21st January 2014

Dear Pharmacist,

DANTRIUM® IV (dantrolene sodium)

I am writing with regard to the supply of DANTRIUM® IV.

Norgine is currently experiencing a manufacturing issue with regard to DANTRIUM® IV, which is currently under urgent investigation. Although we do not anticipate a shortage of DANTRIUM® IV in the immediate future in the UK, in order to ensure on going supply whilst the issue is resolved, Norgine has shared extended stability data with the Department of health and NHS QA Pharmacists. The NHS QA Pharmacists have agreed that these data support an additional 6 month shelf life of the batches detailed below.

This pertains to the following batches only:

Country	Product Name	Batch Number	Original Expiration Date	New Expiration Date
UK	DANTRIUM IV AMP 20MG 12HP	124001	30/11/2013	30/05/2014
UK	DANTRIUM IV AMP 20MG 12HP	124001	30/11/2013	30/05/2014
UK	DANTRIUM IV AMP 20MG 12HP	132001	30/11/2013	30/05/2014
UK	DANTRIUM IV AMP 20MG 12HP	142001	29/04/2014	29/10/2014
UK	DANTRIUM IV AMP 20MG 12HP	150001	29/04/2014	29/10/2014
UK	DANTRIUM IV AMP 20MG 12HP	202001	28/02/2014	28/08/2014
UK	DANTRIUM IV AMP 20MG 12HP	205001L	30/08/2014	28/02/2015
UK	DANTRIUM IV AMP 20MG 12HP	205001L	31/08/2014	28/02/2015
UK	DANTRIUM IV AMP 20MG 12HP	206003	30/09/2014	30/03/2015
UK	DANTRIUM IV AMP 20MG 12HP	209001L	30/03/2014	30/09/2014
UK	DANTRIUM IV AMP 20MG 12HP	209001L	31/03/2014	30/09/2014
UK	DANTRIUM IV AMP 20MG 12HP	212001L	30/04/2014	30/10/2014
UK	DANTRIUM IV 36 PACK VIALS	133001	30/04/2014	30/10/2014
UK	DANTRIUM IV 36 PACK VIALS	133001	29/04/2014	29/10 2014
UK	DANTRIUM IV 36 PACK VIALS	150001L	30/08/2014	28/02/2015
UK	DANTRIUM IV 36 PACK VIALS	150001L	31/08/2014	28/02/2015
UK	DANTRIUM IV 36 PACK VIALS	215001L	30/11/2014	28/05/2015

Please do take the time to clearly mark this extended expiry date on every product pack currently held in your pharmacy.

We are committed to ensuring availability of DANTRIUM® IV for all patients who need it. We are working hard to resolve the manufacturing issue and will update you in due course.

If you have any questions regarding this letter, please contact us on 01895 826606.

Yours sincerely

Dr Amr Radwan
Medical Director
Norgine Pharmaceuticals Limited

DANTRIUM® IV (dantrolene sodium) – Abbreviated prescribing Information. Each box contains 12 or 36 vials. Each vial contains 20 mg dantrolene sodium formulated as powder for solution for injection to be reconstituted with 60 ml of Water for Injections. **Indications:** Treatment of malignant hyperthermia (MH). **Dosage and administration:** As soon as MH is recognised, all anaesthetic agents should be discontinued. An initial dose of 1 mg/kg should be given rapidly into the vein. This dose may be repeated up to a cumulative dose of 10 mg/kg. Clinical experience has shown that the average dose of Dantrium® IV required has been 2.5 mg/kg. If a relapse or recurrence occurs, Dantrium® IV ® should be re-administered at the last effective dose. Dantrium® IV is not recommended for use in children. **Special warnings and precautions:** In some subjects, as much as 10 mg/kg of Dantrium® IV has been needed to reverse MH. The 3000 mg of mannitol present in each vial of Dantrium IV® should be taken into consideration when calculating total mannitol dose for the prevention or treatment of renal complications of MH. Care must be taken to prevent extravasation of the intravenous solution. The use of Dantrium® IV in the management of MH is not a substitute for supportive measures. Whilst the licensed indications of intravenous dantrolene sodium do not generally necessitate prolonged therapy, the risk of hepatic dysfunction may increase with dose and duration of treatment, based on experience with oral therapy. However in some patients it is of an idiosyncratic or hypersensitivity type, and could occur after a single dose. Dantrium® IV should not be mixed with other intravenous infusions. **Interactions:** It is recommended that the combination of Dantrium® IV and calcium channel blockers, such as verapamil, is not used during the reversal of a MH crisis. Administration of dantrolene may potentiate vecuronium-induced neuromuscular block. **Pregnancy and lactation:** The safety of Dantrium® IV in pregnant women has not been established. Dantrium® IV should be given during pregnancy only when the potential benefits outweigh the possible risk to mother and child. **Effects on ability to drive and use machines:** Patients must not operate an automobile or engage in other hazardous activity for up to 48 hours. **Side-effects:** There have been occasional reports of death following MH crisis even when treated with intravenous dantrolene sodium. There have been rare reports of pulmonary oedema developing during the treatment. Injection site reactions, thrombophlebitis, extravasation and hepatic dysfunction may occur, including fatal hepatic failure. Refer to SmPC for full product information and list of side-effects. **MA:** PL 34413/0003.
MA Holder: SpePharm Holding B.V., Kingsfordweg 151, 1043 GR Amsterdam, The Netherlands. **Legal category:** POM. **NHS Price:** 12 X 20mg £612; 36 X 20mg £1,836. **Date of revision:** Mar 2013, DA/3383/MAR/13.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.
Adverse events should also be reported to SpePharm on 0844 800 7579.