



988170 Nebraska Medical Center • Omaha, NE 68198-8170 • 1-800-222-1222 • www.NebraskaPoison.com

Serving Nebraska, Idaho, Wyoming, American Samoa, and Federated States of Micronesia

From: Ron Kirschner, MD, Medical Director  
To: ALL HEALTH CARE PROFESSIONALS  
Subject: Alternatives to physostigmine for anticholinergic delirium  
Date: 4/13/23

---

- When given intravenously, the short-acting cholinesterase inhibitor physostigmine can reverse delirium in anticholinergic poisoning but many providers felt uncomfortable administering it due to unfamiliarity.
- Due to a current shortage, physostigmine is often unavailable so alternatives must be considered (1).
- Rivastigmine works by a similar mechanism but is only available in oral or topical formulations.
- The physostigmine analogs neostigmine and pyridostigmine are quaternary amines with poor CNS penetration, so are unlikely to be effective in treating mental status changes.
- In 2021 Hughes reported successful treatment of anticholinergic delirium with oral rivastigmine (2).
- Rivastigmine is a tertiary amine that readily enters the CNS. It is available as a 1.5 or 3 mg pill with peak absorption in 1 hour and duration of action ~10 h, but there is no IV formulation.
- A transdermal rivastigmine preparation is available, but absorption is slower (peak thought to be ~ 8 hours).
- In a recent series of 20 delirious anticholinergic patients treated with oral and/or topical rivastigmine, delirium resolved in 3-12 hours and no adverse reactions were noted (3).
- If there is a need to rapidly titrate delirium control due to severe agitation or critical illness, intravenous dexmedetomidine may be a preferable option (1).
- We encourage you to call and discuss your patients so that we can provide more case-specific individualized recommendations.

#### References

1. Whitley JD. Shortages of agents used to treat muscarinic delirium. *Am J Emerg Med* 2023; 67: 163-167.
2. Hughes AR. Letter in response to rivastigmine for the treatment of anticholinergic delirium. *Clin Toxicol* 2021; 59: 855-56.
3. Greene SC. Antimuscarinic delirium reversed by rivastigmine: a case series. *J Med Toxicol* 2023; 19: 80 (abstract 29).

**Our certified specialists in poison information and physician toxicologists  
are available 24 hours a day to answer your questions.**