Derbyshire Healthcare
NHS Foundation Trust

Lithium Carbonate

Supplementary guidance for switching patients who are currently prescribed Priadel® 200mg and 400mg tablets

Please refer to the Supply Disruption Alert (SDA/2020/012) that was issued by the Department of Health and Social Care on the 21st August 2020 for information about this product discontinuation and the steps required to ensure patient health and safety is maintained.

This document reproduces key elements of SDA/2020/012 (boxed text) and provides supplementary advice for healthcare professionals working collaboratively to support the switching process in Derbyshire.

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.

Ordering Lithium Treatment Packs (updated 15/09/2020)

Please note that Primary Care practices should order "Lithium Treatment Packs" from the Primary Care Support England portal:
https://secure.pcse.england.nhs.uk/_forms/pcsssignin.aspx?ReturnUrl=%2f_layouts%2f15%2fAuthenticate.aspx%3fSource%3d%252F&Source=%2F

There is currently a limit of 10 packs per practice per order. This has been escalated to NHS England in the hope that quantities can be more generous during the switching process.

Secondary Care providers should order "Lithium Treatment Packs" from the Xerox online portal:
http://www.nhsforms.co.uk/

- 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 GPs 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.

Derbyshire GPs can access specialist medication advice from the Derbyshire Healthcare NHSFT mental health pharmacists through Consultant Connect.

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.

Derbyshire Healthcare prescribers can access specialist medication advice from the Pharmacy Department by using their usual email and telephone contact methods.

Mental Health Services in Derbyshire do not currently have an electronic prescribing system, so this is not a route for proactively identifying patients who are prescribed Priadel®.

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.

Prescribers should note that the 250mg tablets mentioned above should be prescribed as:
"Lithium Carbonate Essential Pharma 250mg tablets' to ensure dispensing of the intended product.

Pharmacies and dispensing doctors should be aware that **Lithium Carbonate Essential Pharma 250mg tablets** are kept by wholesalers but the precise product name can differ between suppliers. The PIP code is 1205327 and the EAN code is 5060334120114.

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.

Baseline lithium levels can be taken from a satisfactory assay completed within the preceding 6 months if there has been no significant change in the patient's health or presentation. Otherwise a fresh assay should be arranged before switching.

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.

Before formulating the switching plan with individuals check the lithium level result and ask about any problems with side effects.

The following tables are provided to guide decision-making on achieving specific doses using available products. These do not replace clinical judgement and the switching process presents a good opportunity to optimise lithium doses in partnership with the patient.

Essential Pharma state that the score lines on their tablets (both 250mg and 400mg MR) are not to facilitate splitting into equal doses. In any situation where patients are asked to split tablets, consideration should be given to the legal and practical implications of this and the patient's ability to comply consistently and safely.

Target dose	Lithium Carbonate Essential Pharma 250mg tablets	Camcolit® 400mg MR tablets	Total(mg)	Liskonum 450mg MR tablets	Total (mg)
	Please note that a combination of these two products will incur **two prescription charges** for the patient although their pharmacokinetic properties are similar.				
200*	1		**250**		
300*	1	1	**250 or 400**	0.5	**225**
400		1	**400**	1	**450**
500	2		**500**		
600*	1	1	**650**		
700*	1 3	1	**650 or 750**	1.5	**675**
800		2	**800**		
900	2	1	**900**	2	**900**
1000	4		**1000**		
1100*	1 3	2 1	**1050 or 1150**	2.5	**1125**
1200		3	**1200**		

(*) These target doses cannot be achieved with the use of Essential Pharma products as whole tablets or with Liskonum tablets and there will be a need for the dose prescribed to be rounded-up or rounded down. As a general guide:
In elderly patients who sometimes respond to lower levels and are more sensitive to higher levels, round doses down initially
In bipolar disorder: round down if the previous stable plasma level was 0.7mmol/L or more, and round up if the previous stable plasma level was below 0.7mmol/L
In unipolar depression: round down if the previous stable plasma level was 0.5mmol/L or more and round up if the previous stable plasma level was less than 0.5mmol/L

Combining products from two manufacturers is not recommended as it may lead to confusion about which product(s) a patient is being prescribed. Also be aware that Essential Pharma 250mg tablets are not marketed as modified-release but have broadly similar pharmacokinetic properties to Camcolit® 400mg MR tablets.

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.

Guidance on target lithium levels:

Lithium dosing is by slow upwards titration to achieve a target serum level usually between **0.4 – 0.8mmol/L.**

In **bipolar disorder** the target level should be **0.6 – 0.8mmol/L** but consider maintaining a target level of **0.8-1.0mmol/L** for a trial of at least six months in those who have relapsed while taking lithium previously or who have subthreshold symptoms with functional impairment.

Levels at the lower end of the therapeutic range **0.4 – 0.8mmol/L** may be advisable in older adults or those at risk of renal impairment, heart disease or interacting concomitant medicine.

Brands of lithium are not interchangeable due to considerable differences in product bioavailability, inter-individual variability and narrow therapeutic index and should be **prescribed by brand name.**

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/

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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

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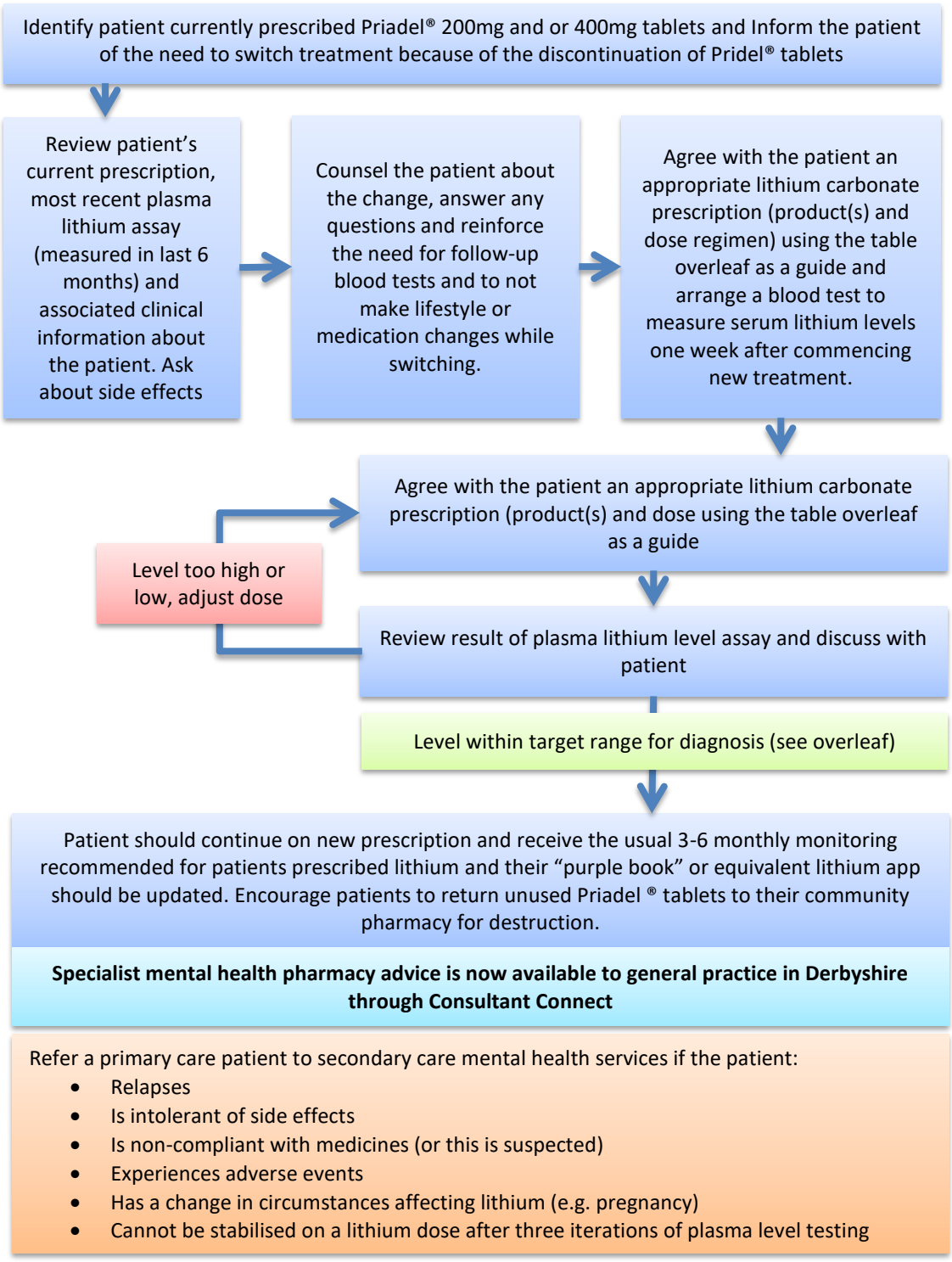
Lithium Carbonate

Supplementary guidance for switching patients who are currently prescribed Priadel® 200mg and 400mg tablets – Quick Reference Guide for Primary Care

This summarises information in the complete guidance document as an aid to practice when switching patients from Priadel® tablets. It should not be used as a guide to maintenance treatment with lithium, for which there is a Shared Care Guideline.



Specialist mental health pharmacy advice is now available to general practice in Derbyshire through Consultant Connect

Refer a primary care patient to secondary care mental health services if the patient:

- Relapses
- Is intolerant of side effects
- Is non-compliant with medicines (or this is suspected)
- Experiences adverse events
- Has a change in circumstances affecting lithium (e.g. pregnancy)
- Cannot be stabilised on a lithium dose after three iterations of plasma level testing

Guidance on product and dose selection for initial switch:

Target dose	Lithium Carbonate Essential Pharma 250mg tablets	Camcolit® 400mg MR tablets	Total(mg)	Liskonum 450mg MR tablets	Total (mg)
	Please note that a combination of these two products will incur **two prescription charges** for the patient although their pharmacokinetic properties are similar.				
200*	1		**250**	0.5	**225**
300*	1	1	**250 or 400**		
400		1	**400**	1	**450**
500	2		**500**		
600*	1	1	**650**	1.5	**675**
700*	1 3	1	**650 or 750**		
800		2	**800**	2	**900**
900	2	1	**900**		
1000	4		**1000**		
1100*	1 3	2 1	**1050 or 1150**	2.5	**1125**
1200		3	**1200**		

(*) These target doses cannot be achieved with the use of Essential Pharma products as whole tablets or with Liskonum tablets and there will be a need for the dose prescribed to be rounded-up or rounded down. As a general guide:
In elderly patients who sometimes respond to lower levels and are more sensitive to higher levels, round doses down initially
In bipolar disorder: round down if the previous stable plasma level was 0.7mmol/L or more, and round up if the previous stable plasma level was below 0.7mmol/L
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Levels at the lower end of the therapeutic range **0.4 – 0.8mmol/L** may be advisable in older adults or those at risk of renal impairment, heart disease or interacting concomitant medicine.

Brands of lithium are not interchangeable due to considerable differences in product bioavailability, inter-individual variability and narrow therapeutic index and should be **prescribed by brand name.**

Suggested wording for letters, leaflets, webpages, etc

Discontinuation of Priadel® 200mg and 400mg tablets
Information for Patients

The manufacturer of Priadel® tablets has decided to stop making and supplying these items by April 2021.
This is a decision outside of the control of your healthcare professionals, and is solely the choice of the manufacturer. We want to let you know what will happen to carry on your lithium treatment once Priadel® can no longer be obtained. It is very important that you do not stop taking your medicines without speaking to your doctor or mental health team first.

Our intention is to work with you to find other lithium tablets so that you can continue your treatment and maintain your health and safety.

Changing your lithium tablets will mean that you need to have extra blood tests so that we can be sure you are prescribed a dose that suits you. For some people just one blood test will be needed but others might need more while we get the dose just right for you. Not all lithium tablets are the same. Once we have found tablets and a dose that suits you, it will be important to carry on your treatment exactly as prescribed.

Blood tests will be needed around one week after any change in tablets or dose. You should take your tablets at about 10pm on the night before a blood test and then have the test the following morning before taking any more lithium. This means we can use your test result to understand whether your dose is right for you or if we need to change it.

During the change of tablets we advise you not to make any major lifestyle changes. In particular you should drink the same amount of liquid as usual and keep to the same level of exercise. Wherever possible, other medicines should not be started, stopped or changed while we are changing your lithium tablets. This includes medicines that you might buy over-the-counter from a pharmacy or shop.

Once your lithium tablets have been changed, any left-over Priadel® tablets should be returned to your Community Pharmacy for safe disposal and to avoid any confusion about what you are now taking.

There is an NHS medicines guide that provides useful information for patients who take lithium. It can be found at https://www.nhs.uk/medicines/lithium

If you pay for your prescriptions it is important to make you aware that if you are now prescribed a combination of two different lithium tablets you may need to pay two prescription charges each time. For people who are prescribed several medicines it is often possible to save money by purchasing a prescription prepayment certificate. Details of these can be found at https://www.nhs.uk/using-the-nhs/help-with-health-costs/save-money-with-a-prescription-prepayment-certificate-ppc/