



Lamictal

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ELEMENTS FOR A PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Epilepsy

Epilepsy is a serious illness where a person has repeated seizures, sometimes called convulsions or fits. Seizures are caused by short bursts of too much electrical activity in the brain.

More than 50 million people in the world have epilepsy, and about 1 in 30 people will develop epilepsy during their life. Epilepsy can start at any age but it most often starts in children under the age of 2 or in people aged over 60. In many people with epilepsy no cause for the seizures is found.

There are medicines that can help people to control their seizures. Some people will only need to regularly take a single drug but others may need to take more than one drug. Other people will not be able to control their seizures with medicines and will require extra help from their doctor.

Bipolar disorder

Bipolar disorder, sometimes called manic depression, is a serious long-term illness where a person's mood swings between one extreme and another. One extreme is called depression where a person feels very low or down, and the other extreme is called mania where a person feels very high or excited.

Between 1 in 40 and 1 in 250 people will develop bipolar disorder, usually before the age of 30, and often as children and teenagers. Bipolar disorder can be very serious if not treated. There is a much bigger risk of a person with bipolar disorder thinking about dying or trying to kill themselves when feeling very low than there is in a healthy person.

There are medicines that can help to treat and prevent periods of mania and depression in people with bipolar disorder. Treating periods of depression with medicines is not always as easy as treating periods of mania.

VI.2.2 Summary of treatment benefits

Epilepsy

Lamotrigine has been studied in, and used by, epilepsy patients for over 20 years to help control their seizures. In adults and children over 13 years of age lamotrigine has been shown to help control seizures either when taken on its own or when taken with other epilepsy medicines.

In 2-12 year old children lamotrigine has been shown to help control seizures when taken with another epilepsy medicine. In these children, lamotrigine can also be taken on its own to help treat a type of epilepsy that often only occurs in children and young people called “typical absence seizures”. Children often grow out of this type of epilepsy by the time they are adults.

Bipolar disorder

In tests on adults with bipolar disorder who had recently had a period of feeling either very low or very high, doctors gave the patients either lamotrigine or a sugar pill (placebo). They then timed how long it took before the patients had a new period of feeling either very low or very high where the doctors had to give them an extra medicine or treatment to help them feel better. These tests showed that lamotrigine taken once a day by adults can help to increase the time between new periods of depression in adults with bipolar disorder.

Lamotrigine is not approved in any country for the treatment of bipolar disorder in patients below 18 years of age.

VI.2.3 Unknowns relating to treatment benefits

Lamotrigine has been used for over 20 years to treat patients with epilepsy and for over 10 years to treat adults with bipolar disorder. The benefits for patients within these groups who the medicine works for are well known.

Lamotrigine has not been shown to help patients with bipolar disorder under the age of 18.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Severe allergic skin reactions(hypersensitivity)	<p>A reaction often starts with parts of the skin becoming red or raised (skin rash) that can become serious and may be seen with or without other signs such as swelling of the mouth, throat or face, a sore throat, feeling hot and cold (fever), and having odd bruises or bleeding.</p> <p>Most rashes seen in patients taking lamotrigine are not serious but in some patients the rash can be very serious with blisters and peeling skin and the patient may need to go to hospital. In the most severe cases it can lead to death.</p> <p>There is no way to tell if a mild rash will become a more serious rash but it may be the first sign of a patient having a severe allergic reaction to lamotrigine.</p> <p>Serious skin rashes occur in about 1 in 500 adult epilepsy patients and in about 1 in 1,000 adult bipolar disorder patients.</p> <p>Children are more at risk with from 1 in 300 to 1 in 100 children taking lamotrigine for epilepsy getting a serious skin rash.</p> <p>Most rashes occur in the first 8 weeks after a patient starts taking lamotrigine and often get better once the patient stops taking the medicine.</p>	<p>The chance of a patient developing rash has been shown to be linked with the dose of lamotrigine given when they start their treatment.</p> <p>As a result, doctors use a guide so that the patient starts with a smaller dose of lamotrigine, and then increase the dose they take bit by bit over a number of weeks until it helps their epilepsy or bipolar disorder.</p> <p>Epilepsy patients who have had a rash after taking other medicines for their epilepsy need to be very careful, and should talk to their doctor, as they have a higher chance of getting a rash if they start taking lamotrigine.</p>
Having thoughts about killing yourself or trying to kill yourself (suicide risk)	Having thoughts about or trying to kill yourself is common in patients with bipolar disorder. Between 1 in 4 and 1 in 2 bipolar disorder patients	Having thoughts about killing yourself is a major risk in bipolar patients and can also be a risk in

Risk	What is known	Preventability
	<p>try to kill themselves at least once during their lives.</p> <p>Although the risk is not nearly as great in patients with epilepsy, epilepsy patients are more likely to have these thoughts or to try to kill themselves compared to people without epilepsy. It is not clear if this is due to epilepsy or due to the medicines taken to treat epilepsy.</p> <p>In tests of epilepsy patients taking lamotrigine compared to those who were taking a sugar pill (placebo), the number of patients who had thoughts about killing themselves was too small to show any change due to lamotrigine use. In bipolar patients, the number of patients who had thoughts about killing themselves was similar for those taking lamotrigine and those taking the sugar pill (placebo).</p> <p>Any patient with epilepsy who has symptoms of bipolar disorder or feeling low has an increased risk of having thoughts about killing themselves. Young adults and patients who have had thoughts about killing themselves in the past may be at greater risk of these symptoms starting.</p> <p>When a bipolar disorder patient starts to take lamotrigine, or when they start to take a bigger dose of lamotrigine than they have before, their symptoms may get worse rather than better, or they may start to have new symptoms that they did not have before.</p>	<p>epilepsy patients.</p> <p>It is not possible to tell in advance if a patient will get thoughts about killing themselves or when these thoughts may happen. A patient should call their doctor straight away if they have any of these thoughts. The doctor may change or stop the treatment.</p> <p>If a bipolar disorder patient has new symptoms or if the symptoms they have quickly get worse while taking lamotrigine, the patient, their family, friends or carers should tell their doctor who may change or stop treatment.</p>

Risk	What is known	Preventability
<p>Taking more than one drug at the same time that the body processes in a similar way can change how well each drug works and how long they stay in the body (drug interactions)</p>	<p>Other medicines for epilepsy</p> <p>Taking lamotrigine at the same time as another medicine for epilepsy called valproate can slow down how quickly the body processes lamotrigine. This can lead to a larger amount of lamotrigine being in the body for longer than is wanted and this can cause side-effects. As a result, if a person is also taking valproate, their doctor should prescribe a smaller amount of lamotrigine than for someone who is only taking lamotrigine.</p> <p>Taking lamotrigine at the same time as some other medicines for epilepsy (phenytoin, carbamazepine, phenobarbitone, primidone) can speed up how quickly the body processes lamotrigine. This can lead to a smaller amount of lamotrigine being in the body than is wanted and the patient may not benefit from the medicine. People taking lamotrigine at the same time as one of these medicines should be prescribed a larger amount of lamotrigine than someone who is only taking lamotrigine for their epilepsy.</p> <p>While these other medicines for epilepsy can change how quickly the body processes lamotrigine, lamotrigine does not seem to affect how quickly the body processes those medicines.</p> <p>Hormonal contraceptives</p> <p>Females taking “the pill” to help stop them getting pregnant should tell their doctor before starting lamotrigine. “The pill” can make the body process lamotrigine about twice as quickly and this can lead to a smaller amount of lamotrigine being in the body than is wanted. The doctor will decide on the right amount of lamotrigine to take.</p> <p>Tests have also shown that</p>	<p>Other medicines for epilepsy</p> <p>The risk can be reduced by a doctor changing either the amount of lamotrigine given to the patient or the amount of the other medicines given to the patient at the same time.</p> <p>Any side-effects or loss of benefit that are due to a medicine being taken at the same time as lamotrigine will often improve when the amount of lamotrigine or the other medicine given to the patient is changed by a doctor.</p> <p>Hormonal contraceptives</p> <p>Women wanting to start or stop taking “the pill” while taking lamotrigine should speak to their doctor first.</p> <p>Other medicines</p> <p>Doctors are advised not to give both lamotrigine and some other medicines such as dofetilide (a medicine used to treat some heart problems) to a patient at the same time.</p>

Risk	What is known	Preventability
	<p>lamotrigine can speed up how quickly the body processes "the pill". The effect of this is not clear but it may make "the pill" work less well.</p>	
<p>Use in children and in patients with kidney problems (renal impairment) and liver problems (hepatic impairment)</p>	<p>Lamotrigine is processed by the body more quickly in children than in adults, especially in children under 5. Children are more likely to get a serious rash or allergic reaction than adults.</p> <p>In tests people with kidney problems have been shown to process lamotrigine more slowly than healthy people. This can lead to a larger amount of lamotrigine being in the body for longer than is wanted in people with kidney problems and this can cause side-effects.</p> <p>Lamotrigine is mainly processed by the body in the liver and in tests people with liver problems have been shown to process lamotrigine more slowly than healthy people. This can lead to a larger amount of lamotrigine being in the body for longer than is wanted in people with liver problems and this can cause side-effects.</p>	<p>The dose of lamotrigine given to a child when they start treatment should be based on their weight and if they are taking any other epilepsy medicines at the same time. This will help make sure that the child gets the benefit of treatment and limits the chance of side-effects. A child's response to starting lamotrigine should be watched closely by their doctor as the medicine's strength is increased slowly.</p> <p>A patient with kidney problems should talk to their doctor about the dose of lamotrigine that is best for them.</p> <p>A patient with liver problems should talk to their doctor about the dose of lamotrigine that is best for them.</p>
<p>Being given the wrong medicine or the wrong strength of medicine (medication errors) by a doctor (a prescribing error) or a pharmacist (a dispensing error)</p>	<p>Patients taking lamotrigine (LAMICTAL) have sometimes been given the wrong medicine because many medicines have similar names, such as LAMISIL and lamivudine. Some patients have also been given the wrong dose or type of lamotrigine.</p> <p>Sometimes patients taking a different medicine (such as LAMISIL to help treat an infection) are given LAMICTAL by mistake.</p> <p>Taking the wrong medicine may be serious as the patient will not receive the benefit of the medicine they are meant to be taking for their illness. The patient may also be at risk of getting a side effect, which</p>	<p>The different lamotrigine tablets and the bottle or box they are in look different to make them stand out from each other and from other medicines.</p> <p>Doctors and pharmacists are given information to help stop them giving a patient the wrong medicine, or the wrong type or dose of lamotrigine.</p> <p>Patient should check that they get the right tablets when they collect their medicine.</p>

Risk	What is known	Preventability
	<p>may be serious.</p> <p>Side effects due to a patient taking the wrong medicine may go away when the patient stops taking the wrong medicine, when they start taking the right medicine or after treatment.</p>	

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
<p>Sudden death of an epilepsy patient with no known cause (Sudden Unexplained Death in Epilepsy (SUDEP))</p>	<p>Some healthy people with epilepsy can die suddenly without the cause for their death being known. This is called Sudden Unexplained Death in Epilepsy or "SUDEP".</p> <p>Patients who have a type of seizure called "tonic clonic seizures" are at a greater risk of SUDEP.</p> <p>In tests the risk of SUDEP in patients taking lamotrigine was not shown to be much different to the risk of SUDEP in patients taking other medicines for epilepsy.</p> <p>In tests the risk of SUDEP does not seem to change if a patient takes a medicine for their epilepsy, though it is still not certain if taking lamotrigine increases this risk.</p> <p>Doctors should consider the known risks for SUDEP when thinking about giving lamotrigine to a patient.</p>
<p>Use in patients during pregnancy and when breastfeeding (lactation)</p>	<p>Over 8,000 women who took lamotrigine as the only medicine for their epilepsy during the first 13 weeks of being pregnant have been studied to see whether there are any effects of taking lamotrigine when pregnant.</p> <p>A small number of tests have shown a bigger chance of the newborn baby having a type of birth defect (congenital abnormality) called an oral cleft (where the lips or mouth do not form properly) if the mother took lamotrigine during the first 13 weeks of pregnancy.</p> <p>When all the current information is put together there is not a clear sign of a large increase in the risk of birth defects in babies whose mothers had taken lamotrigine when pregnant.</p> <p>Changes in the body during pregnancy can lower the amount of lamotrigine in a patient's body. This may mean that there is not enough medicine in the body to help stop or control the pregnant patient's seizures. This can be a risk to both the patient's and the unborn baby's safety.</p>

Risk	What is known (Including reason why it is considered a potential risk)
	Lamotrigine can pass from the mother to the baby in breast milk and the level of the medicine in the baby can reach half of the level in the mother. This is a large enough amount of medicine in the baby to have side-effects.

Missing information

Nothing has been identified at this time.

VI.2.5 Summary of additional risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other healthcare professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet. The measures in these documents are known as routine risk minimisation measures.

The SmPC and the package leaflet for LAMICTAL can be found in the LAMICTAL EPAR page.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

None.

VI.2.7 Summary of changes to the Risk Management Plan over time

None.