



Paracetamol Overdose: New Guidance on Treatment with Intravenous Acetylcysteine

Acetylcysteine (Parvolex) is licensed for the treatment of paracetamol poisoning. Its mode of action is to reduce the hepatic toxicity of NAPQI (n-acetyl-p-benzo-quinoneimine) which is the highly reactive intermediate metabolite produced following ingestion of a high dose of paracetamol. Acetylcysteine acts as a precursor for the synthesis of glutathione and, therefore, maintains cellular glutathione at a level sufficient to inactivate NAPQI.

Paracetamol overdose can result in liver damage which may be fatal. Intravenous acetylcysteine (Parvolex) is the antidote to treat paracetamol overdose and is highly efficacious in preventing liver damage if administered within 8 hours of the overdose. After this time efficacy of acetylcysteine declines progressively.

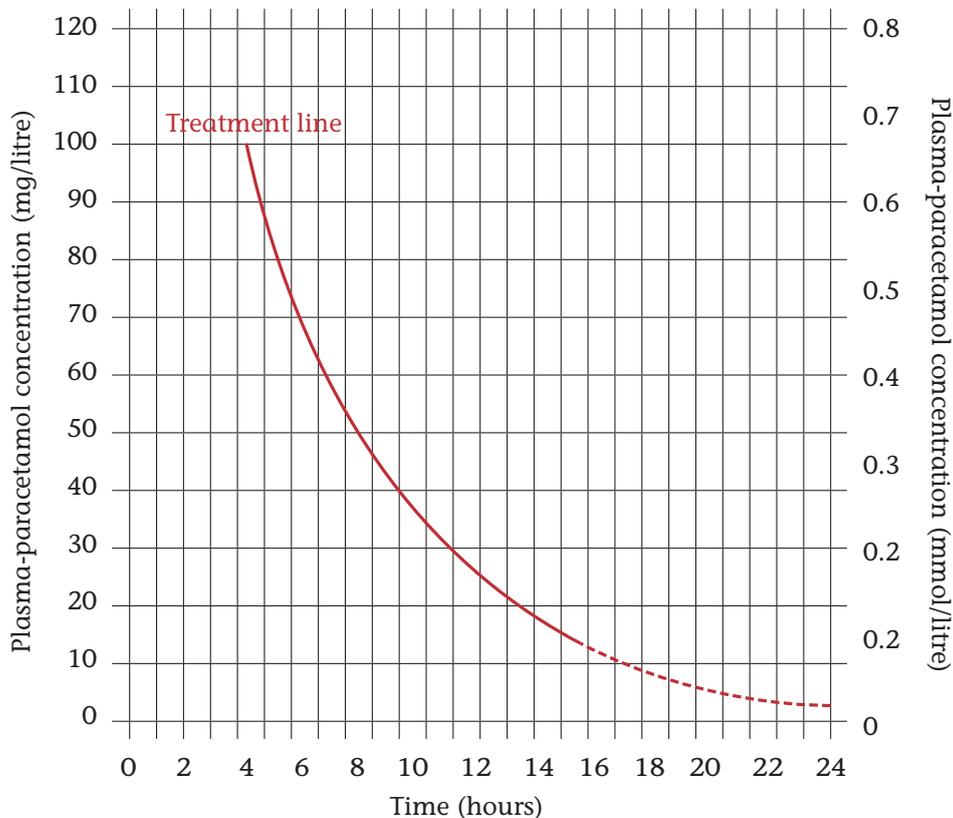
New simplified guidance on the treatment of acute paracetamol overdose with acetylcysteine has been approved by the Irish Medicines Board (IMB). The simplified guidance is aligned with the findings of a review undertaken by the Commission of Human Medicines (CHM-UK) and includes an updated treatment nomogram. Previously healthcare professionals treating patients for paracetamol overdose were advised to assess for risk factors of hepatotoxicity (i.e. poor nutritional intake, chronic alcohol consumption, concomitant medications etc). This assessment of risk factors resulted in two separate lines on the treatment nomogram—one for patients with risk factors and one for those without risk factors.

Advice to Healthcare Professionals:

- The previous treatment nomogram has been amended to a single treatment line (previously high risk line) so all patients with a plasma paracetamol level of 100mg/litre at 4 hours are recommended to have treatment (figure 1).
- Regardless of risk factors for hepatotoxicity, all patients with a timed plasma paracetamol level on or above a single treatment line joining points of 100mg/L at 4 hours and 15 mg/L at 15 hours after ingestion should receive acetylcysteine based on the new treatment nomogram.
- The new nomogram (figure 1) is therefore a single line joining the points of 100mg/L at 4 hours and 15mg/L at 15 hours after ingestion of paracetamol on or above which all patients should receive treatment with acetylcysteine.
- If there is doubt over the over the timing of paracetamol ingestion including when ingestion has occurred over a period of one hour or more (i.e. staggered overdose), acetylcysteine should be given without delay (i.e. the nomogram should not be used).
- To reduce the risk of anaphylactoid reactions, initial loading dose infusion should be increased from 15 minutes to 60 minutes.
- To minimise the risk of administration errors, a clear comprehensive weight based dosage table will be included in the product information for both adults and children.
- Please note that hypersensitivity has been removed as a contraindication to the administration of acetylcysteine from the product information



Figure 1. New treatment nomogram for paracetamol overdose



Key message

All patients with a timed plasma paracetamol level on or above a single treatment line joining points of 100mg/L at 4 hours and 15mg/L at 15 hours after ingestion should receive acetylcysteine (Parvolex) based on a new treatment nomogram, regardless of risk factors for hepatotoxicity (see Figure 1 above).

Where there is doubt over the timing of paracetamol ingestion, including when ingestion has occurred over a period of one hour or more (that is 'staggered overdose'), acetylcysteine should be given without delay.

An increase in the duration of administration of the first dose of intravenous acetylcysteine from 15 minutes to 60 minutes.

Removal of hypersensitivity as a contraindication to treatment with acetylcysteine.

The provision of weight-based acetylcysteine dosing tables for adults and children.

The product information has been updated to reflect this new guidance and is available from the IMB website (www.imb.ie), where a more detailed version of this guidance is also accessible.