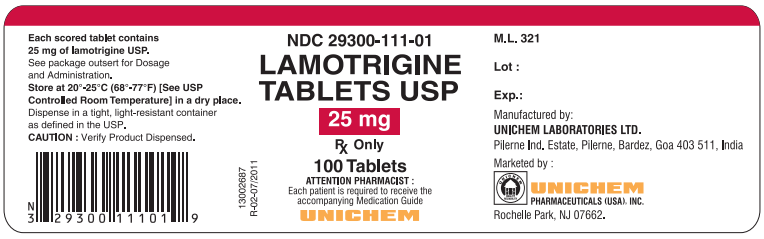
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 090170

LABELING

(b) (4)



Each scored tablet contains 25 mg of lamotrigine USP.
See package outsert for Dosage and Administration.
Store at 20°-25°C (68°-77°F) [See USP Controlled Room Temperature] in a dry place.
Dispense in a tight, light-resistant container as defined in the USP.
CAUTION : Verify Product Dispensed.

N 3 29300 11101 9

13002687
R-02-07/2011

NDC 29300-111-01

LAMOTRIGINE TABLETS USP

25 mg

℞ Only

100 Tablets

ATTENTION PHARMACIST :
Each patient is required to receive the accompanying Medication Guide

UNICHEM

M.L. 321

Lot :

Exp.:

Manufactured by:
UNICHEM LABORATORIES LTD.
Pilerne Ind. Estate, Pilerne, Bardez, Goa 403 511, India

Marketed by :
UNICHEM PHARMACEUTICALS (USA) INC.
Rochelle Park, NJ 07662.

(b) (4)

Each scored tablet contains 25 mg of lamotrigine USP.
See package outsert for Dosage and Administration.
Store at 20°-25°C (68°-77°F) [See USP Controlled Room Temperature] in a dry place.
Dispense in a tight, light-resistant container as defined in the USP.
CAUTION : Verify Product Dispensed.

N 3 29300 11105 7

13002688
R-02-07/2011

NDC 29300-111-05

LAMOTRIGINE TABLETS USP

25 mg

℞ Only

500 Tablets

ATTENTION PHARMACIST :
Each patient is required to receive the accompanying Medication Guide

UNICHEM

M.L. 321

Lot :

Exp.:

Manufactured by:
UNICHEM LABORATORIES LTD.
Pilerne Ind. Estate, Pilerne, Bardez, Goa 403 511, India

Marketed by :
UNICHEM
PHARMACEUTICALS (USA), INC.
Rochelle Park, NJ 07662.

(b) (4)

Each scored tablet contains 25 mg of lamotrigine USP.
See package outsert for Dosage and Administration.
Store at 20°-25°C (68°-77°F) [See USP Controlled Room Temperature] in a dry place.
Dispense in a tight, light-resistant container as defined in the USP.
CAUTION : Verify Product Dispensed.

N 3 29300 11110 1

13002689
R-02-07/2011

NDC 29300-111-10

LAMOTRIGINE TABLETS USP

25 mg

℞ Only

1000 Tablets

ATTENTION PHARMACIST :
Each patient is required to receive the accompanying Medication Guide

UNICHEM

M.L. 321

Lot :

Exp.:

Manufactured by:
UNICHEM LABORATORIES LTD.
Pilerne Ind. Estate, Pilerne, Bardez, Goa 403 511, India

Marketed by :
UNICHEM
PHARMACEUTICALS (USA), INC.
Rochelle Park, NJ 07662.

(b) (4)

Each scored tablet contains 100 mg of lamotrigine USP.
See package outsert for Dosage and Administration.
Store at 20°-25°C (68°-77°F) [See USP Controlled Room Temperature] in a dry place.
Dispense in a tight, light-resistant container as defined in the USP.
CAUTION : Verify Product Dispensed.

N 3 29300 11201 6

13002690
R-02-07/2011

NDC 29300-112-01

LAMOTRIGINE TABLETS USP

100 mg

℞ Only

100 Tablets

ATTENTION PHARMACIST :
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UNICHEM

M.L. 321

Lot :

Exp.:

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Marketed by :
UNICHEM PHARMACEUTICALS (USA), INC.
Rochelle Park, NJ 07662.

(b) (4)

Each scored tablet contains 100 mg of lamotrigine USP.
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Store at 20°-25°C (68°-77°F) [See USP Controlled Room Temperature] in a dry place.
Dispense in a tight, light-resistant container as defined in the USP.
CAUTION :
Verify Product Dispensed.

N 3 29300 11205 4

13002691
R-02-07/2011

NDC 29300-112-05

LAMOTRIGINE TABLETS USP

100 mg

℞ Only

500 Tablets

ATTENTION PHARMACIST :
Each patient is required to receive the accompanying Medication Guide

UNICHEM

M.L. 321

Lot :

Exp.:

Manufactured by:
UNICHEM LABORATORIES LTD.
Pilerne Ind. Estate, Pilerne,
Bardez, Goa 403 511, India

Marketed by :
UNICHEM
PHARMACEUTICALS (USA), INC.
Rochelle Park, NJ 07662.

Each scored tablet contains 100 mg of lamotrigine USP.
See package outsert for Dosage and Administration.
Store at 20°-25°C (68°-77°F) [See USP Controlled Room Temperature] in a dry place.
Dispense in a tight, light-resistant container as defined in the USP.
CAUTION :
Verify Product Dispensed.

N 3 29300 11210 8

13002692
R-02-07/2011

NDC 29300-112-10

LAMOTRIGINE TABLETS USP

100 mg

℞ Only

1000 Tablets

ATTENTION PHARMACIST :
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UNICHEM

M.L. 321

Lot :

Exp.:

Manufactured by:
UNICHEM LABORATORIES LTD.
Pilerne Ind. Estate, Pilerne,
Bardez, Goa 403 511, India

Marketed by :
UNICHEM
PHARMACEUTICALS (USA), INC.
Rochelle Park, NJ 07662.

(b) (4)

Each scored tablet contains 150 mg of lamotrigine USP.
See package outsert for Dosage and Administration.
Store at 20°-25°C (68°-77°F) [See USP Controlled Room Temperature] in a dry place.
Dispense in a tight, light-resistant container as defined in the USP.
CAUTION : Verify Product Dispensed.

N 3 29300 11316 7

13002693
R-02-07/2011

NDC 29300-113-16

LAMOTRIGINE TABLETS USP

150 mg

℞ Only

60 Tablets

ATTENTION PHARMACIST :
Each patient is required to receive the accompanying Medication Guide

UNICHEM

M.L. 321

Lot :

Exp.:

Manufactured by:
UNICHEM LABORATORIES LTD.
Pilerne Ind. Estate, Pilerne, Bardez, Goa 403 511, India

Marketed by :
UNICHEM
PHARMACEUTICALS (USA), INC.
Rochelle Park, NJ 07662.

Each scored tablet contains 150 mg of lamotrigine USP.
See package outsert for Dosage and Administration.
Store at 20°-25°C (68°-77°F) [See USP Controlled Room Temperature] in a dry place.
Dispense in a tight, light-resistant container as defined in the USP.
CAUTION :
Verify Product Dispensed.

N 3 29300 11305 1

13002694
R-02-07/2011

NDC 29300-113-05

LAMOTRIGINE TABLETS USP

150 mg

℞ Only

500 Tablets

ATTENTION PHARMACIST :
Each patient is required to receive the accompanying Medication Guide

UNICHEM

M.L. 321

Lot :

Exp.:

Manufactured by:
UNICHEM LABORATORIES LTD.
Pilerne Ind. Estate, Pilerne, Bardez, Goa 403 511, India

Marketed by :
UNICHEM
PHARMACEUTICALS (USA), INC.
Rochelle Park, NJ 07662.

Each scored tablet contains 150 mg of lamotrigine USP.
See package outsert for Dosage and Administration.
Store at 20°-25°C (68°-77°F) [See USP Controlled Room Temperature] in a dry place.
Dispense in a tight, light-resistant container as defined in the USP.
CAUTION :
Verify Product Dispensed.

N 3 29300 11310 5

13002695
R-02-07/2011

NDC 29300-113-10

LAMOTRIGINE TABLETS USP

150 mg

℞ Only

1000 Tablets

ATTENTION PHARMACIST :
Each patient is required to receive the accompanying Medication Guide

UNICHEM

M.L. 321

Lot :

Exp.:

Manufactured by:
UNICHEM LABORATORIES LTD.
Pilerne Ind. Estate, Pilerne,
Bardez, Goa 403 511, India

Marketed by :
UNICHEM
PHARMACEUTICALS (USA), INC.
Rochelle Park, NJ 07662.

(b) (4)

Each scored tablet contains 200 mg of lamotrigine USP.
See package outsert for Dosage and Administration.
Store at 20°-25°C (68°-77°F) [See USP Controlled Room Temperature] in a dry place.
Dispense in a tight, light-resistant container as defined in the USP.
CAUTION : Verify Product Dispensed.

N 3 29300 11416 4

13002696
R-02-07/2011

NDC 29300-114-16

LAMOTRIGINE TABLETS USP

200 mg

℞ Only

60 Tablets

ATTENTION PHARMACIST :
Each patient is required to receive the accompanying Medication Guide

UNICHEM

M.L. 321

Lot :

Exp.:

Manufactured by:
UNICHEM LABORATORIES LTD.
Pilerne Ind. Estate, Pilerne, Bardez, Goa 403 511, India

Marketed by:
UNICHEM
PHARMACEUTICALS (USA), INC.
Rochelle Park, NJ 07662.

Each scored tablet contains 200 mg of lamotrigine USP.
See package outsert for Dosage and Administration.
Store at 20°-25°C (68°-77°F) [See USP Controlled Room Temperature] in a dry place.
Dispense in a tight, light-resistant container as defined in the USP.
CAUTION :
Verify Product Dispensed.

N 3 29300 11405 8

13002697
R-02-07/2011

NDC 29300-114-05

LAMOTRIGINE TABLETS USP

200 mg

℞ Only

500 Tablets

ATTENTION PHARMACIST :
Each patient is required to receive the accompanying Medication Guide

UNICHEM

M.L. 321

Lot :

Exp.:

Manufactured by:
UNICHEM LABORATORIES LTD.
Pilerne Ind. Estate, Pilerne, Bardez, Goa 403 511, India

Marketed by:
UNICHEM PHARMACEUTICALS (USA), INC.
Rochelle Park, NJ 07662.

Each scored tablet contains 200 mg of lamotrigine USP.
See package outsert for Dosage and Administration.
Store at 20°-25°C (68°-77°F) [See USP Controlled Room Temperature] in a dry place.
Dispense in a tight, light-resistant container as defined in the USP.
CAUTION :
Verify Product Dispensed.

N 3 29300 11410 2

13002698
R-02-07/2011

NDC 29300-114-10

LAMOTRIGINE TABLETS USP

200 mg

℞ Only

1000 Tablets

ATTENTION PHARMACIST :
Each patient is required to receive the accompanying Medication Guide

UNICHEM

M.L. 321

Lot :

Exp.:

Manufactured by:
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Marketed by :
UNICHEM
PHARMACEUTICALS (USA), INC.
Rochelle Park, NJ 07662.

MEDICATION GUIDE
LAMOTRIGINE TABLETS USP
13002701

MEDICATION GUIDE
LAMOTRIGINE TABLETS USP

Read this Medication Guide before you start taking lamotrigine tablets and each time you get a refill. There may be new information. This information does not take he place of talking with your hea thcare provider about your medical condition or treatment. If you have questions about lamotrigine tablets, ask your heal hcare provider or pharmacist.

What is the most important information I should know about Lamotrigine tablets?

1. Lamotrigine tablets may cause a serious skin rash that may cause you to be hospitalized or to stop lamotrigine tablets; it may rarely cause death.

There is no way to tell if a mild rash will develop into a more serious reaction. These serious skin reactions are more likely to happen when you begin taking lamotrigine tablets, within he first 2 to 8 weeks of treatment. But it can happen in people who have taken lamotrigine tablets for any period of time. Children between 2 to 16 years of age have a higher chance of getting his serious skin eaction while taking lamotrigine tablets.

The risk of getting a rash is higher if you:
- take lamotrigine tablets while taking valproate (valproic acid or divalproex sodium)
- take a higher starting dose of lamotrigine tablets han your healthcare provider prescribed
- increase your dose of lamotrigine tablets faster han prescribed.

Lamotrigine tablets can also cause other types of allergic reactions or serious problems which may affect organs and other parts of your body like the liver or blood cells. You may or may not have a rash with these types of reactions.

Call your healthcare provider right away if you have any of the following:
- **a skin rash**
- **hives**
- **fever**
- **swollen lymph glands**
- **painful sores in the mouth or around your eyes**
- **swelling of your lips or tongue**
- **yellowing of your skin or eyes**
- **unusual bruising or bleeding**
- **severe fatigue or weakness**
- **severe muscle pain**
- **frequent infections**

These symptoms may be the first signs of a serious reaction. A heal hcare provider should examine you to decide if you should continue taking lamotrigine tablets.

2. Like other antiepileptic drugs, lamotrigine tablets may cause suicidal thoughts or actions in a very small number of people, about 1 in 500.

Call a healthcare provider right away if you have any of these symptoms, especially if they are new, worse, or worry you:
- thoughts about suicide or dying
- attempt to commit suicide
- new or worse depression
- new or worse anxiety
- feeling agitated or restless
- panic attacks
- trouble sleeping (insomnia)
- new or worse irritability
- acting agg essive, being angry, or violent
- acting on dangerous impulses
- an extreme increase in activity and talking (mania)
- other unusual changes in behavior or mood

Do not stop lamotrigine tablets without first talking to a healthcare provider.
- Stopping lamotrigine tablets suddenly can cause serious problems.
- Suicidal houghts or actions can be caused by hings o her than medicines. If you have suicidal thoughts or actions, your healthcare provider may check for other causes.

How can I watch for early symptoms of suicidal thoughts and actions?
- Pay attention to any changes, especially sudden changes, in mood, behaviors, houghts, or feelings.
- Keep all follow-up visits wi h your heal hca e provider as scheduled.
- Call your healthcare provider between visits as needed, especially if you are worried about symptoms.

3. Lamotrigine tablets may rarely cause aseptic meningitis, a serious inflammation of the protective membrane that covers the brain and spinal cord.

Call your healthcare provider right away if you have any of the following symptoms:
- Headache
- Fever
- Nausea
- Vomiting
- Stiff neck
- Rash
- Unusual sensitivity to light
- Muscle pains
- Chills
- Confusion
- Drowsiness

Meningitis has many causes o her han lamotrigine tablets, which your doctor would check for if you developed meningitis while taking lamotrigine tablets.

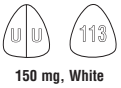
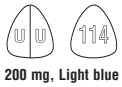
Lamotrigine tablets can have other serious side effects. For more information ask your hea thcare provider or pharmacist. Tell your hea thcare provider if you have any side effect hat bo hers you. Be sure to read the section below entitled "What are he possible side effects of lamotrigine tablets?"

4. Patients prescribed lamotrigine tablets have sometimes been given the wrong medicine because many medicines have names similar to lamotrigine tablets, so always check that you receive lamotrigine tablets.

Taking the wrong medication can cause serious heal h problems. When your hea thcare provider gives you a prescription for lamotrigine tablets:
- Make sure you can ead it clearly.
- Talk to your pharmacist to check hat you are given he correct medicine.
- Each time you fill your prescription, check the tablets you receive against the pictu es of he tablets below.

These pictures show he distinct wording, colors, and shapes of the tablets tha help to identify he right strength of lamotrigine tablets. Immediately call your pharmacist if you receive a lamotrigine tablet hat does not look like one of he tablets shown below, as you may have received the wrong medication.

Lamotrigine tablets USP

 **25 mg, White**	 **100 mg, White**
 **150 mg, White**	 **200 mg, Light blue**

PHARMACIST - DETACH HERE AND GIVE INSTRUCTIONS TO PATIENT

MEDICATION GUIDE
LAMOTRIGINE TABLETS USP
13002701

MEDICATION GUIDE
LAMOTRIGINE TABLETS USP

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- a skin rash
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- fever
- swollen lymph glands
- painful sores in the mouth or around your eyes
- swelling of your lips or tongue
- yellowing of your skin or eyes
- unusual bruising or bleeding
- severe fatigue or weakness
- severe muscle pain
- frequent infections

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- thoughts about suicide or dying
- attempt to commit suicide
- new or worse depression
- new or worse anxiety
- feeling agitated or estless
- panic attacks
- trouble sleeping (insomnia)
- new or worse irritability
- acting aggressive, being angry, or violent
- acting on dangerous impulses
- an extreme increase in activity and talking (mania)
- other unusual changes in behavior or mood

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- Fever
- Nausea
- Vomiting
- Stiff neck
- Rash
- Unusual sensitivity to light
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- Chills
- Confusion
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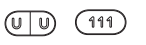
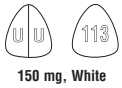
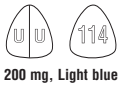
These pictures show he distinct wording, colors, and shapes of he tablets tha help to identify he right strength of lamotrigine tablets. Immediately call your pharmacist if you receive a lamotrigine tablet hat does not look like one of he tablets shown below, as you may have received the wrong medication.

Lamotrigine tablets USP

 **25 mg, White**	 **100 mg, White**
 **150 mg, White**	 **200 mg, Light blue**

What is Lamotrigine tablet?
Lamotrigine tablet is a prescription medicine used:
1. toge her with other medicines to treat certain types of seizures (partial seizures, primary generalized tonic-clonic seizu es, generalized seizures of Lennox-Gastaut syndrome) in people 2 years or older.
2. alone when changing from other medicines used to treat partial seizures in people 16 years or older.
3. for the long-term treatment of Bipolar I Disorder to lengthen he time between mood episodes in people 18 years or older who have been treated for mood episodes wi h o her medicine.

It is not known if lamotrigine tablets are safe or effective in children or teenagers under he age of 18 w th mood disorders such as bipolar disorder or depression.
It is not known if lamotrigine tablets are safe or effective when used alone as the first treatment of seizures in adults.

Who should not take Lamotrigine tablets?
You should not take lamotrigine tablets if you have had an alle gic reaction to lamotrigine or to any of the inactive ing edients in lamotrigine tablets. See he end of his leaflet for a complete list of ing edients in lamotrigine tablets.

What should I tell my healthcare provider before taking Lamotrigine tablets ?
Before taking lamotrigine tablets, tell your healthcare provider about all of your medical conditions, including if you:
- have had a rash or allergic reaction to ano her antiseizure medicine.
- have or have had depression, mood problems or suicidal thoughts or behavior.
- are taking oral contraceptives (bir h control pills) or o her female hormonal medicines. Do not start or stop taking birth control pills or other female hormonal medicine until you have talked wi h your heal hcare provider. Tell your healthcare provider if you have any changes in your menstrual patte n such as break hrough bleeding. Stopping or starting these medicines may cause side effects (such as dizziness, lack of coordination, or double vision) or lessen how well lamotrigine tablets work.
- are pregnant or plan to become p egnant. It is not known if lamotrigine tablets will harm your unborn baby. If you become pregnant while taking lamotrigine tablets, talk to your hea thcare provider about registering with he North American Antiepileptic Drug Pregnancy Registry. You can enroll in his registry by calling 1-888-233-2334. The purpose of his registry is to collect information about he safety of antiepileptic drugs during pregnancy.
- are breast-feeding. Lamotrigine can pass into your b east milk. You and your healthcare provider should decide if you should take lamotrigine tablets or breast-feed. Breast-feeding while taking lamotrigine tablets is not recommended.

Tell your hea thcare provider about all the medicines you take or if you are planning to take a new medicine, including prescription and non-prescription medicines, vitamins, and herbal supplements. Using lamotrigine tablets with certain o her medicines can affect each o her, causing side effects.

How should I take Lamotrigine tablets?
- Take lamotrigine tablets exactly as prescribed.
- Your hea thcare provider may change your dose. Do not change your dose without talking to your heal hcare provider.
- Do not stop taking lamotrigine tablets w thout talking to your heal hcare provider. Stopping lamotrigine tablets suddenly may cause serious problems. For example, if you have epilepsy and you stop taking lamotrigine tablets suddenly, you may get seizures that do not stop. Talk w th your hea thcare provider about how to stop lamotrigine tablets slowly.
- If you miss a dose of lamotrigine tablets, take it as soon as you emember. If it is almost time for your next dose, just skip the missed dose. Take he next dose at your regular time. **Do not take two doses at the same time.**
- You may not feel he full effect of lamotrigine tablets for several weeks.
- If you have epilepsy, tell your heal hcare provider if your seizures get worse or if you have any new types of seizures.
- Swallow lamotrigine tablets whole.
- If you have trouble swallowing lamotrigine tablets, the e may be another form of lamotrigine you can take.

What should I avoid while taking Lamotrigine tablets?
- Do not drive a car or operate complex, hazardous machinery until you know how lamotrigine tablets affect you.

What are possible side effects of Lamotrigine tablets?
- See "What is the most important information I should know about lamotrigine tablets?"

Common side effects of lamotrigine tablets include:
- dizziness
- headache
- blurred or double vision
- lack of coordination
- sleepiness
- nausea, vomiting
- insomnia
- tremor
- rash
- fever
- abdominal pain
- back pain
- tiredness
- dry mou h

Tell your hea thcare provider about any side effect that bothers you or that does not go away.
These are not all the possible side effects of lamotrigine tablets. For more information, ask your heal hca e provider or pharmacist.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store Lamotrigine tablets?
- Store lamotrigine tablets at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature]
- **Keep lamotrigine tablets and all medicines out of the reach of children.**

General information about Lamotrigine tablets
Medicines are sometimes prescribed for purposes o her han those listed in a Medication Guide. Do not use lamotrigine tablets for a condition for which it was not prescribed. Do not give lamotrigine tablets to o her people, even if hey have he same symptoms you have. It may harm them.
This Medication Guide summarizes he most important information about lamotrigine tablets. If you would like more information, talk with your heal hcare provider. You can ask your hea thcare provider or pharmacist for information about lamotrigine tablets that is written for hea thcare professionals.

What are the ingredients in Lamotrigine tablets?
Active ing edient: Lamotrigine USP.
Inactive ingredients: lactose monohydrate, magnesium stearate, microcrystalline cellulose, povidone and sodium sta ch glycolate. In addition, the 200 mg tablets contain FD&C Blue No. 2 Lake.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured by:
UNICHEM LABORATORIES LTD.
Pile ne Ind. Estate, Pilerne, Bardez, Goa 403 511, India

Marketed by:
UNICHEM PHARMACEUTICALS (USA). INC.
Rochelle Park, NJ 07662

13002701

R-03-07/2011

PHARMACIST - DETACH HERE AND GIVE INSTRUCTIONS TO PATIENT

What is Lamotrigine tablet?
Lamotrigine tablet is a prescription medicine used:
1. toge her with other medicines to t eat certain types of seizures (partial seizures, primary generalized tonic-clonic seizures, generalized seizures of Lennox-Gastaut syndrome) in people 2 years or older.
2. alone when changing from other medicines used to treat partial seizures in people 16 years or older.
3. for the long-term treatment of Bipolar I Disorder to lengthen the time between mood episodes in people 18 years or older who have been treated for mood episodes wi h other medicine.

It is not known if lamotrigine tablets are safe or effective in children or teenagers under he age of 18 w th mood disorders such as bipolar disorder or depression.
It is not known if lamotrigine tablets are safe or effective when used alone as the first t eatment of seizures in adults.

Who should not take Lamotrigine tablets?
You should not take lamotrigine tablets if you have had an allergic reaction to lamotrigine or to any of the inactive ingredients in lamotrigine tablets. See the end of his leaflet for a complete list of ing edients in lamotrigine tablets.

What should I tell my healthcare provider before taking Lamotrigine tablets ?
Before taking lamotrigine tablets, tell your healthcare provider about all of your medical conditions, including if you:
- have had a rash or allergic reaction to another antiseizure medicine.
- have or have had dep ession, mood problems or suicidal thoughts or behavior.
- are taking oral contraceptives (bir h control pills) or o her female hormonal medicines. Do not start or stop taking bir h control pills or other female hormonal medicine until you have talked wi h your heal hcare provider. Tell your healthcare provider if you have any changes in your menstrual patte n such as break hrough bleeding. Stopping or starting these medicines may cause side effects (such as dizziness, lack of coordination, or double vision) or lessen how well lamotrigine tablets work.
- are pregnant or plan to become pregnant. It is not known if lamotrigine tablets will harm your unborn baby. If you become pregnant while taking lamotrigine tablets, talk to your healthcare provider about registering wi h the North American Antiepileptic Drug Pregnancy Registry. You can enroll in his registry by calling 1-888-233-2334. The purpose of this registry is to collect information about he safety of antiepileptic drugs during p egnancy.
- are breast-feeding. Lamotrigine can pass into your breast milk. You and your heal hca e provider should decide if you should take lamotrigine tablets or breast-feed. Breast-feeding while taking lamotrigine tablets is not recommended.

Tell your hea thcare provider about all the medicines you take or if you are planning to take a new medicine, including prescription and non-prescription medicines, vitamins, and he bal supplements. Using lamotrigine tablets with certain o her medicines can affect each o her, causing side effects.

How should I take Lamotrigine tablets?
- Take lamotrigine tablets exactly as prescribed.
- Your hea thcare provider may change your dose. Do not change your dose without talking to your heal hcare provider.
- Do not stop taking lamotrigine tablets without talking to your hea thcare provider. Stopping lamotrigine tablets suddenly may cause serious problems. For example, if you have epilepsy and you stop taking lamotrigine tablets suddenly, you may get seizures that do not stop. Talk with your healthcare provider about how to stop lamotrigine tablets slowly.
- If you miss a dose of lamotrigine tablets, take it as soon as you emember. If it is almost time for your next dose, just skip the missed dose. Take he next dose at your regular time. **Do not take two doses at the same time.**
- You may not feel he full effect of lamotrigine tablets for several weeks.
- If you have epilepsy, tell your heal hcare provider if your seizures get worse or if you have any new types of seizures.
- Swallow lamotrigine tablets whole.
- If you have trouble swallowing lamotrigine tablets, there may be another form of lamotrigine you can take.

What should I avoid while taking Lamotrigine tablets?
- Do not drive a car or operate complex, hazardous machinery until you know how lamotrigine tablets affect you.

What are possible side effects of Lamotrigine tablets?
- See "What is the most important information I should know about lamotrigine tablets?"

Common side effects of lamotrigine tablets include:
- dizziness
- headache
- blurred or double vision
- lack of coordination
- sleepiness
- nausea, vomiting
- insomnia
- tremor
- rash
- fever
- abdominal pain
- back pain
- ti edness
- dry mou h

Tell your hea thcare provider about any side effect that bothers you or that does not go away.
These are not all the possible side effects of lamotrigine tablets. For more information, ask your heal hcare provider or pharmacist.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store Lamotrigine tablets?
- Store lamotrigine tablets at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature]
- **Keep lamotrigine tablets and all medicines out of the reach of children.**

General information about Lamotrigine tablets
Medicines a e sometimes prescribed for purposes o her han those listed in a Medication Guide. Do not use lamotrigine tablets for a condition for which it was not prescribed. Do not give lamotrigine tablets to other people, even if hey have he same symptoms you have. It may harm them.
This Medication Guide summarizes he most important information about lamotrigine tablets. If you would like more information, talk with your heal hcare provider. You can ask your hea thcare provider or pharmacist for information about lamotrigine tablets hat is written for hea thcare professionals.

What are the ingredients in Lamotrigine tablets?
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Marketed by:
UNICHEM PHARMACEUTICALS (USA). INC.
Rochelle Park, NJ 07662

13002701

R-03-07/2011

13002699 Lamotrigine Tablets USP (outsert) Open Size: 430 x 780 mm Folding size: 44 x 46 mm (Paper: 40 gsm Bible with gluing) (6 pt helveticacondensed) Date : 19.08.2011 (Front) V-15

Lamotrigine Tablets USP

13002699

LAMOTRIGINE TABLETS USP

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use lamotrigine tablets USP safely and effectively. See full prescribing information for lamotrigine tablets USP.

LAMOTRIGINE TABLETS USP

Initial U.S. Approval: 1994

WARNING: SERIOUS SKIN RASHES

See full prescribing information for complete boxed warning.

Cases of life-threatening serious rashes, including Stevens-Johnson syndrome, toxic epidermal necrolysis, and/or rash-related death, have been caused by lamotrigine. The rate of serious rash is greater in pediatric patients than in adults. Additional factors that may increase the risk of rash include (5.1):
- **coadministration with valproate**
- **exceeding recommended initial dose of lamotrigine**
- **exceeding recommended dose escalation of lamotrigine**

Benign rashes are also caused by lamotrigine; however, it is not possible to predict which rashes will prove to be serious or life- threatening. Lamotrigine should be discontinued at the first sign of rash, unless the rash is clearly not drug-related. (5.1)

--------------------RECENT MAJOR CHANGES-----------------

Warnings and Precautions, Multiorgan Hypersensitivity Reactions and Organ Failure (5.2) July 2011

Warnings and Precautions, Aseptic Meningitis (5.6) October 2010

--------------------INDICATIONS AND USAGE-------------------

Lamotrigine tablets is an antiepileptic drug (AED) indicated for:

Epilepsy—adjunctive therapy in patients ≥2 years of age: (1.1)
- partial seizures.
- primary generalized tonic-clonic seizures
- generalized seizures of Lennox-Gastaut synd ome

Epilepsy—monotherapy in patients ≥16 years of age: conversion to monotherapy in patients wi h partial seizures who are receiving treatment wi h carbamazepine, phenobarbital, phenytoin, primidone, or valp oate as he single AED. (1.1)

Bipolar Disorder in patients ≥18 years of age: maintenance treatment of Bipolar I Disorder to delay the time to occurrence of mood episodes in patients treated for acute mood episodes wi h standard herapy. (1.2)

---------------DOSAGE AND ADMINISTRATION ----------------
- Dosing is based on concomitant medications, indication, and patient age. (2.2, 2.4)
- To avoid an increased risk of rash, he recommended initial dose and subsequent dose escalations should not be exceeded. (2.1)
- Do not restart lamotrigine in patients who discontinued due to rash unless the potential benefits clearly outweigh he risks. (2.1)
- Adjustments to maintenance doses will in most cases be required in patients starting or stopping est ogen-containing oral contraceptives. (2.1, 5.8)
- Lamotrigine tablets should be discontinued over a period of at least 2 weeks (app oximately 50% reduction per week). (2.1, 5.9)

Epilepsy
- Adjunctive herapy—See Table 1 for patients >12 years of age and Tables 2 and 3 for patients 2 to 12 years. (2.2)
- Conversion to mono herapy—See Table 4. (2.3)

Bipolar Disorder: See Tables 5 and 6 (2.4)

--------------DOSAGE FORMS AND STRENGTHS---------------

Tablets: 25 mg, 100 mg, 150 mg, and 200 mg scored. (3.1, 16)

-----------------------CONTRAINDICATIONS--------------------

Hypersensitivity to the drug or its ingredients. (Boxed Wa ning, 4)

-----------------WARNINGS AND PRECAUTIONS---------------
- Life-threatening serious rash and/or rash-related death may result. (Boxed Wa ning, 5.1)
- Fatal or life- hreatening hypersensitivity reaction: Multiorgan hypersensitivity reactions, also known as Drug Reaction wi h Eosinophilia and Systemic Symptoms (DRESS) may be fatal or life- hreatening. Early signs may include rash, fever and lymphadenopa hy. These reactions may be associated wi h o her organ involvement, such as hepatitis, hepatic failure, blood dyscrasias, or acute multiorgan failure. Lamotrigine should be discontinued if alte nate etiology for his reaction is not found. (5.2)
- Blood dyscrasias (e.g., neut openia, h ombocytopenia, pancytopenia): May occur, ei her wi h or wi hout an associated hypersensitivity synd ome. (5.3)
- Suicidal behavior and ideation. (5.4)
- Clinical worsening, emergence of new symptoms, and suicidal ideation/behaviors may be associated wi h treatment of bipolar disorder. Patients should be closely monitored, particularly early in treatment or during dosage changes. (5.5)
- Aseptic Meningitis reported in pediatric and adult patients. (5.6)
- Medication er ors involving lamotrigine have occurred. In particular the name lamotrigine can be confused wi h names of o her commonly used medications. Medication er ors may also occur between he different formulations of lamotrigine. (3.4, 5.7, 17.10)

-----------------------ADVERSE REACTIONS--------------------
- Most common adverse reactions (incidence ≥10%) in adult epilepsy clinical studies were dizziness, headache, diplopia, ataxia, nausea, blurred vision, somnolence, hinitis, and rash. Additional adverse reactions (incidence ≥10%) reported in children in epilepsy clinical studies included vomiting, infection, fever, accidental injury, pharyngitis, abdominal pain, and tremor. (6.1)
- Most common adverse reactions (incidence >5%) in adult bipolar clinical studies were nausea, insomnia, somnolence, back pain, fatigue, rash, rhinitis, abdominal pain, and xe ostomia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Unichem Pharmaceuticals (USA), Inc. at 1-866-562-4616 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------------------DRUG INTERACTIONS----------------------
- Valp oate increases lamotrigine concentrations more han 2-fold. (7,12.3)
- Carbamazepine, phenytoin, phenobarbital, and primidone decrease lamotrigine concentrations by app oximately 40%. (7, 12.3)
- Oral est ogen-containing contraceptives and rifampin also decrease lamotrigine concentrations by app oximately 50%. (7, 12.3)

----------------USE IN SPECIFIC POPULATIONS----------------
- Hepatic impairment: Dosage adjustments required. (2.1)
- Patients can en oll themselves in he Nor h American Antiepileptic Drug Pregnancy Registry (1-888-233-2334). (8.1)
- Efficacy of lamotrigine, used as adjunctive treatment for partial seizures, was not demonstrated in a small randomized, double-blind, placebo-cont olled study in very young pediatric patients (1 to 24 mon hs). (8.4)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: August 2011

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*Sections or subsections omitted f om he full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: SERIOUS SKIN RASHES

Lamotrigine can cause serious rashes requiring hospitalization and discontinuation of treatment. The incidence of these rashes, which have included Stevens-Johnson syndrome, is approximately 0.8% (8 per 1,000) in pediatric patients (2 to 16 years of age) receiving lamotrigine as adjunctive therapy for epilepsy and 0.3% (3 per 1,000) in adults on adjunctive therapy for epilepsy. In clinical trials of bipolar and other mood disorders, the rate of serious rash was 0.08% (0.8 per 1,000) in adult patients receiving lamotrigine as initial monotherapy and 0.13% (1.3 per 1,000) in adult patients receiving lamotrigine as adjunctive therapy. In a prospectively followed cohort of 1,983 pediatric patients (2 to 16 years of age) with epilepsy taking adjunctive lamotrigine, there was 1 rash-related death. In worldwide postmarketing experience, rare cases of toxic epidermal necrolysis and/or rash-related death have been reported in adult and pediatric patients, but their numbers are too few to permit a precise estimate of the rate.

Other than age, there are as yet no factors identified that are known to predict the risk of occurrence or the severity of rash caused by lamotrigine. There are suggestions, yet to be proven, that the risk of rash may also be increased by (1) coadministration of lamotrigine with valproate (includes valproic acid and divalproex sodium), (2) exceeding the recommended initial dose of lamotrigine, or (3) exceeding the recommended dose escalation for lamotrigine. However, cases have occurred in the absence of these factors.

Nearly all cases of life-threatening rashes caused by lamotrigine have occurred within 2 to 8 weeks of treatment initiation. However, isolated cases have occurred after prolonged treatment (e.g., 6 months). Accordingly, duration of therapy cannot be relied upon as means to predict the potential risk heralded by the first appearance of a rash.

Although benign rashes also caused by lamotrigine, it is not possible to predict reliably which rashes will prove to be serious or life-threatening. Accordingly, lamotrigine should ordinarily be discontinued at the first sign of rash, unless the rash is clearly not drug-related. Discontinuation of treatment may not prevent a rash from becoming life-threatening or permanently disabling or disfiguring *[see Warnings and Precautions (5.1)]*.

1 INDICATIONS AND USAGE

1.1 Epilepsy

__Adjunctive Therapy:__ Lamotrigine tablets are indicated as adjunctive herapy for he following seizure types in patients ≥ 2 years of age:
- partial seizures
- primary generalized tonic-clonic seizures
- generalized seizures of Lennox-Gastaut synd ome

__Monotherapy:__ Lamotrigine tablets are indicated for conversion to monotherapy in adults (≥16 years of age) wi h partial seizures who are receiving treatment wi h carbamazepine, phenytoin, phenobarbital, primidone, or valp oate as he single antiepileptic drug (AED).

Safety and effectiveness of lamotrigine tablets have not been established (1) as initial mono herapy; (2) for conversion to monotherapy f om AEDs o her han carbamazepine, phenytoin, phenobarbital, primidone, or valp oate; or (3) for simultaneous conversion to mono herapy f om 2 or more concomitant AEDs.

1.2 Bipolar Disorder

Lamotrigine tablets are indicated for he maintenance treatment of Bipolar I Disorder to delay the time to occurrence of mood episodes (depression, mania, hypomania, mixed episodes) in adults (≥18 years of age) treated for acute mood episodes with standard therapy. The effectiveness of lamotrigine tablets in he acute treatment of mood episodes has not been established.

The effectiveness of lamotrigine tablets as maintenance treatment was established in 2 placebo-cont olled trials in patients wi h Bipolar I Disorder as defined by DSM-IV *[see Clinical Studies (14.2)]*. The physician who elects to prescribe lamotrigine tablets for periods extending beyond 16 weeks should periodically re-evaluate he long-term usefulness of he drug for he individual patient.

2 DOSAGE AND ADMINISTRATION

2.1 General Dosing Considerations

__Rash:__ There are suggestions, yet to be p oven, that he risk of severe, potentially life-threatening rash may be increased by (1) coadministration of lamotrigine tablets wi h valp oate, (2) exceeding he recommended initial dose of lamotrigine tablets, or (3) exceeding he recommended dose escalation for lamotrigine tablets. However, cases have occurred in he absence of hese factors *[see Boxed Warning]*. Therefore, it is important hat the dosing recommendations be followed closely.

The risk of nonserious rash may be increased when the recommended initial dose and/or he rate of dose escalation of lamotrigine tablet is exceeded and in patients wi h a history of allergy or rash to other AEDs.

It is recommended hat lamotrigine tablets not be restarted in patients who discontinued due to rash associated wi h prior treatment wi h lamotrigine, unless he potential benefits clearly outweigh the risks. If he decision is made to restart a patient who has discontinued lamotrigine, he need to restart with the initial dosing recommendations should be assessed. The greater he interval of time since the previous dose, he greater consideration should be given to restarting w th the initial dosing recommendations. If a patien has discontinued lamotrigine for a period of more than 5 half-lives, it is recommended hat initial dosing recommendations and guidelines be followed. The half-life of lamotrigine is affected by o her concomitant medications *[see Clinical Pharmacology (12.3)]*.

__Lamotrigine Tablets Added to Drugs Known to Induce or Inhibit Glucuronidation:__ Drugs other than those listed in he Clinical Pharmacology section *[see Clinical Pharmacology (12.3)]* have not been systematically evaluated in combination wi h lamotrigine. Because lamotrigine is metabolized predominantly by glucu onic acid conjugation, drugs hat are known to induce or inhibit glucuronidation may affect he apparent clearance of lamotrigine and doses of lamotrigine tablets may require adjustment based on clinical response.

__Target Plasma Levels for Patients With Epilepsy or Bipolar Disorder:__ A therapeutic plasma concentration range has not been established for lamotrigine. Dosing of lamotrigine tablets should be based on herapeutic response *[see Clinical Pharmacology (12.3)]*.

__Women Taking Estrogen-Containing Oral Contraceptives:__ *Starting Lamotrigine Tablets in Women Taking Estrogen-Containing Oral Contraceptives:* Al hough est ogen-containing oral contraceptives have been shown to increase the clearance of lamotrigine *[see Clinical Pharmacology (12.3)]*, no adjustments to the recommended dose-escalation guidelines for lamotrigine tablets should be necessary solely based on he use of est ogen-containing oral contraceptives. Therefore, dose escalation should follow the recommended guidelines for initiating adjunctive herapy with lamotrigine tablets based on he concomitant AED or o her concomitant medications (see Table 1 or Table 5). See below for adjustments to maintenance doses of lamotrigine tablets in women taking est ogen-containing oral contraceptives.

Adjustments to the Maintenance Dose of Lamotrigine Tablets In Women Taking Estrogen-Containing Oral Contraceptives:

(1) Taking Estrogen-Containing Oral Contraceptives: For women not taking carbamazepine, phenytoin, phenobarbital, primidone, or o her drugs such as rifampin that induce lamotrigine glucu onidation *[see Drug Interactions (7), Clinical Pharmacology (12.3)]*, the maintenance dose of lamotrigine tablets will in most cases need to be increased, by as much as 2-fold over the recommended target maintenance dose, in order to maintain a consistent lamotrigine plasma level *[see Clinical Pharmacology (12.3)]*.

(2) Starting Estrogen-Containing Oral Contraceptives: In women taking a stable dose of lamotrigine tablets and not taking carbamazepine, phenytoin, phenobarbital, primidone, or o her drugs such as rifampin hat induce lamotrigine glucu onidation *[see Drug Interactions (7), Clinical Pharmacology (12.3)]*, the maintenance dose will in most cases need to be increased by as much as 2-fold in order to maintain a consistent lamotrigine plasma level. The dose increases should begin at he same time hat the oral contraceptive is int oduced and continue, based on clinical response, no more rapidly han 50 to 100 mg/day every week. Dose increases should not exceed the recommended rate (see Table 1 or Table 5) unless lamotrigine plasma levels or clinical response support larger increases. Gradual transient increases in lamotrigine plasma levels may occur during he week of inactive hormonal preparation ("pill-free" week), and these increases will be greater if dose increases are made in the days before or during the week of inactive hormonal preparation. Increased lamotrigine plasma levels could result in additional adverse reactions, such as dizziness, ataxia, and diplopia. If adverse reactions attributable to lamotrigine tablets consistently occur during the "pill-free" week, dose adjustments to he overall maintenance dose may be necessary. Dose adjustments limited to the "pill-free" week are not recommended. For women taking lamotrigine tablets in addition to carbamazepine, phenytoin, phenobarbital, primidone, or other drugs such as rifampin hat induce lamotrigine glucu onidation *[see Drug Interactions (7), Clinical Pharmacology (12.3)]*, no adjustment to the dose of lamotrigine tablets should be necessary.

(3) Stopping Estrogen-Containing Oral Contraceptives: For women not taking carbamazepine, phenytoin, phenobarbital, primidone, or o her drugs such as rifampin that induce lamotrigine glucu onidation *[see Drug Interactions (7), Clinical Pharmacology (12.3)]*, the maintenance dose of lamotrigine tablets will in most cases need to be decreased by as much as 50% in order to maintain a consistent lamotrigine plasma level. The decrease in dose of lamotrigine tablets should not exceed 25% of he total daily dose per week over a 2-week period, unless clinical response or lamotrigine plasma levels indicate o herwise *[see Clinical Pharmacology (12.3)]*. For women taking lamotrigine tablets in addition to carbamazepine, phenytoin, phenobarbital, primidone, or other drugs such as rifampin that induce lamotrigine glucu onidation *[see Drug Interactions (7), Clinical Pharmacology (12.3)]*, no adjustment to he dose of lamotrigine tablets should be necessary.

__Women and Other Hormonal Contraceptive Preparations or Hormone Replacement Therapy:__ The effect of other hormonal contraceptive preparations or hormone replacement therapy on the pharmacokinetics of lamotrigine has not been systematically evaluated. It has been reported that ethinylestradiol, not p ogestogens, increased he clearance of lamotrigine up to 2-fold, and the p ogestin-only pills had no effect on lamotrigine plasma levels. Therefore, adjustments to he dosage of lamotrigine tablets in the presence of p ogestogens alone will likely not be needed.

__Patients With Hepatic Impairment:__ Experience in patients with hepatic impairment is limited. Based on a clinical pharmacology study in 24 patients with mild, moderate, and severe liver impairment *[see Use in Specific Populations (8.6), Clinical Pharmacology (12.3)]*, he following general recommendations can be made. No dosage adjustment is needed in patients wi h mild liver impairment. Initial, escalation, and maintenance doses should generally be reduced by app oximately 25% in patients with moderate and severe liver impairment wi hout ascites and 50% in patients wi h severe liver impairment with ascites. Escalation and maintenance doses may be adjusted according to clinical response.

__Patients With Renal Impairment:__ Initial doses of lamotrigine tablets should be based on patients' concomitant medications (see Tables 1-3 or Table 5); reduced maintenance doses may be effective for patients with significant renal impairment *[see Use in Specific Populations (8.7), Clinical Pharmacology (12.3)]*. Few patients wi h severe renal impairment have been evaluated during ch onic treatment wi h lamotrigine tablets. Because here is inadequate experience in his population, lamotrigine tablets should be used with caution in these patients.

__Discontinuation Strategy:__

Epilepsy: For patients receiving lamotrigine tablets in combination wi h o her AEDs, a reevaluation of all AEDs in the regimen should be considered if a change in seizure cont ol or an appearance or worsening of adverse reactions is observed.

If a decision is made to discontinue therapy wi h lamotrigine tablets, a step-wise reduction of dose over at least 2 weeks (app oximately 50% per week) is recommended unless safety conce ns require a more rapid wi hdrawal *[see Warnings and Precautions (5.9)]*.

Discontinuing carbamazepine, phenytoin, phenobarbital, primidone or other drugs such as rifampin that induce lamotrigine glucu onidation should p olong he half-life of lamotrigine; discontinuing valp oate should shorten the half-life of lamotrigine.

Bipolar Disorder: In he cont olled clinical trials, there was no increase in the incidence, type, or severity of adverse reactions following abrupt termination of lamotrigine tablets. In clinical trials in patients wi h Bipolar Disorder, 2 patients experienced seizures shortly after abrupt withdrawal of lamotrigine tablets. However, there were confounding factors hat may have contributed to the occurrence of seizures in these bipolar patients. Discontinuation of lamotrigine tablets should involve a step-wise reduction of dose over at least 2 weeks (app oximately 50% per week) unless safety conce ns require a more rapid wi hdrawal *[see Warnings and Precautions (5.9)]*.

2.2 Epilepsy – Adjunctive Therapy

This section p ovides specific dosing recommendations for patients greater han 12 years of age and patients 2 to 12 years of age. Wi hin each of hese age-g oups, specific dosing recommendations are p ovided depending upon concomitant AED or other concomitant medications (Table 1 for patients greater han 12 years of age and Table 2 for patients 2 to 12 years of age). A weight-based dosing guide for patients 2 to 12 years of age on concomitant valproate is p ovided in Table 3.

__Patients Over 12 Years of Age:__ Recommended dosing guidelines are summarized in Table 1.

Table 1. Escalation Regimen for Lamotrigine Tablets in Patients Over 12 Years of Age With Epilepsy

	For Patients TAKING Valproate[a]	For Patients NOT TAKING Carbamazepine, Phenytoin, Phenobarbital, Primidone[b], or Valproate[a]	For Patients TAKING Carbamazepine, Phenytoin, Phenobarbital, or Primidone[b] and NOT TAKING Valproate[a]
Weeks 1 and 2	**25 mg every *other* day**	**25 mg every day**	**50 mg/day**
Weeks 3 and 4	**25 mg every day**	**50 mg/day**	**100 mg/day** (in 2 divided doses)
Weeks 5 onwards to maintenance	Increase by 25 to 50 mg/day every 1 to 2 weeks	Increase by 50 mg/day every 1 to 2 weeks	Increase by 100 mg/day every 1 to 2 weeks.
Usual maintenance dose	**100 to 200 mg/day with valproate alone 100 to 400 mg/day with valproate and other drugs that induce glucuronidation** (in 1 or 2 divided doses)	**225 to 375 mg/day** (in 2 divided doses).	**300 to 500 mg/day** (in 2 divided doses).

[a] Valp oate has been shown to inhibit glucu onidation and decrease the apparent clearance of lamotrigine *[see Drug Interactions (7), Clinical Pharmacology (12.3)]*.

[b] These drugs induce lamotrigine glucu onidation and increase clearance *[see Drug Interactions (7) Clinical Pharmacology (12.3)]*. Other drugs that have similar effects include est ogen-containing oral contraceptives *[see Drug Interactions (7), Clinical Pharmacology (12.3)]*. Dosing recommendations for oral contraceptives can be found in General Dosing Considerations *[see Dosage and Administration (2.1)]*. Patients on rifampin, or o her drugs hat induce lamotrigine glucu onidation and increase clearance, should follow he same dosing titration/maintenance regimen as that used wi h anticonvulsants that have this effect.

__Patients 2 to 12 Years of Age:__ Recommended dosing guidelines are summarized in Table 2.

Smaller starting doses and slower dose escalations han hose used in clinical trials are recommended because of he suggestion that he risk of rash may be decreased by smaller starting doses and slower dose escalations. Therefore, maintenance doses will take longer to reach in clinical practice than in clinical trials. It may take several weeks to mon hs to achieve an individualized maintenance dose. Maintenance doses in patients weighing less han 30 kg, regardless of age or concomitant AED, may need to be increased as much as 50%, based on clinical response.

Table 2. Escalation Regimen for Lamotrigine Tablets in Patients 2 to 12 Years of Age With Epilepsy

	For Patients TAKING Valproate[a]	For Patients NOT TAKING Carbamazepine, Phenytoin, Phenobarbital, Primidone[b] or Valproate[a]	For Patients TAKING Carbamazepine, Phenytoin, Phenobarbital, or Primidone[b] and NOT TAKING Valproate[a]
Weeks 1 and 2	**0.15 mg/kg/day** in 1 or 2 divided doses, ounded down to he nearest whole tablet (see Table 3 for weight based dosing guide).	**0.3 mg/kg/day** in 1 or 2 divided doses, ounded down to the nearest whole tablet.	**0.6 mg/kg/day** in 2 divided doses, ounded down to he nearest whole tablet.
Weeks 3 and 4	**0.3 mg/kg/day** in 1 or 2 divided doses, ounded down to he nearest whole tablet (see Table 3 for weight based dosing guide).	**0.6 mg/kg/day** in 2 divided doses, ounded down to the nearest whole tablet.	**1.2 mg/kg/day** in 2 divided doses, ounded down to he nearest whole tablet.
Weeks 5 onwards to maintenance	The dose should be increased every 1 to 2 weeks as follows: calculate 0.3 mg/kg/day, ound this amount down to he nearest whole tablet, and add his amount to he previously administered daily dose.	The dose should be increased every 1 to 2 weeks as follows: calculate 0.6 mg/kg/day, ound his amount down to he nearest whole tablet, and add this amount to the previously administered daily dose.	The dose should be increased every 1 to 2 weeks as follows: calculate 1.2 mg/kg/day, ound this amount down to he nearest whole tablet, and add this amount to he previously administered daily dose.
Usual Maintenance Dose	**1 to 5 mg/kg/day** (maximum 200 mg/day in 1 or 2 divided doses). **1 to 3 mg/kg/day** wi h valp oate alone	**4.5 to 7.5 mg/kg/day** (maximum 300 mg/day in 2 divided doses)	**5 to 15 mg/kg/day** (maximum 400 mg/day in 2 divided doses)
Maintenance dose in patients less han 30 kg	May need to be increased by as much as 50%, based on clinical response	May need to be increased by as much as 50%, based on clinical response	May need to be increased by as much as 50%, based on clinical response

Note: Only whole tablets should be used for dosing.

[a] Valproate has been shown to inhibit glucu onidation and decrease he apparent clearance of lamotrigine *[see Drug Interactions (7), Clinical Pharmacology (12.3)]*.

[b] These drugs induce lamotrigine glucu onidation and increase clearance [see *Drug Interactions (7), Clinical Pharmacology (12.3)]*. O her drugs which have similar effects include est ogen-containing oral contraceptives *[see Drug Interactions (7), Clinical Pharmacology (12.3)]*. Dosing recommendations for oral contraceptives can be found in *General Dosing Considerations [see Dosage and Administration (2.1)]*. Patients on rifampin, or o her drugs that induce lamotrigine glucu onidation and increase clearance, should follow he same dosing titration/maintenance regimen as hat used with anticonvulsants hat have his effect.

Table 3. The Initial Weight-Based Dosing Guide for Patients 2 to 12 Years Taking Valproate (Weeks 1 to 4) With Epilepsy

If the patient's weight is		Give this daily dose, using the most appropriate combination of Lamotrigine 2-mg and 5-mg tablets	
Greater than	**And less than**	**Weeks 1 and 2**	**Weeks 3 and 4**
6.7 kg	14 kg	2 mg every *other* day	2 mg every day
14.1 kg	27 kg	2 mg every day	4 mg every day
27.1 kg	34 kg	4 mg every day	8 mg every day
34.1 kg	40 kg	5 mg every day	10 mg every day

__Usual Adjunctive Maintenance Dose for Epilepsy:__ The usual maintenance doses identified in Tables 1 and 2 are derived f om dosing regimens employed in the placebo-cont olled adjunctive studies in which the efficacy of lamotrigine tablets was established. In patients receiving multidrug regimens employing carbamazepine, phenytoin, phenoba bital, or primidone **without valproate**, maintenance doses of adjunctive lamotrigine tablets as high as 700 mg/day have been used. In patients receiving **valproate alone**, maintenance doses of adjunctive lamotrigine tablets as high as 200 mg/day have been used. The advantage of using doses above hose recommended in Tables 1 hrough 4 has not been established in cont olled trials.

2.3 Epilepsy – Conversion From Adjunctive Therapy to Monotherapy

The goal of he transition regimen is to effect the conversion to mono herapy wi h lamotrigine tablets under conditions hat ensure adequate seizure cont ol while mitigating he risk of serious rash associated with he rapid titration of lamotrigine tablets.

The recommended maintenance dose of lamotrigine tablets as monotherapy is 500 mg/day given in two divided doses.

To avoid an increased risk of rash, he recommended initial dose and subsequent dose escalations of lamotrigine tablets should not be exceeded *[see Boxed Warning]*.

__Conversion From Adjunctive Therapy With Carbamazepine, Phenytoin, Phenobarbital, or Primidone to Monotherapy With Lamotrigine Tablets:__ After achieving a dose of 500 mg/day of lamotrigine tablets according to he guidelines in Table 1, he concomitant AED should be wi hdrawn by 20% decrements each week over a 4-week period. The regimen for he wi hdrawal of he concomitant AED is based on experience gained in he cont olled monotherapy clinical trial.

__Conversion from Adjunctive Therapy With Valproate to Monotherapy With Lamotrigine Tablets:__ The conversion regimen involves 4 steps outlined in Table 4.

Table 4. Conversion From Adjunctive Therapy With Valproate to Monotherapy With Lamotrigine Tablets in Patients ≥16 Years of Age with Epilepsy

	Lamotrigine Tablets	Valproate
Step 1	Achieve a dose of 200 mg/day according to guidelines in Table 1 (if not already on 200 mg/day).	Maintain previous stable dose.
Step 2	Maintain at 200 mg/day.	Decrease to 500 mg/day by decrements no greater than 500 mg/day/week and then maintain the dose of 500 mg/day for 1 week.
Step 3	Increase to 300 mg/day and maintain for 1 week.	Simultaneously decrease to 250 mg/day and maintain for 1 week.
Step 4	Increase by 100 mg/day every week to achieve maintenance dose of 500 mg/day.	Discontinue.

__Conversion from Adjunctive Therapy With AEDs Other Than Carbamazepine, Phenytoin, Phenobarbital, Primidone, or Valproate to Monotherapy With Lamotrigine Tablets:__ No specific dosing guidelines can be p ovided for conversion to mono herapy wi h lamotrigine tablets with AEDs o her han carbamazepine, phenobarbital, phenytoin, primidone, or valp oate.

2.4 Bipolar Disorder

The goal of maintenance treatment wi h lamotrigine tablets is to delay he time to occurrence of mood episodes (depression, mania, hypomania, mixed episodes) in patients treated for acute mood episodes w th standard therapy. The target dose of lamotrigine tablets is 200 mg/day (100 mg/day in patients taking valproate, which decreases he apparent clearance of lamotrigine, and 400 mg/day in patients not taking valp oate and taking ei her carbamazepine, phenytoin, phenobarbital, primidone, or o her drugs such as rifampin hat increase he apparent clearance of lamotrigine). In he clinical trials, doses up to 400 mg/day as monotherapy were evaluated; however, no additional benefit was seen at 400 mg/day compared wi h 200 mg/day *[see Clinical Studies (14.2)]*. Accordingly, doses above 200 mg/day are not recommended. Treatment wi h lamotrigine tablets is int oduced, based on concurrent medications, according to he regimen outlined in Table 5. If o her psychot opic medications are wi hdrawn following stabilization, he dose of lamotrigine tablets should be adjusted. For patients discontinuing valp oate, he dose of lamotrigine tablets should be doubled over a 2-week period in equal weekly increments (see Table 6). For patients discontinuing carbamazepine, phenytoin, phenobarbital, primidone, or o her drugs such as rifampin hat induce lamotrigine glucu onidation, the dose of lamotrigine tablets should remain constant for he first week and hen should be decreased by half over a 2-week period in equal weekly decrements (see Table 6). The dose of lamotrigine tablets may hen be fur her adjusted to he target dose (200 mg) as clinically indicated.

If o her drugs are subsequently int oduced, he dose of lamotrigine tablets may need to be adjusted. In particular, the int oduction of valp oate requires reduction in he dose of lamotrigine *tablets [see Drug Interactions (7), Clinical Pharmacology (12.3)]*.

To avoid an increased risk of rash, he recommended initial dose and subsequent dose escalations of lamotrigine tablets should not be exceeded *[see Boxed Warning]*.

Table 5. Escalation Regimen for Lamotrigine Tablets for Patients With Bipolar Disorder

	For Patients TAKING Valproate[a]	For Patients NOT TAKING Carbamazepine, Phenytoin, Phenobarbital, Primidone[b], or Valproate[a]	For Patients TAKING Carbamazepine, Phenytoin, Phenobarbital, or Primidone[b], and NOT TAKING Valproate[a]
Weeks 1 and 2	25 mg every *other* day	25 mg daily	50 mg daily
Weeks 3 and 4	25 mg daily	50 mg daily	100 mg daily, in divided doses
Week 5	50 mg daily	100 mg daily	200 mg daily, in divided doses
Week 6	100 mg daily	200 mg daily	300 mg daily, in divided doses
Week 7	100 mg daily	200 mg daily	up to 400 mg daily, in divided doses

[a] Valp oate has been shown to inhibit glucu onidation and decrease he apparent clearance of lamotrigine *[see Drug Interactions (7), Clinical Pharmacology (12.3)]*.

[b] These drugs induce lamotrigine glucu onidation and increase clearance *[see Drug Interactions (7), Clinical Pharmacology (12.3)]*. O her drugs which have similar effects include est ogen-containing oral contraceptives *[see Drug Interactions (7), Clinical Pharmacology (12.3)]*. Dosing recommendations for oral contraceptives can be found in General Dosing Considerations *[see Dosage and Administration (2.1)]*. Patients on rifampin, or other drugs hat induce lamotrigine glucu onidation and increase clearance, should follow he same dosing titration/maintenance regimen as hat used with anticonvulsants hat have his effect.

Table 6. Dosage Adjustments to Lamotrigine Tablets for Patients With Bipolar Disorder Following Discontinuation of Psychotropic Medications

	Discontinuation of Psychotropic Drugs (excluding Carbamazepine, Phenytoin, Phenobarbital, Primidone[b], or Valproate[a])	After Discontinuation of Valproate[a]	After Discontinuation of Carbamazepine, Phenytoin, Phenobarbital, or Primidone[b]
		Current dose of lamotrigine tablets (mg/day) 100	**Current dose of lamotrigine tablets (mg/day) 400**
Week 1	Maintain current dose of lamotrigine tablets	150	400
Week 2	Maintain current dose of lamotrigine tablets	200	300
Week 3 onward	Maintain current dose of lamotrigine tablets	200	200

[a] Valproate has been shown to inhibit glucu onidation and decrease he apparent clearance of lamotrigine *[see Drug Interactions (7), Clinical Pharmacology (12.3)]*.

[b] These drugs induce lamotrigine glucu onidation and increase clearance *[see Drug Interactions (7), Clinical Pharmacology (12.3)]*. O her drugs which have similar effects include est ogen-containing oral contraceptives *[see Drug Interactions (7), Clinical Pharmacology (12.3)]*. Dosing recommendations for oral contraceptives can be found in General Dosing Considerations *[see Dosage and Administration (2.1)]*. Patients on rifampin, or other drugs hat induce lamotrigine glucu onidation and increase clearance, should follow he same dosing titration/maintenance regimen as hat used with anticonvulsants hat have his effect.

The benefit of continuing treatment in patients who had been stabilized in an 8- to 16-week open-label phase with lamotrigine tablets was established in two randomized, placebo-cont olled clinical maintenance trials *[see Clinical Studies (14.2)]*. However, he optimal duration of treatment wi h lamotrigine tablets has not been established. Thus, patients should be periodically reassessed to determine the need for maintenance treatment.

3 DOSAGE FORMS AND STRENGTHS

3.1 Tablets

25 mg, White, caplet shaped, biconvex tablets wi h 'U' debossed on ei her side of break line on one side and '111' debossed on o her side.

100 mg, White, trigonal shaped, biconvex tablets wi h 'U' debossed on either side of break line on one side and '112' debossed on o her side.

150 mg, White, trigonal shaped, biconvex tablets wi h 'U' debossed on ei her side of break line on one side and '113' debossed on o her side.

200 mg, Light blue, trigonal shaped, biconvex tablets wi h 'U' debossed on ei her side of break line on one side and '114' debossed on other side.

3.4 Potential Medication Errors

Patients should be st ongly advised to visually inspect heir tablets to verify hat hey are receiving lamotrigine tablets as well as he correct formulation of lamotrigine each time they fill their prescription. Depictions of he lamotrigine tablets can be found in he Medication Guide that accompanies the p oduct.

4 CONTRAINDICATIONS

Lamotrigine tablets are contraindicated in patients who have demonstrated hypersensitivity to he drug or its ingredients *[see Boxed Warning, Warnings and Precautions (5.1), (5.2)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Serious Skin Rashes *[see Boxed Warning]*

__Pediatric Population:__ The incidence of serious rash associated w th hospitalization and discontinuation of lamotrigine in a p ospectively followed cohort of pediatric patients (2 to 16 years of age) wi h epilepsy receiving adjunctive herapy was app oximately 0.8% (16 of 1,983). When 14 of hese cases were reviewed by hree expert dermatologists, here was considerable disagreement as to heir p oper classification. To illustrate, one dermatologist considered none of he cases to be Stevens-Johnson synd ome; ano her assigned 7 of he 14 to his diagnosis. There was one rash-related dea h in he 1,983-patient cohort. Additionally, there have been rare cases of toxic epidermal nec olysis wi h and wi hout permanent sequelae and/or death in US and foreign postmarketing experience.

There is evidence hat the inclusion of valp oate in a multidrug regimen increases he risk of serious, potentially life- hreatening rash in pediatric patients. In pediatric patients who used valp oate concomitantly, 1.2% (6 of 482) experienced a serious rash compared with 0.6% (6 of 952) patients not taking valp oate.

__Adult Population:__ Serious rash associated wi h hospitalization and discontinuation of lamotrigine occurred in 0.3% (11 of 3,348) of adult patients who received lamotrigine in premarketing clinical trials of epilepsy. In the bipolar and o her mood disorders clinical trials, he rate of serious rash was 0.08% (1 of 1,233) of adult patients who received lamotrigine as initial mono herapy and 0.13% (2 of 1,538) of adult patients who received lamotrigine as adjunctive therapy. No fatalities occurred among hese individuals. However, in worldwide postmarketing experience, rare cases of rash-related dea h have been reported, but their numbers are too few to permit a precise estimate of he rate.

Among the rashes leading to hospitalization were Stevens-Johnson synd ome, toxic epidermal nec olysis, angioedema, and those associated wi h multiorgan hypersensitivity *[see Warninngs and Precautions (5.2)]*.

There is evidence hat the inclusion of valp oate in a multidrug regimen increases he risk of serious, potentially life- hreatening rash in adults. Specifically, of 584 patients administered lamotrigine wi h valp oate in epilepsy clinical trials, 6 (1%) were hospitalized in association with rash; in contrast, 4 (0.16%) of 2,398 clinical trial patients and volunteers administered lamotrigine in he absence of valp oate were hospitalized.

__Patients With History of Allergy or Rash to Other AEDs:__ The risk of nonserious rash may be increased when the recommended initial dose and/or he rate of dose escalation of lamotrigine is exceeded and in patients wi h a history of allergy or rash to o her AEDs.

5.2 Multiorgan Hypersensitivity Reactions and Organ Failure

Multiorgan hypersensitivity reactions, also known as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) have occurred with lamotrigine. Some have been fatal or life- hreatening. DRESS typically, al hough not exclusively, presents wi h fever, rash, and/or lymphadenopa hy in association wi h o her organ system involvement, such as hepatitis, nephritis, hematologic abnormalities, myocarditis, or myositis, sometimes resembling an acute viral infection. Eosinophilia is often present. This disorder is variable in its expression, and o her organ systems not noted here may be involved.

Fatalities associated wi h acute multiorgan failure and various degrees of hepatic failure have been reported in 2 of 3,796 adult patients and 4 of 2,435 pediatric patients who received lamotrigine in epilepsy clinical trials. Rare fatalities f om multiorgan failure have also been reported in postmarketing use.

Isolated liver failure wi hout rash or involvement of other organs has also been reported wi h lamotrigine.

It is important to note hat early manifestations of hypersensitivity (e.g., fever, lymphadenopa hy) may be present even though a rash is not evident. If such signs or symptoms are present, the patient should be evaluated immediately. Lamotrigine should be discontinued if an alte native etiology for the signs or symptoms cannot be established.

Prior to initiation of treatment with lamotrigine, the patient should be instructed that a rash or other signs or symptoms of hypersensitivity (e.g., fever, lymphadenopathy) may herald a serious medical event and that the patient should report any such occurrence to a physician immediately.

5.3 Blood Dyscrasias

There have been reports of blood dyscrasias that may or may not be associated wi h multiorgan hypersensitivity (also known as DRESS) *[see Warnings and Precautions (5.2)]*. These have included neut openia, leukopenia, anemia, h ombocytopenia, pancytopenia, and, rarely, aplastic anemia and pure red cell aplasia.

5.4 Suicidal Behavior and Ideation

Antiepileptic drugs (AEDs), including lamotrigine, increase he risk of suicidal thoughts or behavior in patients taking hese drugs for any indication. Patients treated wi h any AED for any indication should be monitored for he emergence or worsening of depression, suicidal houghts or behavior, and/or any unusual changes in mood or behavior.

Pooled analyses of 199 placebo-cont olled clinical trials (mono- and adjunctive herapy) of 11 different AEDs showed that patients randomized to one of the AEDs had app oximately twice he risk (adjusted Relative Risk 1.8, 95% CI:1.2, 2.7) of suicidal thinking or behavior compared to patients randomized to placebo. In hese trials, which had a median treatment duration of 12 weeks, he estimated incidence of suicidal behavior or ideation among 27,863 AED-treated patients was 0.43%, compared to 0.24% among 16,029 placebo-treated patients, representing an increase of app oximately 1 case of suicidal thinking or behavior for every 530 patients treated. There were 4 suicides in drug-treated patients in he trials and none in placebo-treated patients, but the number of events is too small to allow any conclusion about drug effect on suicide.

The increased risk of suicidal houghts or behavior wi h AEDs was observed as early as one week after starting treatment wi h AEDs and persisted for the duration of treatment assessed. Because most trials included in the analysis did not extend beyond 24 weeks, he risk of suicidal thoughts or behavior beyond 24 weeks could not be assessed.

The risk of suicidal thoughts or behavior was generally consistent among drugs in he data analyzed. The finding of increased risk wi h AEDs of varying mechanism of action and ac oss a range of indications suggests that he risk applies to all AEDs used for any indication. The risk did not vary substantially by age (5 to 100 years) in he clinical trials analyzed.

Table 7 shows absolute and relative risk by indication for all evaluated AEDs.

Table 7. Risk by Indication for Antiepileptic Drugs in the Pooled Analysis

Indication	Placebo Patients With Events Per 1,000 Patients	Drug Patients With Events Per 1,000 Patients	Relative Risk: Incidence of Events in Drug Patients/Incidence in Placebo Patients	Risk Difference: Additional Drug Patients With Events Per 1,000 Patients
Epilepsy	1.0	3.4	3.5	2.4
Psychiatric	5.7	8.5	1.5	2.9
Other	1.0	1.8	1.9	0.9
Total	2.4	4.3	1.8	1.9

The relative risk for suicidal houghts or behavior was higher in clinical trials for epilepsy than in clinical trials for psychiatric or o her conditions, but the absolute risk differences were similar for he epilepsy and psychiatric indications.

Anyone considering prescribing lamotrigine or any o her AED must balance the risk of suicidal houghts or behavior wi h he risk of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal houghts and behavior. Should suicidal houghts and behavior emerge during treatment, the prescriber needs to consider whether he emergence of these symptoms in any given patient may be related to he illness being treated.

Patients, their caregivers, and families should be informed that AEDs increase he risk of suicidal thoughts and behavior and should be advised of he need to be alert for he emergence or worsening of he signs and symptoms of depression, any unusual changes in mood or behavior, or he emergence of suicidal houghts, behavior, or houghts about self-harm. Behaviors of conce n should be reported immediately to heal hcare p oviders.

5.5 Use in Patients With Bipolar Disorder

__Acute Treatment of Mood Episodes:__ Safety and effectiveness of lamotrigine in the acute treatment of mood episodes have not been established.

__Children and Adolescents (less than 18 years of age):__ Safety and effectiveness of lamotrigine in patients below the age of 18 years with mood disorders have not been established *[see Suicidal Behavior and Ideation (5.4)]*.

__Clinical Worsening and Suicide Risk Associated With Bipolar Disorder:__ Patients with bipolar disorder may experience worsening of heir depressive symptoms and/or he emergence of suicidal ideation and behaviors (suicidality) whe her or not hey are taking medications for bipolar disorder. Patients should be closely monitored for clinical worsening (including development of new symptoms) and suicidality, especially at he beginning of a course of treatment, or at the time of dose changes.

In addition, patients with a history of suicidal behavior or thoughts, hose patients exhibiting a significant degree of suicidal ideation prior to commencement of treatment, and young adults are at an increased risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment *[see Suicidal Behavior and Ideation (5.4)]*.

Consideration should be given to changing he herapeutic regimen, including possibly discontinuing he medication, in patients who experience clinical worsening (including development of new symptoms) and/or the emergence of suicidal ideation/behavior especially if hese symptoms are severe, abrupt in onset, or were not part of he patient's presenting symptoms.

Prescriptions for lamotrigine should be written for the smallest quantity of tablets consistent wi h good patient management in order to reduce the risk of overdose. Overdoses have been reported for lamotrigine, some of which have been fatal *[see Overdosage (10.1)]*.

5.6 Aseptic Meningitis

Therapy wi h lamotrigine increases he risk of developing aseptic meningitis. Because of he potential for serious outcomes of untreated meningitis due to o her causes, patients should also be evaluated for o her causes of meningitis and treated as app opriate.

Postmarketing cases of aseptic meningitis have been reported in pediatric and adult patients taking lamotrigine for various indications. Symptoms upon presentation have included headache, fever, nausea, vomiting, and nuchal rigidity. Rash, photophobia, myalgia, chills, altered consciousness, and somnolence were also noted in some cases. Symptoms have been reported to occur wi hin 1 day to one and a half mon hs following the initiation of treatment. In most cases, symptoms were reported to resolve after discontinuation of lamotrigine. Re-exposure resulted in a rapid retu n of symptoms (f om within 30 minutes to 1 day following re-initiation of treatment) hat were frequently more severe. Some of he patients treated with lamotrigine who developed aseptic meningitis had underlying diagnoses of systemic lupus ery hematosus or other autoimmune diseases.

Cereb ospinal fluid (CSF) analyzed at the time of clinical presentation in reported cases was characterized by a mild to moderate pleocytosis, normal glucose levels, and mild to moderate increase in p otein. CSF white blood cell count differentials showed a predominance of neut ophils in a majority of he cases, al hough a predominance of lymphocytes was reported in app oximately one hird of the cases. Some patients also had new onset of signs and symptoms of involvement of other organs (predominantly hepatic and renal involvement), which may suggest that in hese cases he aseptic meningitis observed was part of a hypersensitivity reaction *[see Warnings and Precautions (5.2)]*.

5.7 Potential Medication Errors

Medication er ors involving lamotrigine have occurred. In particular, the name lamotrigine can be confused wi h he names of o her commonly used medications. Medication er ors may also occur between he different formulations of lamotrigine. To reduce he potential of medication er ors, write and say lamotrigine clearly. Depictions of the lamotrigine tablets, can be found in the Medication Guide that accompanies he p oduct to highlight the distinctive markings, colors, and shapes hat serve to identify he different presentations of he drug and hus may help reduce he risk of medication er ors. To avoid he medication er or of using he w ong drug or formulation, patients should be st ongly advised to visually inspect heir tablets to verify hat hey are lamotrigine tablets, as well as the correct formulation of lamotrigine, each time they fill heir prescription.

5.8 Concomitant Use With Oral Contraceptives

Some est ogen-containing oral contraceptives have been shown to decrease serum concentrations of lamotrigine *[see Clinical Pharmacology (12.3)]*. **Dosage adjustments will be necessary in most patients who start or stop estrogen-containing oral contraceptives while taking lamotrigine** *[see Dosage and Administration (2.1)]*. During he week of inactive hormone preparation ("pill-free" week) of oral contraceptive herapy, plasma lamotrigine levels are expected to rise, as much as doubling at the end of he week. Adverse reactions consistent with elevated levels of lamotrigine, such as dizziness, ataxia, and diplopia, could occur.

5.9 Withdrawal Seizures

As wi h o her AEDs, lamotrigine should not be abruptly discontinued. In patients wi h epilepsy here is a possibility of increasing seizure frequency. In clinical trials in patients with Bipolar Disorder, 2 patients experienced seizures shortly after abrupt wi hdrawal of lamotrigine; however, here were confounding factors that may have contributed to the occurrence of seizures in hese bipolar patients. Unless safety conce ns require a more rapid wi hdrawal, the dose of lamotrigine should be tapered over a period of at least 2 weeks (app oximately 50% reduction per week) *[see Dosage and Administration (2.1)]*.

5.10 Status Epilepticus

Valid estimates of he incidence of treatment-emergent status epilepticus among patients treated wi h lamotrigine are difficult to obtain because reporters participating in clinical trials did not all employ identical rules for identifying cases. At a minimum, 7 of 2,343 adult patients had episodes that could unequivocally be described as status epilepticus. In addition, a number of reports of variably defined episodes of seizure exacerbation (e.g., seizure clusters, seizure flurries etc.) were made.

5.11 Sudden Unexplained Death in Epilepsy (SUDEP)

During the premarketing development of lamotrigine, 20 sudden and unexplained dea hs were recorded among a cohort of 4,700 patients with epilepsy (5,747 patient-years of exposure).

Some of hese could represent seizure-related dea hs in which he seizure was not observed, e.g., at night. This represents an incidence of 0.0035 dea hs per patient-year. Although this rate exceeds hat expected in a healthy population matched for age and sex, it is wi hin he range of estimates for he incidence of sudden unexplained dea hs in patients with epilepsy not receiving lamotrigine (ranging f om 0.0005 for he general population of patients with epilepsy, to 0.004 for a recently studied clinical trial population similar to hat in the clinical development p ogram for lamotrigine, to 0.005 for patients wi h refractory epilepsy). Consequently, whe her hese figures are reassuring or suggest conce n depends on he comparability of he populations reported upon to the cohort receiving lamotrigine and the accuracy of the estimates p ovided. P obably most reassuring is he similarity of estimated SUDEP rates in patients receiving lamotrigine and hose receiving other AEDs, chemically unrelated to each other, that underwent clinical testing in similar populations. Importantly, that drug is chemically unrelated to lamotrigine. This evidence suggests, al hough it certainly does not p ove, that he high SUDEP rates reflect population rates, not a drug effect.

5.12 Addition of lamotrigine to a Multidrug Regimen That Includes Valproate

Because valp oate reduces he clearance of lamotrigine, he dosage of lamotrigine in he presence of valp oate is less han half of hat required in its absence.

5.13 Binding in the Eye and Other Melanin Containing Tissues

Because lamotrigine binds to melanin, it could accumulate in melanin-rich tissues over time. This raises the possibility that lamotrigine may cause toxicity in hese tissues after extended use.

Although oph halmological testing was performed in one cont olled clinical trial, he testing was inadequate to exclude subtle effects or injury occurring after long-term exposure. Moreover, he capacity of available tests to detect potentially adverse consequences, if any, of lamotrigine's binding to melanin is unknown *[see Clinical Pharmacology (12.2)]*.

Accordingly, al hough there are no specific recommendations for periodic ophthalmological monitoring, prescribers should be aware of he possibility of long-term oph halmologic effects.

5.14 Laboratory Tests

The value of monitoring plasma concentrations of lamotrigine in patients treated wi h lamotrigine has not been established. Because of he possible pharmacokinetic interactions between lamotrigine and o her drugs including AEDs (see Table 15), monitoring of he plasma levels of lamotrigine and concomitant drugs may be indicated, particularly during dosage adjustments. In general, clinical judgment should be exercised regarding monitoring of plasma levels of lamotrigine and o her drugs and whether or not dosage adjustments are necessary.

6 ADVERSE REACTIONS

The following adverse reactions are described in more detail in the Wa nings and Precautions section of he label:
- Serious skin rashes *[see Warnings and Precautions (5.1)]*
- Multiorgan hypersensitivity reactions and organ failure *[see Warnings and Precautions (5.2)]*
- Blood dyscrasias *[see Warnings and Precautions (5.3)]*
- Suicidal behavior and ideation *[see Warnings and Precautions (5.4)]*
- Aseptic meningitis *[see Warnings and Precautions (5.6)]*
- Wi hdrawal seizures *[see Warnings and Precautions (5.9)]*
- Status epilepticus *[see Warnings and Precautions (5.10)]*
- Sudden unexplained death in epilepsy *[see Warnings and Precautions (5.11)]*

6.1 Clinical Trials

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared wi h rates in the clinical trials of ano her drug and may not reflect he rates observed in practice.

Lamotrigine has been evaluated for safety in patients wi h epilepsy and in patients w th Bipolar I Disorder. Adverse reactions reported for each of hese patient populations are p ovided below. Excluded are adverse reactions considered too general to be informative and hose not reasonably attributable to he use of the drug.

__Epilepsy:__

Most Common Adverse Reactions in All Clinical Studies: Adjunctive Therapy in Adults With Epilepsy: The most commonly observed (≥5% for lamotrigine and more common on drug han placebo) adverse reactions seen in association wi h lamotrigine during adjunctive herapy in adults and not seen at an equivalent frequency among placebo-treated patients were: dizziness, ataxia, somnolence, headache, diplopia, blurred vision, nausea, vomiting, and rash. Dizziness, diplopia, ataxia, blurred vision, nausea, and vomiting were dose-related. Dizziness, diplopia, ataxia, and blurred vision occurred more commonly in patients receiving carbamazepine wi h lamotrigine han in patients receiving o her AEDs wi h lamotrigine. Clinical data suggest a higher incidence of rash, including serious rash, in patients receiving concomitant valp oate than in patients not receiving valp oate *[see Warnings and Precautions (5.1)]*.

App oximately 11% of he 3,378 adult patients who received lamotrigine as adjunctive herapy in premarketing clinical trials discontinued treatment because of an adverse reaction. The adverse reactions most commonly associated with discontinuation were rash (3.0%), dizziness (2.8%), and headache (2.5%).

In a dose-response study in adults, he rate of discontinuation of lamotrigine for dizziness, ataxia, diplopia, blurred vision, nausea, and vomiting was dose-related.

Monotherapy in Adults With Epilepsy: The most commonly observed (≥5% for lamotrigine and more common on drug than placebo) adverse reactions seen in association wi h the use of lamotrigine during he mono herapy phase of the cont olled trial in adults not seen at an equivalent rate in the cont ol g oup were vomiting, coordination abnormality, dyspepsia, nausea, dizziness, hinitis, anxiety, insomnia, infection, pain, weight decrease, chest pain, and dysmenor hea. The most commonly observed (≥5% for lamotrigine and more common on drug than placebo) adverse reactions associated wi h the use of lamotrigine during the conversion to mono herapy (add-on) period, not seen at an equivalent frequency among low-dose valp oate-treated patients, were dizziness, headache, nausea, as henia, coordination abnormality, vomiting, rash, somnolence, diplopia, ataxia, accidental injury, tremor, blurred vision, insomnia, nystagmus, diarrhea, lymphadenopa hy, pruritus, and sinusitis.

App oximately 10% of he 420 adult patients who received lamotrigine as monotherapy in premarketing clinical trials discontinued treatment because of an adverse reaction. The adverse reactions most commonly associated wi h discontinuation were rash (4.5%), headache (3.1%), and as henia (2.4%).

Adjunctive Therapy in Pediatric Patients With Epilepsy: The most commonly observed (≥5% for lamotrigine and more common on drug han placebo) adverse reactions seen in association wi h he use of lamotrigine as adjunctive treatment in pediatric patients 2 to 16 years of age and not seen at an equivalent rate in he cont ol g oup were infection, vomiting, rash, fever, somnolence, accidental injury, dizziness, diar hea, abdominal pain, nausea, ataxia, tremor, asthenia, b onchitis, flu synd ome, and diplopia.

In 339 patients 2 to 16 years of age with partial seizures or generalized seizures of Lennox-Gastaut synd ome, 4.2% of patients on lamotrigine and 2.9% of patients on placebo discontinued due to adverse reactions. The most commonly reported adverse reaction that led to discontinuation of lamotrigine was rash.

App oximately 11.5% of he 1,081 pediatric patients 2 to 16 years of age who received lamotrigine as adjunctive herapy in premarketing clinical trials discontinued treatment because of an adverse reaction. The adverse reactions most commonly associated wi h discontinuation were rash (4.4%), reaction aggravated (1.7%), and ataxia (0.6%).

Controlled Adjunctive Clinical Studies in Adults With Epilepsy: Table 8 lists treatment-emergent adverse reactions hat occurred in at least 2% of adult patients with epilepsy treated with lamotrigine in placebo-cont olled trials and were numerically more common in the patients treated wi h lamotrigine. In these studies, either lamotrigine or placebo was added to the patient's current AED herapy. Adverse reactions were usually mild to moderate in intensity.

Table 8. Treatment-Emergent Adverse Reaction Incidence in Placebo-Controlled Adjunctive Trials in Adult Patients With Epilepsy[a] (Adverse reactions in at least 2% of patients treated with lamotrigine and numerically more frequent than in the placebo group.)

Body System/ Adverse Reaction	Percent of Patients Receiving Adjunctive lamotrigine (n = 711)	Percent of Patients Receiving Adjunctive Placebo (n = 419)
Body as a whole		
Headache	29	19
Flu synd ome	7	6
Fever	6	4
Abdominal pain	5	4
Neck pain	2	1
Reaction aggravated (seizure exace bation)	2	1
Digestive		
Nausea	19	10
Vomiting	9	4
Diar hea	6	4
Dyspepsia	5	2
Constipation	4	3
Anorexia	2	1
Musculoskeletal		
Ar hralgia	2	0
Nervous		
Dizziness	38	13
Ataxia	22	6
Somnolence	14	7
Incoordination	6	2
Insomnia	6	2
Tremor	4	1
Depression	4	3
Anxiety	4	3
Convulsion	3	1
Irritability	3	2
Speech disorder	3	0
Concentration disturbance	2	1
Respiratory		
Rhinitis	14	9
Pharyngitis	10	9
Cough increased	8	6
Skin and appendages		
Rash	10	5
Pruritus	3	2
Special senses		
Diplopia	28	7
Blurred vision	16	5
Vision abnormality	3	1
U ogenital		
Female patients only	(n = 365)	(n = 207)
Dysmenor hea	7	6
Vaginitis	4	1
Amenor hea	2	1

[a] Patients in hese adjunctive studies were receiving 1 to 3 of he following concomitant AEDs (carbamazepine, phenytoin, phenobarbital, or primidone) in addition to lamotrigine or placebo. Patients may have reported multiple adverse reactions during he study or at discontinuation; thus, patients may be included in more han one category.

In a randomized, parallel study comparing placebo and 300 and 500 mg/day of lamotrigine, some of he more common drug-related adverse reactions were dose-related (see Table 9).

Table 9. Dose-Related Adverse Reactions From a Randomized, Placebo-Controlled Adjunctive Trial in Adults With Epilepsy

	Percent of Patients Experiencing Adverse Reactions		
Adverse Reaction	**Placebo (n = 73)**	**Lamotrigine 300 mg (n = 71)**	**Lamotrigine 500 mg (n = 72)**
Ataxia	10	10	28[ab]
Blurred vision	10	11	25[ab]
Diplopia	8	24[a]	49[ab]
Dizziness	27	31	54[ab]
Nausea	11	18	25[a]
Vomiting	4	11	18[a]

[a] Significantly greater than placebo group (p<0.05).

[b] Significantly greater han g oup receiving lamotrigine 300 mg (p<0.05).

The overall adverse reaction p ofile for lamotrigine was similar between females and males, and was independent of age. Because the largest non-Caucasian racial subg oup was only 6% of patients exposed to lamotrigine in placebo-cont olled trials, here are insufficient data to support a statement regarding he distribution of adverse reaction reports by race. Generally, females receiving either lamotrigine as adjunctive therapy or placebo were more likely to report adverse reactions than males. The only adverse reaction for which the reports on lamotrigine were greater han 10% more frequent in females han males (without a corresponding difference by gender on placebo) was dizziness (difference = 16.5%). There was little difference between females and males in he rates of discontinuation of lamotrigine for individual adverse reactions.

Controlled Monotherapy Trial in Adults With Partial Seizures: Table 10 lists treatment-emergent adverse reactions hat occurred in at least 5% of patients with epilepsy treated wi h mono herapy wi h lamotrigine in a double-blind trial following discontinuation of ei her concomitant carbamazepine or phenytoin not seen at an equivalent frequency in he cont ol g oup.

Table 10. Treatment-Emergent Adverse Reaction Incidence in Adults With Partial Seizures in a Controlled Monotherapy Trial[a] (Adverse reactions in at least 5% of patients treated with lamotrigine and numerically more frequent than in the valproate group.)

Body System/ Adverse Reaction	Percent of Patients Receiving Lamotrigine as Monotherapy[b] (n = 43)	Percent of Patients Receiving Low-Dose Valproate[c] Monotherapy (n = 44)
Body as a whole		
Pain	5	0
Infection	5	2
Chest pain	5	2
Digestive		
Vomiting	9	0
Dyspepsia	7	2
Nausea	7	2
Metabolic and nutritional		
Weight decrease	5	2
Nervous		
Coordination abnormality	7	0
Dizziness	7	0
Anxiety	5	0
Insomnia	5	2
Respiratory		
Rhinitis	7	2
U ogenital (female patients only)	(n = 21)	(n = 28)
Dysmenor hea	5	0

[a] Patients in these studies were converted to lamotrigine or valp oate monotherapy f om adjunctive herapy wi h carbamazepine or phenytoin. Patients may have reported multiple adverse reactions during he study; hus, patients may be included in more han one category.

[b] Up to 500 mg/day.

[c] 1,000 mg/day.

Adverse reactions hat occurred wi h a frequency of less han 5% and greater han 2% of patients receiving lamotrigine and numerically more frequent than placebo were:

Body as a Whole: Asthenia, fever.

Digestive: Anorexia, dry mou h, rectal hemor hage, peptic ulcer.

Metabolic and Nutritional: Peripheral edema.

Nervous System: Amnesia, ataxia, depression, hypesthesia, libido increase, decreased reflexes, increased reflexes, nystagmus, irritability, suicidal ideation.

Respiratory: Epistaxis, b onchitis, dyspnea.

Skin and Appendages: Contact dermatitis, dry skin, sweating.

Special Senses: Vision abnormality.

Incidence in Controlled Adjunctive Trials in Pediatric Patients With Epilepsy: Table 11 lists adverse reactions hat occurred in at least 2% of 339 pediatric patients with partial seizures or generalized seizures of Lennox-Gastaut synd ome, who received lamotrigine up to 15 mg/kg/day or a maximum of 750 mg/day. Reported adverse reactions were classified using COSTART terminology.

Table 11. Treatment-Emergent Adverse Reaction Incidence in Placebo-Controlled Adjunctive Trials in Pediatric Patients With Epilepsy (Adverse reactions in at least 2% of patients treated with lamotrigine and numerically more frequent than in the placebo group.)

Body System/ Adverse Reaction	Percent of Patients Receiving Lamotrigine (n = 168)	Percent of Patients Receiving Placebo (n = 171)
Body as a whole		
Infection	20	17
Fever	15	14
Accidental injury	14	12
Abdominal pain	10	5
As henia	8	4
Flu synd ome	7	6
Pain	5	4
Facial edema	2	1
Photosensitivity	2	0
Cardiovascular		
Hemor hage	2	1
Digestive		
Vomiting	20	16
Diar hea	11	9
Nausea	10	2
Constipation	4	2
Dyspepsia	2	1
Hemic and lymphatic		
Lymphadenopathy	2	1
Metabolic and nutritional		
Edema	2	0
Nervous system		
Somnolence	17	15
Dizziness	14	4
Ataxia	11	3
Tremor	10	1
Emotional lability	4	2
Gait abnormality	4	2
Thinking abnormality	3	2
Convulsions	2	1
Nervousness	2	1
Vertigo	2	1
Respiratory		
Pharyngitis	14	11
B onchitis	7	5
Increased cough	7	6
Sinusitis	2	1
B onchospasm	2	1
Skin		
Rash	14	12
Eczema	2	1
Pruritus	2	1
Special senses		
Diplopia	5	1
Blurred vision	4	1
Visual abnormality	2	0
U ogenital		
Male and female patients		
Urinary tract infection	3	0

__Bipolar Disorder:__ The most commonly observed (≥5%) treatment-emergent adverse reactions seen in association wi h he use of lamotrigine as mono herapy (100 to 400 mg/day) in adult patients (≥18 years of age) wi h Bipolar Disorder in he 2 double-blind, placebo-cont olled trials of 18 mon hs' duration, and numerically more frequent than in placebo-treated patients are included in Table 12. Adverse reactions hat occurred in at least 5% of patients and were numerically more common during he dose-escalation phase of lamotrigine in hese trials (when patients may have been receiving concomitant medications) compared w th he mono herapy phase were: headache (25%), rash (11%), dizziness (10%), diar hea (8%), dream abnormality (6%), and pruritus (6%).

During the mono herapy phase of he double-blind, placebo-cont olled trials of 18 mon hs' duration, 13% of 227 patients who received lamotrigine (100 to 400 mg/day), 16% of 190 patients who received placebo, and 23% of 166 patients who received li hium discontinued herapy because of an adverse reaction. The adverse reactions which most commonly led to discontinuation of lamotrigine were rash (3%) and mania/hypomania/mixed mood adverse reactions (2%). App oximately 16% of 2,401 patients who received lamotrigine (50 to 500 mg/day) for Bipolar Disorder in premarketing trials discontinued herapy because of an adverse reaction; most commonly due to rash (5%) and mania/hypomania/mixed mood adverse reactions (2%).

The overall adverse reaction p ofile for lamotrigine was similar between females and males, between elderly and nonelderly patients, and among racial g oups.

Table 12. Treatment-Emergent Adverse Reaction Incidence in Two Placebo-Controlled Trials in Adults With Bipolar I Disorder[a] (Adverse reactions in at least 5% of patients treated with lamotrigine as monotherapy and numerically more frequent than in the placebo group.)

Body System/ Adverse Reaction	Percent of Patients Receiving Lamotrigine (n = 227)	Percent of Patients Receiving Placebo (n = 190)
General		
Back pain	8	6
Fatigue	8	5
Abdominal pain	6	3
Digestive		
Nausea	14	11
Constipation	5	2
Vomiting	5	2
Nervous System		
Insomnia	10	6
Somnolence	9	7
Xerostomia (dry mou h)	6	4
Respiratory		
Rhinitis	7	4
Exacerbation of cough	5	3
Pharyngitis	5	4
Skin		
Rash (nonserious)[b]	7	5

[a] Patients in hese studies were converted to lamotrigine (100 to 400 mg/day) or placebo mono herapy f om add-on herapy with o her psychot opic medications. Patients may have reported multiple adverse reactions during he study; thus, patients may be included in more han one category.

[b] In he overall bipolar and o her mood disorders clinical trials, the rate of serious rash was 0.08% (1 of 1,233) of adult patients who received lamotrigine as initial mono herapy and 0.13% (2 of 1,538) of adult patients who received lamotrigine as adjunctive herapy *[see Warnings and Precautions (5.1)]*.

These adverse reactions were usually mild to moderate in intensity. O her reactions hat occurred in 5% or more patients but equally or more frequently in he placebo g oup included: dizziness, mania, headache, infection, influenza, pain, accidental injury, diar hea, and dyspepsia.

Adverse reactions hat occurred wi h a frequency of less han 5% and greater han 1% of patients receiving lamotrigine and numerically more frequent than placebo were:

General: Fever, neck pain.

Cardiovascular: Migraine.

Digestive: Flatulence

Metabolic and Nutritional: Weight gain, edema.

Musculoskeletal: Ar hralgia, myalgia.

Nervous System: Amnesia, depression, agitation, emotional lability, dyspraxia, abnormal houghts, dream abnormality, hypoes hesia.

Respiratory: Sinusitis.

Urogenital: Urinary frequency.

Adverse Reactions Following Abrupt Discontinuation: In he two maintenance trials, here was no increase in he incidence, severity or type of adverse reactions in Bipolar Disorder patients after abruptly terminating herapy wi h lamotrigine. In clinical trials in patients wi h Bipolar Disorder, two patients experienced seizures shortly after abrupt wi hdrawal of lamotrigine. However, there were confounding factors hat may have contributed to he occurrence of seizures in hese bipolar patients *[see Warnings and Precautions (5.9)]*.

Mania/Hypomania/Mixed Episodes: During the double-blind, placebo-cont olled clinical trials in Bipolar I Disorder in which patients were converted to mono herapy wi h lamotrigine (100 to 400 mg/day) f om o her psychot opic medications and followed for up to 18 months, he rates of manic or hypomanic or mixed mood episodes reported as adverse reactions were 5% for patients treated wi h lamotrigine (n = 227), 4% for patients treated wi h lithium (n = 166), and 7% for patients treated wi h placebo (n = 190). In all bipolar cont olled trials combined, adverse reactions of mania (including hypomania and mixed mood episodes) were reported in

PHARMACIST - DETACH HERE AND GIVE INSTRUCTIONS TO PATIENT

MEDICATION GUIDE
LAMOTRIGINE TABLETS USP

Read this Medication Guide before you start taking lamotrigine tablets and each time you get a refill. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or treatment. If you have questions about lamotrigine tablets, ask your healthcare provider or pharmacist.

What is the most important information I should know about Lamotrigine tablets?

1. Lamotrigine tablets may cause a serious skin rash that may cause you to be hospitalized or to stop lamotrigine tablets; it may rarely cause death.

There is no way to tell if a mild rash will develop into a more serious reaction. These serious skin reactions are more likely to happen when you begin taking lamotrigine tablets, within the first 2 to 8 weeks of treatment. But it can happen in people who have taken lamotrigine tablets for any period of time. Children between 2 to 16 years of age have a higher chance of getting this serious skin reaction while taking lamotrigine tablets.

The risk of getting a rash is higher if you:
- take lamotrigine tablets while taking valproate (valproic acid or divalproex sodium)
- take a higher starting dose of lamotrigine tablets than your healthcare provider prescribed
- increase your dose of lamotrigine tablets faster than prescribed.

Lamotrigine tablets can also cause other types of allergic reactions or serious problems which may affect organs and other parts of your body like the liver or blood cells. You may or may not have a rash with these types of reactions.

Call your healthcare provider right away if you have any of the following:
- **a skin rash**
- **hives**
- **fever**
- **swollen lymph glands**
- **painful sores in the mouth or around your eyes**
- **swelling of your lips or tongue**
- **yellowing of your skin or eyes**
- **unusual bruising or bleeding**
- **severe fatigue or weakness**
- **severe muscle pain**
- **frequent infections**

These symptoms may be the first signs of a serious reaction. A healthcare provider should examine you to decide if you should continue taking lamotrigine tablets.

2. Like other antiepileptic drugs, lamotrigine tablets may cause suicidal thoughts or actions in a very small number of people, about 1 in 500.

Call a healthcare provider right away if you have any of these symptoms, especially if they are new, worse, or worry you:
- thoughts about suicide or dying
- attempt to commit suicide
- new or worse depression
- new or worse anxiety
- feeling agitated or restless
- panic attacks
- trouble sleeping (insomnia)
- new or worse irritability
- acting aggressive, being angry, or violent
- acting on dangerous impulses
- an extreme increase in activity and talking (mania)
- other unusual changes in behavior or mood

Do not stop lamotrigine tablets without first talking to a healthcare provider.
- Stopping lamotrigine tablets suddenly can cause serious problems.
- Suicidal thoughts or actions can be caused by things other than medicines. If you have suicidal thoughts or actions, your healthcare provider may check for other causes.

How can I watch for early symptoms of suicidal thoughts and actions?
- Pay attention to any changes, especially sudden changes, in mood, behaviors, thoughts, or feelings.
- Keep all follow-up visits with your healthcare provider as scheduled.
- Call your healthcare provider between visits as needed, especially if you are worried about symptoms.

3. Lamotrigine tablets may rarely cause aseptic meningitis, a serious inflammation of the protective membrane that covers the brain and spinal cord.

Call your healthcare provider right away if you have any of the following symptoms:
- Headache
- Fever
- Nausea
- Vomiting
- Stiff neck
- Rash
- Unusual sensitivity to light
- Muscle pains
- Chills
- Confusion
- Drowsiness

Meningitis has many causes other than lamotrigine tablets, which your doctor would check for if you developed meningitis while taking lamotrigine tablets.

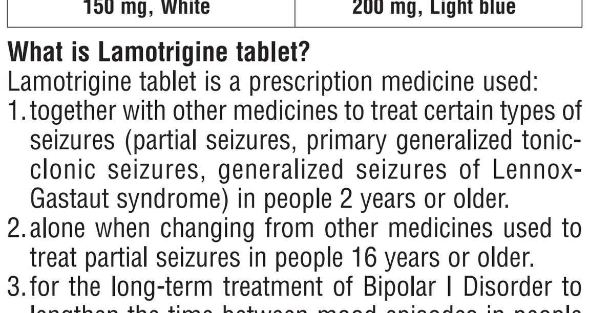
Lamotrigine tablets can have other serious side effects. For more information ask your healthcare provider or pharmacist. Tell your healthcare provider if you have any side effect that bothers you. Be sure to read the section below entitled "What are the possible side effects of lamotrigine tablets?"

4. Patients prescribed lamotrigine tablets have sometimes been given the wrong medicine because many medicines have names similar to lamotrigine tablets, so always check that you receive lamotrigine tablets.

Taking the wrong medication can cause serious health problems. When your healthcare provider gives you a prescription for lamotrigine tablets:
- Make sure you can read it clearly.
- Talk to your pharmacist to check that you are given the correct medicine.
- Each time you fill your prescription, check the tablets you receive against the pictures of the tablets below.

These pictures show the distinct wording, colors, and shapes of the tablets that help to identify the right strength of Lamotrigine Tablets. Immediately call your pharmacist if you receive a lamotrigine tablet that does not look like one of the tablets shown below, as you may have received the wrong medication.

Lamotrigine Tablets USP



What is Lamotrigine tablet?

Lamotrigine tablet is a prescription medicine used:
1. together with other medicines to treat certain types of seizures (partial seizures, primary generalized tonic-clonic seizures, generalized seizures of Lennox-Gastaut syndrome) in people 2 years or older.
2. alone when changing from other medicines used to treat partial seizures in people 16 years or older.
3. for the long-term treatment of Bipolar I Disorder to lengthen the time between mood episodes in people 18 years or older who have been treated for mood episodes with other medicine.

It is not known if lamotrigine tablets are safe or effective in children or teenagers under the age of 18 with mood disorders such as bipolar disorder or depression.

It is not known if lamotrigine tablets are safe or effective when used alone as the first treatment of seizures in adults.

Who should not take Lamotrigine tablets?

You should not take lamotrigine tablets if you have had an allergic reaction to lamotrigine or to any of the inactive ingredients in lamotrigine tablets. See the end of this leaflet for a complete list of ingredients in lamotrigine tablets.

What should I tell my healthcare provider before taking Lamotrigine tablets?

Before taking lamotrigine tablets, tell your healthcare provider about all of your medical conditions, including if you:
- have had a rash or allergic reaction to another antiseizure medicine.
- have or have had depression, mood problems or suicidal thoughts or behavior.
- are taking oral contraceptives (birth control pills) or other female hormonal medicines. Do not start or stop taking birth control pills or other female hormonal medicine until you have talked with your healthcare provider. Tell your healthcare provider if you have any changes in your menstrual pattern such as breakthrough bleeding. Stopping or starting these

medicines may cause side effects (such as dizziness, lack of coordination, or double vision) or lessen how well lamotrigine tablets work.

- are pregnant or plan to become pregnant. It is not known if lamotrigine tablets will harm your unborn baby. If you become pregnant while taking lamotrigine tablets, talk to your healthcare provider about registering with the North American Antiepileptic Drug Pregnancy Registry. You can enroll in this registry by calling 1-888-233-2334. The purpose of this registry is to collect information about the safety of antiepileptic drugs during pregnancy.
- are breast-feeding. Lamotrigine can pass into your breast milk. You and your healthcare provider should decide if you should take lamotrigine tablets or breast-feed. Breast-feeding while taking lamotrigine tablets is not recommended.

Tell your healthcare provider about all the medicines you take or if you are planning to take a new medicine, including prescription and non-prescription medicines, vitamins, and herbal supplements. Using lamotrigine tablets with certain other medicines can affect each other, causing side effects.

How should I take Lamotrigine tablets?

- Take lamotrigine tablets exactly as prescribed.
- Your healthcare provider may change your dose. Do not change your dose without talking to your healthcare provider.
- Do not stop taking lamotrigine tablets without talking to your healthcare provider. Stopping lamotrigine tablets suddenly may cause serious problems. For example, if you have epilepsy and you stop taking lamotrigine tablets suddenly, you may get seizures that do not stop. Talk with your healthcare provider about how to stop lamotrigine tablets slowly.
- If you miss a dose of lamotrigine tablets, take it as soon as you remember. If it is almost time for your next dose, just skip the missed dose. Take the next dose at your regular time. **Do not take two doses at the same time.**
- You may not feel the full effect of lamotrigine tablets for several weeks.
- If you have epilepsy, tell your healthcare provider if your seizures get worse or if you have any new types of seizures.
- Swallow lamotrigine tablets whole.
- If you have trouble swallowing lamotrigine tablets, there may be another form of lamotrigine you can take.

What should I avoid while taking Lamotrigine tablets?

- Do not drive a car or operate complex, hazardous machinery until you know how lamotrigine tablets affect you.

What are possible side effects of Lamotrigine tablets?

- See "What is the most important information I should know about lamotrigine tablets?"

Common side effects of lamotrigine tablets include:

- dizziness
- headache
- blurred or double vision
- lack of coordination
- sleepiness
- nausea, vomiting
- insomnia
- tremor
- rash
- fever
- abdominal pain
- back pain
- tiredness
- dry mouth

Tell your healthcare provider about any side effect that bothers you or that does not go away.

These are not all the possible side effects of lamotrigine tablets. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store Lamotrigine tablets?

- Store lamotrigine tablets at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature]
- **Keep lamotrigine tablets and all medicines out of the reach of children.**

General information about Lamotrigine tablets

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use lamotrigine tablets for a condition for which it was not prescribed. Do not give lamotrigine tablets to other people, even if they have the same symptoms you have. It may harm them.

This Medication Guide summarizes the most important information about lamotrigine tablets. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about lamotrigine tablets that is written for healthcare professionals.

What are the ingredients in Lamotrigine tablets?

Active ingredient: Lamotrigine USP.

Inactive ingredients: lactose monohydrate, magnesium stearate, microcrystalline cellulose, povidone and sodium starch glycolate. In addition, the 200 mg tablets contain FD&C Blue No. 2 Lake.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured by:
UNICHEM LABORATORIES LTD.
Pilerne Ind. Estate, Pilerne, Bardez, Goa 403 511, India

Marketed by:

UNICHEM PHARMACEUTICALS (USA), INC.
Rochelle Park, NJ 07662

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5% of patients treated wi h lamotrigine (n = 956), 3% of patients treated wi h li hium (n = 280), and 4% of patients treated with placebo (n = 803).

6.2 Other Adverse Reactions Observed in All Clinical Trials

Lamotrigine has been administered to 6,694 individuals for whom complete adverse reaction data was captured during all clinical trials, only some of which were placebo cont olled. During hese trials, all adverse reactions were recorded by he clinical investigators using terminology of heir own choosing. To p ovide a meaningful estimate of the p oportion of individuals having adverse reactions, similar types of adverse reactions were g ouped into a smaller number of standardized categories using modified COSTART dictionary terminology. The frequencies presented represent the p oportion of the 6,694 individuals exposed to lamotrigine who experienced an event of the type cited on at least one occasion while receiving lamotrigine. All reported adverse reactions are included except hose already listed in he previous tables or elsewhere in the labeling, hose too general to be informative, and those not reasonably associated wi h he use of he drug.

Adverse reactions are fur her classified wi hin body system categories and enumerated in order of decreasing frequency using he following definitions: *frequent* adverse reactions are defined as those occurring in at least 1/100 patients; *infrequent* adverse reactions are hose occurring in 1/100 to 1/1,000 patients; *rare* adverse reactions are hose occurring in fewer than 1/1,000 patients.

Body as a Whole: *Infrequent:* Allergic reaction, chills, and malaise.

Cardiovascular System: *Infrequent:* Flushing, hot flashes, hypertension, palpitations, postural hypotension, syncope, tachycardia, and vasodilation.

Dermatological: *Infrequent:* Acne, alopecia, hirsutism, maculopapular rash, skin discoloration, and urticaria. *Rare:* Angioedema, ery hema, exfoliative dermatitis, fungal dermatitis, herpes zoster, leukoderma, multiforme ery hema, petechial rash, pustular rash, Stevens-Johnson synd ome, and vesiculobullous rash.

Digestive System: *Infrequent:* Dysphagia, eructation, gastritis, gingivitis, increased appetite, increased salivation, liver function tests abnormal, and mou h ulceration. *Rare:* Gat ointestina hemor hage, glossitis, gum hemor hage, gum hyperplasia, hematemesis, hemor hagic colitis, hepatitis, melena, stomach ulcer, stomatitis, and tongue edema.

Endocrine System: *Rare:* Goiter and hypothy oidism.

Hematologic and Lymphatic System: *Infrequent:* Ecchymosis and leukopenia. *Rare:* Anemia, eosinophilia, fibrin decrease, fibrinogen decrease, i on deficiency anemia, leukocytosis, lymphocytosis, mac ocytic anemia, petechia, and th ombocytopenia.

Metabolic and Nutritional Disorders: *Infrequent:* Aspartate transaminase increased. *Rare:* Alcohol intolerance, alkaline phosphatase increase, alanine transaminase increase, bilirubinemia, general edema, gamma glutamyl transpeptidase increase, and hyperglycemia.

Musculoskeletal System: *Infrequent:* Ar hritis, leg cramps, myasthenia, and twitching. *Rare:* Bursitis, muscle at ophy, pa hological fracture, and tendinous contracture.

Nervous System: *Frequent:* Confusion and paresthesia. *Infrequent:* Aka hisia, apathy, aphasia, (CNS) depression, depersonalization, dysarthria, dyskinesia, euphoria, hallucinations, hostility, hyperkinesia, hypertonia, libido decreased, memory decrease, mind racing, movement disorder, myoclonus, panic attack, paranoid reaction, personality disorder, psychosis, sleep disorder, stupor, and suicidal ideation. *Rare:* Choreoathetosis, delirium, delusions, dysphoria, dystonia, extrapyramidal synd ome, faintness, grand mal convulsions, hemiplegia, hyperalgesia, hyperes hesia, hypokinesia, hypotonia, manic depression reaction, muscle spasm, neuralgia, neu osis, paralysis, and peripheral neuritis.

Respiratory System: *Infrequent:* Yawn. *Rare:* Hiccup and hyperventilation.

Special Senses: *Frequent:* Amblyopia. *Infrequent:* Abnormality of accommodation, conjunctivitis, dry eyes, ear pain, photophobia, taste perversion, and tinnitus. *Rare:* Deafness, lacrimation disorder, oscillopsia, pa osmia, ptosis, strabismus, taste loss, uveitis, and visual field defect.

Urogenital System: *Infrequent:* Abnormal ejaculation, hematuria, impotence, menor hagia, polyuria, and urinary incontinence. *Rare:* Acute kidney failure, anorgasmia, breast abscess, breast neoplasm, creatinine increase, cystitis, dysuria, epididymitis, female lactation, kidney failure, kidney pain, nocturia, urinary retention, and urinary urgency.

6.3 Post-marketing Experience

The following adverse events (not listed above in clinical trials or other sections of the prescribing information) have been identified during post-app oval use of lamotrigine. Because these events are reported voluntarily f om a population of uncertain size, it is not always possible to reliably estimate heir frequency or establish a causal relationship to drug exposure.

Blood and Lymphatic: Agranulocytosis, hemolytic anemia.

Gastrointestinal: Esophagitis.

Hepatobiliary Tract and Pancreas: Pancreatitis.

Immunologic: Lupus-like reaction, vasculitis.

Lower Respiratory: Apnea.

Musculoskeletal: Rhabdomyolysis has been observed in patients experiencing hypersensitivity reactions.

Neurology: Exacerbation of Parkinsonian symptoms in patients w th pre-existing Parkinson's disease, tics.

Non-site Specific: P ogressive immunosuppression.

7 DRUG INTERACTIONS

Significant drug interactions wi h lamotrigine are summarized in Table 13. Additional details of hese drug interaction studies are p ovided in he Clinical Pharmacology section *[see Clinical Pharmacology (12.3)]*.

Table 13. Established and Other Potentially Significant Drug Interactions

Concomitant Drug	Effect on Concentration of Lamotrigine or Concomitant Drug	Clinical Comment
Est ogen-containing oral contraceptive preparations containing 30 mcg e hinylestradiol and 150 mcg levonorgestrel	↓ lamotrigine	Decreased lamotrigine levels app oximately 50%.
	↓ levonorgestrel	Decrease in levonorgestrel component by 19%.
Carbamazepine (CBZ) and CBZ epoxide	↓ lamotrigine	Addition of carbamazepine decreases lamotrigine concentration app oximately 40%.
	? CBZ epoxide	May increase CBZ epoxide levels
Phenobarbital/Primidone	↓ lamotrigine	Decreased lamotrigine concentration app oximately 40%.
Phenytoin (PHT)	↓ lamotrigine	Decreased lamotrigine concentration app oximately 40%
Rifampin	↓ lamotrigine	Decreased lamotrigine AUC app oximately 40%
Valp oate	↑ lamotrigine	Increased lamotrigine concentrations slightly more than 2-fold.
	? valp oate	Decreased valp oate concentrations an average of 25% over a 3-week period hen stabilized in heal hy volunteers; no change in cont olled clinical trials in epilepsy patients.

↓= Decreased (induces lamotrigine glu onidation).
↑= Increased (inhibits lamotrigine glucu onidation).
?= Conflicting data.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic Effects: Pregnancy Category C. No evidence of teratogenicity was found in mice, rats, or rabbits when lamotrigine was orally administered to pregnant animals during he period of organogenesis at doses up to 1.2, 0.5, and 1.1 times, respectively, on a mg/m² basis, he highest usual human maintenance dose (i.e., 500 mg/day). However, mate nal toxicity and secondary fetal toxicity p oducing reduced fetal weight and/or delayed ossification were seen in mice and rats, but not in rabbits at these doses. Teratology studies were also conducted using bolus intravenous administration of the ise hionate salt of lamotrigine in rats and rabbits. In rat dams administered an intravenous dose at 0.6 times he highest usual human maintenance dose, the incidence of intrauterine dea h wi hout signs of teratogenicity was increased.

A behavioral teratology study was conducted in rats dosed during the period of organogenesis. At day 21 postpartum, offspring of dams receiving 5 mg/kg/day or higher displayed a significantly longer latent period for open field exploration and a lower frequency of rearing. In a swimming maze test performed on days 39 to 44 postpartum, time to completion was increased in offspring of dams receiving 25 mg/kg/day. These doses represent 0.1 and 0.5 times the clinical dose on a mg/m² basis, respectively.

Lamotrigine did not affect fertility, teratogenesis, or postnatal development when rats were dosed prior to and during mating, and th oughout gestation and lactation at doses equivalent to 0.4 times he highest usua human maintenance dose on a mg/m² basis. When pregnant rats were orally dosed at 0.1, 0.14, or 0.3 times the highest human maintenance dose (on a mg/m² basis) during the latter part of gestation (days 15 to 20), mate nal toxicity and fetal dea h were seen. In dams, food consumption and weight gain were reduced, and he gestation period was slightly p olonged (22.6 vs. 22.0 days in the cont ol g oup). Stillbo n pups were found in all 3 drug-treated g oups wi h the highest number in he high-dose g oup. Postnatal dea h was also seen, but only in he 2 highest doses, and occurred between days 1 and 20. Some of hese deaths appear to be drug-related and not secondary to he mate nal toxicity. A no-observed-effect level (NOEL) could not be determined for this study.

Al hough lamotrigine was not found to be teratogenic in the above studies, lamotrigine decreases fetal folate concentrations in rats, an effect known to be associated wi h teratogenesis in animals and humans. There are no adequate and well-cont olled studies in pregnant women. Because animal rep oduction studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefit justifies he potential risk to he fetus.

Non-Teratogenic Effects: As with other AEDs, physiological changes during pregnancy may affect lamotrigine concentrations and/or herapeutic effect. There have been reports of decreased lamotrigine concentrations during pregnancy and restoration of pre-partum concentrations after delivery. Dosage adjustments may be necessary to maintain clinical response.

Pregnancy Exposure Registry:

To p ovide information regarding the effects of in ute o exposure to lamotrigine, physicians are advised to recommend hat pregnant patients taking lamotrigine en oll in the North American Antiepileptic Drug (NAAED) Pregnancy Registry. This can be done by calling the toll free number 1-888-233-2334, and must be done by patients hemselves. Information on he registry can also be found at he website http://www.aedpregnancyregistry.org/.

8.2 Labor and Delivery

The effect of lamotrigine on labor and delivery in humans is unknown.

8.3 Nursing Mothers

Preliminary data indicate that lamotrigine passes into human milk. Because he effects on the infant exposed to lamotrigine by this oute are unknown, breastfeeding while taking lamotrigine is not recommended.

8.4 Pediatric Use

Lamotrigine is indicated for adjunctive therapy in patients ≥2 years of age for partial seizures, he generalized seizures of Lennox-Gastaut synd ome, and primary generalized tonic-clonic seizures.

Safety and efficacy of lamotrigine, used as adjunctive treatment for partial seizures, were not demonstrated in a small randomized, double-blind, placebo-cont olled, wi hdrawal study in very young pediatric patients (1 to 24 mon hs). Lamotrigine was associated wi h an increased risk for infectious adverse reactions (lamotrigine 37%, Placebo 5%), and respiratory adverse reactions (lamotrigine 26%, Placebo 5%). Infectious adverse reactions included b onchiolitis, b onchitis, ear infection, eye infection, otitis exte na, pharyngitis, urinary tract infection, and viral infection. Respiratory adverse reactions included nasal congestion, cough, and apnea. Safety and effectiveness in patients below he age of 18 years wi h Bipolar Disorder have not been established.

8.5 Geriatric Use

Clinical studies of lamotrigine for epilepsy and in Bipolar Disorder did not include sufficient numbers of subjects 65 years of age and over to determine whether they respond differently f om younger subjects or exhibit a different safety p ofile han that of younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting he greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or o her drug therapy.

8.6 Patients With Hepatic Impairment

Experience in patients wi h hepatic impairment is limited. Based on a clinical pharmacology study in 24 patients wi h mild, moderate, and severe liver impairment *[see Clinical Pharmacology (12.3)]*, he following general recommendations can be made. No dosage adjustment is needed in patients wi h mild liver impairment. Initial, escalation, and maintenance doses should generally be reduced by app oximately 25% in patients wi h moderate and severe liver impairment wi hout ascites and 50% in patients with severe liver impairment wi h ascites. Escalation and maintenance doses may be adjusted according to clinical response *[see Dosage and Administration (2.1)]*.

8.7 Patients With Renal Impairment

Lamotrigine is metabolized mainly by glucu onic acid conjugation, wi h the majority of he metabolites being recovered in he urine. In a small study comparing a single dose of lamotrigine in patients wi h varying degrees of renal impairment wi h hea thy volunteers, he plasma half-life of lamotrigine was significantly longer in the patients wi h renal impairment *[see Clinical Pharmacology (12.3)]*.

Initial doses of lamotrigine should be based on patients' AED regimens; reduced maintenance doses may be effective for patients wi h significant renal impairment. Few patients wi h severe renal impairment have been evaluated during ch onic treatment wi h lamotrigine. Because here is inadequate experience in his population, lamotrigine should be used wi h caution in hese patients *[see Dosage and Administration (2.1)]*.

10 OVERDOSAGE

10.1 Human Overdose Experience

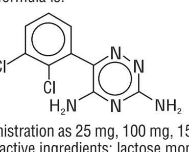
Overdoses involving quantities up to 15 g have been reported for lamotrigine, some of which have been fatal. Overdose has resulted in ataxia, nystagmus, increased seizures, decreased level of consciousness, coma, and intraventricular conduction delay.

10.2 Management of Overdose

There are no specific antidotes for lamotrigine. Following a suspected overdose, hospitalization of he patient is advised. General supportive care is indicated, including frequent monitoring of vital signs and close observation of he patient. If indicated, emesis should be induced; usual precautions should be taken to p otect the airway. It should be kept in mind hat lamotrigine is rapidly absorbed *[see Clinical Pharmacology (12.3)]*. It is uncertain whe her hemodialysis is an effective means of removing lamotrigine f om he blood. In 6 renal failure patients, about 20% of the amount of lamotrigine in he body was removed by hemodialysis during a 4-hour session. A Poison Cont ol Center should be contacted for information on the management of overdosage of lamotrigine.

11 DESCRIPTION

Lamotrigine, an AED of the phenyltriazine class, is chemically unrelated to existing AEDs. Its chemical name is 3,5-diamino-6-(2,3-dichlo ophenyl)-*as*-triazine, its molecular formula is $C_9H_7N_5Cl_2$, and its molecular weight is 256.09. Lamotrigine is a white to pale cream-colored powder and has a pKa of 5.7. Lamotrigine is very slightly soluble in water (0.17 mg/mL at 25°C) and slightly soluble in 0.1 M HCl (4.1 mg/mL at 25°C). The structural formula is:



Lamotrigine tablets USP are supplied for oral administration as 25 mg, 100 mg, 150 mg or 200 mg tablets. Each tablet contains he labeled amount of lamotrigine and the following inactive ingredients: lactose monohydrate, magnesium stearate, mic ocrystalline cellulose, povidone and sodium starch glycolate. In addition, the 200 mg tablets contain FD&C Blue No. 2 Lake.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The precise mechanism(s) by which lamotrigine exerts its anticonvulsant action are unknown. In animal models designed to detect anticonvulsant activity, lamotrigine was effective in preventing seizure spread in he maximum electroshock (MES) and pentylenetetrazol (scMet) tests, and prevented seizures in the visually and electrically evoked after-discharge (EEAD) tests for antiepileptic activity. Lamotrigine also displayed inhibitory p operties in he kindling model in rats bo h during kindling development and in the fully kindled state. The relevance of hese models to human epilepsy, however, is not known.

One p oposed mechanism of action of lamotrigine, the relevance of which remains to be established in humans, involves an effect on sodium channels. In vit o pharmacological studies suggest hat lamotrigine inhibits voltage-sensitive sodium channels, thereby stabilizing neu onal membranes and consequently modulating presynaptic transmitter release of excitatory amino acids (e.g., glutamate and aspartate).

Al hough he relevance for human use is unknown, he following data characterize he performance of lamotrigine in receptor binding assays. Lamotrigine had a weak inhibitory effect on he se otonin 5-HT_3 receptor (IC_{50} = 18 μM). It does not exhibit high affinity binding (IC_{50}>100 μM) to the following neu otransmitter receptors: adenosine A_1 and A_2; adrenergic α_1, α_2, and β; dopamine D_1 and D_2; γ-aminobutyric acid (GABA) A and B; histamine H_1; kappa opioid; muscarinic acetylcholine; and se otonin 5-HT_2. Studies have failed to detect an effect of lamotrigine on dihyd opyridine-sensitive calcium channels. It had weak effects at sigma opioid receptors (IC_{50} = 145 μM). Lamotrigine did not inhibit he uptake of norepinephrine, dopamine, or se otonin, (IC_{50}>200 μM) when tested in rat synaptosomes and/or human platelets in vit o.

Effect of Lamotrigine on N-Methyl d-Aspartate-Receptor Mediated Activity: Lamotrigine did not inhibit N-me hyl d-aspartate (NMDA)-induced depolarizations in rat cortical slices or NMDA-induced cyclic GMP formation in immature rat cerebellum, nor did lamotrigine displace compounds that are either competitive or noncompetitive ligands at his glutamate receptor complex (CNQX, CGS, TCHP). The IC_{50} for lamotrigine effects on NMDA-induced currents (in the presence of 3 μM of glycine) in cultured hippocampal neu ons exceeded 100 μM.

The mechanisms by which lamotrigine exerts its herapeutic action in Bipolar Disorder have not been established.

12.2 Pharmacodynamics

Folate Metabolism: In vit o, lamotrigine inhibited dihyd ofolate reductase, he enzyme hat catalyzes the reduction of d hyd ofolate to tetrahyd ofolate. Inhibition of his enzyme may interfere wi h the biosyn hesis of nucleic acids and p oteins. When oral daily doses of lamotrigine were given to pregnant rats during organogenesis, fetal, placental, and mate nal folate concentrations were reduced. Significantly reduced concentrations of folate are associated wi h teratogenesis *[see Use in Specific Populations (8.1)]*. Folate concentrations were also reduced in male rats given repeated oral doses of lamotrigine. Reduced concentrations were partially retu ned to normal when supplemented wi h folinic acid.

Accumulation in Kidneys: Lamotrigine accumulated in the kidney of he male rat, causing ch onic p ogressive neph osis, nec osis, and mineralization. These findings are attributed to α-2 mic oglobulin, a species- and sex-specific p otein hat has not been detected in humans or o her animal species.

Melanin Binding: Lamotrigine binds to melanin-containing tissues, e.g., in the eye and pigmented skin. It has been found in the uveal tract up to 52 weeks after a single dose in odents.

Cardiovascular: In dogs, lamotrigine is extensively metabolized to a 2-N-me hyl metabolite. This metabolite causes dose-dependent p olongations of he PR interval, widening of he QRS complex, and, at higher doses, complete AV conduction block. Similar cardiovascular effects are not anticipated in humans because only trace amounts of the 2-N-methyl metabolite (<0.6% of lamotrigine dose) have been found in human urine *[see Clinical Pharmacology (12.3)]*. However, it is conceivable that plasma concentrations of his metabolite could be increased in patients wi h a reduced capacity to glucu onidate lamotrigine (e.g., in patients wi h liver disease).

12.3 Pharmacokinetics

The pharmacokinetics of lamotrigine have been studied in patients wi h epilepsy, heal hy young and elderly volunteers, and volunteers wi h ch onic renal failure. Lamotrigine pharmacokinetic parameters for adult and pediatric patients and heal hy normal volunteers are summarized in Tables 14 and 16.

Table 14. Mean[a] Pharmacokinetic Parameters in Healthy Volunteers and Adult Patients With Epilepsy

Adult Study Population	Number of Subjects	T_{max} : Time of Maximum Plasma Concentration (hr)	$t_{½}$: Elimination Half-life (hr)	Cl/F: Apparent Plasma Clearance (mL/min/kg)
Healthy volunteers taking no other medications:				
Single-dose lamotrigine	179	2.2 (0.25-12.0)	32.8 (14.0-103.0)	0.44 (0.12-1.10)
Multiple-dose lamotrigine	36	1.7 (0.5-4.0)	25.4 (11.6-61.6)	0.58 (0.24-1.15)
Healthy volunteers taking valproate:				
Single-dose lamotrigine	6	1.8 (1.0-4.0)	48.3 (31.5-88.6)	0.30 (0.14-0.42)
Multiple-dose lamotrigine	18	1.9 (0.5-3.5)	70.3 (41.9-113.5)	0.18 (0.12-0.33)
Patients with epilepsy taking valproate only:				
Single-dose lamotrigine	4	4.8 (1.8-8.4)	58.8 (30.5-88.8)	0.28 (0.16-0.40)
Patients with epilepsy taking carbamazepine, phenytoin, phenobarbital, or primidone[b] plus valproate:				
Single-dose lamotrigine	25	3.8 (1.0-10.0)	27.2 (11.2-51.6)	0.53 (0.27-1.04)
Patients with epilepsy taking carbamazepine, phenytoin, phenobarbital, or primidone[b]:				
Single-dose lamotrigine	24	2.3 (0.5-5.0)	14.4 (6.4-30.4)	1.10 (0.51-2.22)
Multiple-dose lamotrigine	17	2.0 (0.75-5.93)	12.6 (7.5-23.1)	1.21 (0.66-1.82)

[a] The majority of parameter means determined in each study had coefficients of variation between 20% and 40% for half-life and Cl/F and between 30% and 70% for T_{max}. The overall mean values were calculated f om individual study means hat were weighted based on he number of volunteers/patients in each study. The numbers in paren heses below each parameter mean represent he range of individual volunteer/patient values ac oss studies.

[b] Carbamazepine, phenobarbital, phenytoin, and primidone have been shown to increase he apparent clearance of lamotrigine. Est ogen-containing oral contraceptives and o her drugs such as rifampin that induce lamotrigine glucu onidation have also been shown to increase he apparent clearance of lamotrigine *[see Drug Interactions (7)]*.

Absorption: Lamotrigine is rapidly and completely absorbed after oral administration with negligible first-pass metabolism (absolute bioavailability is 98%). The bioavailability is not affected by food. Peak plasma concentrations occur anywhere f om 1.4 to 4.8 hours following drug administration. The lamotrigine chewable/dispersible tablets were found to be equivalent, whether they were administered as dispersed in water, chewed and swallowed, or swallowed as whole, to he lamotrigine compressed tablets in terms of rate and extent of absorption. In terms of rate and extent of absorption, lamotrigine orally disintegrating tablets whe her disintegrated in the mou h or swallowed whole w th water were equivalent to he lamotrigine compressed tablets swallowed w th water.

Dose Proportionality: In healthy volunteers not receiving any other medications and given single doses, he plasma concentrations of lamotrigine increased in direct p oportion to he dose administered over the range of 50 to 400 mg. In 2 small studies (n = 7 and 8) of patients wi h epilepsy who were maintained on other AEDs, there also was a linear relationship between dose and lamotrigine plasma concentrations at steady state following doses of 50 to 350 mg twice daily.

Distribution: Estimates of he mean apparent volume of distribution (Vd/F) of lamotrigine following oral administration ranged f om 0.9 to 1.3 L/kg. Vd/F is independent of dose and is similar following single and multiple doses in bo h patients w th epilepsy and in healthy volunteers.

Protein Binding: Data f om in vitro studies indicate hat lamotrigine is app oximately 55% bound to human plasma p oteins at plasma lamotrigine concentrations from 1 to 10 mcg/mL (10 mcg/mL is 4 to 6 times the t ough plasma concentration observed in the cont olled efficacy trials). Because lamotrigine is not highly bound to plasma p oteins, clinically significant interactions with other drugs h ough competition for p otein binding sites are unlikely. The binding of lamotrigine to plasma p oteins did not change in the presence of herapeutic concentrations of phenytoin, phenobarbital, or valp oate. Lamotrigine did not displace o her AEDs (carbamazepine, phenytoin, phenobarbital) f om p otein binding sites.

Metabolism: Lamotrigine is metabolized predominantly by glucu onic acid conjugation; he major metabolite is an inactive 2-N-glucu onide conjugate. After oral administration of 240 mg of ^{14}C-lamotrigine (15 μCi) to 6 heal hy volunteers, 94% was recovered in the urine and 2% was recovered in he feces. The radioactivity in the urine consisted of unchanged lamotrigine (10%), the 2-N-glucu onide (76%), a 5-N-glucu onide (10%), a 2-N-methyl metabolite (0.14%), and other unidentified minor metabolites (4%).

Enzyme Induction: The effects of lamotrigine on he induction of specific families of mixed-function oxidase isozymes have not been systematically evaluated.

Following multiple administrations (150 mg twice daily) to normal volunteers taking no other medications, lamotrigine induced its own metabolism, resulting in a 25% decrease in $t_{½}$ and a 37% increase in Cl/F at steady state compared with values obtained in he same volunteers following a single dose. Evidence ga hered f om o her sources suggests hat self-induction by lamotrigine may not occur when lamotrigine is given as adjunctive therapy in patients receiving enzyme-inducing drugs such as carbamazepine, phenytoin, phenobarbital, primidone, or drugs such as rifampin hat induce lamotrigine glucu onidation *[see Drug Interactions (7)]*.

Elimination: The elimination half-life and apparent clearance of lamotrigine following administration of lamotrigine to adult patients wi h epilepsy and heal hy volunteers is summarized in Table 14. Half-life and apparent oral clearance vary depending on concomitant AEDs.

Drug Interactions: The apparent clearance of lamotrigine is affected by he coadministration of certain medications *[see Warnings and Precautions (5.8, 5.12), Drug Interactions (7)]*.

The net effects of drug interactions wi h lamotrigine are summarized in Tables 13 and 15, followed by details of the drug interaction studies below.

Table 15. Summary of Drug Interactions With Lamotrigine

Drug	Drug Plasma Concentration With Adjunctive Lamotrigine[a]	Lamotrigine Plasma Concentration With Adjunctive Drugs[b]
Oral contraceptives (e.g. ethinylestradiol/levonorgestrel)[c]	↔[d]	↓
Bup opion	Not assessed	↔
Carbamazepine (CBZ)	↔	↓
CBZ epoxide[e]	?	
Felbamate	Not assessed	↔
Gabapentin	Not assessed	↔
Levetiracetam	↔	↔
Lithium	↔	Not assessed
Olanzapine	↔	↔[f]
Oxcarbazepine	↔	↔
10-monohyd oxy oxcarbazepine metabolite[g]	↔	
Phenobarbital/primidone	↔	↓
Phenytoin (PHT)	↔	↓
Pregabalin	↔	↔
Rifampin	Not assessed	↓
Topiramate	↔[h]	↔
Valp oate	↓	↑
Valp oate + PHT and/or CBZ	Not assessed	↔
Zonisamide	Not assessed	↔

[a] F om adjunctive clinical trials and volunteer studies.
[b] Net effects were estimated by comparing the mean clearance values obtained in adjunctive clinical trials and volunteers studies.
[c] The effect of o her hormonal contraceptive preparations or hormone replacement herapy on he pharmacokinetics of lamotrigine has not been systematically evaluated in clinical trials, al hough he effect may be similar to that seen with the e hinylestradiol/levonorgestrel combinations.
[d] Modest decrease in levonorgestrel.
[e] Not administered, but an active metabolite of carbamazepine.
[f] Slight decrease, not expected to be clinically relevant.
[g] Not administered, but an active metabolite of oxcarbazepine.
[h] Slight increase not expected to be clinically relevant.
↔ = No significant effect.
? = Conflicting data.

Estrogen-Containing Oral Contraceptives: In 16 female volunteers, an oral contraceptive preparation containing 30 mcg e hinylestradiol and 150 mcg levonorgestrel increased he apparent clearance of lamotrigine (300 mg/day) by app oximately 2-fold with mean decreases in AUC of 52% and in C_{max} of 39%. In his study, t ough serum lamotrigine concentrations gradually increased and were app oximately 2-fold higher on average at the end of he week of he inactive hormone preparation compared wi h t ough lamotrigine concentrations at he end of the active hormone cycle.

Gradual transient increases in lamotrigine plasma levels (app oximate 2-fold increase) occurred during he week of inactive hormone preparation ("pill-free" week) for women not also taking a drug that increased the clearance of lamotrigine (carbamazepine, phenytoin, phenobarbital, primidone, or o her drugs such as rifampin hat induce lamotrigine glucu onidation *[see Drug Interactions (7)]*). The increase in lamotrigine plasma levels will be greater if he dose of lamotrigine is increased in the few days before or during he "pill-free" week. Increases in lamotrigine plasma levels could result in dose-dependent adverse reactions.

In he same study, coadministration of lamotrigine (300 mg/day) in 16 female volunteers did not affect he pharmacokinetics of he e hinylestradiol component of he oral contraceptive preparation. There were mean decreases in he AUC and C_{max} of the levonorgestrel component of 19% and 12%, respectively. Measurement of serum p ogesterone indicated hat here was no hormonal evidence of ovulation in any of he 16 volunteers, al hough measurement of serum FSH, LH, and estradiol indicated hat here was some loss of suppression of the hypo halamic-pituitary-ovarian axis.

The effects of doses of lamotrigine other han 300 mg/day have not been systematically evaluated in cont olled clinical trials.

The clinical significance of the observed hormonal changes on ovulatory activity is unknown. However, he possibility of decreased contraceptive efficacy in some patients cannot be excluded. Therefore, patients should be instructed to p omptly report changes in heir menstrual patte n (e.g., break- h ough bleeding).

Dosage adjustments may be necessary for women receiving est ogen-containing oral contraceptive preparations *[see Dosage and Administration (2.1)]*.

Other Hormonal Contraceptives or Hormone Replacement Therapy: The effect of other hormonal contraceptive preparations or hormone replacement herapy on he pharmacokinetics of lamotrigine has not been systematically evaluated. It has been reported hat ethinylestradiol, not p ogestogens, increased he clearance of lamotrigine up to 2-fold, and the p ogestin-only pills had no effect on lamotrigine plasma levels. Therefore, adjustments to the dosage of lamotrigine in the presence of p ogestogens alone will likely not be needed.

Bupropion: The pharmacokinetics of a 100-mg single dose of lamotrigine in healthy volunteers (n = 12) were not changed by coadministration of bup opion sustained-release formulation (150 mg twice daily) starting 11 days before lamotrigine.

Carbamazepine: Lamotrigine has no appreciable effect on steady-state carbamazepine plasma concentration. Limited clinical data suggest here is a higher incidence of dizziness, diplopia, ataxia, and blurred vision in patients receiving carbamazepine wi h lamotrigine han in patients receiving other AEDs wi h lamotrigine *[see Adverse Reactions (6.1)]*. The mechanism of his interaction is unclear. The effect of lamotrigine on plasma concentrations of carbamazepine-epoxide is unclear. In a small subset of patients (n = 7) studied in a placebo cont olled trial, lamotrigine had no effect on carbamazepine-epoxide plasma concentrations, but in a small, uncont olled study (n = 9), carbamazepine-epoxide levels increased.

The addition of carbamazepine decreases lamotrigine steady-state concentrations by app oximately 40%.

Felbamate: In a study of 21 healthy volunteers, coadministration of felbamate (1,200 mg twice daily) with lamotrigine (100 mg twice daily for 10 days) appeared to have no clinically relevant effects on the pharmacokinetics of lamotrigine.

Folate Inhibitors: Lamotrigine is a weak inhibitor of d hyd ofolate reductase. Prescribers should be aware of his action when prescribing o her medications hat inhibit folate metabolism.

Gabapentin: Based on a ret ospective analysis of plasma levels in 34 patients who received lamotrigine bo h wi h and wi hout gabapentin, gabapentin does not appear to change the apparent clearance of lamotrigine.

Levetiracetam: Potential drug interactions between levetiracetam and lamotrigine were assessed by evaluating serum concentrations of bo h agents during placebo-cont olled clinical trials. These data indicate hat lamotrigine does not influence he pharmacokinetics of levetiracetam and hat levetiracetam does not influence the pharmacokinetics of lamotrigine.

Lithium: The pharmacokinetics of lithium were not altered in heal hy subjects (n = 20) by coadministration of lamotrigine (100 mg/day) for 6 days.

Olanzapine: The AUC and C_{max} of olanzapine were similar following he addition of olanzapine (15 mg once daily) to lamotrigine (200 mg once daily) in heal hy male volunteers (n = 16) compared wi h he AUC and C_{max} in hea thy male volunteers receiving olanzapine alone (n = 16).

In he same study, he AUC and C_{max} of lamotrigine were reduced on average by 24% and 20%, respectively, following he addition of olanzapine to lamotrigine in heal hy male volunteers compared wi h those receiving lamotrigine alone. This reduction in lamotrigine plasma concentrations is not expected to be clinically relevant.

Oxcarbazepine: The AUC and C_{max} of oxcarbazepine and its active 10-monohyd oxy oxcarbazepine metabolite were not significantly different following he addition of oxcarbazepine (600 mg twice daily) to lamtrigine (200 mg once daily) in heal hy male volunteers (n = 13) compared wi h heal hy male volunteers receiving oxcarbazepine alone (n = 13).

In the same study, he AUC and C_{max} of lamotrigine were similar following he addition of oxcarbazepine (600 mg twice daily) to lamotrigine in healthy male volunteers compared wi h those receiving lamotrigine alone. Limited clinical data suggest a higher incidence of headache, dizziness, nausea, and somnolence wi h coadministration of lamotrigine and oxcarbazepine compared wi h lamotrigine alone or oxcarbazepine alone.

Phenobarbital, Primidone: The addition of phenobarbital or primidone decreases lamotrigine steady-state concentrations by app oximately 40%.

Phenytoin: Lamotrigine has no appreciable effect on steady-state phenytoin plasma concentrations in patients w th epilepsy. The addition of phenytoin decreases lamotrigine steady-state concentrations by app oximately 40%.

Pregabalin: Steady-state t ough plasma concentrations of lamotrigine were not affected by concomitant pregabalin (200 mg 3 times daily) administration. There are no pharmacokinetic interactions between lamotrigine and pregabalin.

Rifampin: In 10 male volunteers, rifampin (600 mg/day for 5 days) significantly increased the apparent clearance of a single 25-mg dose of lamotrigine by app oximately 2-fold (AUC decreased by app oximately 40%).

Topiramate: Topiramate resulted in no change in plasma concentrations of lamotrigine. Administration of lamotrigine resulted in a 15% increase in topiramate concentrations.

Valproate: When lamotrigine was administered to heal hy volunteers (n = 18) receiving valp oate, he trough steady-state valp oate plasma concentrations decreased by an average of 25% over a 3-week period, and then stabilized. However, adding lamotrigine to he existing herapy did not cause a change in valp oate plasma concentrations in ei her adult or pediatric patients in controlled clinical trials.

The addition of valp oate increased lamotrigine steady-state concentrations in normal volunteers by slightly more han 2-fold. In one study, maximal inhibition of lamotrigine clearance was reached at valp oate doses between 250 and 500 mg/day and did not increase as he valp oate dose was fur her increased.

Zonisamide: In a study of 18 patients with epilepsy, coadministration of zonisamide (200 to 400 mg/day) wi h lamotrigine (150 to 500 mg/day for 35 days) had no significant effect on the pharmacokinetics of lamotrigine.

Known Inducers or Inhibitors of Glucuronidation: Drugs other han hose listed above have not been systematically evaluated in combination wi h lamotrigine. Since lamotrigine is metabolized predominately by glucu onic acid conjugation, drugs hat are known to induce or inhibit glucu onidation may affect he apparent clearance of lamotrigine and doses of lamotrigine may require adjustment based on clinical response.

Other: Results of in vit o experiments suggest hat clearance of lamotrigine is unlikely to be reduced by concomitant administration of amitriptyline, clonazepam, clozapine, fluoxetine, haloperidol, lorazepam, phenelzine, risperidone, sertraline, or trazodone.

Results of in vit o experiments suggest that lamotrigine does not reduce the clearance of drugs eliminated predominantly by CYP2D6.

Special Populations:

Patients With Renal Impairment: Twelve volunteers wi h ch onic renal failure (mean creatinine clearance: 13 mL/min; range: 6 to 23) and another 6 individuals undergoing hemodialysis were each given a single 100-mg dose of lamotrigine. The mean plasma half-lives determined in he study were 42.9 hours (ch onic renal failure), 13.0 hours (during hemodialysis), and 57.4 hours (between hemodialysis) compared wi h 26.2 hours in heal hy volunteers. On average, app oximately 20% (range: 5.6 to 35.1) of he amount of lamotrigine present in the body was eliminated by hemodialysis during a 4-hour session *[see Dosage and Administration (2.1)]*.

Hepatic Disease: The pharmacokinetics of lamotrigine following a single 100-mg dose of lamotrigine were evaluated in 24 subjects with mild, moderate, and severe hepatic impairment (Child-Pugh Classification system) and compared with 12 subjects wi hout hepatic impairment. The patients with severe hepatic impairment were without ascites (n = 2) or with ascites (n = 5). The mean apparent clearances of lamotrigine in patients wi h mild (n = 12), moderate (n = 5), severe wi hout ascites (n = 2), and severe wi h ascites (n = 5) liver impairment were 0.30 ± 0.09, 0.24 ± 0.1, 0.21 ± 0.04, and 0.15 ± 0.09 mL/min/kg, respectively, as compared with 0.37 ± 0.1 mL/min/kg in the heal hy cont ols. Mean half-lives of lamotrigine in patients wi h mild, moderate, severe wi hout ascites, and severe wi h ascites hepatic impairment were 46 ± 20, 72 ± 44, 67 ± 11, and 100 ± 48 hours, respectively, as compared with 33 ± 7 hours in heal hy cont ols *[see Dosage and Administration (2.1)]*.

Age: Pediatric Patients: The pharmacokinetics of lamotrigine following a single 2-mg/kg dose were evaluated in 2 studies of pediatric patients (n = 29 for patients 10 months to 5.9 years of age and n = 26 for patients 5 to 11 years of age). Forty-three patients received concomitant herapy with other AEDs and 12 patients received lamotrigine as monotherapy. Lamotrigine pharmacokinetic parameters for pediatric patients are summarized in Table 16.

Population pharmacokinetic analyses involving patients 2 to 18 years of age demonstrated that lamotrigine clearance was influenced predominantly by total body weight and concurrent AED herapy. The oral clearance of lamotrigine was higher, on a body weight basis, in pediatric patients han in adults. Weight-normalized lamotrigine clearance was higher in those subjects weighing less han 30 kg, compared with those weighing greater than 30 kg. Accordingly, patients weighing less han 30 kg may need an increase of as much as 50% in maintenance doses, based on clinical response, as compared wi h subjects weighing more han 30 kg being administered he same AEDs *[see Dosage and Administration (2.2)]*. These analyses also revealed hat, after accounting for body weight, lamotrigine clearance was not significantly influenced by age. Thus, the same weight-adjusted doses should be administered to children irrespective of differences in age. Concomitant AEDs which influence lamotrigine clearance in adults were found to have similar effects in children.

Table 16. Mean Pharmacokinetic Parameters in Pediatric Patients With Epilepsy

Pediatric Study Population	Number of Subjects	T_{max} (hr)	$t_{½}$ (hr)	Cl/F (mL/min/kg)
Ages 10 months-5.3 years				
Patients taking carbamazepine, phenytoin, phenobarbital, or primidone[a]	10	3.0 (1.0-5.9)	7.7 (5.7-11.4)	3.62 (2.44-5.28)
Patients taking AEDs wi h no known effect on the apparent clearance of lamotrigine	7	5.2 (2.9-6.1)	19.0 (12.9-27.1)	1.2 (0.75-2.42)
Patients taking valp oate only	8	2.9 (1.0-6.0)	44.9 (29.5-52.5)	0.47 (0.23-0.77)
Ages 5-11 years				
Patients taking carbamazepine, phenytoin, phenobarbital, or primidone[a]	7	1.6 (1.0-3.0)	7.0 (3.8-9.8)	2.54 (1.35-5.58)
Patients taking carbamazepine, phenytoin, phenobarbital, or primidone[a] plus valp oate	8	3.3 (1.0-6.4)	19.1 (7.0-31.2)	0.89 (0.39-1.93)
Patients taking valp oate only[b]	3	4.5 (3.0-6.0)	65.8 (50.7-73.7)	0.24 (0.21-0.26)
Ages 13-18 years				
Patients taking carbamazepine, phenytoin, phenobarbital, or primidone[a]	11	[c]	[c]	1.3
Patients taking carbamazepine, phenytoin, phenobarbital, or primidone[a] plus valp oate	8	[c]	[c]	0.5
Patients taking valp oate only	4	[c]	[c]	0.3

[a] Carbamazepine, phenobarbital, phenytoin, and primidone have been shown to increase the apparent clearance of lamotrigine. Est ogen-containing oral contraceptives and rifampin have also been shown to increase he apparent clearance of lamotrigine *[see Drug Interactions (7)]*.
[b] Two subjects were included in he calculation for mean T_{max}
[c] Parameter not estimated.

Elderly: The pharmacokinetics of lamotrigine following a single 150-mg dose of lamotrigine were evaluated in 12 elderly volunteers between the ages of 65 and 76 years (mean creatinine clearance = 61 mL/min, range: 33 to 108 mL/min). The mean half-life of lamotrigine in hese subjects was 31.2 hours (range: 24.5 to 43.4 hours), and the mean clearance was 0.40 mL/min/kg (range: 0.26 to 0.48 mL/min/kg).

Gender: The clearance of lamotrigine is not affected by gender. However, during dose escalation of lamotrigine in one clinical trial in patients w th epilepsy on a stable dose of valp oate (n = 77), mean t ough lamotrigine concentrations, unadjusted for weight, were 24% to 45% higher (0.3 to 1.7 mcg/mL) in females than in males.

Race: The apparent oral clearance of lamotrigine was 25% lower in non-Caucasians than Caucasians.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No evidence of carcinogenicity was seen in one mouse study or two rat studies following oral administration of lamotrigine for up to 2 years at maximum tolerated doses (30 mg/kg/day for mice and 10 to 15 mg/kg/day for rats, doses hat are equivalent to 90 mg/m² and 60 to 90 mg/m², respectively). Steady-state plasma concentrations ranged f om 1 to 4 mcg/mL in he mouse study and 1 to 10 mcg/mL in he rat study. Plasma concentrations associated with the recommended human doses of 300 to 500 mg/day are generally in he range of 2 to 5 mcg/mL, but concentrations as high as 19 mcg/mL have been recorded.

Lamotrigine was not mutagenic in the presence or absence of metabolic activation when tested in two gene mutation assays (he Ames test and he in vit o mammalian mouse lymphoma assay). In two cytogenetic assays (the in vit o human lymphocyte assay and he in vivo rat bone mar ow assay), lamotrigine did not increase he incidence of structural or numerical ch omosomal abnormalities.

No evidence of impairment of fertility was detected in rats given oral doses of lamotrigine up to 2.4 times he highest usua human maintenance dose of 8.33 mg/kg/day or 0.4 times the human dose on a mg/m² basis. The effect of lamotrigine on human fertility is unknown.

14 CLINICAL STUDIES

14.1 Epilepsy

Monotherapy With Lamotrigine in Adults With Partial Seizures Already Receiving Treatment With Carbamazepine, Phenytoin, Phenobarbital, or Primidone as the Single AED: The effectiveness of monotherapy wi h lamotrigine was established in a multicenter, double-blind clinical trial en olling 156 adult outpatients wi h partial seizures. The patients experienced at least four simple partial, complex partial, and/or secondarily generalized seizures during each of two consecutive 4-week periods while receiving carbamazepine or phenytoin monotherapy during baseline. Lamotrigine (target dose of 500 mg/day) or valp oate (1,000 mg/day) was added to ei her carbamazepine or phenytoin mono herapy over a 4-week period. Patients were hen converted to mono herapy wi h lamotrigine or valp oate during the next 4 weeks, hen continued on mono herapy for an additional 12-week period.

Study endpoints were completion of all weeks of study treatment or meeting an escape criterion. Criteria for escape relative to baseline were: (1) doubling of average mon hly seizure count, (2) doubling of highest consecutive 2-day seizure frequency, (3) emergence of a new seizure type (defined as a seizure hat did not occur during the 8-week baseline) that is more severe han seizure types hat occur during study treatment, or (4) clinically significant p olongation of generalized tonic-clonic (GTC) seizures. The primary efficacy variable was the p oportion of patients in each treatment g oup who met escape criteria.

The percentages of patients who met escape criteria were 42% (32/76) in he g oup receiving lamotrigine and 69% (55/80) in he valp oate g oup. The difference in the percentage of patients meeting escape criteria was statistically significant (p= 0.0012) in favor of lamotrigine. No differences in efficacy based on age, sex, or race were detected.

Patients in he cont ol g oup were intentionally treated wi h a relatively low dose of valp oate; as such, he sole objective of his study was to demonstrate the effectiveness and safety of mono herapy with lamotrigine, and cannot be interpreted to imply he superiority of lamotrigine to an adequate dose of valp oate.

Adjunctive Therapy With Lamotrigine in Adults With Partial Seizures: The effectiveness of lamotrigine as adjunctive herapy (added to other AEDs) was established in three multicenter, placebo-cont olled, double-blind clinical trials in 355 adults wi h refractory partial seizures. The patients had a history of at least four partial seizures per mon h in spite of receiving one or more AEDs at herapeutic concentrations and, in two of the studies, were observed on heir established AED regimen during baselines hat varied between 8 to 12 weeks. In the hird, patients were not observed in a p ospective baseline. In patients continuing to have at least four seizures per month during he baseline, lamotrigine or placebo was hen added to the existing therapy. In all three studies, change f om baseline in seizure frequency was he primary measure of effectiveness. The results given below are for all partial seizures in he intent-to-treat population (all patients who received at least one dose of treatment) in each study, unless o herwise indicated. The median seizure frequency at baseline was 3 per week while the mean at baseline was 6.6 per week for all patients en olled in efficacy studies.

One study (n = 216) was a double-blind, placebo-cont olled, parallel trial consisting of a 24-week treatment period. Patients could not be on more han two o her anticonvulsants and valp oate was not allowed. Patients were randomized to receive placebo, a target dose of 300 mg/day of lamotrigine, or a target dose of 500 mg/day of lamotrigine. The median reductions in the frequency of all partial seizures relative to baseline were 8% in patients receiving placebo, 20% in patients receiving 300 mg/day of lamotrigine, and 36% in patients receiving 500 mg/day of lamotrigine. The seizure frequency reduction was statistically significant in he 500-mg/day g oup compared wi h the placebo g oup, but not in the 300-mg/day g oup.

A second study (n = 98) was a double-blind, placebo-cont olled, randomized, c ossover trial consisting of two 14-week treatment periods (the last 2 weeks of which consisted of dose tapering) separated by a 4-week washout period. Patients could not be on more than two o her anticonvulsants and valp oate was not allowed. The target dose of lamotrigine was 400 mg/day. When he first 12 weeks of he treatment periods were analyzed, he median change in seizure frequency was a 25% reduction on lamotrigine compared with placebo (p<0.001).

The hird study (n = 41) was a double-blind, placebo-cont olled, c ossover trial consisting of two 12-week treatment periods separated by a 4-week washout period. Patients could not be on more han two o her anticonvulsants. Thirteen patients were on concomitant valp oate; hese patients received 150 mg/day of lamotrigine. The 28 other patients had a target dose of 300 mg/day of lamotrigine. The median change in seizure frequency was a 26% reduction on lamotrigine compared w th placebo (p<0.01).

No differences in efficacy based on age, sex, or race, as measured by change in seizure frequency, were detected.

Adjunctive Therapy With Lamotrigine in Pediatric Patients With Partial Seizures: The effectiveness of lamotrigine as adjunctive herapy in pediatric patients wi h partial seizures was established in a multicenter, double-blind, placebo-cont olled trial in 199 patients 2 to 16 years of age (n = 98 on lamotrigine, n = 101 on placebo). Following an 8-week baseline phase, patients were randomized to 18 weeks of treatment wi h lamotrigine or placebo added to their current AED regimen of up to two drugs. Patients were dosed based on body weight and valp oate use. Target doses were designed to app oximate 5 mg/kg/day for patients taking valp oate (maximum dose: 250 mg/day) and 15 mg/kg/day for the patients not taking valp oate (maximum dose: 750 mg/day). The primary efficacy endpoint was percentage change f om baseline in all partial seizures. For he intent-to-treat population, he median reduction of all partial seizures was 36% in patients treated wi h lamotrigine and 7% on placebo, a difference that was statistically significant (p<0.01).

Adjunctive Therapy With Lamotrigine in Pediatric and Adult Patients With Lennox-Gastaut Syndrome: The effectiveness of lamotrigine as adjunctive herapy in patients wi h PGTC seizures was established in a multicenter, double-blind, placebo-cont olled trial in 169 patients 3 to 25 years of age (n = 79 on lamotrigine, n = 90 on placebo). Following a 4-week single-blind, placebo phase, patients were randomized to 16 weeks of treatment w th lamotrigine or placebo added to their current AED regimen of up to three drugs. Patients were dosed on a fixed-dose regimen based on body weight and valp oate use. Target doses were designed to app oximate 5 mg/kg/day for patients taking valp oate (maximum dose: 200 mg/day) and 15 mg/kg/day for patients not taking valp oate (maximum dose: 400 mg/day). The primary efficacy endpoint was percentage change from baseline in major motor seizures (atonic, tonic, major myoclonic, and tonic-clonic seizures). For the intent-to-treat population, he median reduction of major motor seizures was 32% in patients treated with lamotrigine and 9% on placebo, a difference that was statistically significant (p<0.05). D op attacks were significantly reduced by lamotrigine (34%) compared wi h placebo (9%), as were tonic-clonic seizures (36% reduction versus 10% increase for lamotrigine and placebo, respectively).

Adjunctive Therapy With Lamotrigine in Pediatric and Adult Patients With Primary Generalized Tonic-Clonic Seizures: The effectiveness of lamotrigine as adjunctive herapy in patients wi h primary generalized tonic-clonic seizures was established in a multicenter, double-blind, placebo-controlled trial in 117 pediatric and adult patients ≥2 years (n = 58 on lamotrigine, n = 59 on placebo). Patients wi h at least hree primary generalized tonic-clonic seizures during an 8-week baseline phase were randomized to 19 to 24 weeks of treatment wi h lamotrigine or placebo added to heir current AED regimen of up to 2 drugs. Patients were dosed on a fixed-dose regimen, wi h target doses ranging f om 3 mg/kg/day to 12 mg/kg/day for pediatric patients and f om 200 mg/day to 400 mg/day for adult patients based on concomitant AED.

The primary efficacy endpoint was percentage change f om baseline in primary generalized tonic-clonic seizures. For he intent-to-treat population, the median percent reduction of primary generalized tonic-clonic seizures was 66% in patients treated wi h lamotrigine and 34% on placebo, a difference hat was statistically significant (p = 0.006).

14.2 Bipolar Disorder

The effectiveness of lamotrigine in he maintenance treatment of Bipolar I Disorder was established in two multicenter, double-blind, placebo-cont olled studies in adult patients who met DSM-IV criteria for Bipolar I Disorder. Study 1 en olled patients wi h a current or recent (wi hin 60 days) depressive episode as defined by DSM-IV and Study 2 included patients with a current or recent (within 60 days) episode of mania or hypomania as defined by DSM-IV. Bo h studies included a cohort of patients (30% of 404 patients in Study 1 and 28% of 171 patients in Study 2) wi h rapid cycling Bipolar Disorder (4 to 6 episodes per year).

In bo h studies, patients were titrated to a target dose of 200 mg of lamotrigine, as add-on herapy or as mono herapy, wi h gradual withdrawal of any psychot opic medications during an 8- to 16-week open-label period. Overall 81% of 1,305 patients participating in the open-label period were receiving one or more other psychot opic medications, including benzodiazepines, selective se otonin reuptake inhibitors (SSRIs), atypical antipsychotics (including olanzapine), valp oate, or li hium, during titration of lamotrigine. Patients wi h a CGI-severity score of 3 or less maintained for at least 4 continuous weeks, including at least the final week on mono herapy wi h lamotrigine, were randomized to a placebo-cont olled, double-blind treatment period for up to 18 months. The primary endpoint was TIME (time to intervention for a mood episode or one hat was emerging, time to discontinuation for ei her an adverse event that was judged to be related to Bipolar Disorder, or for lack of efficacy). The mood episode could be depression, mania, hypomania, or a mixed episode.

In Study 1, patients received double-blind monotherapy wi h lamotrigine 50 mg/day (n = 50), lamotrigine 200 mg/day (n = 124), lamotrigine 400 mg/day (n = 47), or placebo (n = 121). Lamotrigine (200- and 400-mg/day treatment g oups combined) was superior to placebo in delaying he time to occurrence of a mood episode. Separate analyses of he 200- and 400-mg/day dose g oups revealed no added benefit f om he higher dose.

In Study 2, patients received double-blind mono herapy wi h lamotrigine (100 to 400 mg/day, n = 59), or placebo (n = 70). Lamotrigine was superior to placebo in delaying time to occurrence of a mood episode. The mean dose of lamotrigine was about 211 mg/day.

Al hough these studies were not designed to separately evaluate time to he occurrence of depression or mania, a combined analysis for the 2 studies revealed a statistically significant benefit for lamotrigine over placebo in delaying he time to occurrence of both depression and mania, although the finding was more obust for depression.

16 HOW SUPPLIED/STORAGE AND HANDLING

Lamotrigine Tablets USP, 25 mg

White, caplet shaped, biconvex tablets wi h 'U' debossed on either side of break line on one side and '111' debossed on o her side.

Bottles of 100: NDC 29300-111-01
Bottles of 500: NDC 29300-111-05
Bottles of 1000: NDC 29300-111-10

Lamotrigine Tablets USP, 100 mg

White, trigonal shaped, biconvex tablets wi h 'U' debossed on either side of break line on one side and '112' debossed on o her side.

Bottles of 100: NDC 29300-112-01
Bottles of 500: NDC 29300-112-05
Bottles of 1000: NDC 29300-112-10

Lamotrigine Tablets USP, 150 mg

White, trigonal shaped, biconvex tablets wi h 'U' debossed on either side of break line on one side and '113' debossed on o her side.

Bottles of 60: NDC 29300-113-16
Bottles of 500: NDC 29300-113-05
Bottles of 1000: NDC 29300-113-10

Lamotrigine Tablets USP, 200 mg

Light blue, trigonal shaped, biconvex tablets with 'U' debossed on ei her side of break line on one side and '114' debossed on o her side.

Bottles of 60: NDC 29300-114-16
Bottles of 500: NDC 29300-114-05
Bottles of 1000: NDC 29300-114-10

Store at 20°-25°C (68°-77°F) [see USP Cont olled Room Temperature] in a dry place.
Dispense in tight, light-resistant container as defined in the USP.

17 PATIENT COUNSELING INFORMATION

See Medication Guide that accompanies the product.

17.1 Rash

Prior to initiation of treatment wi h lamotrigine, the patient should be instructed that a rash or other signs or symptoms of hypersensitivity (e.g., fever, lymphadenopa hy) may herald a serious medical event and hat he patient should report any such occurrence to a physician immediately.

17.2 Multiorgan Hypersensitivity Reactions, Blood Dyscrasias and Organ Failure

Patients should be instructed hat multiorgan hypersensitivity reactions and acute multiorgan failure may occur wi h lamotrigine. Isolated organ failure or isolated blood dyscrasias wi hout evidence of multiorgan hypersensitivity may also occur. Patients should contact their physician immediately if they experience any signs or symptoms of hese conditions *[see Warnings and Precautions (5.2, 5.3)]*.

17.3 Suicidal Thinking and Behavior

Patients, heir caregivers, and families should be counseled hat AEDs, including lamotrigine, may increase he risk of suicidal houghts and behavior and should be advised of the need to be alert for he emergence or worsening of symptoms of depression, any unusual changes in mood or behavior, or he emergence of suicidal houghts, behavior, or houghts about self-harm. Behaviors of conce n should be reported immediately to healthcare p oviders.

17.4 Worsening of Seizures

Patients should be advised to notify their physician if worsening of seizure cont ol occurs.

17.5 CNS Adverse Effects

Patients should be advised hat lamotrigine may cause dizziness, somnolence, and o her symptoms and signs of central nervous system (CNS) depression. Accordingly, they should be advised nei her to drive a car nor to operate o her complex machinery until hey have gained sufficient experience on lamotrigine to gauge whether or not it adversely affects their mental and/or motor performance.

17.6 Pregnancy

Patients should be advised to notify their physicians if they become pregnant or intend to become pregnant during herapy. Patients should be advised to notify heir physicians if hey intend to breastfeed or are breastfeeding an infant.

Patients should also be encouraged to en oll in he NAAED Pregnancy Registry if they become pregnant. This registry is collecting information about the safety of antiepileptic drugs during pregnancy. To en oll, patients can call the toll-free number 1-888-233-2334 *[see Use in Specific Populations (8.1)]*.

17.7 Oral Contraceptive Use

Women should be advised to notify heir physician if hey plan to start or stop use of oral contraceptives or o her female hormonal preparations. Starting est ogen-containing oral contraceptives may significantly decrease lamotrigine plasma levels and stopping est ogen-containing oral contraceptives (including the "pill-free" week) may significantly increase lamotrigine plasma levels *[see Warnings and Precautions (5. 8), Clinical Pharmacology (12.3)]*. Women should also be advised to p omptly notify heir physician if hey experience adverse reactions or changes in menstrual patte n (e.g., break- h ough bleeding) while receiving lamotrigine in combination wi h hese medications.

17.8 Discontinuing Lamotrigine

Patients should be advised to notify heir physician if hey stop taking lamotrigine for any reason and not to resume lamotrigine wi hout consulting heir physician.

17.9 Aseptic Meningitis

Patients should be advised that lamotrigine may cause aseptic meningitis. Patients should be advised to notify their physician immediately if hey develop signs and symptoms of meningitis such as headache, fever, nausea, vomiting, stiff neck, rash, abnormal sensitivity to light, myalgia, chills, confusion, or d owsiness while taking lamotrigine.

17.10 Potential Medication Errors

Medication er ors involving lamotrigine have occurred. In particular the name lamotrigine can be confused with the names of o her commonly used medications. Medication er ors may also occur between he different formulations of lamotrigine. To reduce he potential of medication er ors, write and say lamotrigine clearly. Depictions of he lamotrigine tablets, can be found in he Medication Guide hat accompanies the p oduct to highlight he distinctive markings, colors, and shapes that serve to identify the different presentations of he drug and hus may help reduce he risk of medication er ors. **To avoid a medication error of using the wrong drug or formulation, patients should be strongly advised to visually inspect their tablets to verify that they are lamotrigine tablets, as well as the correct formulation of lamotrigine, each time they fill their prescription** *[see Dosage Forms and Strengths (3.1), How Supplied/Storage and Handling (16)]*.

R-04-08/2011

MEDICATION GUIDE

LAMOTRIGINE TABLETS USP

Read his Medication Guide before you start taking lamotrigine tablets and each time you get a refill. There may be new information. This information does not take he place of talking wi h your healthcare p ovider about your medical condition or treatment. If you have questions about lamotrigine tablets, ask your healthcare p ovider or pharmacist.

What is the most important information I should know about Lamotrigine tablets?

1. Lamotrigine tablets may cause a serious skin rash that may cause you to be hospitalized or to stop lamotrigine tablets; it may rarely cause death.

There is no way to tell if a mild rash will develop into a more serious reaction. These serious skin reactions are more likely to happen when you begin taking lamotrigine tablets, wi hin he first 2 to 8 weeks of treatment. But it can happen in people who have taken lamotrigine tablets for any period of time. Children between 2 to 16 years of age have a higher chance of getting his serious skin reaction while taking lamotrigine tablets.

The risk of getting a rash is higher if you:

- take lamotrigine tablets while taking valp oate (valp oic acid or divalp oex sodium)
- take a higher starting dose of lamotrigine tablets han your healthcare p ovider prescribed
- increase your dose of lamotrigine tablets faster than prescribed.

Lamotrigine tablets can also cause other types of allergic reactions or serious problems which may affect organs and other parts of your body like the liver or blood cells. You may or may not have a rash with these types of reactions.

Call your healthcare provider right away if you have any of the following:

- **a skin rash**
- **hives**
- **fever**
- **swollen lymph glands**
- **painful sores in the mouth or around your eyes**
- **swelling of your lips or tongue**
- **yellowing of your skin or eyes**
- **unusual bruising or bleeding**
- **severe fatigue or weakness**
- **severe muscle pain**
- **frequent infections**

These symptoms may be he first signs of a serious reaction. A healthcare p ovider should examine you to decide if you should continue taking lamotrigine tablets.

2. Like other antiepileptic drugs, lamotrigine tablets may cause suicidal thoughts or actions in a very small number of people, about 1 in 500.

Call a healthcare provider right away if you have any of these symptoms, especially if they are new, worse, or worry you:

- houghts about suicide or dying
- attempt to commit suicide
- new or worse depression
- new or worse anxiety
- feeling agitated or restless
- panic attacks
- t ouble sleeping (insomnia)
- new or worse irritability
- acting aggressive, being angry, or violent
- acting on dange ous impulses
- an extreme increase in activity and talking (mania)
- o her unusual changes in behavior or mood

Do not stop lamotrigine tablets without first talking to a healthcare provider.

- Stopping lamotrigine tablets suddenly can cause serious p oblems.
- Suicidal houghts or actions can be caused by hings other han medicines. If you have suicidal houghts or actions, your heal hcare p ovider may check for o her causes.

How can I watch for early symptoms of suicidal thoughts and actions?

- Pay attention to any changes, especially sudden changes, in mood, behaviors, thoughts, or feelings.
- Keep all follow-up visits wi h your heal hcare provider as scheduled.
- Call your heal hcare p ovider between visits as needed, especially if you are worried about symptoms.

3. Lamotrigine tablets may rarely cause aseptic meningitis, a serious inflammation of the protective membrane that covers the brain and spinal cord.

Call your healthcare provider right away if you have any of the following symptoms:

- Headache
- Fever
- Nausea
- Vomiting
- Stiff neck
- Rash
- Unusual sensitivity to light
- Muscle pains
- Chills
- Confusion
- D owsiness

Meningitis has many causes o her han lamotrigine tablets, which your doctor would check for if you developed meningitis while taking lamotrigine tablets.

Lamotrigine tablets can have other serious side effects. For more information ask your heal hcare p ovider or pharmacist. Tell your heal hcare p ovider if you have any side effect that bothers you. Be sure to read he section below entitled "What are he possible side effects of lamotrigine tablets?"

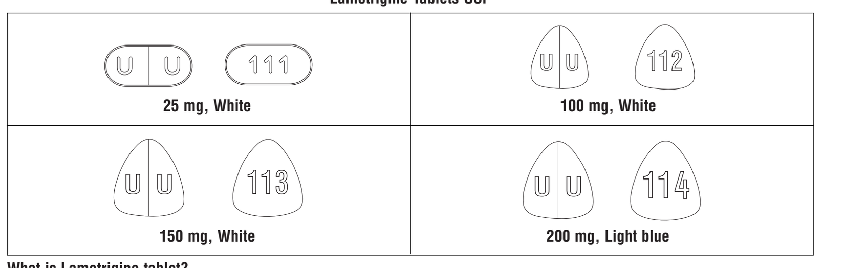
4. Patients prescribed lamotrigine tablets have sometimes been given the wrong medicine because many medicines have names similar to lamotrigine tablets, so always check that you receive lamotrigine tablets.

Taking he wrong medication can cause serious heal h p oblems. When your heal hcare p ovider gives you a prescription for lamotrigine tablets:

- Make sure you can read it clearly.
- Talk to your pharmacist to check that you are given he correct medicine.
- Each time you fill your prescription, check the tablets you receive against the pictures of he tablets below.

These pictures show he distinct wording, colors, and shapes of he tablets hat help to identify the right streng h of lamotrigine tablets. Immediately call your pharmacist if you receive a lamotrigine tablet that does not look like one of he tablets shown below, as you may have received he w ong medication.

Lamotrigine Tablets USP



25 mg, White | **100 mg, White** | **150 mg, White** | **200 mg, Light blue**

What is Lamotrigine tablet?

Lamotrigine tablet is a prescription medicine used:

1. together wi h o her medicines to treat certain types of seizures (partial seizures, primary generalized tonic-clonic seizures, generalized seizures of Lennox-Gastaut synd ome) in people 2 years or older.
2. alone when changing f om other medicines used to treat partial seizures in people 16 years or older.
3. for he long-term treatment of Bipolar I Disorder to leng hen he time between mood episodes in people 18 years or older who have been treated for mood episodes with other medicine.

It is not known if lamotrigine tablets are safe or effective in children or teenagers under he age of 18 wi h mood disorders such as bipolar disorder or depression.

It is not known if lamotrigine tablets are safe or effective when used alone as the first treatment of seizures in adults.

Who should not take Lamotrigine tablets?

You should not take lamotrigine tablets if you have had an allergic reaction to lamotrigine or to any of the inactive ingredients in lamotrigine tablets. See the end of his leaflet for a complete list of ingredients in lamotrigine tablets.

What should I tell my healthcare provider before taking Lamotrigine tablets?

Before taking lamotrigine tablets, tell your healthcare p ovider about all of your medical conditions, including if you:

- have had a rash or allergic reaction to ano her antiseizure medicine.
- have or have had depression, mood p oblems or suicidal houghts or behavior.
- are taking oral contraceptives (birth cont ol pills) or other female hormonal medicines. Do not start or stop taking birth cont ol pills or other female hormonal medicine until you have talked with your heal hcare p ovider. Tell your healthcare provider if you have any changes in your menstrual patte n such as breakth ough bleeding. Stopping or starting these medicines may cause side effects (such as dizziness, lack of coordination, or double vision) or lessen how well lamotrigine tablets work.
- are pregnant or plan to become pregnant. It is not known if lamotrigine tablets will harm your unbo n baby. If you become pregnant while taking lamotrigine tablets, talk to your heal hcare p ovider about registering wi h the North American Antiepileptic Drug Pregnancy Registry. You can en oll in his registry by calling 1-888-233-2334. The purpose of his registry is to collect information about he safety of antiepileptic drugs during pregnancy.
- are breast-feeding. Lamotrigine can pass into your breast milk. You and your heal hcare p ovider should decide if you should take lamotrigine tablets or breast-feed. Breast-feeding while taking lamotrigine tablets is not recommended.

Tell your healthcare p ovider about all he medicines you take or if you are planning to take a new medicine, including prescription and non-prescription medicines, vitamins, and herbal supplements. Using lamotrigine tablets wi h certain o her medicines can affect each other, causing side effects.

How should I take Lamotrigine tablets?

- Take lamotrigine tablets exactly as prescribed.
- Your heal hcare p ovider may change your dose. Do not change your dose wi hout talking to your heal hcare p ovider.
- Do not stop taking lamotrigine tablets wi hout talking to your heal hcare p ovider. Stopping lamotrigine tablets suddenly may cause serious p oblems. For example, if you have epilepsy and you stop taking lamotrigine tablets suddenly, you may get seizures hat do not stop. Talk with your healthcare p ovider about how to stop lamotrigine tablets slowly.
- If you miss a dose of lamotrigine tablets, take it as soon as you remember. If it is almost time for your next dose, just skip he missed dose. Take he next dose at your regular time. **Do not take two doses at the same time.**
- You may not feel he full effect of lamotrigine tablets for several weeks.
- If you have epilepsy, tell your heal hcare p ovider if your seizures get worse or if you have any new types of seizures.
- Swallow lamotrigine tablets whole.
- If you have t ouble swallowing lamotrigine tablets, here may be ano her form of lamotrigine you can take.

What should I avoid while taking Lamotrigine tablets?

- Do not drive a car or operate complex, hazardous machinery until you know how lamotrigine tablets affect you.

What are possible side effects of Lamotrigine tablets?

- See "What is he most important information I should know about lamotrigine tablets?"

Common side effects of lamotrigine tablets include:

- dizziness
- headache
- blurred or double vision
- lack of coordination
- sleepiness
- nausea, vomiting
- insomnia
- tremor
- rash
- fever
- abdominal pain
- back pain
- tiredness
- dry mou h

Tell your heal hcare p ovider about any side effect hat bothers you or hat does not go away.

These are not all he possible side effects of lamotrigine tablets. For more information, ask your healthcare p ovider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store Lamotrigine tablets?

- Store lamotrigine tablets at 20° to 25°C (68° to 77°F). [See USP Cont olled Room Temperature]
- **Keep lamotrigine tablets and all medicines out of the reach of children.**

General information about Lamotrigine tablets

Medicines are sometimes prescribed for purposes o her than hose listed in a Medication Guide. Do not use lamotrigine tablets for a condition for which it was not prescribed. Do not give lamotrigine tablets to o her people, even if hey have the same symptoms you have. It may harm hem.

This Medication Guide summarizes the most important information about lamotrigine tablets. If you would like more information, talk wi h your heal hcare p ovider. You can ask your heal hcare p ovider or pharmacist for information about lamotrigine tablets hat is written for healthcare p ofessionals.

What are the ingredients in Lamotrigine tablets?

Active ingredient: Lamotrigine USP.

Inactive ingredients: lactose monohydrate, magnesium stearate, mic ocrystalline cellulose, povidone and sodium starch glycolate. In addition, he 200 mg tablets contain FD&C Blue No. 2 Lake.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

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PHARMACIST - DETACH HERE AND GIVE INSTRUCTIONS TO PATIENT