Act 39 or The Patient Choice and Control at End of Life Act, allows Vermont residents with terminal diseases to be prescribed a dose of medication that, if taken, will hasten the end of their life. The compound below is the medication dispensed by Rutland Pharmacy.

**Compound name:** C- DDMA *PB- POWDER SUSPENSION (ACT 39)

**Dosage form:** Powder reconstitution

**Strength:** DIGOXIN 100mg, DIAZEPAM 1gm, MORPHINE 15gm, AMITRIPTYLINE 5gm, PHENOBARBITAL 5gm

**Recommended beyond use date:** 6 months

**Storage conditions:** Room temperature

**Prior to ingestion:** Add 3 to 4 ounces of water, or clear liquid (ie: apple juice), bitterness suppressor and flavoring (optional) to this bottle, then shake until smoothly mixed

**CAUTION:** This bottle contains a combination of lethal doses of medication. Taking this medication will result in death.

**Components-**

DIGOXIN:

- Digoxin is an antiarrhythmic generally used to treat atrial fibrillation and heart failure.
- MOA – Inhibits sodium-potassium ATPase which leads to an increase in intracellular sodium and calcium concentration. This causes vagomimetic action and baroreceptor sensitization.
- A healthy adult can experience life-threatening toxicity with acute ingestions of about 5mg or more. Ingesting 10mg or more can cause cardiac arrest in healthy adults. The strength of digoxin used in DDMA *PB is 100mg.
- The effects of overdosing on digoxin are an extension of the therapeutic effects. The increase in intracellular calcium leads to early afterdepolarization, cardiac irritability, and dysrhythmias. Increased vagal and decreased sympathetic tones lead to bradycardia and heart block. Inhibition of the sodium-potassium ATPase pump causes hyperkalemia which can lead to cardiac arrhythmias.
- Digoxin also interacts with diazepam which increases the risk of digoxin toxicity.

DIAZEPAM:

- Diazepam is a benzodiazepine generally used for anxiety, seizures or as a muscle relaxant.

- MOA – The mechanism of action is not fully known, but it may involve potentiation of GABA neurotransmission resulting from binding at the benzodiazepine site of the GABA-A receptor.
- Generally, a healthy adult can ingest up to 2000mg of diazepam with only minor toxicity. The strength of diazepam used in DDMA *PB is 1gm. Increased GABA activity causes CNS depression. Alone 1gm of diazepam may not cause toxicity, but in combination with the other components of DDMA *PB there is additive CNS and respiratory depression.

MORPHINE:

- Morphine is an opioid generally used for pain.
- MOA - Morphine is a pure opioid agonist, selective to the mu receptor, with primary actions in the brain through transitory stimulation prior to depression. In the CNS, it promotes analgesia and respiratory depression by decreasing brainstem respiratory centers response to carbon dioxide tension and electrical stimulation. It also decreases gastric, biliary and pancreatic secretion, induces peripheral vasodilation and promotes opioid-induced hypotension due to histamine release
- The therapeutic and toxic effects of morphine are mediated by different receptors. The Mu 1 receptor mediates supraspinal and peripheral analgesia, sedation, and euphoria. The Mu 2 receptor mediates spinal analgesia, respiratory depression, physical dependence, gastrointestinal dysmotility, bradycardia and pruritus. The Kappa 1 receptor mediates spinal analgesia and miosis, Kappa 2 receptor mediates dysphoria and psychotomimesis and the Kappa 3 receptor mediates supraspinal analgesia.
- Severe toxicity may lead to respiratory depression leading to apnea, hypoxia, coma, bradycardia, seizures, acute lung injury, and death.
- Morphine also interacts with diazepam, amitriptyline and phenobarbital increasing both CNS and respiratory depression.

AMITRIPTYLINE:

- Amitriptyline is a tricyclic antidepressant generally used for depression.
- MOA- Amitriptyline promotes neuronal activity by blocking the membrane pump mechanism which is responsible for the absorption of serotonin and norepinephrine in serotonergic and adrenergic neurons. Amitriptyline exhibits a sedative property.
- Ingestion of amitriptyline greater than 5mg/kg can is considered potentially toxic and can lead to coma, seizures, QRS prolongation with ventricular dysrhythmias, and respiratory failure.
- The strength of amitriptyline used in DDMA *PB is 5gm. 5 grams of amitriptyline far exceeds the 5mg/kg that an adult could ingest. An adult taking 5gm of amitriptyline would need to weigh 1000 kg (2,200 lbs) or more to stay below toxic levels.
- Amitriptyline also interacts with morphine and diazepam increasing the risk of serotonin syndrome and psychomotor deficits.

PHENOBARBITAL:

- Phenobarbital is a barbiturate generally used for epilepsy and sedation.

- MOA – Phenobarbital's probable mechanism of action is through prolonging the opening time of Cl- ion channels in postsynaptic neuronal membranes. It depresses the central nervous system and causes sedation. It also decreases intraneuronal Na+ concentrations and inhibits Ca2+ influx into depolarized synaptosomes which may be the reason for its anticonvulsant properties.
- Oral therapeutic doses of phenobarbital for adults' range from 20 to 200mg/day in divided doses. The strength of phenobarbital used in DDMA *PB is 5gm, 25 times the upper limit and not in divided doses.
- Toxic levels of phenobarbital can lead to enhanced GABA activity causing central nervous system depression, along with direct myocardial depression leading to hypotension.
- Phenobarbital was first added to DDMA to add a 3rd class of sedative that will be additive to respiratory depression. It was also added to help prevent seizure activity in at-risk patients as the other components in DDMA increase that risk further.

**Interactions-**

| Drugs | Severity | Interaction |
|---|---|---|
| Amitriptyline – morphine | Major | Increased risk of paralytic ileus and serotonin syndrome |
| Diazepam – morphine | Major | Increased risk of respiratory and CNS depression |
| Diazepam – phenobarbital | Major | Additive respiratory depression |
| Morphine – phenobarbital | Major | Increased risk of respiratory and CNS depression |
| Amitriptyline – diazepam | Moderate | May result in psychomotor deficits |
| Diazepam – digoxin | Moderate | May result in digoxin toxicity (nausea, vomiting, cardiac arrhythmias) |