Dantrolene (Agilus®)

Administration guidance is for the management of malignant hyperthermia crisis, or neuroleptic malignant syndrome (unlicensed)

Dantrium® (20mg dantrolene powder for solution for injection) has been discontinued however stock may be available.
Check form of dantrolene before administration – Dantrium® or Agilus®

Form	120mg dantrolene sodium hemiheptahydrate powder for solution for injection (Agilus®)	Store at room temperature in outer box for light protection.

Reconstitution

- Add 20mL **sterile water for injection** and shake until solution dissolved
- Shake vial for approximately 1 minute until the solution is free from particles (this may take longer than 1 minute).
- The reconstituted solution should be a yellow-orange colour and free from particulates. The volume of solution in a reconstituted vial is 22.6 mL (**5.3mg/mL** dantrolene sodium hemiheptahydrate)
- Reconstituted solution must be protected from light. Do not store above 25 °C and do not refrigerate

Bodyweight (kg)	Number of vials to prepare for loading dose
Up to 48 kg	1 vial
49-96 kg	2 vials
From 97 kg	3 vials

Compatibility & Stability

No further dilution permitted

Administration

Bolus intravenous injection

Management of malignant hyperthermia crisis, or neuroleptic malignant syndrome (unlicensed)

- Give by rapid injection over at least 1 minute
- Administer an initial dose: 2.5 mg/kg body weight intravenously
- If there is no response after 5 minutes repeat a dose of 1 mg/kg. Further doses can be given every 5 minutes, until ETCO2 <6 kPa and temp <38.5°C
- Repeat 1mg/kg to maintain ETCO2 <6 kPa and temp <38.5°C even if exceeds maximum dose of 10 mg/kg.
- If a cumulative dose of 10 mg/kg or above is considered, the diagnosis of malignant hyperthermia should be re-examined.
- For a 70kg patient, if a cumulative dose of 10mg/kg is needed this will amount to approximately 6 vials.
- See table below for examples of volume of reconstituted Agilus (5.3mg/mL) to be given

Dosing examples by body weight

Number of vials to be prepared for Loading Dose	Body weight range	Body weight (kg)	Recommended Dose	Dose to be administered (mg)	Volume to be administered[a] (mL)
1	Up to 48 kg	5	2.5mg/kg	12.5 mg	**2.4 mL**
			1mg/kg	5 mg	**0.94 mL**
		10	2.5 mg/kg	25 mg	**4.7 mL**
			1mg/kg	10 mg	**1.9 mL**
		15	2.5 mg/kg	37.5 mg	**7.1 mL**
			1mg/kg	15 mg	**2.8 mL**
		20	2.5 mg/kg	50 mg	**9.4 mL**
			1mg/kg	20 mg	**3.8 mL**
		25	2.5mg/kg	62.5 mg	**11.8 mL**
			1mg/kg	25 mg	**4.7 mL**
		30	2.5 mg/kg	75 mg	**14.2 mL**
			1mg/kg	30 mg	**5.7 mL**
		40	2.5 mg/kg	100 mg	**18.9 mL**
			1mg/kg	40 mg	**7.5 mL**
2	49 kg to 96 kg	50	2.5 mg/kg	125 mg	**23.6 ml**
			1mg/kg	50 mg	**9.4 mL**
		60	2.5 mg/kg	150 mg	**28.3 mL**
			1mg/kg	60 mg	**11.3 mL**
		70	2.5mg/kg	175 mg	**33 mL**
			1mg/kg	70 mg	**13.2 mL**
		80	2.5mg/kg	200 mg	**37.7 mL**
			1mg/kg	80 mg	**15.1 mL**
3	From 97 kg	100	2.5mg/kg	250 mg	**47.2 mL**
			1mg/kg	100 mg	**18.9 mL**
		120	2.5mg/kg	300 mg	**56.6 mL**
			1mg/kg	120 mg	**22.6 mL**
		140	2.5mg/kg	300 mg[b]	**56.6 mL**
			1mg/kg	140 mg	**26.4 mL**

[a]Total volume of one reconstituted vial is 22.6 mL
[b]For all bodyweights, the initial dose and any repeat doses should not exceed 300 mg, equivalent to 2.5 vials.

Monitoring

Monitor blood pressure, respiratory rate, pulse, temperature, pH, pCO_2, K
Recommendations for standards of monitoring during anaesthesia and recovery 2021 | Association of Anaesthetists

Extravasation

Dantrolene sodium has a high pH (pH 9.5) and may cause venous irritation and tissue damage in cases of extravasation. If a central venous access device is unavailable, administer via a large peripheral vein monitoring insertion site closely using a recognised phlebitis scoring tool. Re-site cannula at first signs of inflammation.

Additional Information	• Reference: Association of Anaesthetists Guidelines Guideline Malignant hyperthermia 2020.pdf • Caution should be exercised if **hyperkalaemia** symptoms occur (muscular paralysis, ECG changes, bradycardic arrhythmias) or in cases of pre-existing hyperkalaemia (renal insufficiency, digitalis intoxication etc.), as an increase in serum potassium has been demonstrated in animal trials a result of the co-administration of dantrolene with verapamil. Concomitant use of Agilus® and calcium channel blockers is not recommended. • **Liver damage** may occur during dantrolene therapy. This is dependent on the dosage and duration of therapy and may run a lethal course. • Agilus® contains 3530 mg hydroxypropylbetadex (a cyclodextrin) in each vial, which is equivalent to 156.2 mg/mL in the reconstituted solution. Hydroxypropylbetadex increases solubility of dantrolene and thereby reduces preparation time and fluid volume. Hydroxypropylbetadex has been associated with **ototoxicity** in animal studies; and cases of hearing impairment have been observed in studies in other clinical settings. Cases of hearing impairment have been observed at hydroxypropylbetadex exposure levels comparable to the higher range of recommended Agilus® doses. In most cases the hearing impairment has been transient and of slight to mild severity. • **Stock** kept in ED Antidote press, Theatres, CUMH Theatre

Information provided relates to Agilus®