North Central London
Joint Formulary Committee

Shared Care Guideline
Use of stiripentol in adults with Dravet syndrome

Dear GP

The information in the shared care guideline has been developed in consultation with Primary Care and it has been agreed that it is suitable for shared care.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the Consultant when treatment is initiated. It is important that patients are consulted about treatment and are in agreement with it.

Contents

1. Introduction Target audience 2
2. Shared Care criteria 2
3. Shared care responsibilities 3
   3.1. Consultant and /or Specialist Nurse 3
   3.2. General Practitioner 3
   3.3. Patient responsibility 4
   3.4. Clinical Commissioning Group 4
4. Indications 4
5. Dose and Administration 4
6. Adverse effects 5
7. Cautions 6
8. Clinical Monitoring 6
9. Contraindications 6
10. Drug Interactions 7
11. References 8
12. Contact Details 9

Appendix 1: xxx transfer form: from [Trust] to GP practice 11

1. Introduction and target audience

This document should provide sufficient information to enable you to make an informed decision regarding the clinical and legal responsibility for prescribing this drug.

Stiripentol is indicated for use in conjunction with clobazam and valproate as adjunctive therapy of refractory generalized tonic-clonic seizures in patients with severe myoclonic epilepsy in children, adolescents and adults (SMEI, Dravet's syndrome) whose seizures are not adequately controlled with clobazam and valproate as per NICE NG217. It should only be used under specialist supervision.

The efficacy and safety of the stiripentol/valproate/clobazam combination started at paediatric age has shown to be maintained long term through into adulthood (Balestrini & Sisodiya, 2017; Chiron et al, 2018; Rosati et al, 2019). Such prolonged stiripentol therapy tends to positively impact the late prognosis of epilepsy, especially when initiated before adolescence.

Patients that started treatment with stiripentol during childhood at specialist paediatric services are normally transferred to the adult services at 18 years old. This shared care guideline supports prescribing for continued use in adults (≥18 years of age) whose seizures have previously been well controlled with stiripentol as children. This shared care guideline also supports the off-label initiation of stiripentol in adults with treatment refractory seizures due to Dravet syndrome (as per NCL JFC approval – see minutes from the June 2021 meeting).

Once the child has transitioned to the adult services and achieved a stable, optimal dose, a shared care arrangement with you will be requested. It will clarify responsibilities between the specialist and general practitioner (GP) for managing the prescribing of Stiripentol such as:

- Who will prescribe;
- Who will monitor;
- Any tests required (e.g. blood tests), the exact names/nature of the tests, why they are needed, the frequency of testing, the location in which these will be carried out and action to be taken for any abnormal results
- Which clinician will be responsible for receipt and review of the results;
- Who will communicate any necessary changes in dose to the patient and the GP;

GPs are asked to participate in this shared care arrangement. If the GP is not confident to undertake these roles, the total clinical responsibility for the patient for the epilepsy remains with the specialist. However, the GP is encouraged to contact the consultant to discuss their concerns and consider if further support can be provided to enable shared care. Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the Consultant / specialist nurse when treatment is initiated. It is important that patients are consulted about treatment and are in agreement with it.

2. Shared Care criteria

Patients initiated on stiripentol by a specialist paediatric centre during childhood who have transitioned into the adult services and are stabilised on treatment, or have been initiated stiripentol in adulthood. Patients should be monitored appropriately at baseline and after initiation of treatment with no problems identified during this period at point of transition to adult services. Stiripentol should be prescribed in conjunction with clobazam and valproate.

3. Shared care responsibilities

3.1. Consultant and /or Specialist Nurse

1) Ensure the patient fulfils the criteria for treatment as per NICE guidance
2) Before initiating treatment, perform baseline FBC, U&E's, LFT's tests
3) Discuss the benefits and side effects of stiripentol treatment with the patient. Provide the patient with a Patient Information Leaflet (PIL), explain it and ensure that the patient understands the reason for the treatment, and dosing regimen.
4) Send a letter to the GP along with shared care criteria and transfer form, requesting whether they are willing to participate in shared care. The consultant should ensure that contact details are included within the request to enable the GP to contact them for further support or advice if needed. Indication, dose and frequency to be decided by the hospital team.
5) Adjust the doses of other AEDs as appropriate.
6) Initiate and stabilise treatment with stiripentol and continue to prescribe until the GP formally agrees to share care. Patients will be seen in clinic prior to consideration of shared care.
7) Discuss the shared care arrangement with the patient
8) Provide results of baseline tests and recommend frequency of monitoring to GP. The consultant must also explain what the recommended tests are, why they are needed and the location in which these tests will be carried out
9) Send a letter to the GP after each clinic attendance ensuring current dose, weight, most recent blood results and frequency of monitoring are stated
10) Inform GP of blood test results, actions to take in case of abnormal results, and advise the GP on when to adjust the dose, stop treatment, or consult with specialist
11) Periodically review the patient's condition and communicate promptly with the GP when treatment is changed. Counsel the patient on any dose changes that are made during clinic appointments
12) Evaluate adverse effects reported by GP or patient
13) Report adverse events to the MHRA (via yellow card scheme) and GP
14) Inform GP of patients who do not attend clinic appointments
15) Ensure that clear backup arrangements exist for GPs to obtain advice and support. Consultant and clinical nurse contacts must be included in the Shared Care Guideline.

3.2. General Practitioner

1) Complete transfer form and send back to hospital confirming acceptance/ rejection of shared care for patient. If GP unable to agree to shared care, inform the Hospital team stating reasons within ***14 days*** of receipt of request. If no response is received with 14 days, the Consultant will assume the GP has accepted shared care.
2) Monitor patient's overall health and well-being
3) Prescribe the drug treatment as described (but not to alter the dose unless advised to do so by the specialist). The term "as directed" **SHOULD NOT** be used
4) Ensure that the patient understands the dosing
5) Ensure the patient understands that he/she must report the warning symptoms as listed under "adverse effects"
6) Ensure compatibility with concomitant medication

7) Monitor results at recommended frequencies as described under “clinical monitoring” or as directed by the specialist and inform the Consultant if abnormal
8) Adjust the dose as advised by the specialist (where applicable) and counsel patient on any dose changes
9) Report any adverse events and non-compliance to the hospital specialist, where appropriate
10) Stop treatment on advice of specialist or immediately if urgent need arises
11) Help in monitoring the progression of disease and inform the hospital team of any changes to medication
12) Report adverse events to the specialist and MHRA via the yellow card scheme.
13) All requests for repeat prescriptions should be reviewed individually prior to issuing

3.3. Patient responsibility

1) Attend all hospital and GP appointments.
2) Take stiripentol at the prescribed dose and frequency.
3) Report to the specialist or GP if he/she does not have a clear understanding of the treatment.
4) Inform specialist or GP of any other medication being taken, including over-the-counter products.
5) Report any adverse effects or warning symptoms to GP or specialist.
6) Inform hospital and GP of any changes in address or telephone numbers.
7) Share any concerns in relation to treatment with Stiripentol with Consultant neurologist.
8) Have regular monitoring blood tests undertaken according to an agreed programme.
9) Report any changes in disease symptoms to the Consultant neurologist or GP.

3.4. Clinical Commissioning Group

1) To provide feedback to Trusts from the standard letter, via the NCL shared care group.
2) To support GPs to make the decision whether or not to accept clinical responsibility for prescribing.
3) To support Trusts in the resolving issues that may arise as a result of shared care.

4. Indications

Stiripentol is indicated for use in conjunction with clobazam and valproate as adjunctive therapy of refractory generalized tonic-clonic seizures in patients with severe myoclonic epilepsy in children, adolescents and adults (SMEI, Dravet's syndrome) whose seizures are not adequately controlled with clobazam and valproate as per NICE NG 217. It should only be used under specialist supervision.

Stiripentol is licensed for the use in infancy, however the Summary of Product Characteristics (SPC) does suggest that treatment can be continued for as long as efficacy is observed. In NCL, stiripentol is also used off-label for the initiation in adults with treatment refractory seizures due to Dravet syndrome (as per NCL JFC approval – see minutes from the June 2021 meeting). Usually, the first six months of treatment is offered from the specialist, and only continued in primary care if effective and safe.

5. Dose and Administration

Stiripentol is initiated with an increasing dosing schedule to reach a dose of 50mg/kg/day which is administered in 2-3 divided doses and is given in conjunction with clobazam and valproate. Doses must always be taken with food to avoid the degradation of stiripentol in an acidic environment. Stiripentol should not be taken with milk or dairy products, carbonated drinks, fruit juice or food and drinks that contain caffeine or theophylline.

The sachet formulation has a slightly higher C_{max} than the capsules, thus the formulations are not bioequivalent. Clinical supervision by GP with support/advice from consultant and/or specialist nurse is recommended if switching between formulations, in case of problems with tolerability.

Preparations available (BNF, November 2025)

Stiripentol is available as 250mg and 500mg capsules or sachets under the brand name Diacomit®. Bioavailability differs between the sachet and capsule preparations and therefore clinical supervision by GP with support/advice from consultant and/or specialist nurse is recommended if switching between formulations.

BNF list prices (correct to November 2025)

Diacomit® 250mg (60 pink capsules pack): £284.00

Diacomit® 500mg (60 white capsules pack): £493.00

Diacomit® 250mg (60 sachets pack): £284.00

Diacomit® 500mg (60 sachets pack): £493.00

6. Adverse effects

Adverse effect	Frequency	Suggested management by GP
Loss of appetite, weight loss, anorexia	Very Common	If weight loss unexplained or severe (>5% compared to baseline) refer to the specialist for advice
Ataxia, drowsiness, hypotonia, dystonia	Very Common	If severe or unexplained symptoms refer back to the specialist for advice
Neutropenia	Common	If moderate to severe neutropenia refer back to the specialist for advice (see monitoring section below)
Nausea and vomiting	Common	If other reasons excluded and thought to be an allergy, stop immediately and refer back to the specialist for advice
Behavioural disorders, sleep disorders, aggressiveness, irritability	Common	If severe or unexplained behavioural disorders, refer back to the specialist for advice
Hyperkinesia	Common	If severe or unexplained hyperkinesia, refer back to the specialist for advice
Diplopia	Uncommon	If severe or unexplained diplopia, refer back to the specialist for advice
Photosensitivity, rash, cutaneous allergy and urticaria	Uncommon	If other reasons excluded and thought to be an allergy, stop immediately and refer back to the specialist for advice
Abnormal liver function tests	Rare	If LFTs >5 times the upper limit of normal, refer back to the specialist for advice (see monitoring section below)
Thrombocytopaenia	Rare	If moderate to severe thrombocytopaenia, refer back to the specialist for advice (see monitoring section below)

If referred back to the specialist, the specialist will consider withdrawal/ dose adjustment/interactions with clobazam or valproate
In case of an allergic reaction, stiripentol should be immediately discontinued and the consultant and/or specialist nurse should be informed.

For a full list of adverse effects, refer to the Summary of Product Characteristics (https://www.medicines.org.uk/emc/product/10300/smpc).

Serious suspected reactions (even if well recognised or causal link uncertain) should be reported to the Commission on Human Medicines (CHM) via *http://yellowcard.mhra.gov.uk*

7. Cautions

- Neutropenia may be associated with the use of stiripentol, valproate and clobazam. Blood counts should be assessed prior to starting treatment with stiripentol. Unless otherwise clinically indicated, blood counts should be checked every 6 months;
- Stiripentol is not recommended for use in patients with impaired hepatic and/or renal function.

For a full list of cautions, refer to the Summary of Product Characteristics (https://www.medicines.org.uk/emc/product/10300/smpc).

8. Clinical Monitoring

Blood test	Frequency	Action if out of range
Full blood count	Six-monthly	If moderate to severe neutropenia is observed (<1.0 x 10^9/L), refer back to the specialist for advice
Liver function test	Six-monthly	If abnormal LFTs are observed (i.e. ALT/AST >5 times the upper limit of normal), refer back to the specialist for advice
Urea and electrolytes	Six-monthly	If deterioration in renal function is observed, refer back to the specialist for advice

The specialist may conduct additional investigations as required e.g. EEG if changes in seizure pattern or increased drowsiness, levels of all concomitant antiepileptic drugs if side effects, etc. The results will be sent to the GP.

9. Contraindications

- Hypersensitivity to Stiripentol or to any of the Diacomit® excipients;
- A past history of psychoses in the form of episodes of delirium;
- Patients with liver and/or renal impairment;
- Stiripentol (Diacomit®) sachets contain aspartame and therefore should be avoided in patients with phenylketonuria;
- Stiripentol (Diacomit®) sachets contain glucose and should be avoided in patients with glucose-galactose malabsorption;
- Stiripentol (Diacomit®) sachets contain sorbitol and should be avoided in patients with hereditary fructose intolerance.

For a full list of contraindications, refer to the Summary of Product Characteristics.

10. Drug Interactions

Interactant	Information
Food and drinks containing milk, dairy products, carbonated drinks, fruit juices, caffeine or theophylline	**Avoid taking at the same time as stiripentol**
Immunosuppressants (tacrolimus, ciclosporin, sirolimus)	Stiripentol raises blood levels of immunosuppressants - **to be avoided unless strictly necessary**
Statins	Increased risk of dose-dependent adverse reactions e.g. rhabdomyolysis - **to be avoided unless strictly necessary**
Rye ergot alkaloids (ergotamine, dihydroergotamine)	Ergotism with possibility of necrosis of the extremities by inhibition of hepatic elimination of rye ergot - **to be avoided unless strictly necessary**
Cisapride, halofantrine, pimozide, quinidine, bepridil	Increased risk of cardiac arrhythmias and torsades de pointes/wave burst arrhythmia in particular-**to be avoided unless strictly necessary**
Midazolam	Increased plasma benzodiazepine levels which can lead to excessive sedation – **combination with stiripentol requires precaution**
Chlopromazine	Enhances the central depressant effect of chlorpromazine - **combination with stiripentol requires precaution**
Theophylline, caffeine	Increased levels of theophylline and caffeine - **combination with stiripentol requires precaution**
Phenobarbital, primidone, phenytoin, carbamazepine, clobazam, valproate, diazepam, ethosuximide and tiagabine	Stiripentol is an inhibitor of cytochrome P450 thus increase plasma levels of these drugs with potential risk of overdose - **Doses of these drugs must be reduced. Monitor plasma levels of antiepileptic drugs where this is possible, when combined with stiripentol**.
Drugs metabolised by CYP2D6 e.g. betablockers, antidepressants (fluoxetine, paroxetine, sertraline, imipramine, clomipramine), antipsychotics (haloperidol), analgesics (codeine, dextromethorphan, tramadol)	**In- vitro stiripentol showed inhibition of CYP2D6, therefore drugs metabolised by this enzyme may require dose adjustments.**

For a full list of drug interactions, refer to the Summary of Product Characteristics

11. References

Epilepsies: diagnosis and management, NICE Clinical Guidance 137, http://www.nice.org.uk/guidance/cg137 last updated 11 February 2020

BNF Stiripentol, https://bnf.nice.org.uk/drug/stiripentol.html last accessed on 05/05/20

Spc Diacomit® 500mg hard capsules, Alan Pharmaceuticals, https://www.medicines.org.uk/emc/product/10305/smpc last updated on 31/05/2019

Spc Diacomit® 250mg hard capsules, Alan Pharmaceuticals, https://www.medicines.org.uk/emc/product/10300/smpc last updated on 31/05/2019

Spc Diacomit® 500mg sachets, Alan Pharmaceuticals, https://www.medicines.org.uk/emc/product/10308/smpc last updated on 31/05/2019

Spc Diacomit® 250mg sachets, Alan Pharmaceuticals, https://www.medicines.org.uk/emc/product/10304/smpc last updated on 31/05/2019

Balestrini S et al 2016. Audit of use of stiripentol in adults with Dravet syndrome. Acta Neurol Scand. 2017 Jan;135(1):73-79 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5157719 last accessed on 05/05/20

Chiron C, Helias M, Kaminska A, Laroche C4, de Toffol B5, Dulac Oet al. Do children with Dravet syndrome continue to benefit from stiripentol for long through adulthood? *Epilepsia*. 2018;59:1705-1717
https://www.ncbi.nlm.nih.gov/pubmed/30132836 last accessed 05/05/20

Stiripentol use in adults with Dravet Syndrome, https://cdn.ymaws.com/www.theabn.org/resource/collection/0F3D17B6-B02E-4B65-B0EA-4AF6F605EF42/Stiripentol_MHRA_5Mar19_Final_SMS.pdf; last accessed 1/5/2020

https://www.scottishmedicines.org.uk/SMC_Advice/Advice/524_08_stiripentol__DIACOMIT_/stiripentol_Diacomit; last accessed 1/5/2020

Chiron C, Marchand MC, Tran A, Rey E, d'Athis P, Vincent J, et al. Stiripentol in severe myoclonic epilepsy in infancy: a randomised placebo-controlled syndrome-dedicated trial. STICLO study group. *Lancet*. 2000;356:1638–1642

Strzelczyk A, Schubert-Bast S, Reese JP, Rosenow F, Stephani U, Boor R. Evaluation of health-care utilization in patients with Dravet syndrome and on adjunctive treatment with stiripentol and clobazam. *Epilepsy Behav*. 2014;34:86–91

Inoue Y, Ohtsuka Y, Oguni H, Tohyama J, Baba H, Fukushima K, et al. Stiripentol open study in Japanese patients with Dravet syndrome. *Epilepsia* 2009;50:2362–2368.

Inoue Y, Ohtsuka Y, STP-1 Study Group .Effectiveness of add-on stiripentol to clobazam and valproate in Japanese patients with Dravet syndrome: additional supportive evidence. *Epilepsy Res.* 2014;108:725–731.

Inoue Y, Ohtsuka Y, STP-1 Study Group. Long-term safety and efficacy of stiripentol for the treatment of Dravet syndrome: a multicenter, open-label study in Japan. *Epilepsy Res*. 2015;113:90–97.

Wirrell EC, Laux L, Franz DN, Sullivan J, Saneto RP, Morse RP, et al. Stiripentol in Dravet syndrome: results of a retrospective U.S. study. *Epilepsia* 2013;54:1595–1604.

Myers KA, Lightfoot P, Patil SG, Cross JH, Scheffer IE. Stiripentol efficacy and safety in Dravet syndrome: a 12-year observational study. *Dev Med Child Neurol*. 2018;60:574–578.

Rosati A, Boncristiano A, Doccini V, et al. Long-term efficacy of add-on stiripentol treatment in children, adolescents, and young adults with refractory epilepsies: A single center prospective observational study. Epilepsia. 2019;60(11):2255-2262.

12. Contact Details

Hospital

Hospital switchboard:	020 3448 1901
Consultant: Name	Simona Balestrini / Sanjay Sisodiya 01494 601300
NHNN Pharmacy	020 3448 3140

Document control

Date	Version	Amendments
21/04/2021	1.0	New document
23/12/2022	2.0	Updated to include initiation in adult patients – as per NCL JFC June 2021 minutes
21/01/2026	2.1	Minor amendment (CG 137 has now been replaced by NG217)
26/03/2026	2.2	Updated with extended review date to 30/06/2026

Groups / Individuals who have overseen the development of this guidance:	Dr S Balestrini Dr S Sisodiya Ms A Fariah Ms N Patel NCL CCG – Barnet borough MMT
Groups which were consulted and have given approval:	NCL Shared Care Group NCL CCG NCL Provider Trusts
File name:	Shared Care Guideline: Use of stiripentol in adults with Dravet syndrome
Version number:	2.2
Available on:	www.ncl-mon.nhs.uk
Disseminated to:	Formulary Pharmacists and Commissioners
Equality impact assessment:	Nil identified
NCL Shared Care Group Approval date:	23/12/2022
Review date:	30/06/2026

Appendix 1: xxx transfer form: from [Trust] to GP practice

Section A: to be completed by secondary care *Send to practice*

This document is to request the shared care pathway of your patient and comprises an agreement between the GP a named consultant. The patient will continue to be seen by the named consultant as regular follow up.

Fix address label here (ensure NHS no. on)	Clinic stamp *or give details below*

Department			
Clinic phone			
Consultant		Email	
Indication for prescription			
Drug prescribed			
Date	Drug started	Current dose	
Relevant conditions			
Monitoring variations			
Date next blood test		Next disease review due in	months' time.

Section B: [Accept Shared Care] to be completed by practice *Send back **FAO referring consultant** above*

The above patient has been accepted into our monitoring service.

Practice date for next blood test		Practice stamp
Signed / Designation		
Date		

Section B: [Reject Shared Care] to be completed by practice *Send back **FAO referring consultant** above*

The above patient has not been accepted into our monitoring service.

Reason		Practice stamp
Signed / Designation		
Date		

Section C: Shared Care Agreement (Trust specific information)

This section (and reference to it: Consultant Shared Care Responsibilities point 3) can be removed if all Trusts and CCGs have the same contractual arrangements.

Contact details	
Clinic / service	
Address	
Email	
Telephone	

Contractual details

CCG 1	
No. weeks Trust to prescribe	
Treatment reviews to be conducted by trust (frequency)	

CCG 2	
No. weeks Trust to prescribe	
Treatment reviews to be conducted by trust (frequency)	

CCG 3	
No. weeks Trust to prescribe	
Treatment reviews to be conducted by trust (frequency)	