ADVERSE REACTIONS

5.7 Laboratory Tests

Aseptic Meningitis, Serositis, Nephropathy.

Serious Skin Rashes

Discontinue at the first sign of rash, unless the rash is life threatening. DRESS typically, although not exclusively, presents with fever, rash, and/or lymphadenopathy in association with other organ system involvement. Some cases of DRESS with lamotrigine have been fatal or life threatening. DRESS may occur more frequently in patients with human leukocyte antigen (HLA) B*5701.

Blood dyscrasias (e.g., neutropenia, thrombocytopenia, aplastic anemia) may herald a serious medical event and that the patient should report any such occurrence to a physician immediately.

Laboratory Tests

Clinical Worsening and Suicide Risk Associated With Bipolar Disorder:

Clinical Worsening and Suicide Risk Associated With Bipolar Disorder:

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

Epilepsy:

• Withdrawal seizures
• Status epilepticus
• Seizures with no apparent precipitating cause

• Suicidal behavior and ideation

• Mental status changes

Bipolar Disorder:

• Depression
• Mania

Other:

• Hemorrhage
• Seizures
• Hypothyroidism

5.8 Other Information

5.9 Pregnancy

5.10 Nursing Mothers

5.11 Sudden Unexplained Death in Epilepsy (SUDEP)

5.12 Lactation

5.13 Children

5.14 Geriatric Use

5.15 Renal Impairment

5.16 hepatic impairment

5.17 Use in Specific Populations

5.17.1 Pregnancy

There have been reports of blood dyscrasias that may or may not be associated with multiorgan hypersensitivity (also known as DRESS) which may be fatal with lamotrigine. DRESS has been reported in all age groups and in both males and females. The risk of DRESS may be increased in patients taking lamotrigine with concomitant valproate or carbamazepine. Other AEDs that may increase the risk of DRESS include carbamazepine, phenytoin, phenobarbital, primidone, the protease inhibitors lopinavir/ritonavir, and the protease inhibitors lopinavir/ritonavir.

5.17.2 Lactation

5.17.3 Children

5.17.4 Geriatric Use

5.17.5 Renal Impairment

5.17.6 Hepatic Impairment

5.17.7 Use in Specific Populations

5.18 Carcinogenesis, Mutagenesis, Impairment of Fertility

5.18.1 Carcinogenesis

5.18.2 Mutagenesis

5.18.3 Impairment of Fertility

5.19 Human Pharmacology

5.19.1 Drug Interactions

5.19.2 Laboratory Tests

5.19.3 Other Information

5.20 Animal Toxicology

5.20.1 Acute Toxicity

5.20.2 Chronic Toxicity

5.20.3 Reproductive Toxicology

5.20.4 Carcinogenicity

5.20.5 Mutagenicity

5.20.6 Impairment of Fertility

5.20.7 Human Pharmacology

5.20.8 Drug Interactions

5.20.9 Laboratory Tests

5.20.10 Other Information

5.21 Additional Information

5.21.1 Carcinogenesis

5.21.2 Mutagenesis

5.21.3 Impairment of Fertility

5.21.4 Human Pharmacology

5.21.5 Drug Interactions

5.21.6 Laboratory Tests

5.21.7 Other Information

5.22 References

5.23 US Patent

5.24 Other Information

5.25 Additional Information

5.26 References

5.27 US Patent

5.28 Other Information

5.29 Additional Information

5.30 References

5.31 US Patent

5.32 Other Information

5.33 Additional Information

5.34 References

5.35 US Patent

5.36 Other Information

5.37 Additional Information

5.38 References

5.39 US Patent

5.40 Other Information

5.41 Additional Information

5.42 References

5.43 US Patent

5.44 Other Information

5.45 Additional Information

5.46 References

5.47 US Patent

5.48 Other Information

5.49 Additional Information

5.50 References

5.51 US Patent

5.52 Other Information

5.53 Additional Information

5.54 References

5.55 US Patent

5.56 Other Information

5.57 Additional Information

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5.59 US Patent

5.60 Other Information

5.61 Additional Information

5.62 References

5.63 US Patent

5.64 Other Information

5.65 Additional Information

5.66 References

5.67 US Patent

5.68 Other Information

5.69 Additional Information

5.70 References

5.71 US Patent

5.72 Other Information

5.73 Additional Information

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5.75 US Patent

5.76 Other Information

5.77 Additional Information

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5.79 US Patent

5.80 Other Information

5.81 Additional Information

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5.83 US Patent

5.84 Other Information

5.85 Additional Information

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5.87 US Patent

5.88 Other Information

5.89 Additional Information

5.90 References

5.91 US Patent

5.92 Other Information

5.93 Additional Information

5.94 References

5.95 US Patent

5.96 Other Information

5.97 Additional Information

5.98 References

5.99 US Patent

5.100 Other Information

5.101 Additional Information

5.102 References
Clinical Comment

• ↑ adverse reactions are defined as those occurring in at least 1/100 patients; Experience in patients with hepatic impairment is limited. Based on a clinical pharmacology study in 24 subjects with mild, moderate, and severe liver impairment disease or other drug therapy.

• Respond differently from younger patients or exhibit a different safety profile than that of younger patients. In general, dose selection for an elderly patient should

• Be guided more by drug therapy and less by age. Other factors to consider include (1) dosage regimen, (2) body composition change, (3) decreased hepatic, renal, and drug metabolism, and (4) increased sensitivity to drug effects; for a complete discussion, see Clinical Pharmacology section

• Pregnancy Registry:

• lamotrigine. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish

• Relationship to drug exposure. Generally, systemic drug exposure was increased in patients aged ≥65 years (mean creatinine clearance = 61 mL/min, range: 33 to 108 mL/min). The mean half-life of lamotrigine in these subjects was 31.2 hours (range: 24.5 to 43.4 hours), with a range of 24.5 to 96.5 hours among the elderly patients who participated in clinical studies. For further information, see Clinical Pharmacology section

• Cardiovascular System:

• Acne, alopecia, hirsutism, maculopapular rash, skin discoloration, urticaria.

• Changes in electrolyte levels may occur. Monitor serum electrolytes regularly during therapy, especially in patients with hepatic impairment. Increase the plasma levels of lamotrigine in patients with hepatic impairment and monitor for possible signs of toxicity.

• Increase in the incidence of rash in patients with normal renal function compared to patients with renal impairment.

• Clinical Pharmacology section

• Lamotrigine is known to induce phase I enzymes, including CYP 2C9, CYP 2C19, and CYP 3A4, and phase II enzymes, including UGT 1A9 and 1A1. There may be a decreased metabolism of drugs that are substrates for these enzymes. As a result, the plasma levels of certain drugs may increase when lamotrigine is added or decreased. Therefore, the plasma levels of drugs that are substrates for these enzymes should be monitored, and the dose of the concomitant drug(s) should be adjusted if necessary.

• Lamotrigine is a substrate for CYP 2C9, CYP 2C19, and CYP 3A4. As a result, the plasma levels of drugs that are substrates for these enzymes may be decreased when lamotrigine is added or decreased. Therefore, the plasma levels of drugs that are substrates for these enzymes should be monitored, and the dose of the concomitant drug(s) should be increased if necessary.

• Significant drug interactions with lamotrigine are summarized in this section. Additional details of these drug interaction studies are provided in the Clinical Pharmacology section

• In an open-label study, 24 healthy volunteers (12 males and 12 females) received lamotrigine 400 mg daily for 7 days. On Days 1 and 7, the plasma concentrations of metabolites of lamotrigine were determined by high-performance liquid chromatography. The mean half-life of lamotrigine was 31.2 hours (range: 24.5 to 43.4 hours), with a range of 24.5 to 96.5 hours among the elderly patients who participated in clinical studies. For further information, see Clinical Pharmacology section

• The pharmacokinetics of lamotrigine following a single 100-mg dose of lamotrigine were evaluated in 24 subjects with mild, moderate, and severe liver impairment disease or other drug therapy.

• Inhibition of lamotrigine glucuronidation by drugs that induce CYP 2C9 and CYP 3A4 may increase lamotrigine plasma concentrations at steady state following doses of 50 to 350 mg twice daily. In 2 small studies (n = 7 and 8) of patients with epilepsy who were maintained on other AEDs, there was a linear relationship between dose and lamotrigine plasma concentrations at steady state following doses of 50 to 350 mg twice daily.

• There is no way to tell if a mild rash will become more serious. A serious skin rash can happen at any time during treatment with lamotrigine.

• Do not take 2 doses at the same time.