

ALTERNATIVES TO PHYSOSTIGMINE SALICYLATE FOR ANTICHOLINERGIC TOXICITY

GENERAL INFORMATION:

Physostigmine salicylate is the preferred antidote for central anticholinergic toxicity (delirium), but it requires Special Access Program authorization from Health Canada and may not be available on-site. This document outlines alternative management strategies for moderate/severe anticholinergic delirium, including rivastigmine.

Contact the Poison Centre for additional guidance.

RIVASTIGMINE FOR ANTICHOLINERGIC TOXICITY

MECHANISM OF ACTION:

Rivastigmine inhibits acetylcholinesterase, increasing synaptic acetylcholine to overcome central and peripheral muscarinic receptor blockade. [See Appendix 1](#) for comparison of physostigmine and rivastigmine properties.

INDICATIONS:

Adults: Patients with anticholinergic-induced agitation or delirium unresponsive to non-pharmacologic measures, **AND** either:

- Physostigmine is unavailable; **OR**
- The patient has a confirmed salicylate allergy

Pediatrics: Consult Poison Centre before use and to discuss dosing.

ADULT DOSING ([See Appendix 2](#)):

Initial dose:

Route	Dose	Notes
Oral (preferred given faster onset)	6 mg PO	Onset: ~1 hour
Transdermal patch	9.5 mg/24h	Slower onset of action Apply to upper back to reduce removal risk and improve bioavailability

Reassessment & Additional Doses ([See Appendix 2](#)):

- Reassess 1–2 hours after the initial dose. If CNS symptoms persist, give 3 mg PO or apply a 9.5 mg/24-hour patch (if not already used). If a patch is started at this stage, do not give additional oral doses for the next 24 hours.
- Reassess again 3–4 hours after the initial dose. If symptoms continue and the maximum daily dose has not been reached, give a final 3 mg PO dose

Maximum daily dose:

- Rivastigmine 12mg PO; **OR**
- Rivastigmine 6mg PO + rivastigmine 9.5mg/24h patch



Duration of treatment and observation:

- Continue rivastigmine treatment until CNS symptoms have resolved.
- Remove patch after 24 hours if not already removed due to symptom resolution.
- Monitor for at least 12 hours after last oral dose or patch removal to ensure anticholinergic symptoms do not recur.

SPECIAL POPULATIONS:

- Patients >100 kg: when oral dosing not possible, consider starting with the 13.3mg/24h patch.
- Pediatric patients: consult Poison Centre before use.
- Patients already on rivastigmine: follow same protocol but reduce initial and additional doses as needed to stay within the maximum daily dose.

CONTRAINDICATIONS:

- Cardiac conduction abnormalities, particularly QRS widening (> 100 msec not related to bundle branch block) and PR > 200 msec
- Bradycardia or sick sinus syndrome
- Unexplained syncopal episodes
- Severe asthma/COPD
- Seizure disorder
- Hypersensitivity to rivastigmine
- Severe hepatic impairment (use has not studied in this population)

ADVERSE EFFECTS:

Stop if there is evidence of cholinergic toxicity including any of the following:

- Bradycardia
- Nausea/vomiting/diarrhea
- Syncope
- Seizures (rare)

OTHER AGENTS FOR ANTICHOLINERGIC TOXICITY

Benzodiazepines: Indicated for agitation, seizures, or sedation if physostigmine and rivastigmine are unavailable or insufficient. Benzodiazepines do not reverse anticholinergic toxicity but may reduce symptom burden.

Other acetylcholinesterase inhibitors:

- **Neostigmine, pyridostigmine:** Not recommended due to poor CNS penetration
- **Donepezil, galantamine:** May be helpful theoretically but are not recommended at this time given lack of evidence. Other concerns include donepezil's long half-life if adverse events develop and drug-drug interactions (both metabolized by CYP3A4 and 2D6).



**Ontario
Poison
Centre** | **Centre
Anti-Poison
de l'Ontario**

Ontario: 1 (800) 268-9017
Manitoba: 1 (855) 776-4766
Nunavut: 1 (866) 913-7897

DO NOT ARCHIVE

APPENDIX 1

COMPARISON OF PHYSOSTIGMINE AND RIVASTIGMINE PROPERTIES

	Physostigmine IV	Rivastigmine	
		Oral	Transdermal Patch
Onset	5 - 10 min	10 min – 2 hours	30 -60 min
Median Time to Resolution of Delerium	Minutes	2 hours	5 hours
Duration of Action	30 min – 5 hours**	Approx. 10 hours**	Sustained while patch applied** 3-9 hours once removed
Elimination Half-life (T_{1/2})	15-40 min**	1-2 hours**	3-4 hours**

**Duration of cholinesterase inhibition and therefore the duration of effect is greater than the elimination half-life would suggest



**Ontario
Poison
Centre** | **Centre
Anti-Poison
de l'Ontario**

Ontario: 1 (800) 268-9017
Manitoba: 1 (855) 776-4766
Nunavut: 1 (866) 913-7897

DO NOT ARCHIVE

APPENDIX 2

RIVASTIGMINE DOSING ALGORITHM

