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MOOD-STABILISING MEDICATIONS

LIZ HOLLAND

AFTER READING THIS CHAPTER, YOU WILL BE ABLE TO:

- Discuss what we mean by the term 'bipolar disorder' and understand what a
 person with bipolar disorder may experience
- Discuss the five most commonly prescribed medicines that are used to help stabilise mood
- Define the term 'polypharmacy' and relate this to bipolar disorder
- Be aware of the monitoring requirements for the drug lithium
- Understand the risks of lithium toxicity
- Discuss the complexities of prescribing mood-stabilising medicines for women of childbearing age
- Apply this knowledge to a clinical scenario

WHEN MIGHT MOOD-STABILISING MEDICATIONS BE USED?

The use of mood-stabilising medication is seen when someone is being treated for 'bipolar disorder'.

Bipolar disorder is a mood disorder characterised by extreme fluctuations in mood. A person with bipolar disorder will have periods of very low mood and low energy (depressive episodes) and periods of very high mood and high energy (manic episodes). The person may also have periods of time where they seem excitable and elated but are not as high as when they are in a full manic episode; this is known as 'hypomania'.

There are three known categories of bipolar disorder. Bipolar 1 is characterised by both depressive episodes and manic episodes and can lead to the







person needing hospital care very quickly, as the manic episodes can be quite extreme. A person with bipolar 2 also has depressive episodes, but the episodes of elated mood only ever reach the hypomanic threshold. 'Cyclothymia' (bipolar 3) is the mildest form of bipolar disorder, where the person will have periods of both high and low mood but will not reach the levels of a full depressive or hypomanic episode.

When people are going through an episode of mania their behaviour can become erratic and bizarre: they may say and do things that they would not normally say and do, and behave in ways that they would not normally behave. When people are manic they may also develop symptoms of psychosis. Manic episodes are the time in which people with bipolar disorder are most likely to need the support of hospital admission and care (National Institute of Mental Health. 2016):

I began to believe that my step father was behind why I was in hospital and wouldn't let him see me, I thought that the doctors and nurses were a gang holding me hostage. I was fearful of everything, talking and singing to myself, unable to sit still and became quite agitated at times with the staff and patients, which is completely out of character for me. I simply didn't know what was real or unreal and I was so frightened of the staff and others while my brain was in this state.

(In a blog for the Time to Change campaign, 2017, Sarah details her experience of having a psychotic episode whilst going through a period of mania)

Bipolar disorder can respond very well to medicines, but often more than one medicine is used in order to help the person. The term that we use when people take more than one medicine is 'polypharmacy'. The person will often take an antidepressant medicine that will help with their tendency to low mood, and a mood-stabilising medicine that will help their mood to remain stable. The use of antidepressant medications in people with bipolar disorder needs to be managed very carefully, as taking too much of an antidepressant medication can cause someone to become elated in their mood and consequently develop a manic episode. When the person is going through a manic episode they may take some extra medication (such as a benzodiazepine) in order to quickly help them feel calmer. A person may also take some short-term medicine to help them with their sleep when they are having a severe depressive or manic episode, as both of these can have a notable impact on sleeping patterns. If the person develops signs and symptoms of psychosis whilst in a manic episode, an antipsychotic medicine may be used in order to help.

This chapter will discuss the use of mood-stabilising medications as information on antidepressant medications is covered in Chapter 1, and information







on medicines that can quickly calm someone down is covered in both Chapter 3 and Chapter 6. Information on medicines that help with sleep is covered in Chapter 3. Information on antipsychotic medications is discussed in Chapter 5.

WHICH MEDICATIONS ARE USED TO HELP STABILISE MOOD?

There are five key medications that are often used in practice as mood-stabilising medications in the UK. These are:

- Lithium
- Valproate
- Carbamazepine
- Lamotrigine
- Asenapine.

The current NICE guidelines (2015) for management of bipolar disorder state that choosing what to prescribe is bespoke to each individual and should be informed by other medications the person is taking and any known previous responses to medications. The NICE (2020) update specifies that any person being treated with lithium or valproate should be under a specialist secondary mental health service before starting this medication.

The Independent Medicines and Medical Devices Safety Review (IMMDS, 2020) notes the risks of valproate, and this has led to the development of a national "Valporate Safety Implementation Group" hosted by NHS England, which is coordinating work that aims, by 2023, to reduce by 50 per cent the use of valproate in people who can get pregnant, and to help prevent unplanned pregnancies in this group of patients. You can read more about the group and the actions they are taking at: www.england.nhs.uk/patient-safety/ sodium-valproate

GO FURTHER ...

If you would like to read more about how different medicines prescribed for mood stabilisation compare with each other, a good read to start you off is an article by Keck and McElroy (2002).







These are not all from the same family of medicines. Lithium is a natural mineral, rather than a drug that is artificially developed by the pharmaceutical industry. Asenapine is an antipsychotic by nature but is not used for the treatment of psychosis at present; it is only used for mood stabilisation. As it is a very new drug, there is still not much information or evidence behind it. Valproate, lamotrigine and carbamazepine are all anticonvulsant medications. This means that they are often prescribed for the management of epilepsy and seizures, but they have also been found to have mood-stabilising properties.

GO FURTHER ...

If you would like to read more about how anticonvulsant medications work, then the article by Stahl (2004) is recommended.

Choosing which mood-stabilising medicine is right for someone is a difficult decision to make, as they all have their own side effects, and these can be severe. In general, lithium is found to be particularly effective in people who have bipolar 1. Asenapine is only likely to be prescribed if other mood stabilisers have been found to be ineffective. Carbamazepine or valproate can be a good choice for people who move quickly between periods of high mood and low mood. Lamotrigine is more likely to be used in bipolar 2 than bipolar 1.

Of all of these medications, lithium has the most complex side effect profile, and is subject to special monitoring requirements.

LITHIUM MONITORING

Due to the risks and side effects associated with lithium, special monitoring processes are required. When a person is commenced on lithium, they will be assigned a lithium treatment pack in order to help keep this monitoring process on track, and to provide a clear record of the monitoring. This pack is in purple, and all the information associated with lithium monitoring will also be in purple. The pack includes a booklet in which all blood test results can be recorded, a Lithium Alert Card for the person to keep with them that will indicate that they are taking lithium, and a lithium therapy information booklet. Some organisations/NHS trusts will also have their own booklets or monitoring documents that need to be completed, so do check what your organisations are using.







The Lithium Alert Card can be seen in Figure 2.1.

Lithium Alert Card			
This patient is taking lithium therapy This card should be carried at all times and shown to healthcare profession			
Name of patent:	lame of patent:		
Address:			
Postcode:	Telephone:		
GP:			
NHS number:			

Figure 2.1 Lithium Alert Card

All patients taking lithium will need to have regular blood tests in order to assess their lithium level, which is the measure of how much lithium there is in their blood. The safe range for the lithium level is 0.4–1.0mmol/L.

The factors that influence a person's lithium level are varied, but include metabolic rate, weight, salt intake, exercise levels and fluid consumption. A person's dose of lithium will be adjusted until their lithium level falls to within the safe range of 0.4–1.0mmol/L. Once a person's lithium dose is stable, the person will be asked not to adjust any lifestyle factors that could affect their fluid balance, such as fluid consumption and salt intake.

All blood tests for lithium levels should be taken around 12 hours after a person has taken their dose of lithium. When a person is starting on lithium treatment or has undergone a dose change, the person should have their lithium level taken weekly until the bloods are returning stable results. The person should then go to three-monthly monitoring. If the person has any lifestyle changes that may affect sodium and fluid levels, they will need to go back to weekly monitoring until their blood levels are stable.

In addition to the above blood monitoring, the person will need additional health monitoring. Prior to anyone starting on lithium, their baseline renal, cardiac and thyroid function will need to be tested, and then renal, cardiac and thyroid function should be assessed every six months.







LITHIUM TOXICITY

When a person's blood lithium level goes higher than 1.5mmol/L, the person is at risk of lithium toxicity. Lithium toxicity can occur at any time in a person taking lithium. Any concerns about lithium toxicity must be acted upon quickly, because if it is not treated promptly, it can be fatal.

Lithium toxicity will present with some key symptoms. These are:

- Blurred vision
- Dizziness
- Difficulty walking
- Slurred speech
- Muscle twitches in the arms and legs
- Trembling hands and legs
- Vomiting or severe nausea
- Persistent diarrhoea
- Swollen feet and/or legs
- An irregular heartbeat
- A rash.

If a person who is taking lithium presents with any of the above symptoms, they should be closely monitored, and their blood should be taken in order to obtain a lithium level immediately. They should not be given their next dose of lithium until their blood results come back and are normal. These should be processed as 'urgent'.

SUPPORTING THE TREATMENT OF BIPOLAR WITH ANTIPSYCHOTIC MEDICATIONS

As mentioned above, we are increasingly seeing people who live with bipolar disorder taking antipsychotic medication as part of their treatment plans. Prescribing an antipsychotic medication needs careful consideration of risks and benefits, in particular around the risks of physical health complications and weight gain (see Chapter 6).

Antipsychotic medication is often used for those who are experiencing a manic episode, as it can be helpful with agitation, distress and difficulty sleeping, hallucinations or delusions that the person is currently experiencing. The use of antipsychotics can also impact on how other medications are working. The medications we tend to see being used most often are olanzapine and quetiapine. Please see Chapter 6 for more information on these medications, side effects and monitoring.







THE MEDICINES LIST

This medicines list will provide information on the five key mood-stabilising medicines that are used in the UK, as outlined above. This is not an exhaustive list of all the possible treatments that can be used for the treatment of bipolar.

Drug name: Lithium

UK brand names: Camcolit, Liskonum, Lithonate, Priadel, Litarex, Li-Liquid

Average doses: Depends on the individual patient and is determined by regularly monitoring the lithium level in the blood. An average starting dose on lithium tablets may be around 400mg a day. The person's age and weight should also be considered when lithium is being prescribed

What form does it come in? Liquid and tablet

Does it interact with any other medications? Yes. The following interactions are known:

Lithium should not be taken with: Antibiotic medications or steroid
medications without medical advice, medicines containing caffeine,
water tablets, creams containing urea, non-steroidal anti-inflammatory
(NSAID) analgesic medications (such as ibuprofen). Medical advice
should be obtained for anyone on blood pressure or cardiac medication if they are also prescribed lithium

Additional information: See the section above on lithium monitoring. Lithium should not be taken by anyone with severe kidney or thyroid difficulties. Lithium can cause an itchy rash in some people. If this occurs, it should be stopped immediately and medical advice should be sought

Anticonvulsant medications

In rare cases, these medicines can be associated with an increased risk of suicidal thoughts. People taking these medicines should also keep an







eye out for any skin rashes and serious flu-like symptoms, as these can be warning signs of Stevens-Johnson syndrome, which can be fatal.

Drug name: Valproate

UK brand names: Epilim, Depakote

Average doses: Usually, between 1000 and 2000mg per day

What form does it come in? Liquid and tablet

Does it interact with any other medicines? Yes. The following interactions are known:

- Other medicines: Medical advice must be sought if valproate is being taken with salicylate painkillers (e.g. aspirin), other medicines for epilepsy, blood-thinning medications, medicines to reduce cholesterol, medicines for HIV, medicines for cancer, antidepressant medications, antipsychotic medications
- MAOI antidepressants: Valproate must not be taken with MAOI antidepressants

Additional information: Valproate should not be taken by anyone with liver problems

Drug name: Carbamazepine

UK brand names: Carbagen SR, Tegretol, Tegretol Retard, Teril Retard

Average doses: Usually, up to 1200mg per day

What form does it come in? Liquid and tablet

Does it interact with any other medicines? Yes. The following interactions are known:

- MAOI antidepressants: Carbamazepine must not be taken with any MAOI antidepressants
- St John's wort: Carbamazepine must not be taken with St John's wort

(Continued)





(1)



Other medicines: Medical advice must be sought before starting carbamazepine if a person is taking other medicines for epilepsy, anticoagulants, omeprazole, any antipsychotic medication, any antidepressant medication, any medicine used to treat sickness, antibiotics, water tablets, hormone replacement therapy (HRT), antifungals, corticosteroids, painkillers, asthma medicines, oral contraceptives (as efficacy of these can be decreased), levothyroxine, medicines for cancer, medicines for HIV, bupropion, antihistamines, vitamin B supplements

Additional information: MAOI antidepressants must have been stopped at least two weeks prior to starting carbamazepine. Carbamazepine should not be taken by anyone with a heart condition. The patient on carbamazepine must not drink alcohol or eat/drink grapefruit

Drug name: Lamotrigine

UK brand names: Lamictal

Average doses: Usually, 100-400mg per day

What form does it come in? Tablet and dispersible tablet

Does it interact with any other medicines? Yes. The following interactions are known:

 Other medicines: Medical advice must be sought if lamotrigine is being taken with any other medicines for epilepsy, olanzapine, risperidone, lithium, aripiprazole, carbamazepine, bupropion, rifampicin, medicines for HIV, oral contraceptives

Additional information: Caution should be taken for people with kidney problems

Asenapine

Asenapine is a second-generation antipsychotic. A key side effect of asenapine is that it can initially cause low blood pressure. This may cause





(1)



some people to feel dizzy or to faint when they move or stand up suddenly. As enapine is also associated with involuntary rhythmic movements of the tongue, mouth and face, and it carries a risk of neuroleptic malignant syndrome (NMS). You can read more about NMS in Chapter 5.

Drug name: Asenapine

UK brand names: Sycrest

Average doses: One 5mg or 10mg tablet, twice per day. Usual daily maximum is 20mg.

What form does it come in? 5mg and 10mg sublingual tablets (these should be placed under the tongue until they dissolve)

Does it interact with any other medications: Yes. The following interactions are known:

- Antidepressant: Asenapine can interact with antidepressant medication (in particular, fluvoxamine, fluoxetine or paroxetine)
- Medicines for Parkinson's disease: These can make asenapine less effective
- Medicines that lower blood pressure: Asenapine should not be taken
 with any other medicines that lower blood pressure

Additional information: Asenapine should not be used in older adults (usually over 60). People with liver problems should not take asenapine. You should not drink alcohol when taking asenapine. You must not eat or drink for at least ten minutes after taking a dose of asenapine. If you are taking more than one medicine, asenapine should always be taken last

MEDICINES FOR MOOD STABILISATION IN PREGNANT WOMEN AND BREASTFEEDING MOTHERS

It should be noted that all of the mood-stabilising medications carry risks in relation to unborn children, and for pregnant women taking mood stabilisers there is currently no preferred option. Any women who are pregnant or planning on becoming pregnant and who are taking a mood-stabilising







medication will need to work with a specialist in order to plan the safest possible treatment for both them and their baby.

The highest risk types of mood-stabilising medication for unborn babies are the anticonvulsant medications. Taking an anticonvulsant when pregnant can lead to 'fetal anticonvulsant syndrome', which can cause both physical and cognitive defects in the baby and is associated with developmental delay. The first three months of pregnancy is the highest-risk time for this

Valproate carries the highest potential risks of all the anticonvulsant medications. It is best practice to avoid prescribing valproate to any woman of childbearing age due to the potential risks to the baby if she were to get pregnant. If valproate is seen as the best treatment choice, then the clinician and the woman would need to discuss if and when she would like to get pregnant, and her current use of contraception. Specific risks of valproate in relation to the unborn baby include an increased risk of spina bifida and other spinal abnormalities, cleft palate and cleft lip abnormalities, heart defects, abnormal fingers and toes, extra fingers and toes and an increased risk of the baby being born with an intellectual disability.

Anticonvulsant medicines are much less risky once the baby is born, and the risks associated with breastfeeding and taking such medicines are low.

As as enapine is such a new drug, there is currently very little research available, and knowledge about its use in pregnant and breastfeeding mothers is limited.

Taking lithium during pregnancy carries noted risks both to the mother and to the unborn child, and very careful monitoring of both mother and baby is required if it is decided that continuing with lithium treatment is the best course of action. In relation to the baby, the most well-known risk is that of heart defects if lithium is taken during early pregnancy. There is also an increased risk of a baby being stillborn or of sudden death after the baby is born. As discussed above, careful fluid balancing is always important to anyone taking lithium, and this is particularly important if a woman is pregnant. During pregnancy, liver and kidney function change, as do fluid and hormone levels, meaning that a woman's lithium level can change rapidly during pregnancy. Extra lithium-level monitoring is therefore required for pregnant women. Childbirth itself is also a high-risk time for pregnant women taking lithium due to both the sudden changes in fluid balance and to the fact that the way in which the body metabolises lithium changes in labour.

Women taking lithium are advised not to breastfeed as lithium is passed through the breast milk from mother to baby and can lead to the baby having harmful lithium levels in their blood.







CONSIDERATIONS FOR DIFFERENT AGE GROUPS

The peak age of onset for bipolar disorder is in late adolescence or early adult life, with a further small increase in incidence in mid to late life (NICE, 2015). Diagnosis and treatment of any possible bipolar disorder in a child should be undertaken by a specialist service as the diagnostic criteria are not tailored to young people, and consequent treatment will be bespoke.

For those over 65, treatment by someone who specialises in working with older adults is recommended. The NICE guidelines state that approaches to treatment will be the same, but doses may need to be lower and to be calculated with age in mind. The falls risks associated with sedating medications must also be considered. NICE (2020) states that for medications given to older adults, the following considerations must be applied:

- use medication at lower doses
- take into account the increased risk of drug interactions
- take into account the negative impact that anticholinergic medication, or drugs with anticholinergic activity, can have on cognitive function and mobility
- ensure that medical comorbidities have been recognised and treated.

LEARNING FROM A CASE STUDY: TEST YOUR KNOWLEDGE

Dana is 31 years old and was diagnosed with bipolar disorder at the age of 19. Dana takes the mood-stabilising drug lithium in tablet form, which works really well for her. She has not had a hospital admission in over three years. Dana has a lithium information pack at home and carries her Lithium Alert Card in her purse. She has been taking the same dose of lithium for the last three years and manages her fluid and salt intake to ensure that this remains stable.

1 What colour is Dana's information pack and card?

Dana has been dating a new partner, Delroy, for almost a year, and things are getting serious. They have just decided to move in together, and hope for a future that involves marriage and children. Delroy asks her for more information about her lithium treatment so that he can support her. He would like to know about what monitoring she requires and if there are any risks.

(Continued)







- 2 How often does Dana need to have her lithium bloods taken, and what is the safe range for her lithium blood levels?
- 3 Does Dana need any other regular health checks?
- 4 If Dana and Delroy decide to try for a baby, does Dana need to think about anything concerning her medications before she stops taking her contraceptive pill?

One day, Dana comes home from work early as she has not been feeling well. She feels sick and has had diarrhoea for the last few days. When Delroy comes home from work, he notices that Dana does not seem her usual self. Her speech is slurred, and she seems wobbly on her feet. He notices that her hands are shaking. Dana tells Delroy that she feels dizzy and her heart is pounding. Delroy gets cross with Dana and starts shouting at her, telling her that she is clearly drunk.

5 Is there another explanation that may be causing Dana's symptoms? What should Delrov do?

IF I REMEMBER 5 THINGS FROM THIS CHAPTER...

- 1 There are five commonly used mood-stabilising medicines used in the UK. These are: lithium, carbamazepine, valproate, lamotrigine and asenapine.
- There are considerable risks when any mood-stabilising medicine is taken by a pregnant woman, and the fetus is at risk of harm. Valproate carries the highest risk to the baby. Specialist advice must be sought if a woman who takes a mood-stabilising medicine becomes pregnant or wishes to become pregnant.
- 3 Anyone who takes lithium will have a purple lithium information pack.
- 4 Anyone who takes lithium must have regular blood monitoring tests; the safe lithium blood level is: 0.4-1.0mmol/L.
- 5 Lithium toxicity occurs when a person's lithium level is over 1.5 mmol/L. It can occur to anyone at any time, and symptoms must be looked out for at all times because if it is not treated early it can be fatal.

ANSWERS TO THE CASE STUDY QUESTIONS

- 1 Purple.
- 2 Dana should be having her lithium levels checked every three months, and the safe range is 0.4-1.0 mmol/L.







- 3 In addition, Dana should be having her renal, cardiac and thyroid function checked every six months.
- 4 Yes. Dana needs to meet with her doctor before she comes off her contraceptive pill in order to obtain some advice. If she continues on her lithium and becomes pregnant then there are risks to both her and her baby, and so additional monitoring will need to be arranged for them both.
- 5 These could also be signs that Dana's lithium level is becoming toxic. Delroy should take Dana to A&E immediately, and he should also take her lithium information pack, blood test record book and Alert Card with him. He should explain that Dana is on lithium and that he is very worried that she is becoming toxic because of the symptoms that she is demonstrating. He should clearly describe these symptoms. He should take Dana's lithium tablets with them to A&E.

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