Department of Health & Social Care

NHS

Supply Disruption Alert

SDA/2020/012 Issued: 21/08/2020

Lithium carbonate (Priadel®) 200mg and 400mg modified release tablets – Supply Disruption

Summary

- Priadel® (lithium carbonate) 200mg and 400mg modified-release tablets are being discontinued in the UK and remaining supplies of both strengths are expected to be exhausted by April 2021.
- Lithium (Priadel®, Camcolit® and Liskonum® brands) is a first line treatment for patients with bipolar disorder. It is also licensed for the treatment and prophylaxis of *recurrent depression*, and *aggressive or self-harming behaviour*, and used off-license in the treatment of *cluster headaches*.
- Clinical guidance advises that patients must be maintained on the same brand of lithium to ensure that a consistent serum lithium level is maintained. The switching of brands necessitated by this SDA will require individualised determination of dose, close monitoring of serum lithium levels and vigilance for relapse and tolerability in all cases.
- Other brands of lithium carbonate tablets remain available including Liskonum® 450mg modified-release tablets, Camcolit® 400mg modified-release tablets and lithium carbonate Essential Pharma 250mg tablets.

Action

All healthcare professionals in primary, secondary or specialist healthcare services should be aware of the following advice.

For all prescribers managing patients receiving treatment with Priadel® (lithium carbonate) 200mg and 400mg modified release tablets, the advice provided in the below section should be used in conjunction with actions listed below for specific healthcare settings:

- Lithium should continue to be prescribed as appropriate.
- Prescribers should not initiate new patients on Priadel® brand (200mg & 400mg) modified-release tablets.
- All patients currently prescribed Priadel® (200mg & 400mg) modified-release tablets should be switched to an alternative lithium brand at the nearest equivalent dose once baseline serum lithium levels have been established (with the help of mental health specialists where appropriate).
- When switching patients to an alternative brand of lithium, prescribers should follow the monitoring advice in the SPC (see Supporting Information section) and later sections of this SDA to ensure safe switching; switches should be made without cross tapering (lowering the dose of one medicine while simultaneously increasing the dose of the new medicine) and without interruption to treatment.
- When switching patients to an alternative lithium brand, prescribers (GPs and if necessary, in conjunction with a mental health specialist) should ensure patients are individually assessed so that the most appropriate treatment is selected. Advice provided in later sections of this alert should be used to do this.
- Prescribers should ensure all patients being switched to an alternative lithium formulation have individualised management plans. For those taking lithium for psychiatric conditions, this may be a valuable opportunity to review relapse indicators and recovery plans.

- Prescribers are actively encouraged to ensure patient and/or carer involvement in the decision-making process.
- Prescribers should ensure that all patients have a 'Lithium treatment pack'. The pack consists of a patient information booklet, lithium alert card, and a record book for tracking serum-lithium concentration. (Packs can be ordered from 3M Tel:- 0845 610 111 Email: nhsforms@mmm.uk.com)
- Monitoring requirements and prescriber responsibility should also be explained to the patient/carer as part of a safe switch between lithium brands.
- When patients are transferred between healthcare services, patients and service providers should have a clear understanding of who is responsible for their care.

For patients prescribed Priadel® modified-release tablets in Primary Care GP's should:

- Proactively identify all patients prescribed Priadel® modified-release tablets for all indications (including off-license indications);
- Make early contact with all patients/carers to alert them of the requirement to switch brands of lithium and ensure individualised treatment plans are made in conjunction with mental health specialists if required;
- Ensure patients are switched to an alternative lithium brand at the earliest opportunity. Where prescribers are unable to switch patients to an alternative therapy safely, they are advised to refer patients to specialist services; and
- Ensure that patients currently prescribed Priadel® modified-release tablets for the treatment of cluster headaches are reviewed and switched to an alternative brand and if required, GP's should discuss with and/or refer to neurology services, not mental health specialists.

For patients prescribed Priadel® modified-release tablets in Mental Health Services, prescribers should:

- Proactively identify all patients under their care (including those referred by primary care) who are currently prescribed Priadel® modified-release tablets; and
- Ensure patients are reviewed and, where ongoing lithium therapy is required, switched to an alternative brand of lithium in a timely manner, that individualised management plans are agreed and enacted, and that this is communicated to the patient's GP.

For patients prescribed Priadel® modified-release tablets in a Health and Justice setting, prescribers should:

- Proactively identify all patients currently prescribed Priadel® modified-release tablets;
- Follow the principles outlined for the switching of brands in Primary care or Mental Health Services but in addition;
  - Take length of sentence and remand status into consideration and ensure appropriate communication is shared with the patient's Healthcare Professional(s) outside of the Health and Justice system to ensure continuity of care during and immediately after the switching process in the event of patient release;
  - Switch patients to an alternative lithium brand at the earliest opportunity. Where prescribers are unable to switch patients to an alternative therapy safely, patients should be referred to the relevant specialist services to ensure the safe and timely switching to alternative brands of lithium.
- For all patients newly admitted into custody, careful monitoring of serum lithium levels will be required due to the changes in their lifestyle and possible alteration of medication that takes place during clinical reviews at admission.

Deadlines for actions

Actions initiated:	on receipt of this alert
Actions completed:	as soon as possible

Product details

Priadel® (lithium carbonate) 200mg and 400mg modified-release tablets.

Problem / background

Essential Pharma will discontinue Priadel® 200mg and 400mg modified-release tablets with supplies expected to be exhausted by April 2021.

Lithium is indicated for the treatment and prophylaxis of mania, bipolar disorder, recurrent depression and the treatment of aggressive or self-harming behaviour. It may also be used for unlicensed indications such as cluster headache and augmentation therapy in treatment resistant depression.

Clinical guidance advises that patients must be maintained on the same brand of lithium. As Priadel® modified-release tablets are being discontinued, there is a need to ensure patients are safely stabilised on a new brand of lithium therapy. This will require close monitoring of each patient.

When prescribed as prophylaxis in bipolar disorder (the most common indication for lithium), sudden discontinuation of lithium is associated with relapse in up to 50% of patients. Relapse is often into mania. It is therefore important that therapeutic serum levels are maintained with NO interruptions to treatment when switching brands of lithium.

Alternative brands

There are several alternative licensed lithium brands available (see table 1 below). In selecting an alternative brand and implementing a switch, prescribers may find the advice in the following sections useful when developing individualised treatment plans.

Table 1. Lithium brands

Brand	Salt	Strength	Presentation	Availability
Priadel®	Lithium Carbonate	200mg	Modified-release tablets	Discontinued April 2021
Priadel®	Lithium Carbonate	400mg	Modified-release tablets	Discontinued April 2021
Essential Pharma*	Lithium Carbonate	250mg	Film-coated (f/c) tablets	Remains Available
Camcolit®	Lithium Carbonate	400mg	Modified-release tablets	Remains Available
Liskonum®	Lithium Carbonate	450mg	Modified-release tablets	Remains Available

*This product was previously Camcolit® brand and whilst genericised in 2015, these continue to have Camcolit inscribed on the tablet.

Please note: liquid preparations exist for lithium but as these contain lithium citrate, not lithium carbonate, information on switching to these preparations is not included within this alert; if prescribers deem a switch to a liquid formulation appropriate, relevant guidance should be consulted to ensure safe switching.

Advice on switching patients to alternative lithium brands

To expedite the safe transfer of patients from Priadel® (lithium carbonate) modified-release tablets to alternative brands, prescribers may wish to incorporate the following points into individualised treatment plans. These should not be considered formal guidance, rather a framework to facilitate the development of local strategies.

Switching brands of lithium

- If switching to Camcolit® or Essential Pharma Lithium carbonate film-coated tablets or Liskonum®; discontinue Priadel® modified-release tablets and start the alternative brand at a dose schedule as

close as possible to the previous prescription. Ensure that there is NO interruption to treatment or "double dosing".

- In many cases, a direct switch from Priadel® modified-release tablets to the same dose of a different brand will be feasible, e.g. Priadel® modified-release tablets 800mg at night to Camcolit® modified-release 800mg at night. In some cases, a directly comparable dose switch will not be feasible, e.g. Priadel® modified-release tablets 600mg at night may need to be changed to Camcolit® modified-release 400mg plus Lithium carbonate 250mg f/c tablets to total 650mg at night or to Lithium carbonate f/c tablets 500mg (2 x 250mg f/c tablets) at night. The dose selected should be based on the baseline 12-hour serum lithium level and the target therapeutic range. Illness stability, current and past propensity to toxicity, and any potential for drug interactions should also be considered.
- Serum lithium levels should be measured in line with relevant national guidance and manufacturers information.

Monitoring for switching lithium brands

- A baseline serum lithium level should be taken before switching. Serum lithium levels should be taken 12 hours after the last dose (range 11-13 hours post-dose). Consult specialist literature for information on appropriate lithium levels. Where the appropriate lithium level is unknown, the patient's specialist should be consulted for guidance.
- Switches should only be undertaken if services are in place to permit regular and, if necessary, frequent monitoring of serum lithium levels.

Safety considerations when switching brands of lithium

For patients prescribed lithium, prescribers and patients (and their carers where appropriate) should be aware of the common signs and symptoms of lithium toxicity. Lithium toxicity can occur within the typical therapeutic range, especially in the elderly. However, it is more commonly seen when 12-hour sample levels exceed 1mmol/L. Signs of toxicity include, but are not limited to, the following (prescribers should consult product literature for further information):

- Nausea, diarrhoea, blurred vision, polyuria, light headedness, fine resting tremor, muscular weakness, drowsiness and increasing confusion.

Lithium should always be prescribed by brand, and the strengths available may be the principal determinant of the brand selected. Note that for some brands of lithium tablets (e.g. Camcolit®), the tablet score line is only to facilitate ease of swallowing and not to divide into equal doses. Prescribers should consult the brand SPC and/or seek the advice of specialist pharmacists in cases of uncertainty.

Considerations when switching patients to alternative lithium brands

Dosing schedules and lithium levels

A change in brand of lithium requires the same precautions as an initiation of treatment – particular attention should be paid to the monitoring requirement recommendations. In developing individualised treatment plans with patients taking lithium, prescribers should ensure that they are aware of each patient's individual therapeutic target range; if prescribers are unsure, they should seek specialist advice.

When switching patients from Priadel® modified-release tablets prescribers should aim, where possible, to switch patients to the brand and dose that reflects their current therapy most closely.

In many cases, switching to the same dose of a different brand will be possible. This does not guarantee the same therapeutic effect or tolerability, for reasons related to bioavailability differences between brands. In some instances, an exact dose conversion will not be possible and here, individualised, agreed, documented and communicated treatment plans are important.

Monitoring patients after switching

Lithium has a narrow therapeutic range. Serum levels should be checked 7 days after switching brands.

Lithium samples should be taken 12-hours after the last dose (range 11-13) hours post dose and referenced against the target range (see national guidelines for the various indications). After any change in dose or brand, serum lithium levels should be checked once steady state levels have been achieved (typically 4-7 days). The development of toxicity or signs of relapse should prompt earlier measurement.

When switching patients to an alternative brand of lithium carbonate, prescribers should consider the following monitoring advice:

- Lithium levels should be taken 7 days after any change in brand, dose or formulation and 12-hours after the last dose of lithium (range 11-13 hours post-dose).
- Follow monitoring guidelines as per initiation guidance in the SPC/other reference sources.
- Despite equivalent 12-hour serum levels, some patients may not tolerate different brands of lithium in the same way.
- Additional monitoring and intervention may be required if signs of lithium toxicity occur with dosage alteration, and in the presence of significant intercurrent disease, symptoms of mania or depressive relapse, or significant changes in sodium or fluid intake.
- More frequent monitoring is required if patients are receiving any drug treatment that interacts with and/or affects renal clearance of lithium e.g. diuretics, ACE-I and NSAIDs.
- The patient's clinical condition and mental state will require careful monitoring, and a review is indicated in all cases where the brand of lithium is switched.

Interpretation of serum lithium levels
The BNF quotes the reference range for serum lithium levels as 0.4 – 1.0mmol/L. Lower serum lithium levels may prove therapeutic in elderly patients and they are more likely to show toxic symptoms at lower concentrations than working-age adults.

Prescribers should also be aware that there are a number of factors that should be considered in determining what lithium level is safe and effective for individual patients, such as the duration of therapy, the dose schedule and the timing of the sample in relation to the last dose. Switching should be individualised, but with reference to NICE guidance (https://www.nice.org.uk/guidance/cg185, https://www.nice.org.uk/guidance/cg90) and the relevant manufacturers SPC as appropriate.

Patient/Carer Counselling

All patients will require careful counselling on the need to switch brands of lithium and alerted to the requirements for monitoring before and after switching. Advice should be provided on who they should contact if they experience side effects on the alternative brand of lithium tablets.

Patients should be reminded not to make any major lifestyle changes during the process of switching; in particular they should maintain stable levels of fluid intake and exercise. If possible, other medications should not be initiated or altered until stabilisation on the new brand of lithium has been achieved. This is particularly important for medications with known interactions with lithium, including over the counter medications such as NSAIDs.

Following the switch in brand, patients should be encouraged to return any unused Priadel® modified-release tablets to their Community Pharmacy for safe disposal and to avoid confusion.

There is a Medicine Guide for lithium on the NHS website which provides useful information for patients taking this medicine and can be found at the following link: https://www.nhs.uk/medicines/lithium/

Care Arrangements

GPs and mental health specialists should work collaboratively to support patients and their carers in managing the switch of Priadel® modified-release tablets to alternative brands of lithium carbonate tablets.

Supporting Information

Summary of Product Characteristics for remaining lithium presentations can be found at the following:

- Camcolit 400 mg, controlled release Lithium Carbonate
- Lithium Carbonate Essential Pharma 250 mg film-coated tablets
- Liskonum 450mg tablets

Distribution

Trusts (NHS boards in Scotland)

CAS and SABS (NI) liaison officers for onward distribution to all relevant staff including:

- Chief pharmacists
- Clinical governance leads
- Clinical Procurement Specialists
- Community hospitals
- Community nurses
- District nurses
- Hospital pharmacies
- Hospital pharmacists
- Immunologists
- Medical directors
- Mental Health Trusts
- Mental Health Specialists
- Outpatient clinics
- Pharmaceutical advisors
- Pharmacists
- Gynaecologists
- Psychiatrists
- Haematologists

NHS England regional teams

For onward distribution to Community Pharmacists.

General Practice

For onward distribution to all relevant staff including GPs, Practice Managers and Practice Nurses.

Independent distribution

Establishments registered with the Care Quality Commission (CQC) (England only)

Enquiries

Send enquiries about this notice to the DHSC Supply Resilience Team, quoting reference number **SDA/2020/012 -** Email:supplyresiliencemd@dhsc.gov.uk

References

1. Grandjean EM, Aubry J-M. Lithium: Updated Human Knowledge Using an Evidence-Based Approach Part III: Clinical Safety. *Cns Drugs.* 2009;23(5):397-418.
2. Cooper TB, Simpson GM, Lee JH, Bergner PEE. Evaluation of a slow-release lithium-carbonate formulation. *American Journal of Psychiatry.* 1978;135(8):917-922.
3. Ward ME, Musa MN, Bailey L. Clinical pharmacokinetics of lithium. *Journal of Clinical Pharmacology.* 1994;34(4):280-285.
4. Alda M. Pharmacokinetics of lithium. In: Baur M, Grof P, Müller-Oerlinghausen B, eds. *Lithium in neuropsychiatry: the comprehensive guide.* UK: Oxon; 2006:321-328.
5. Shelley RK, Silverstone T. Single dose pharmacokinetics of 5 formulations of lithium - a controlled comparison in healthy-subjects. *International Clinical Psychopharmacology.* 1986;1(4):324-331.
6. Thornhill DP, Field SP. Distribution of lithium elimination rates in a selected population of psychiatric patients. *European Journal of Clinical Pharmacology.* 1982;21(4):351-354.

7. Carter L, Zolezzi M, Lewczyk A. An Updated Review of the Optimal Lithium Dosage Regimen for Renal Protection. *Canadian Journal of Psychiatry-Revue Canadienne De Psychiatrie.* 2013;58(10):595-600.
8. Singh LK, Nizamie SH, Akhtar S, Praharaj SK. Improving Tolerability of Lithium With a Once-Daily Dosing Schedule. *American Journal of Therapeutics.* 2011;18(4):288-291.