L at a rate of 150-250 mL/hr titrating to pH > 7.2
    - Urine alkalinization:
        - 150 mEq/L infused at 150-200 mL/h for a goal urine pH 7.5-7.55
    - Chlorine gas induced injury: 4 mL of 4.2% sodium bicarbonate via nebulizer
- Pediatrics:
    - Drug-induced wide complex dysrhythmia:
        - 1-2 mEq/kg IV (50-100 ml of sodium bicarbonate 8.4%) bolused over 1-2 minutes
        - Repeat boluses until improvement of ECG and hemodynamics, then begin an infusion of 150 mEq/L at twice maintenace
    - Toxin-induced metabolic acidosis:
        - 50-150 mEq/L at twice maintenance titrating to pH > 7.2
    - Urine alkalinization:
        - 150 mEq/L infused at twice maintenance for a goal urine pH 7.5-7.55
    - Chlorine gas induced injury: 4 mL of 4.2% sodium bicarbonate via nebulizer

CONTRAINDICATIONS

- Chloride loss from vomiting, GI suction or diuretics causing alkalosis

Monitoring and Adverse Effects

- In neonates and children: hypernatremia, decrease in CSF pressure, intracranial hemorrhage from rapid injection
- Sodium retention, fluid overload, electrolyte dilution (hypocalcemia, hypokalemia), pulmonary edema
- Caution in renal impairment and heart failure
- Extravasation: cellulitis, tissue necrosis, ulceration, sloughing
- Hypokalemia requiring careful repletion
- Monitor labs: pH, ABG's, CO2, urinary pH, electrolytes, blood glucose, renal function, EKG, serial drug levels

Other important considerations

- Neonates and children < 2 years old should receive sodium bicarbonate slowly: < 10ml/min
- 4.2% concentration is preferred in pediatrics < 2 years old

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. IWK Regional Poison Centre (2015). Antidote Sodium Bicarbonate. Retrieved from https://iwkpoisoncentre.ca/octreotide-adult.html
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Sodium Thiosulfate

Indication

- Reversal of cyanide poisoning used in conjunction with hydroxocobalamin

Dosage forms

- Sodium thiosulfate: 12.5 g/50mL vial (25% solution)

Mechanism of Action

- Provides sulfur molecules to the endogenous enzyme rhodanese, thereby enhancing its biotransformation of cyanide to nontoxic thiocyanate

Dose:

- Adult:
  - 50 mL (12.5 g) of 25% solution sodium thiosulfate. Repeat administration at ½ the initial dose if toxicity persists or recurs
  - Sodium thiosulfate may also be given after hydroxocobalamin
- Pediatric:
  - 1 mL/kg IV of 25% solution (250 mg/kg or 30 to 40 mL/m^2) of sodium thiosulfate; maximum dose: 50 mL (12.5 g) total dose. Repeat administration at ½ the initial dose if toxicity persists or recurs
  - Sodium thiosulfate may also be given after hydroxocobalamin

Monitoring and Adverse Effects

- Monitoring
  - Adequate perfusion and oxygenation for 24-48 hours
  - Recurrent signs of cyanide toxicity
  - Renal function, especially in elderly
  - Hemodynamic stability

Other important considerations

- Requires airway, ventilatory and circulatory support prior to antidotal therapies
- Sodium nitrite: Consider risk of methemoglobinemia with G6PD deficiency and concomitant medications

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. Sodium Thiosulfate. Micromedex 2.0. Truven Health Analytics, Inc. Greenwood Village, CO. Available at: http://www.micromedexsolutions.com. Accessed January 24, 2020.

Succimer (2,3-Dimercaptosuccinic acid or DMSA)

Indication

- Treatment of mild to moderate lead poisoning in children with blood lead concentrations >45 mcg/dL without encephalopathy
- Arsenic and mercury poisoning
- Adults with lead levels >50 mcg/dL (off-label)

Mechanism of Action

- Direct chelator of heavy metal ions inactivating them and allowing increased urinary excretion

Dosage forms

- 100mg oral capsules; no generic available; Chemet®

Dose

- Children: 10 mg/kg/dose (or 350 mg/m^2/dose) PO every 8 hours for 5 days, always round up dose to whole capsules
    - Followed by 10 mg/kg/dose (or 350 mg/m^2/dose) every 12 hours for 14 days
    - Maximum: 500 mg/dose
- Adults: 10 mg/kg every 8 hours for 5 days, always round up dose to whole capsules
    - Followed by 10 mg/kg/dose every 12 hours for 14 days

CONTRAINDICATIONS

- Hypersensitivity to succimer

Monitoring and Adverse Effects

- CBC with differential and transaminases before treatment initiation and weekly during treatment
- BLL on days 3, 6, 9, and 12, then weekly during treatment or until down trending
- Rash, diarrhea, loss of appetite, nausea, and vomiting are common
- Rare, but serious neutropenia has occurred

Other important considerations

- For young children or those unable to swallow capsules, empty content of capsules on soft foods: apple sauce, ice cream, etc.
- Do not make a suspension, do not add to bottle feeds
- A 2-week interval is necessary prior to administration of a second course of succimer unless BLLs are initially >100 mcg/dL or encephalopathy is present

References:

1. Howland M. Vitamin K1. In: Nelson LS, Howland M, Lewin NA, Smith SW, Goldfrank LR, Hoffman RS. eds. Goldfrank's Toxicologic Emergencies, 11e New York, NY: McGraw-Hill
2. Succimer [monograph]. In: Lexicomp Online [online database]. Hudson, OH: Lexi-Comp.
3. Succimer [monograph]. In: Micromedex [online database]. Greenwood Village, CO: Truven Health Analytics.

Thiamine

Indication

- Prevention and treatment of Wernicke encephalopathy and Wernicke-Korsakoff syndrome in patients with, or at risk of, thiamine deficiency, primarily chronically malnourished patients and chronic alcohol users
- Treatment of alcoholic ketoacidosis without concern for encephalopathy
- Adjunctive therapy for ethylene glycol poisoning

Mechanism of Action

- Replenishes thiamine in depleted cells, thereby allowing the progression of multiple metabolic processes including the synthesis of myelin
- Enhances conversion of the toxic ethylene glycol metabolite glyoxylic acid to nontoxic α-hydroxy-β-ketoadipic acid

Dosage forms

- IV solution 100mg/1ml, oral tablet

Dose

- Wernicke encephalopathy and prevention of Wernicke-Korsakoff in at-risk patients with undifferentiated altered mental status: 500 mg IV every 8 hours until improvement in mental status or neurologic abnormality and tolerating a normal diet
- Alcoholic ketoacidosis without encephalopathy: 500 mg IV daily until acidosis resolves and tolerating a normal diet
- Adjunctive therapy for ethylene glycol poisoning: 100 mg IV daily until intoxication resolves

Monitoring and Adverse Effects

- Anaphylactoid reactions have been reported, pain with intramuscular administration
- Respiratory distress, pruritus, shock, and abdominal pain
- Increased risk with repeated IV or IM administration

Other important considerations

- Avoid oral route in patients with chronic alcohol use and patients with encephalopathy or acute illness due to poor absorption
- Give oral tablets with a meal

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. Thiamine. DrugPoints Summary. Micromedex 2.0. Truven Health Analytics, Inc. Greenwood Village, CO. Available at: http://www.micromedexsolutions.com. Accessed December 13, 2019

Uridine Triacetate

Indication

- Treat RNA-related toxicity from fluorouracil and fluorouracil prodrugs such as capecitabine

Ordering

- If considering use, please contact central pharmacy as soon as possible to facilitate ordering as these medications are not kept in stock. If both oncology and toxicology agree that medication is needed, please contact the Main Pharmacy at 2-5120. If emergent ordering in needed during nights, holidays, or weekends please contact the Main Pharmacy and have them reach out to the Pharmacy Supervisor.

Mechanism of Action

- Provides source of uridine to cells poisoned by fluorouracil, thereby allowing RNA synthesis to proceed

Dosage Forms

- Oral granules, 10 g/packet

Dose

- Adult: 1 packet (10 g) orally every 6 hours for 20 doses; mix with soft food and follow with water
- Pediatric: 6.2g/m^2 BSA orally every 6 hours for 20 doses up to a maximum of 10 g/dose; mix with soft food and follow with water

Monitoring and Adverse Effects

- Common: nausea, vomiting, diarrhea
- Monitor: improvement of signs of fluorouracil toxicity (bone marrow suppression, neutropenia, GI toxicity, neurotoxicity, renal toxicity, cardiotoxicity, etc.)

Other important considerations

- Measure pediatric doses with a measuring scale accurate to 0.2 g or a graduated teaspoon accurate to 0.25 teaspoon
- Give an antiemetic 20-30 minutes before dose
- If vomiting occurs within 2 hours of the dose, give another dose within 15 minutes of vomiting and continue with the next dose as scheduled

References

1. Nelson, L. S., Howland, M. A., Lewin, N. A., Smith, S. W., Goldfrank, L. R., Hoffman, R. S., (2019). Goldfrank's toxicologic emergencies (Eleventh ed.). New York: McGraw Hill.
2. Uridine Triacetate. DrugPoints Summary. Micromedex 2.0. Truven Health Analytics, Inc. Greenwood Village, CO. Available at: http://www.micromedexsolutions.com. Accessed December 14, 2019