Lamotridgine® tablets

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Brand Names: Sazar® (Сейзар®) , Lamolep® (Ламолеп®), Lamitor® (Ламитор®), Lamictal® (Ламиктал®)

Active substance: Lamotridgine

Pharmachologic effect: antiepileptic

Pharmacodynamics: Lamotrigine is a voltage-gated sodium channel blocker. It reduces the pathological activity of neurons without inhibiting their function, stabilizes neuronal membranes by influencing Na + channels, blocks excessive release of glutamate without reducing its normal release.

Pharmacokinetics:
Lamotrigine is rapidly and completely absorbed from the intestine with little or no first pass metabolism.
C_{max} in plasma is reached approximately 2.5 hours after oral administration of the drug. T_{max} slightly increases after a meal, but the degree of absorption remains unchanged.
Pharmacokinetics is linear with single doses up to 450 mg (highest dose studied). There are significant inter-individual fluctuations in C_{max} in the equilibrium state, however, with rare fluctuations in each individual.
The enzyme uridine diphosphate glucuronyl transferase (UDP-glucuronyl transferase) is involved in the metabolism of lamotrigine. Lamotrigine slightly increases its own metabolism in a dose dependent manner. However, there is no evidence that lamotrigine affects the pharmacokinetics of other antiepileptic drugs and interactions between lamotrigine and other drugs metabolized by the cytochrome P450 system are possible.
In healthy adults, the steady-state clearance of lamotrigine is on average (39±14) ml/min.
The $T_{1/2}$ of lamotrigine is greatly influenced by co-administered drugs.
The average $T_{1/2}$ decreases to approximately 14 hours when co-administered with drugs that stimulate glucuronidation, such as carbamazepine and phenytoin, and increases to an average of 70 hours when co-administered with valproic acid.

Indications:
Epilepsy: Adults and children (over 12 years of age): epilepsy (partial and generalized seizures, including tonic-clonic seizures, as well as seizures in Lennox-Gastaut syndrome) as part of combination therapy or monotherapy.
Children aged 3 to 12 years: epilepsy (partial and generalized seizures, including tonic-clonic seizures, as well as seizures in Lennox-Gastaut syndrome) as part of combination therapy. Once epilepsy is controlled with combination therapy, concomitant antiepileptic drugs (AEDs) may be discontinued and lamotrigine continued as monotherapy; monotherapy of typical absences;

Bipolar Disorders: Adults (18 years and older): to prevent mood disorders (depression, mania, hypomania, mixed episodes) in patients with bipolar disorder.

Contraindications: hypersensitivity to lamotrigine; children's age up to 3 years (for this dosage form).

Use with caution: chronic renal failure, allergic reactions or skin rash caused by taking other antiepileptic drugs.

Side effects:
Information on side effects is divided into two sections: side effects in patients with epilepsy and side effects in patients with bipolar disorder. However, when considering the safety profile of lamotrigine as a whole, the information in both sections should be taken into account.

Epilepsy :
Often: skin rash, irritability, headache, drowsiness, insomnia, dizziness, tremor, nausea, diarrhea, diplopia, blurred

vision;
Not often : aggressiveness, ataxia,
Rare : Stevens-Johnson syndrome, conjunctivitis
Very rare : toxic epidermal necrolysis, hematological disorders, hypersensitivity syndrome, tics, hallucinations, confusion, agitation, unsteadiness, movement disorders, worsening of Parkinson's symptoms, extrapyramidal disorders, choreoathetosis, increased frequency of seizures, elevated liver enzymes, abnormal liver function, liver failure Lupus-like syndrome.

Bipolar disorder:
Often : skin rash, headache, agitation, drowsiness, dizziness, arthralgia, back pain
Rare : Stevens-Johnson Syndrome

Interaction:
Valproic acid, which inhibits the glucuronization of lamotrigine, reduces the rate of its metabolism and lengthens its average $T_{1/2}$ by almost 2 times. Certain AEDs (such as phenytoin, carbamazepine, phenobarbital, and primidone), which stimulate the liver metabolizing enzyme system, accelerate lamotrigine glucuronidation and metabolism**.**
Taking combined oral contraceptives containing 30 mcg of ethinyl estradiol and 150 mcg of levonorgestrel causes an approximately twofold increase in the clearance of lamotrigine (after oral administration), which leads to a decrease in AUC and C_{max} of lamotrigine by an average of 52 and 39%, respectively. During the week free from taking the active drug, there is an increase in the plasma concentration of lamotrigine, while the concentration of lamotrigine, measured at the end of this week before the next dose, is on average 2 times higher than during the period of active therapy.
Rifampicin increases the clearance of lamotrigine and reduces its $T_{1/2}$ due to the stimulation of hepatic enzymes responsible for glucuronidation.
Myelotoxic drugs increase the manifestations of hematotoxicity of the drug.

Dosing and Administration:

Epilepsy:

Recommended dosage regimen for the treatment of epilepsy in adults and children over 12 years of age

<table>
<tr><th colspan="2">Dosing regimen</th><th>Week 1–2</th><th>Week 3-4</th><th>Maintenance dose</th></tr>
<tr><td colspan="2">Monotherapy</td><td>25 mg / day in 1 dose</td><td>50 mg / day in 1 dose</td><td>100-200 mg / day in 1 or 2 doses. To achieve a therapeutic effect, the dose may be increased by 50-100 mg every 1-2 weeks.</td></tr>
<tr><td colspan="2">Combination therapy with lamotrigine and valproic acid, regardless of other concomitant therapy</td><td>25 mg every other day</td><td>25 mg / day in 1 dose</td><td>100-200 mg / day in 1 or 2 doses. To achieve a therapeutic effect, the dose may be increased by 25-50 mg every 1-2 weeks.</td></tr>
<tr><td rowspan="2">Combination therapy without valproic acid</td><td>This regimen should be used with phenytoin, carbamazepine, phenobarbital, primidone, or other inducers of lamotrigine glucuronidation</td><td>50 mg/day in 1 dose</td><td>100 mg/day in 2 divided doses</td><td>200-400 mg / day in 1-2 doses. To achieve a therapeutic effect, the dose may be increased by 100 mg every 1-2 weeks.</td></tr>
<tr><td>With oxcarbazepine without inducers or inhibitors of lamotrigine glucuronidation</td><td>25 mg/day in 1 dose</td><td>50 mg/day in 1 dose</td><td>100-200 mg / day in 1 or 2 doses. To achieve a therapeutic effect, the dose may be increased by 50-100 mg every 1-2 weeks.</td></tr>
<tr><td colspan="5">In patients taking AEDs for which no pharmacokinetic interactions with lamotrigine are currently known, the regimen recommended for lamotrigine in combination with valproic acid should be used.</td></tr>
</table>

Recommended treatment regimen for children with epilepsy aged 3 to 12 years (total daily dose)

Dosing regimen		Week 1–2	Week 3-4	Maintenance dose
Monotherapy for typical absence seizures		0.3 mg/kg in 1 or 2 doses	0.3 mg/kg in 1 or 2 doses	Increase the dose by 0.6 mg/kg every 1–2 weeks until a maintenance dose of 1–15 mg/kg/day (in 1 or 2 divided doses) is reached, up to a maximum of 200 mg/day
Combination therapy with lamotrigine and valproic acid, regardless of other concomitant therapy		0.15 mg/kg in 1 dose	0.3 mg/kg in 1 dose	Increase the dose by 0.3 mg/kg every 1–2 weeks until a maintenance dose of 1–5 mg/kg/day (in 1 or 2 divided doses) is reached, up to a maximum of 200 mg/day
Combination therapy without valproic acid	This regimen should be used with phenytoin, carbamazepine, phenobarbital, primidone, or other inducers of lamotrigine glucuronidation	0.6 mg/kg in 2 divided doses	1.2 mg/kg in 2 divided doses	Increase the dose by 1.2 mg/kg every 1–2 weeks until a maintenance dose of 5–15 mg/kg/day (in 1 or 2 divided doses) is reached, up to a maximum of 400 mg/day
	With oxcarbazepine without inducers or inhibitors of lamotrigine glucuronidation	0.3 mg/kg in 1 or 2 doses	0.6 mg/kg in 1 or 2 doses	Increase the dose by 0.6 mg/kg every 1–2 weeks until a maintenance dose of 1–10 mg/kg/day (in 1 or 2 divided doses) is reached, up to a maximum of 200 mg/day

Bipolar disorders

Recommended dose escalation regimen to achieve the maintenance daily dose for adults (over 18 years of age) with bipolar disorders

Dosing regimen	Week 1–2	Week 3-4	Week 5	Target stabilization dose (week 5)
Combination therapy with lamotrigine glucuronidation inhibitors, such as valproic acid	25 mg every other day	25 mg / day in 1 dose	50 mg/day in 1 or 2 divided doses	100 mg / day in 1 or 2 doses, the maximum daily dose is up to 200 mg
Combination therapy with lamotrigine glucuronidation inhibitors in patients not taking inhibitors such as valproic acid. This regimen should be used with phenytoin, carbamazepine, phenobarbital, primidone, or other inducers of lamotrigine glucuronidation				400 mg on the 7th week of therapy (in 2 divided doses)
Lamotrigine monotherapy or add-on therapy in patients taking lithium, bupropion, olanzapine, oxcarbazepine, or other drugs that do not significantly induce or inhibit lamotrigine glucuronidation	25 mg / day in 1 dose	50 mg/day in 1 or 2 divided doses	100 mg/day in 1 or 2 divided doses	200 mg (100 to 400 mg in 1 or 2 doses per day)
Note: In patients taking AEDs for which pharmacokinetic interactions with lamotrigine have not been studied, a dose escalation regimen should be used as recommended for lamotrigine in combination with valproic acid.				

The target stabilization dose varies depending on the clinical effect.

Maintenance stabilizing total daily dose for the treatment of bipolar disorder after withdrawal of concomitant psychotropic or antiepileptic drugs

<table>
<tr><th>Dosing regimen</th><th>Week 1</th><th>Week 2</th><th>Week 3, etc</th></tr>
<tr><td>After discontinuation of lamotrigine glucuronidation inhibitors, such as valproic acid</td><td>Double the stabilization dose without exceeding 100 mg/week, i.e. target stabilization dose of 100 mg/day increased on week 1 to 200 mg/day</td><td colspan="2">Maintain dose of 200 mg/day in 2 divided doses</td></tr>
<tr><td rowspan="3">After discontinuation of inducers of glucuronidation of lamotrigine, depending on the initial dose. This regimen should be used when using phenytoin, carbamazepine, phenobarbital, primidone, or other inducers of lamotrigine glucuronidation.</td><td>400mg</td><td>300mg</td><td>200mg</td></tr>
<tr><td>300mg</td><td>225mg</td><td>150mg</td></tr>
<tr><td>200mg</td><td>150mg</td><td>100mg</td></tr>
<tr><td>After discontinuation of other psychotropic or antiepileptic drugs in patients not taking inducers or inhibitors of lamotrigine glucuronidation (including lithium, bupropion, olanzapine, oxcarbazepine)</td><td colspan="3">Maintain target dose achieved during boost regimen (200 mg/day in 2 doses, dose range 100 to 400 mg)</td></tr>
<tr><td colspan="4">Note: in patients taking AEDs, the nature of the pharmacokinetic interaction of which with lamotrigine is currently not studied, a dosing regimen is recommended, as when taking lamotrigine with valproic acid.</td></tr>
</table>

If necessary, the dose can be increased to 400 mg / day.

Adjustment of daily doses of lamotrigine in patients with bipolar disorder after adding other drugs to therapy

<table>
<tr><th>Dosing regimen</th><th>Current stabilization dose of Lamotrigine</th><th>Week 1</th><th>Week 2</th><th>Week 3, etc</th></tr>
<tr><td rowspan="3">Addition of lamotrigine glucuronidation inhibitors (e.g. valproic acid), depending on the initial dose of lamotrigine</td><td>200mg</td><td colspan="3">100mg</td></tr>
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<tr><td>400mg</td><td colspan="3">200mg</td></tr>
<tr><td rowspan="3">Attachment of inducers of glucuronidation of lamotrigine in patients not receiving valproic acid, depending on the initial dose of lamotrigine. This regimen should be used when using phenytoin, carbamazepine, phenobarbital, primidone, or other inducers of lamotrigine glucuronidation.</td><td>200mg</td><td>200mg</td><td>300mg</td><td>400mg</td></tr>
<tr><td>150mg</td><td>150mg</td><td>225mg</td><td>300mg</td></tr>
<tr><td>100mg</td><td>100mg</td><td>150mg</td><td>200mg</td></tr>
<tr><td>Addition of other psychotropic or antiepileptic drugs with no significant pharmacokinetic interaction with lamotrigine (eg lithium preparations, bupropion, olanzapine, oxcarbazepine)</td><td colspan="4">Maintain target dose achieved during boost regimen (200 mg/day; dose range 100 to 400 mg)</td></tr>
<tr><td colspan="5">Note: in patients taking AEDs, the nature of the pharmacokinetic interaction of which with lamotrigine is currently not studied, a dosing regimen is recommended, as when taking lamotrigine with valproic acid.</td></tr>
</table>

Overdose:

Single administrations of doses exceeding the maximum therapeutic dose by 10–20 times have been reported.

Symptoms: nystagmus, ataxia, impaired consciousness up to coma.

Treatment: hospitalization and appropriate symptomatic therapy. In case of recent (less than 2 hours) administration of the drug, gastric lavage should be carried out.

Manufacturer:
Sazar : Alkaloid ad Skopje (North Macedonia)
Lamolep : Gedeon Richter (Hungary)
Lamitor : Torrent Pharmaceutical (India)
Lamictal : GlaxoSmithKline (Poland)

Reliable supplier with fast Worldwide shipping:
RussianMeds Online Store
https://russianmeds.com

Storage:
The temperature is not above 25 °C (77 °F)