

Pregnancy

There are insufficient data available on the use of Lamonil in human pregnancy to evaluate its safety. As with most drugs, Lamonil should not be used in pregnancy unless, in the opinion of the physician, the potential benefits of treatment to the mother outweigh any possible risks to the developing fetus.

Lactation

Preliminary data indicate that lamotrigine passes into breast milk in concentrations usually of the order of 40-45% of the plasma concentration. In the small number of infants known to have been breastfed, the dose of lamotrigine received was calculated to be approximately 0.06-0.75 mg/kg/24 hours, and no adverse experiences were reported.

OVERDOSAGE

Symptoms and signs: Ingestion of between 1.35 and 4 g lamotrigine has been reported in a few patients. Clinical consequences were not severe, signs and symptoms included nystagmus, ataxia, dizziness, somnolence, headache and vomiting.

A patient who ingested a dose calculated to be between 4 and 5 g lamotrigine was admitted to hospital with coma lasting 8-12 Hours followed by recovery over the next 2 to 3 days. A further patient who ingested 5.6 g lamotrigine was found unconscious. Following treatment with activated charcoal for suspected intoxication the patient recovered after sleeping for 16 hours.

MODE OF ACTION

The results pharmacological studies suggest that lamotrigine is a use-dependent blocker of voltage gated sodium channels. It produces a use- and voltage-dependent block of sustained repetitive firing in cultured neurones and inhibits pathological release of glutamate (the amino acid which plays a key role in the generation of epileptic seizures), as well as inhibiting glutamate-evoked bursts of action potentials.

Treatment: In the event of overdosage, the patient should be admitted to hospital and given appropriate supportive therapy. Gastric lavage should be performed if indicated.

PRECAUTIONS

Store below 30°C in a dry place, protect from light.
To be dispensed on the prescription of a registered medical practitioner only.
Keep out of the reach of children.

PRESENTATION

Lamonil tablets are available in following strength.

- Lamonil 25mg tablets in blister pack of 30's
- Lamonil 50mg tablets in blister pack of 30's
- Lamonil 100mg tablets in blister pack of 30's

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر خشک جگہ پر رکھیں،
روشنی سے بچائیں۔ صرف رجسٹرڈ ڈاکٹر کے نسخے پر فروخت کریں۔
بچوں کی پہنچ سے دور رکھیں۔

Manufactured by:

Platinum
Pharmaceuticals (Pvt) Ltd.
A-20, North Western Industrial Zone,
Bin Qasim, Karachi-75020, Pakistan.

QAR No. AW17-0313

[Lamonil]
(Lamotrigine)

[لیمونیل]
(لیموٹریجن)

25mg Tablets

Each tablet contains :
Lamotrigine (U.S.P.)..... 25 mg
Product Complies U.S.P. Specs.

۵۰ ملی گرام ۵۰ ملی گرام اور ۱۰۰ ملی گرام گولیاں

50mg Tablets

Each tablet contains :
Lamotrigine (U.S.P.)..... 50 mg
Product Complies U.S.P. Specs.

100mg Tablets

Each tablet contains :
Lamotrigine (U.S.P.) 100 mg
Product Complies U.S.P. Specs.

INDICATIONS

Adults: Lamonil is indicated for use as adjunctive or monotherapy in the treatment of epilepsy, for partial seizures and generalized seizures, including tonic-clonic seizures and the seizures associated with Lennox-Gastaut Syndrome.

Children: Lamonil is indicated as adjunctive therapy in the treatment of epilepsy, for partial seizures and generalised seizures including tonic-clonic seizures and the seizures associated with Lennox-Gastaut syndrome.

After epileptic control has been achieved during adjunctive therapy, concomitant antiepileptic drugs (AED's) may be withdrawn and patients continued on Lamonil monotherapy.

DOSAGE AND ADMINISTRATION

Dosage in monotherapy

Adults (over 12 years of age): The initial Lamonil dose in monotherapy is 25 mg once a day for two weeks, followed by 50 mg once a day for two weeks. Thereafter, the dose should be increased by a maximum of 50 - 100 mg every 1-2 weeks until the optimal response is achieved. The usual maintenance dose to achieve optimal response is 100 - 200 mg/day given once a day or as two divided doses. Some patients have required 500 mg/day of Lamonil to achieve the desired response.

Recommended dose escalation for adults (over 12 years of age) on monotherapy.

Weeks 1 + 2	Weeks 3 + 4	Maintenance Dose
25 mg (Once a day)	25 mg (Once a day)	100-200mg (once a day or two divided doses) To achieve maintenance, doses may be increased by 50-100mg every 1 -2 weeks

Dosage in add-on therapy

Adults (over 12 years of age): In patients taking valproate with/without any other anti-epileptic drug (AED), the initial Lamonil dose is 25 mg every alternate day for two weeks, followed by 25 mg once a day for two weeks. Thereafter, the dose should be increased by a maximum of 25-50 mg every 1-2 weeks until the optimal response is achieved. The usual maintenance dose to achieve optimal response is 100-200 mg/day given once a day or in two divided doses.

In those patients taking enzyme inducing AEDs with/without other AEDs (except valproate), the initial Lamonil dose is 50 mg once a day for two weeks, followed by 100 mg/day given in two divided doses for two weeks. Thereafter, the dose should be increased by a maximum of 100 mg every 1-2 weeks until the optimal response is achieved. The usual maintenance dose to achieve optimal response is 200-400 mg/day given in two divided doses.

Some patients have required 700 mg/day of Lamoniil to achieve the desired response.

Recommended dose escalation for adults (over 12 years of age) on combined drug therapy.

	Weeks 1 + 2	Weeks 3 + 4	Maintenance Dose
Valproate with/without any other AEDs	12.5mg (given 25 mg alternate days)	25 mg (once a day)	100-200mg (once a day or two divided doses) To achieve maintenance, doses may be increased by 25-50 mg every 1-2 weeks
Enzyme inducing AEDs* without other AEDs (except valproate)	50 mg (once a day)	100 mg (two divided doses)	200-400mg (two divided doses) To achieve maintenance, doses may be increased by 100 mg every 1-2 weeks
*e.g phenytoin, carbamazepine, phenobarbitone and primidone			
NOTE: In patients taking AEDs where the pharmacokinetic interaction with lamotrigine is currently not known, the dose escalation as recommended for lamotrigine with concurrent valproate, should be used.			

Children (2 to 12 years of age): To ensure a therapeutic dose is maintained the weight of a child must be monitored and the dose reviewed as weight changes occur, if the doses calculated for children, according to bodyweight, do not equate to whole tablets the dose to be administered is that equal to the lower number of whole tablets.

In patients taking valproate with/without any other AED, the initial Lamoniil dose is 0.2 mg/kg bodyweight/day given once a day for two weeks, followed by 0.5 mg/kg/day once a day for two weeks. Thereafter, the dose should be increased by a maximum of 0.5-1 mg/kg every 1-2 weeks until the optimal response is achieved. The usual maintenance dose to achieve optimal response is 1-5 mg/kg/day given once a day or in two divided doses, with a maximum of 200 mg/day.

In those patients taking enzyme inducing AEDs with/without other AEDs (except valproate), the initial Lamoniil dose is 2 mg/kg bodyweight/day given in two divided doses for two weeks, followed by 5 mg/kg/day given in two divided doses for two weeks.

Thereafter, the dose should be increased by a maximum of 2-3 mg/kg every 1-2 weeks until the optimal response is achieved. The usual maintenance dose to achieve optimal response is 5-15 mg/kg/day given in two divided doses, with a maximum of 400 mg/day.

Recommended dose escalation for children aged 2-12 years (total daily dose in mg/kg bodyweight/day) on combined drug therapy.

	Weeks 1 + 2	Weeks 3 + 4	Maintenance Dose
Valproate with/without any other AEDs	0.2 mg/ kg** (once a day)	0.5 mg/kg (once a day)	1-5 mg/kg (once a day or two divided doses) To achieve maintenance, doses may be increased by 0.5-1 mg/kg every 1-2 weeks, to a maximum of 200 mg/day
Enzyme inducing AEDs* with/ without other AEDs (except valproate)	2 mg/kg (two divided doses)	5 mg/kg (two divided doses)	5-15 mg/kg (two divided doses) To achieve maintenance, doses may be increased by 2-3 mg/kg every 1-2 weeks, to a maximum of 400 mg/day
*e.g phenytoin, carbamazepine, phenobarbitone and primidone			
NOTE: In patients taking AEDs where the pharmacokinetic interaction with lamotrigine is currently not known, the dose escalation as recommended for lamotrigine with concurrent valproate, should be used.			

**NOTE: If the calculated daily dose in 2.5-5 mg, then 5mg Lamoniil may be taken on alternate days for the first two weeks.

If the calculated daily dose is less than 2.5 mg, then Lamoniil should not be administered. When concomitant antiepileptic drug are withdrawn to achieve Lamoniil paediatric monotherapy consideration should be given to the effect this may have on lamotrigine pharmacokinetics and the dose be adjusted appropriately.

It is likely that patients aged 2-6 years will require a maintenance dose at the higher end of the recommended range.

CONTRA-INDICATIONS

Lamoniil is contraindicated in individuals with known hypersensitivity to lamotrigine.

PRECAUTIONS AND WARNINGS

There have been reports of adverse skin reactions, which have generally occurred within the first 8 weeks after initiation of lamotrigine (Lamoniil) treatment. The majority of rashes are mild and self limiting, however serious, potentially life threatening skin rashes including Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported. The approximate incidence of serious skin rashes in adults is 1 in 1000. The risk is higher in children than in adults. Available data from a number of studies suggest the incidence in children requiring hospitalization ranges from 1 in 300 to 1 in 100. In children, the initial presentation of a rash can be mistaken for an infection, physicians should consider the possibility of a drug reaction in children that develop symptoms of rash and fever during the first eight weeks of therapy.

Additionally the overall risk of rash appears to be strongly associated with:

- High initial doses of lamotrigine and exceeding the recommended dose escalation of lamotrigine therapy (see Dosage and Administration).
- Concomitant use of valproate, which increases the mean half life of lamotrigine nearly two fold

As with other AEDs, abrupt withdrawal of Lamoniil may provoke rebound seizures. Unless safety concerns (for example rash) require an abrupt withdrawal, the dose of Lamoniil should be gradually decreased over a period of 2 weeks. When concomitant antiepileptic drugs are withdrawn to achieve Lamoniil monotherapy or other antiepileptic drugs (AEDs) are added-on to Lamoniil monotherapy consideration should be given to the effect this may have on lamotrigine pharmacokinetics.

In single dose studies in subjects with end stage renal failure, plasma concentrations of lamotrigine were not significantly altered. However, accumulation of the glucuronide metabolite is to be expected; caution should therefore be exercised in treating patients with renal failure. Lamoniil is cleared primarily by metabolism in the liver. No studies have been carried out in patients with significant impairment of hepatic function. Until such data become available Lamoniil cannot be recommended in this condition.

There are reports in the literature that severe convulsive seizures including status epilepticus may lead to rhabdomyolysis, multiorgan dysfunction and disseminated intravascular coagulation, sometimes with fatal outcome. Similar cases have occurred in association with the use of Lamoniil.

DRUG INTERACTIONS

There is no evidence that lamotrigine causes clinically significant induction or inhibition of hepatic oxidative drug-metabolizing enzymes. Lamotrigine may induce its own metabolism but the effect is modest and unlikely to have significant clinical consequences.

Antiepileptic, agents (such as phenytoin, carbamazepine, phenobarbitone and primidone) which induce hepatic drug-metabolizing enzymes enhance the metabolism of lamotrigine. Valproate, which competes with lamotrigine for hepatic drug-metabolizing enzymes, reduces the metabolism of lamotrigine. There have been reports of central nervous system events including dizziness, ataxia, diplopia, blurred vision and nausea in patients taking carbamazepine following the introduction of lamotrigine. These events usually resolve when the dose of carbamazepine is reduced.