Shared Care Guideline
for
Dantrolene (for the treatment of chronic severe spasticity of voluntary skeletal muscle in adults).

This shared care guideline (SCG) has been written to enable the continuation of care by primary care clinicians of patients initiated on Dantrolene by neurologists where this is appropriate and, in the patients' best interests. Primary care will only be requested to take over prescribing of Dantrolene within its licensed indication unless specifically detailed otherwise below.

Introduction

Indication/Licensing information

- Dantrolene is licenced for chronic severe spasticity of voluntary muscle (other licenced conditions are not covered by this shared care guideline).
- It is recommended by NICE as a second-line option to treat spasticity in people with Multiple Sclerosis (MS).

Pharmacology

- Dantrolene acts on skeletal muscle cells by interfering with calcium efflux, thereby stopping the contractile process.

Dosage and administration

- Dantrolene is to be taken orally and is available as a 25mg or 100mg capsule.

- The dosage should be as follows:

Initially 25mg daily, then increased up to 100mg 4 times a day, dose increased at weekly intervals; usual dose 75mg 3 times a day. The lowest compatible dose with optimal response is recommended. A recommended dosage increment scale is shown below:

Week 1	One 25mg capsule daily
Week 2	One 25mg capsule twice daily
Week 3	Two 25mg capsules twice daily
Week 4	Two 25mg capsules three times daily
Week 5	Three 25mg capsules three times daily
Week 6	Three 25mg capsules four times daily
Week 7	One 100mg capsule four times daily

Each dosage level should be maintained for seven days in order to determine the patient's response.

Responsibilities of the specialist clinician initiating treatment

Summary

- To assess the suitability of the patient for treatment and initiate Dantrolene in appropriate patients. (including confirming the patient has no contra-indications to treatment and considering the relevance of any cautions, including interactions).
- To discuss the benefits and side effects of treatment with the patient/carer and the need for long term monitoring if applicable. Obtain informed consent in line with national guidance. This is particularly important for unlicensed products. To discuss the patient's responsibilities (see relevant section) in relation to the shared care agreement.
- To perform baseline tests and if appropriate routine tests until the patient is stable (see details of baseline and routine tests which should be carried out by the specialist in the monitoring section below).
- To prescribe for the first 12 weeks of treatment. The secondary care consultant will only have to review the patient again after initiation if it is clinically indicated.
- To ask the GP whether they are willing to participate in shared care.
- To provide the GP with a summary of information relating to the individual patient to support the GP in undertaking shared care (see shared care request form in Appendix A which includes a link to the shared care guideline).
- To advise the GP of any dosage adjustments required, monitoring required, when to refer back, and when and how to stop treatment (if appropriate).
- To advise the GP when the patient will next be reviewed by the specialist.
- To monitor the patient for adverse events and report to the GP and where appropriate Commission on Human Medicines/MHRA (Yellow Card scheme).
- To provide the GP with contact details in case of queries.
- To provide patient / carer with contact details for support and help if required; both in and out of hours.

Responsibilities of the primary care clinician

Acceptance of Responsibility by the Primary Care Clinician

It is optional for the primary care clinician to participate in taking on responsibility for shared care for the patient. Primary care clinicians will take on shared care only if they are willing and able.

Summary

- To reply to the request for shared care as soon as possible.
- To prescribe and adjust the dose as recommended by the specialist.
- To ensure there are no interactions with any other medications initiated in primary care.
- To continue monitoring as agreed with secondary care in the monitoring section below.
- To inform the specialist if the patient discontinues treatment for any reason.
- To seek the advice of the specialist if any concerns with the patient's therapy. For example:
  - Patient or general practitioner is **not** comfortable to continue with the existing regime due to either change in condition or drug side effects.
  - Advice in respect of concordance.
  - Special situations, (e.g. Pregnancy).
- Discontinue the drug as directed by the specialist if required.
- To conduct an annual medication review or more frequently if required.
- To identify adverse events if the patient presents with any signs and liaise with the hospital specialist where necessary. To report adverse events to the specialist and where appropriate the Commission on Human Medicines/MHRA (Yellow Card scheme).

Responsibilities of Patients or Carers

Summary

- To be fully involved in, and in agreement with, the decision to move to shared care.
- To attend hospital and primary care clinic appointments and to bring monitoring information e.g. booklet (if required). Failure to attend will potentially result in the medication being stopped.
- Present rapidly to the primary care prescriber or specialist should the clinical condition significantly worsen.
- Report any suspected adverse effects to their specialist or primary care prescriber whilst taking Dantrolene
- To read the product information given to them.
- To take Dantrolene as prescribed.
- Inform the specialist, primary care prescriber or community pharmacist dispensing their prescriptions of any other medication being taken – including over-the-counter medication.

Clinical Particulars

The details of side-effects, cautions, contraindications and interactions are not a complete list and the current BNF (MedicinesComplete — CONTENT > BNF > Drug: Dantrolene sodium) and the SPC (Dantrium 25mg Capsules - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)) remain authoritative.

BNF therapeutic class	Muscle Relaxants > Direct Acting.
Cautions and Contraindications	**Cautions** Females (hepatotoxicity); history of liver disorders (hepatotoxicity); if doses greater than 400mg daily (hepatoxicity); impaired cardiac function; impaired pulmonary function; duration of therapy (hepatoxicity most frequently reported between 2 and 12 months of treatment) patients over 30 years (hepatotoxicity); caution in patients with pre-disposition to cardiovascular disease and impaired respiratory function; therapeutic effect may take a few weeks to develop – discontinue if no response within 6-8 weeks. **Contraindications** Acute muscle spasm; avoid when spasticity is useful, for example, locomotion; evidence of hepatic dysfunction; patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.
Pregnancy and breast feeding	**Pregnancy** Although tautological studies in animals have proved satisfactory, dantrolene sodium does cross the placenta, therefore manufacturer advises avoid. **Breast feeding** Present in milk – manufacturer advises avoid. **Paediatric use** Dantrolene is not recommended for use in children.
Adverse Drug Reactions	**Common** Anorexia, mental depression, mental confusion, insomnia, nervousness, seizure, visual disturbance, speech disturbances, headache, pericarditis, pleural effusion with associated eosinophilia, respiratory depression, nausea and/or vomiting, abdominal pain, hepatotoxicity, liver function test disturbances, acne-like rash, skin rash, chills and/or fever. **Uncommon** Exacerbation of pre-existing cardiac insufficiency, dysphagia, constipation, sweating, incontinence, urinary frequency, urinary retention, haematuria, crystalluria.

	Unknown bradycardia, tachycardia, labile blood pressure, dyspnoea, GI bleeding, jaundice, hepatitis. • Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme: www.mhra.gov.uk/yellowcard
Monitoring	It is critical that patients/cares know how to recognise the signs of liver disorder and advise to seek prompt medical attention if symptoms such as anorexia, nausea, vomiting, fatigue, discoloured faeces, abdominal pain, dark urine or pruritus develop. Drowsiness may affect performance of skilled tasks (e.g. driving); effects of alcohol enhanced. There has been reports of hepatotoxicity with raised liver enzyme values, jaundice and hepatitis; fatalities have been reported. In the first report, the 14 fatalities occurred with doses in excess of 200mg daily (Utili, Boitnott & Zimmerman, 1977); a later review found the mean dose associated with 27 fatalities to be 582mg daily (Chan, 1990), while reports of non-fatal liver toxicity (95 cases) were associated with a mean dose of 263mg daily. The onset of hepatic injury was usually between 1 and 6 months after starting treatment and fatalities were not reported in the first 2 months. Only rarely did injury develop before 45 days of treatment. Test liver function before and at intervals during therapy (pre-treatment, at 2 months, 4 months, 6 months and 12 months as per Sheffield neurology team). If target dose is above 200mg per day or if given in combination with Tizanidine repeat at 6 months. If the dose is escalated, repeat the LFTs after a further 2 months. If LFTs are TWICE the upper limit, then check if there is any of potential cause. If no other cause, STOP dantrolene and re-check LFTs. If the LFTs remain raised, refer to gastroenterology. If spasticity becomes troublesome, a routine referral to neurology is warranted.
Interactions	The use of dantrolene with other potentially hepatotoxic drugs should be avoided. The following increase the risk of hepatoxicity: alcohol, atorvastatin, carbamazepine, demeclocycline, tetracycline, flucloxacillin, isoniazid, itraconazole, leflunomide, methotrexate, paracetamol, sulfasalazine, and valproate.
Re-Referral guidelines	The GP should write to the secondary care clinician who started the drug via post or via the secretaries email to refer back into secondary care.

Communication and contact details

Specialist to Primary Care Clinician
The specialist will inform the primary care clinician when they have initiated Dantrolene. When the patient is near completing the satisfactory initiation period, the specialist will write to the primary care clinician to request they take over prescribing and where possible give an indication as to the expected length of treatment. The specialist will also send a shared care request form to support the primary care clinician in undertaking shared care. (Appendix A)

Primary Care Clinician to Specialist
If the primary care clinician has concerns over the prescribing of Dantrolene, they will contact the specialist as soon as possible.

Contact names and details

Contact Details	Telephone number	Email
Dr Aijaz Khan	01226 432386	aijaz.khan@nhs.net
STH Neurology Secretaries	0114 271 1598	sth.neurologysecretaries@nhs.net

References

- BNF Online (Medicines Complete). Dantrolene monograph. https://www.medicinescomplete.com/#/content/bnf/_207282907#content%2Fbnf%2F_207282907%23pot-drugAction Accessed 12th November 2020.
- Chan, CH. (1990) Dantrolene sodium and hepatic injury. Neurology. 40 (9).
- EMC. Dantrium 25mg Capsules. https://www.medicines.org.uk/emc/product/1098/smpc https://www.medicines.org.uk/emc/product/1098/smpc%20Accessed%2012th%20November%202020 Accessed 12th November 2020.
- Nice Guideline [CG186] Multiple sclerosis in adults: management. Last updated November 2019. https://www.nice.org.uk/guidance/cg186/chapter/Recommendations Accessed 12th November 2020.
- Utili, R. Boitnott, JK. Zimmerman, HJ. (1977). Dantrolene-associated hepatic injury. Incidence and character. Gastroenterology. 72(4 Pt 1):610-6

https://www.england.nhs.uk/wp-content/uploads/2018/03/responsibility-prescribing-between-primary-secondary-care-v2.pdf

Development Process

This guidance has been produced by Lauren Clarke – Senior Pharmacist Interface following an AMBER classification status of Dantrolene by the Barnsley Area Prescribing Committee. This guideline was ratified by the Area Prescribing Committee on 9th February 2022.

Appendix A – Shared Care request form (Amber) for Dantrolene

- Specialist to complete when requesting primary care clinician to enter a shared care arrangement.
- Primary care clinician to return signed copy of form to sth.neurologysecretaries@nhs.net
- Both parties should retain a signed copy of the form in the patient's record.

From (**Specialist**): _____ **To** (**Primary care clinician**): _____

As per the agreed Barnsley shared care guideline for Dantrolene, this patient is now suitable for prescribing to move to primary care.

The patient fulfils the criteria for shared care and I am therefore requesting your agreement to participate in shared care. I have carried out baseline tests and initial monitoring as detailed in the shared care guideline.

Patient details

Name: _____ NHS Number: _____

Address: _____ DOB: _____

Diagnosed condition: _____

Amber Drug details

Drug name: _____ Dose and frequency: _____

Date of initiation: _____ Length of treatment: _____

The patient has been provided with sufficient medication to last until: _____

The patient will be reviewed by the consultant on: _____

The patient should be reviewed by the primary care clinician by: _____

Monitoring

The following monitoring should be undertaken by the primary care clinician. Refer to the monitoring section of the shared care guideline.

Parameter	Date next test due	Frequency

Communication

Consultant
Telephone number: _____ Fax number:_____

Email address: _____

Specialist Nurse
Telephone number: _____ Fax number: _____

Email address: _____

Confirmation of acceptance of shared care

Specialist (Doctor/Nurse) name: _____

Specialist (Doctor/Nurse) signature: _____ Date: _____

I, [insert name of primary care clinician] can confirm I :

☐ accept the request to participate in shared care for the patient named above and will complete the monitoring as set out in the shared care guideline for this medicine/condition.

☐ reject the request to participate in shared care for the patient named above. The reason for this being ……

Signature of primary care clinician: _____Date:_____

To save resources you have been sent appendix A of the shared care document. The full document (*Shared Care Guideline for Dantrolene (for the treatment of chronic severe spasticity of voluntary skeletal muscle in adults), date approved February 2022)* can be accessed on the Barnsley BEST website at the following link:
http://best.barnsleyccg.nhs.uk/clinical-support/medicines/shared-care-guidelines/
Or via the Barnsley Area Formulary www.barnsleyformulary.nhs.uk