

SCHEDULING STATUS

S3

PROPRIETARY NAME AND DOSAGE FORM

DYNA-LAMOTRIGINE 25 mg tablets

DYNA-LAMOTRIGINE 50 mg tablets

DYNA-LAMOTRIGINE 100 mg tablets

DYNA-LAMOTRIGINE 200 mg tablets

COMPOSITION

DYNA-LAMOTRIGINE 25 mg: Each tablet contains 25 mg lamotrigine.

DYNA-LAMOTRIGINE 50 mg: Each tablet contains 50 mg lamotrigine.

DYNA-LAMOTRIGINE 100 mg: Each tablet contains 100 mg lamotrigine.

DYNA-LAMOTRIGINE 200 mg: Each tablet contains 200 mg lamotrigine.

PHARMACOLOGICAL CLASSIFICATION

A.2.5 Antiepileptics

PHARMACOLOGICAL ACTION

Lamotrigine blocks voltage-sensitive sodium channels, thereby stabilising neuronal membranes and inhibiting neurotransmitter release, principally that of glutamate, an excitatory amino acid which is thought to play a major role in the generation of epileptic seizures.

Pharmacokinetics:

Lamotrigine is well and completely absorbed from the gut. The absorption is unaffected by food.

The time to peak concentration is 1,4 to 4,8 hours. The mean elimination half-life is 25 ± 10 hours and the pharmacokinetic profile is linear up to 450 mg, the highest single dose tested. The half-life of lamotrigine is affected by concomitant use of enzyme-inducing drugs such as phenytoin, carbamazepine, phenobarbital or primidone with a mean value of approximately 14 hours.

The half-life of lamotrigine increases to approximately 59 hours when co-administered with valproic acid alone (see DOSAGE AND DIRECTIONS FOR USE).

Following multiple administration of lamotrigine (150 mg twice daily) there is modest induction of its own metabolism, resulting in a 25% decrease in the elimination half-life at steady state. Lamotrigine is moderately (55%) bound to plasma proteins.

Clearance adjusted for bodyweight is higher in children aged 12 years and under than in adults, with the highest values in children under 5 years. The half-life of lamotrigine is generally shorter in children than in adults with a mean value of approximately 7 hours when given with enzyme-inducing drugs such as carbamazepine and phenytoin.

INDICATIONS

Adults and children over 12 years

DYNA-LAMOTRIGINE is indicated as monotherapy or add-on treatment of partial epilepsy with or without secondary generalised tonic-clonic seizures and in primary generalised tonic-clonic seizures.

Children 2 to 12 years

DYNA-LAMOTRIGINE is indicated as add-on treatment of partial epilepsy with or without secondary generalised tonic-clonic seizures not satisfactorily controlled with other antiepileptic medicines.

Monotherapy in children under 12 years of age is not recommended until such time as adequate information is made available from controlled trials in this particular target population.

Lennox-Gastaut Syndrome

DYNA-LAMOTRIGINE is indicated as add-on treatment for seizures associated with Lennox-Gastaut Syndrome.

CONTRA-INDICATIONS

DYNA-LAMOTRIGINE is contra-indicated in the following circumstances:

- Individuals with known hypersensitivity to lamotrigine.
- The safety of **DYNA-LAMOTRIGINE** in pregnancy and lactation has not been established.
- Renal and hepatic function impairment. Hepatic metabolism followed by renal excretion is the principle route of elimination of lamotrigine and until more information is available, the use of **DYNA-LAMOTRIGINE** in patients with impairment of hepatic or renal function is contra-indicated.

- Patients over the age of 65 years.

WARNINGS

Severe convulsive seizures including status epilepticus may lead to rhabdomyolysis, multiorgan dysfunction and disseminated intravascular coagulation, usually with fatal outcome. Similar cases have occurred in association with the use of **DYNA-LAMOTRIGINE**.

Patients receiving **DYNA-LAMOTRIGINE** should be closely monitored and changes in hepatic, renal and clotting parameters looked for. Patients should be warned to consult their doctors immediately if rashes or flu-like symptoms associated with hypersensitivity develop, especially within the first month of starting treatment with **DYNA-LAMOTRIGINE**. Withdrawal of therapy should be considered if unexplained rashes, fever, flu-like symptoms, drowsiness or worsening of seizure control occur.

Dosage recommendations should not be exceeded to minimise the risk of developing rash, requiring withdrawal of therapy. Abrupt withdrawal of **DYNA-LAMOTRIGINE** may provoke rebound seizures. The risk may be reduced by tapering off the withdrawal of **DYNA-LAMOTRIGINE** over a period of two weeks.

The weight of a child must be monitored and the dose reviewed as weight changes occur. If the dose calculated for children, according to bodyweight, does not equate to whole tablets, the dose to be administered is that equal to the lower number of whole tablets.

Skin Reactions

Adverse skin reactions have been reported, which have generally occurred within the first 8 weeks of starting **DYNA-LAMOTRIGINE**. Although the majority of rashes usually resolve when lamotrigine is discontinued, irreversible scarring and cases of associated death have been reported. A mild rash may subside even with continuation of **DYNA-LAMOTRIGINE** therapy, however, close monitoring is essential. Less frequently, serious and potentially life-threatening skin rashes including Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported especially in children and in patients using valproate (see **SIDE-EFFECTS AND SPECIAL PRECAUTIONS**). Isolated cases have been reported after prolonged treatment (6 months).

The estimated incidence of serious skin rashes in adults is 1 in 1000. The risk is higher in children than in adults. Some children may require hospitalisation because of the seriousness of skin rashes.

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.

The overall risk of rash appears to be strongly associated with:

- High initial doses of **DYNA-LAMOTRIGINE** and exceeding the recommended dose escalation of **DYNA-LAMOTRIGINE** (see DOSAGE AND DIRECTIONS FOR USE).
- Concomitant use of valproate, which increases the mean half-life of **DYNA-LAMOTRIGINE** nearly two-fold (see DOSAGE AND DIRECTIONS FOR USE).

As it cannot be predicated reliably which rashes will prove to be life-threatening, all patients (adults and children) who develop a rash should be promptly evaluated and **DYNA-LAMOTRIGINE** withdrawn immediately unless the rash is clearly not drug related.

Rash has also been reported as part of a hypersensitivity syndrome associated with a variable pattern of systemic symptoms including fever, lymphadenopathy, pruritus, facial oedema, abnormalities of the blood and liver, and thrombocytopenia. The syndrome shown a wide spectrum of clinical severity and may lead to disseminated intravascular coagulation and multiorgan failure. It is important that early manifestations of hypersensitivity (e.g. fever, lymphadenopathy) may be present even though rash is not evident. If such signs and symptoms are present the patient should be evaluated immediately and **DYNA-LAMOTRIGINE** therapy discontinued if an alternative aetiology cannot be immediately established.

INTERACTIONS

Enzyme-inducing agents (such as phenytoin, carbamazepine, phenobarbitone and primidone) enhance the metabolism of **DYNA-LAMOTRIGINE** leading to an increased clearance and subsequent reduction of the elimination half-life of **DYNA-LAMOTRIGINE**. Concomitant use of valproic acid increases the half-life and plasma concentrations of **DYNA-LAMOTRIGINE** due to competition for hepatic glucuronidation. Plasma concentrations of valproic acid may decrease slightly when **DYNA-LAMOTRIGINE** is added (see pharmacokinetics).

No evidence has shown that **DYNA-LAMOTRIGINE** affects the plasma concentration of other concomitant antiepileptic drugs. **DYNA-LAMOTRIGINE** does not displace other antiepileptic drugs from protein binding sites.

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

DYNA-LAMOTRIGINE does not seem to affect plasma concentrations of ethinyloestradiol and levonorgestrel following the administration of the oral contraceptives pill. However, any change in the menstrual bleeding pattern should be investigated.

PREGNANCY AND LACTATION

The safety of **DYNA-LAMOTRIGINE** in pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE

It is important to adhere to the recommended dosages especially in combination therapy with valproate where one-tenth of the normal DYNA-LAMOTRIGINE dose is used.

Do not exceed the maximum dosage (see WARNINGS).

To ensure a therapeutic dose is maintained the weight of a child must be monitored and the dose reviewed if necessary. If the doses calculated for children, according to bodyweight, does not equate to whole tablets, the dose to be administered is that equal to the lower number of whole tablets.

Dosage in Monotherapy:

Adults and children over 12 years of age:

Initial dose in monotherapy: 25 mg once daily for two weeks, followed by 50 mg once daily for two weeks. The dosage may be increased by a maximum of 50 mg - 100 mg every 1 - 2 weeks until the optimal response is achieved.

Maintenance dose in monotherapy: The usual dose to achieve optimal response is 100 - 200 mg per day given in one dose or two divided doses. Some patients have required 500 mg/day of **DYNA-LAMOTRIGINE** to achieve the desired response.

Adults and Children over 12 years (total daily dose):

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

The recommended initial dose and subsequent dose escalation should not be exceeded to minimise the risk of skin rash (see WARNINGS).

Dosage in Add-On Therapy:**Adults and children over 12 years of age:**

With enzyme-inducing anticonvulsants only: The initial dose is 50 mg once a day for two weeks, then 100 mg a day, divided into two doses, for two weeks. The dosage may be increased by a maximum of 100 mg every 1 - 2 weeks until the optimal response is achieved. The usual maintenance dose is 200 - 400 mg/day given in two divided doses.

With enzyme-inducing anticonvulsants and valproic acid: The initial dose is 25 mg once every other day for two weeks, then 25 mg once a day for two weeks. The dosage may be increased by a maximum of 25 - 50 mg a day every 1 to 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 patients taking antiepileptic drugs where the pharmacokinetic interaction with **DYNA-LAMOTRIGINE** is currently not known, the dose escalation as recommended for **DYNA-LAMOTRIGINE** with concurrent valproate should be used. Thereafter, the dose should be increased until the optimal response is achieved.

Adults and Children over 12 years (total daily dose):

	Weeks 1 & 2	Weeks 3 & 4	Maintenance Dose
Patients not taking sodium valproate	50 mg (once a day)	100 mg (two divided doses)	200 - 400 mg (two divided doses). To achieve maintenance, doses may be increased by 100 mg every 1 - 2 weeks

Patients taking sodium valproate	25 mg (on alternative days)	25 mg (once a day)	100 - 200 mg (once a day or two divided doses). To achieve maintenance, doses may be increased by 25 - 50 mg every 1 - 2 weeks
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The recommended initial dose and subsequent dose escalation should not be exceeded to minimise the risk of skin rash (see WARNINGS).

Children aged 2 to 12 years:

The initial **DYNA-LAMOTRIGINE** dose in those not taking sodium valproate is 0,6 mg/kg body mass/day given in two divided doses for two weeks, followed by 1,2 mg/kg/day for two weeks. Thereafter, the dose should be increased by a maximum of 1,2 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. A maximum daily dose of 400 mg must not be exceeded.

In those patients taking sodium valproate, the initial **DYNA-LAMOTRIGINE** dose is 0,15 mg/kg body mass/day given once a day for two weeks, followed by 0,3 mg/kg/day given once a day for two weeks. Thereafter, the dose should be increased by a maximum of 0,3 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. A maximum daily dose of 200 mg must not be exceeded.

In patients taking antiepileptic drugs where the pharmacokinetic interaction with **DYNA-LAMOTRIGINE** is currently not known, the dose escalation as recommended for **DYNA-LAMOTRIGINE** with concurrent valproate should be used. Thereafter, the dose should be increased until the optimal response is achieved.

Children Aged 2 to 12 Years (Total Daily Dose)

	Weeks 1 & 2	Weeks 3 & 4	Maintenance Dose
Patients not taking sodium valproate	0,6 mg/kg (two divided doses)	1,2 mg/kg (two divided doses)	1,2 mg/kg increments every 1 - 2 weeks to achieve a maintenance dose of 5 - 15 mg/kg (two divided doses) to a maximum of 400 mg/day.
Patients taking sodium valproate	0,15 mg/kg (once a day)	0,3 mg/kg (once a day)	0,3 mg/kg increments every 1 - 2 weeks to achieve a maintenance dose of 1 - 5 mg/kg (once a day or two divided doses) to a maximum of 200 mg.

The recommended initial dose and subsequent dose escalation should not be exceeded to minimise the risk of skin rash (see WARNINGS).

Note: If the calculated daily dose is 1 - 2 mg, then 2 mg **DYNA-LAMOTRIGINE** may be taken on alternate days for the first two weeks. If the calculated daily dose is less than 1 mg, then **DYNA-LAMOTRIGINE** should not be administered.

Patients aged 2 - 6 years may require a maintenance dose at the higher end of the recommended range.

Dosage in seizures associated with Lennox-Gastaut Syndrome

The dosing guidelines outlined above for both adults and children aged 2 - 12 years apply for the treatment of seizures associated with Lennox-Gastaut Syndrome.

Children aged less than 2 years

There is insufficient information on the use of **DYNA-LAMOTRIGINE** in children aged less than two years.

SIDE EFFECTS AND SPECIAL PRECAUTIONS

Side Effects:

Blood and lymphatic system disorders

Less frequent: Blood dyscrasias including anaemia, eosinophilia, leucopenia or thrombocytopenia.

The following have been reported but the frequency is unknown:

Agranulocytosis; disseminated intravascular coagulation; neutropenia; red cell aplasia.

Immune system disorders

Less frequent: Hypersensitivity syndrome. Symptoms such as fever, malaise, influenza-like symptoms, drowsiness, lymphadenopathy, facial oedema, and rarely, hepatic dysfunction, leucopenia and thrombocytopenia have been reported in conjunction with rashes as part of a hypersensitivity syndrome (see WARNINGS).

Skin and subcutaneous disorders

Frequent: Skin rash.

Less frequent: Stevens-Johnson syndrome, toxic epidermal necrolysis, photosensitivity, erythema multiforme. Severe skin rashes, including Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported, especially in children. The skin rash usually occurs within 8 weeks of starting **DYNA-LAMOTRIGINE** and resolves on withdrawal of **DYNA-LAMOTRIGINE**.

Nervous system disorders

Frequent: Headache; tiredness; dizziness; drowsiness; coordination abnormalities; ataxia.

Less frequent: Anxiety; confusion; depression; irritability; increased seizures; nystagmus and insomnia; tremor; amnesia; slurred speech.

Eye disorders

Frequent: Vision abnormalities, including blurred vision and diplopia.

Respiratory, thoracic and mediastinal disorders

Less frequent: Angioedema (trouble in breathing, swelling of face, mouth, hands or feet); rhinitis.

The following have been reported but the frequency is unknown:

Apnoea; oesophagitis.

Gastrointestinal disorders

Frequent: Nausea and vomiting.

Less frequent: Constipation; diarrhoea; dyspepsia.

Musculoskeletal disorders

Less frequent: Asthenia; pain.

General disorders

The following have been reported but the frequency is unknown:

Multi-organ failure; dryness of the mouth.

Special precautions:

DYNA-LAMOTRIGINE inhibits dihydrofolate reductase and should be used with caution with other folate antagonists.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Symptoms and signs

Sedation, ataxia, diplopia, nausea and vomiting have been reported with very high serum lamotrigine concentrations of more than 15 µg/ml.

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.

IDENTIFICATION

DYNA-LAMOTRIGINE 25 mg: Beige, round, flat tablet, embossed "MC" with diameter 6,0 mm.

DYNA-LAMOTRIGINE 50 mg: Beige, round, flat, scored tablets with diameter 8,0 mm.

DYNA-LAMOTRIGINE 100 mg: Beige, round, flat, scored tablets with diameter 9,5 mm.

DYNA-LAMOTRIGINE 200 mg: Beige, round, flat, scored tablets with diameter 12,7 mm.

PRESENTATION

DYNA-LAMOTRIGINE 25 mg, 50 mg, 100 mg and 200 mg are packed into PVC/Aluminium blister pack of 60 tablets, 10 tablets per blister.

STORAGE INSTRUCTIONS

Store below 25 °C in the original pack. Protect against moisture and light. Do not remove the blister from the outer carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS

DYNA-LAMOTRIGINE 25 mg: 40/2.5/0173

DYNA-LAMOTRIGINE 50 mg: 40/2.5/0169

DYNA-LAMOTRIGINE 100 mg: 40/2.5/0166

DYNA-LAMOTRIGINE 200 mg: 40/2.5/0167

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

Pharma Dynamics (Pty) Ltd.

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DATE OF PUBLICATION OF THE PACKAGE INSERT:

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SKEDULERINGSTATUS

S3

EIENDOMSNAAM EN DOSEERVORM

DYNA-LAMOTRIGINE 25 mg tablette

DYNA-LAMOTRIGINE 50 mg tablette

DYNA-LAMOTRIGINE 100 mg tablette

DYNA-LAMOTRIGINE 200 mg tablette

SAMESTELLING

DYNA-LAMOTRIGINE 25 mg: Elke tablet bevat 25 mg lamotrigien.

DYNA-LAMOTRIGINE 50 mg: Elke tablet bevat 50 mg lamotrigien.

DYNA-LAMOTRIGINE 100 mg: Elke tablet bevat 100 mg lamotrigien.

DYNA-LAMOTRIGINE 200 mg: Elke tablet bevat 200 mg lamotrigien.

FARMAKOLOGIESE KLASSIFIKASIE

A.2.5 Anti-epileptika

FARMAKOLOGIESE WERKING

Lamotrigien blokkeer spannings sensitiewe natriumkanale en stabiliseer sodoende neuronale membrane en rem die vrystelling van neurotransmitters, hoofsaaklik dié van glutamaat, 'n eksitatoriese aminosuur wat blykbaar 'n belangrike rol in die ontstaan van epileptiese toevale speel.

Farmakokinetika:

Lamotrigien word goed en volledig uit die spysverteringstelsel geabsorbeer. Die absorpsie word nie deur voedsel beïnvloed nie.

Die tyd tot piek konsentrasie is 1,4 tot 4,8 uur. Die gemiddelde eliminasihalfleeftyd is 25 ± 10 uur en die farmakokinetiese profiel is lineêr tot 450 mg wat die hoogste enkeldosis is wat getoets is. Die halfleeftyd van lamotrigien word deur gelyktydige gebruik van ensieminduseerders soos fenitoïen, karbamasepien, fenobarbitoon of primidoon beïnvloed met 'n gemiddelde waarde van ongeveer 14 uur.

Die halfleeftyd van lamotrigien verleng tot ongeveer 59 uur as dit saam met valproësuur alleen toegedien word (kyk DOSIS EN GEBRUIKSAANWYSINGS).

Na veelvoudige toediening van lamotrigien (150 mg twee keer per dag) is daar 'n matige induksie van sy eie metabolisme wat tot 'n afname van 25% in die eliminasihalfleeftyd by gelykvlakke lei. Lamotrigien bind matig (55%) aan plasmaproteïene.

Die opruiming aangepas vir liggaamsmassa is hoër in kinders van 12 jaar en jonger as in volwassenes, met die hoogste waardes in kinders jonger as 5 jaar. Die halfleeftyd van lamotrigien is oor die algemeen korter in kinders as in volwassenes met 'n gemiddelde waarde van ongeveer 7 uur as dit met ensiemremmers soos karbaamasepien en fenitoïen gegee word.

INDIKASIES

Volwassenes en kinders ouer as 12 jaar

DYNA-LAMOTRIGINE is aangedui as monoterapie of bykomende behandeling vir gedeeltelike epilepsie met of sonder sekondêre algemene tonies-kloniese toevale en vir primêre algemene tonies-kloniese toevale.

Kinders 2 tot 12 jaar

DYNA-LAMOTRIGINE is aangedui as bykomende behandeling vir gedeeltelike epilepsie met of sonder sekondêre algemene tonies-kloniese toevale wat nie bevredigend met ander anti-epileptiese middels beheer word nie.

Totdat voldoende inligting uit gekontroleerde proewe met kinders jonger as 12 jaar beskikbaar kom, word monoterapie vir hierdie besondere teikenpopulasie nie aanbeveel nie.

Lennox-Gastautsindroom

DYNA-LAMOTRIGINE is aangedui as bykomende behandeling vir toevale vanweë die Lennox-Gastautsindroom.

KONTRA-INDIKASIES

DYNA-LAMOTRIGINE is onder die volgende omstandighede teenaangedui:

- Individue met 'n bekende hipersensitiwiteit teenoor lamotrigien.
- Die veiligheid van **DYNA-LAMOTRIGINE** tydens swangerskap en borsvoeding is nie bepaal nie.
- Swak nier- en lewerfunksie. Metabolisme in die lewer gevolg deur uitskeiding deur die nier is die hoofroete van uitskeiding van lamotrigien en totdat meer inligting beskikbaar

is, is die gebruik van **DYNA-LAMOTRIGINE** vir pasiënte met swak lewer of nierfunksie teenaangedui.

- Pasiënte van 65 jaar en ouer.

WAARSKUWINGS

Ernstige konvulsiewe toevale, waaronder status epilepticus, kan tot rabdomiolise, disfunksie van verskeie organe en gedissemineerde intravaskulêre koagulasie lei en gewoonlik met dodelike gevolge. Soortgelyke gevalle het met die gebruik van **DYNA-LAMOTRIGINE** voorgekom.

Pasiënte wat **DYNA-LAMOTRIGINE** ontvang, moet noukeurig gemonitor word en veranderings in lewer- en nierfunksie en bloedstolling moet dopgehou word. Pasiënte moet gewaarsku word om hulle dokters onmiddellik te raadpleeg as veluitslag of griepsimptome aanduidend van hipersensitiwiteit veral in die eerste maand na aanvang van behandeling met **DYNA-LAMOTRIGINE** ontwikkel. Staking van behandeling moet oorweeg word as onverklaarbare veluitslag, koors, griepsimptome, lomerigheid of 'n verergering in toevale voorkom.

Aanbevole dosis moet nie oorskry word nie ten einde die risiko te minimaliseer vir veluitslag wat staking van behandeling kan noodsaak. Skielike onttrekking van **DYNA-LAMOTRIGINE** kan die terugkeer van toevale uitlok. Die risiko kan verminder word deur die onttrekking van **DYNA-LAMOTRIGINE** geleidelik oor 'n periode van twee weke in te faseer.

Die massa van 'n kind moet gemonitor en die dosis moet daarvolgens aangepas word. As die dosis wat volgens liggaamsgewig vir kinders bereken is nie op 'n heel tablet uitwerk nie, moet 'n dosis gelyk aan die kleiner aantal heel tablette toegedien word.

Velreaksies

Nadelige velreaksies is aangemeld wat gewoonlik binne die eerste 8 weke na aanvang van behandeling met **DYNA-LAMOTRIGINE** voorgekom het. Hoewel die meerderheid gevalle van veluitslag gewoonlik opklaar as lamotrigien gestaak word, is onomkeerbare letsels en gevalle van sterftes as gevolg hiervan aangemeld. 'n Ligte veluitslag kan selfs met voortgesette behandeling met **DYNA-LAMOTRIGINE** opklaar, hoewel noukeurige monitoring noodsaaklik is. In enkele gevalle is ernstige en moontlik lewensbedreigende veluitslag, waaronder die Stevens-Johnsonsindroom en toksiese epidermale nekrolise, aangemeld en veral in kinders en in pasiënte wat valproaat gebruik het (kyk **NEWE-EFFEKTE EN**

SPEZIALE VOORSORGMAATREËLS). Enkele gevalle is na langdurige behandeling (6 maande) aangemeld.

Die beraamde voorkoms van ernstige veluitslag in volwassenes is 1 in 1000. Die risiko is hoër in kinders as in volwassenes. Vanweë die graad van die veluitslag mag dit nodig wees om sommige kinders in die hospitaal op te neem.

In kinders kan die aanvanklike voorkoms van 'n veluitslag met 'n infeksie verwar word; dokters moet die moontlikheid van 'n geneesmiddelreaksie in gedagte hou vir kinders wat tydens die eerste agt weke van behandeling simptome van veluitslag en koors ontwikkel.

Dit lyk asof die risiko vir veluitslag sterk saam met die volgende voorkom:

- Hoë aanvanklike dosisse van **DYNA-LAMOTRIGINE** en as die aanbevole eskalering van die dosis van **DYNA-LAMOTRIGINE** oorskry word (kyk DOSIS EN GEBRUIKSAANWYSINGS).
- Gelyktydige gebruik van valproaat wat die gemiddelde halfleeftyd van **DYNA-LAMOTRIGINE** bykans tweevoudig verleng (kyk DOSIS EN GEBRUIKSAANWYSINGS).

Omdat dit nie betroubaar voorspel kan word watter tipe veluitslag lewensbedreigend kan wees nie, moet alle pasiënte (volwassenes en kinders) wat veluitslag ontwikkel spoedig beoordeel word en **DYNA-LAMOTRIGINE** moet onmiddellik onttrek word tensy die veluitslag duidelik nie met die middel verband hou nie.

Veluitslag is ook aangemeld as deel van 'n hipersensitiwiteitsindroom wat met 'n wisselende patroon van sistemiese simptome gepaard gaan, waaronder koors, limfadenopatie, pruritus, edeem in die gesig, abnormaliteite in die bloed en lewer en trombositopenie. Die sindroom het klinies gewissel van minder ernstig tot baie ernstig en kan tot verspreide intravaskulêre koagulاسie en versaking van verskeie organe lei. Dit is belangrik dat vroeë manifestasies van hipersensitiwiteit (bv. koors, limfadenopatie) teenwoordig kan wees selfs as veluitslag nie opvallend is nie. As sulke tekens en simptome teenwoordig is, moet die pasiënt onmiddellik beoordeel en behandeling met **DYNA-LAMOTRIGINE** moet gestaak word as 'n alternatiewe etiologie nie onmiddellik bepaal kan word nie.

INTERAKSIES

Ensieminduseerders (soos fenitoïen, karbamasepien, fenobarbitoon en primidoon) versnel die metabolisme van **DYNA-LAMOTRIGINE** wat tot 'n hoër opruiming en gevolglike afname in die eliminasihalfleeftyd van **DYNA-LAMOTRIGINE** lei. Gelyktydige gebruik van valproësuur verleng die halfleeftyd en verhoog die plasmakonsentrasies van **DYNA-LAMOTRIGINE** vanweë kompetisie vir hepatiese glukuronidering. Plasmakonsentrasies van valproësuur kan effens afneem as **DYNA-LAMOTRIGINE** bygevoeg word (kyk farmakokinetika).

Daar is geen getuienis dat **DYNA-LAMOTRIGINE** die plasmakonsentrasie beïnvloed van ander anti-epileptiese middels wat saam gegee word nie. **DYNA-LAMOTRIGINE** verplaas nie ander anti-epileptiese middels van bindingsplekke aan proteïene nie.

Daar is geen getuienis dat **DYNA-LAMOTRIGINE** beduidende induksie of inhibisie veroorsaak van oksiderende ensieme in die lewer wat geneesmiddels metaboliseer nie. **DYNA-LAMOTRIGINE** kan sy eie metabolisme induseer, maar die effek is matig en het waarskynlik geen klinies beduidende gevolge nie.

Dit lyk nie asof **DYNA-LAMOTRIGINE** plasmakonsentrasies van etinielestadiol en levonorgestrel na toediening van die voorbehoedpil beïnvloed nie. Enige verandering in menstruele bloeding moet egter ondersoek word.

SWANGERSKAP EN BORSVOEDING

Die veiligheid van **DYNA-LAMOTRIGINE** tydens swangerskap en borsvoeding is nie bepaal nie.

DOSIS EN GEBRUIKSAANWYSINGS

Dit is belangrik om by die aanbevole dosisse te hou en veral tydens kombinasiebehandeling met valproaat waar een tiende van die normale dosis van DYNA-LAMOTRIGINE gebruik moet word.

Die maksimum dosis moet nie oorskry word nie (kyk WAARSKUWINGS).

Om te verseker dat 'n terapeutiese dosis volgehou word, moet die gewig van 'n kind gemonitor en die dosis dienooreenkomstig aangepas word. As die dosis bereken vir die kind volgens liggaamsmassa nie op 'n heel tablet uitwerk nie, moet die dosis wat toegedien word die kleiner getal heel tablette wees.

Dosering tydens monoterapie:

Volwassenes en kinders ouer as 12 jaar:

Aanvangsdosis tydens monoterapie: 25 mg een keer per dag vir 2 weke, gevolg deur 50 mg een keer per dag vir 2 weke. Die dosis kan elke 1 - 2 weke met 'n maksimum van 50 - 100 mg verhoog word totdat die optimale respons verkry word.

Onderhoudsdosis tydens monoterapie: Die gewone dosis om optimale respons te bereik, is 100 - 200 mg per dag gegee as een of twee verdeelde doserings. Party pasiënte het 500 mg/dag **DYNA-LAMOTRIGINE** nodig om die verlangde respons te verkry.

Volwassenes en kinders ouer as 12 jaar (totale daaglikse dosis)

Weke 1 & 2	Weke 3 & 4	Onderhoudsdosis
25 mg (een keer per dag)	50 mg (een keer per dag)	100 - 200 mg (een keer per dag of twee verdeelde doserings). Om onderhoud te verkry, kan dosisse elke 1 - 2 weke met 50 - 100 mg verhoog word.

Die aanbevole aanvangsdosis en daaropvolgende verhoging in dosisse moet nie oorskry word nie om die risiko vir veluitslag te verminder (kyk WAARSKUWINGS).

Dosis as bykomende middel:

Volwassenes en kinders ouer as 12 jaar:

Slegs met ensieminduserende antikonvulsante: Die aanvanklike dosis is 50 mg een keer per dag vir twee weke, dan 100 mg per dag verdeel in twee doserings vir twee weke. Die dosis kan elke 1 - 2 weke met 'n maksimum van 100 mg verhoog word totdat die optimale respons verkry word. Die gewone onderhoudsdosis is 200 - 400 mg/dag gegee as twee verdeelde doserings.

Met ensieminduserende antikonvulsante en valproësuur: Die aanvanklike dosis is 25 mg een keer elke tweede dag vir 2 weke, dan 25 mg een keer per dag vir 2 weke. Die dosis kan elke 1 tot 2 weke met 'n maksimum van 25 tot 50 mg per dag verhoog word totdat die optimale respons verkry word. Die gewone onderhoudsdosis om optimale respons te verkry, is 100 tot 200 mg/dag gegee een keer per dag of as twee verdeelde doserings.

Vir pasiënte wat anti-epileptiese middels gebruik waarvan die farmakokinetiese interaksie met **DYNA-LAMOTRIGINE** tans onbekend is, moet die eskalering in die dosis soos aanbeveel vir **DYNA-LAMOTRIGINE** saam met valproaat gebruik word. Daarna moet die dosis verhoog word totdat die optimale respons verkry word.

Volwassenes en kinders ouer as 12 jaar (totale daaglikse dosis)

	Weke 1 & 2	Weke 3 & 4	Onderhoudsdosis
Pasiënte wat nie natriumvalproaat gebruik nie	50 mg (een keer per dag)	100 mg (twee verdeelde doserings)	200 – 400 mg (twee verdeelde doserings). Om onderhoud te bereik, kan die dosis elke 1 - 2 weke met 100 mg verhoog word.
Pasiënte wat natriumvalproaat gebruik	25 mg (op alternatiewe dae)	25 mg (een keer per dag)	100 - 200 mg (een keer per dag of twee verdeelde doserings). Om onderhoud te verkry, kan dosis elke 1 – 2 weke met 25 – 50 mg verhoog word.

Die aanbevole aanvangsdosis en daaropvolgende verhoging in dosis moet nie oorskry word nie om die risiko vir veluitslag te verminder (kyk WAARSKUWINGS).

Kinders 2 tot 12 jaar oud:

Die aanvangsdosis van **DYNA-LAMOTRIGINE** vir diegene wat nie natriumvalproaat gebruik nie, is 0,6 mg/kg liggaamsmassa/dag as twee verdeelde dosis vir twee weke gevolg deur 1,2 mg/kg/dag vir twee weke. Daarna moet die dosis elke 1 tot 2 weke met 'n maksimum van 1,2 mg/kg verhoog word totdat die optimale respons verkry word. Die gewone onderhoudsdosis is 5 - 15 mg/kg/dag gegee as twee verdeelde doserings. 'n Maksimum daaglikse dosis van 400 mg moet nie oorskry word nie.

Die aanvangsdosis van **DYNA-LAMOTRIGINE** vir diegene wat natriumvalproaat gebruik, is 0,15 mg/kg liggaamsmassa/dag een keer per dag vir twee weke gevolg deur 0,3 mg/kg/dag een keer per dag vir twee weke. Daarna moet die dosis elke 1 tot 2 weke met 'n maksimum van 0,3 mg/kg verhoog word totdat die optimale respons verkry word. Die gewone onderhoudsdosis om optimale respons te verkry, is 1 - 5 mg/kg/dag gegee een keer per dag

of as twee verdeelde doserings. 'n Maksimum daaglikse dosis van 200 mg moet nie oorskry word nie.

Vir pasiënte wat anti-epileptiese middels gebruik waarvan die farmakokinetiese interaksie met **DYNA-LAMOTRIGINE** tans onbekend is, moet die eskalering in die dosis soos aanbeveel vir **DYNA-LAMOTRIGINE** saam met valproaat gebruik word. Daarna moet die dosis verhoog word totdat die optimale respons verkry word.

Kinders 2 tot 12 jaar (totale daaglikse dosis)

	Weke 1 & 2	Weke 3 & 4	Onderhoudsdosis
Pasiënte wat nie natriumvalproaat gebruik nie	0,6 mg/kg (twee verdeelde doserings)	1,2 mg/kg (twee verdeelde doserings)	1,2 mg/kg inkrementele elke 1 - 2 weke om 'n onderhoudsdosis van 5 - 15 mg/kg (twee verdeelde doserings) te bereik tot 'n maksimum van 400 mg/dag.
Pasiënte wat natriumvalproaat gebruik	0,15 mg/kg (een keer per dag)	0,3 mg/kg (een keer per dag)	0,3 mg/kg inkrementele elke 1 - 2 weke om 'n onderhoudsdosis van 1 - 5 mg/kg (een keer per dag of twee verdeelde doserings) te bereik tot 'n maksimum van 200 mg.

Die aanbevole aanvangsdosis en daaropvolgende verhoging in dosisse moet nie oorskry word nie om die risiko vir veluitslag te verminder (kyk WAARSKUWINGS).

Let wel: As die berekende daaglikse dosis 1 tot 2 mg is, kan 2 mg **DYNA-LAMOTRIGINE** vir die eerste twee weke op alternatiewe dae gebruik word. As die berekende daaglikse dosis minder as 1 mg is, moet **DYNA-LAMOTRIGINE** nie gebruik word nie.

Pasiënte van 2 - 6 jaar oud kan 'n onderhoudsdosis aan die hoër kant van die aanbevole dosisgebied nodig hê.

Dosis vir toevale saam met die Lennox-Gastautsindroom

Die riglyne vir dosering soos hierbo vir sowel volwassenes en kinders van 2 tot 12 jaar oud geld ook vir die behandeling van toevale wat met die Lennox-Gastautsindroom gepaardgaan.

Kinders jonger as 2 jaar

Daar is onvoldoende inligting oor die gebruik van **DYNA-LAMOTRIGINE** vir kinders jonger as twee jaar.

NEWE EFFEKTE EN SPESIALE VOORSORGMAATREËLS

Nuwe-effekte:

Versteurings van die bloed en limfatiese stelsel

Minder dikwels: Bloeddiskrasie waaronder anemie, eosinofilie, leukopenie of trombositopenie.

Die volgende het voorgekom, maar die frekwensie is onbekend.

Agranulotose; gedissemineerde intravaskulêre koagulasie; neutropenie; rooiselaplasie.

Versteurings van immuunstelsel

Minder dikwels: Die hipersensitiwiteitsindroom. Simptome soos koors, ongesteldheid, griepsimptome, lomerigheid, limfadenopatie, edeem in die gesig en soms lewerdisfunksie, leukopenie en trombositopenie is saam met veluitslag aangemeld as deel van 'n hipersensitiwiteitsindroom (kyk WAARSKUWINGS).

Versteurings van die vel en subkutane weefsel

Dikwels: Veluitslag

Minder dikwels: Stevens-Johnsonsindroom, toksiese epidermale nekrolise, fotosensitiwiteit, multivorme eriteem. Ernstige veluitslag waaronder die Stevens-Johnsonsindroom en toksiese epidermale nekrolise is veral in kinders aangemeld. Die veluitslag verskyn gewoonlik binne 8 weke na aanvang van behandeling met **DYNA-LAMOTRIGINE** en klaar na staking van **DYNA-LAMOTRIGINE** op.

Versteurings van die senustelsel

Dikwels: Hoofpyn, moegheid, duiseligheid, lomerigheid, probleme met koördinasie, ataksie.

Minder dikwels: Angs, verwardheid, depressie, geïrriteerdheid, meer toevale, nistagmus en slaaploosheid, tremor, geheueverlies, sleepspraak.

Oogversteurings

Dikwels: Versteurings in visie, waaronder dowwe visie en diplopie.

Respiratoriese, toragiese en mediastinale versteurings

Minder dikwels: Angio-edeem (probleme met asemhaling, swelling van die gesig, mond, hande of voete).

Die volgende het voorgekom, maar die frekwensie is onbekend.

Apnee, esofagitis.

Gastro-intestinale versteurings

Dikwels: Naarheid en braking.

Minder dikwels: Hardlywigheid, diarree, slegte spysvertering.

Muskuloskeletale versteurings

Minder dikwels: Astenie, pyn.

Algemene versteurings

Die volgende het voorgekom, maar die frekwensie is onbekend.

Multi-orgaanversaking, droë mond.

Spesiale voorsorgmaatreëls

DYNA-LAMOTRIGINE rem dihidrofolaatreduktase en moet versigtig saam met ander folaatantagoniste gebruik word.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VIR DIE BEHANDELING DAARVAN

Simptome en tekens

Sedasie, ataksie, diplopie, naarheid en braking is met baie hoë konsentrasies van meer as 15 µg/ml lamotrigien in die serum aangemeld.

Behandeling

In geval van oordosering moet die pasiënt in die hospitaal opgeneem en geskikte ondersteunende behandeling ontvang. Maagspoeling moet gedoen word, indien aangedui.

IDENTIFIKASIE

DYNA-LAMOTRIGINE 25 mg: Roomkleurige, ronde, plat tablet met "MC" daarop gedruk en deursnit 6,0 mm.

DYNA-LAMOTRIGINE 50 mg: Roomkleurige, ronde, plat tablette met breeklyn en deursnit 8,0 mm.

DYNA-LAMOTRIGINE 100 mg: Roomkleurige, ronde, plat tablette met breeklyn en deursnit 9,5 mm.

DYNA-LAMOTRIGINE 200 mg: Roomkleurige, ronde, plat tablette met breeklyn en deursnit 12,7 mm.

AANBIEDING

DYNA-LAMOTRIGINE 25 mg, 50 mg, 100 mg en 200 mg is verpak in PVC/Aluminiumstulppak met 60 tablette, 10 tablette per stulppak.

BERGINGSINSTRUKSIES

Bewaar benede 25°C in die oorspronklike houer. Beskerm teen vog en lig. Hou die stulpstrok in die karton totdat dit benodig word.

HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMERS

DYNA-LAMOTRIGINE 25 mg: 40/2.5/0173

DYNA-LAMOTRIGINE 50 mg: 40/2.5/0169

DYNA-LAMOTRIGINE 100 mg: 40/2.5/0166

DYNA-LAMOTRIGINE 200 mg: 40/2.5/0167

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT

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