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Lamotrigine and skin reactions

Lamotrigine is an anti-epileptic medication which may also be used as a "mood-stabiliser" in the treatment of bipolar disorder. It is known to have the potential to cause skin reactions varying in severity from mild rashes to serious, potentially life-threatening reactions such as Stevens-Johnson syndrome and toxic epidermal necrosis. Serious skin reactions occur in about 1 in 1000 adult patients and 1 in 50-300 children, and usually manifest within the first eight weeks of lamotrigine treatment. Other rare but serious side effects of lamotrigine that can present with a rash include multi-organ hypersensitivity syndrome and aseptic meningitis.

Although many lamotrigine-related skin reactions are mild, mild rashes can progress to severe rashes or to systemic involvement and there is no way to reliably predict which will develop into potentially life-threatening reactions. Discontinuation of lamotrigine is therefore recommended at the first sign of rash (unless it is clearly not drug related). If necessary, a specialist opinion should be sought. The majority of rashes reported with lamotrigine resolve on withdrawal, however some patients have developed irreversible scarring and there have been rare cases with fatal outcomes. It is important to note that, as with other anticonvulsant drugs used for the treatment of epilepsy, abrupt discontinuation may provoke rebound seizures. In general, rechallenge with lamotrigine (with lower initial doses and slower escalation) should only be considered if the rash was mild and the potential benefit clearly outweighs the risk.

The main risk factors for serious skin reactions with lamotrigine have been identified as: high initial doses; rapid dose escalation; and concurrent use with sodium valproate (which decreases lamotrigine clearance). A history of anti-epileptic induced rash appears to increase the risk of non-serious rash with lamotrigine.

Dosing guidelines for lamotrigine (which specify initial doses, dose titration schedules, and maintenance doses) have been developed in order to minimise the likelihood of rash occurring and should be followed carefully - clinicians can refer to the Australian Medicines Handbook for details. Dosing varies according to whether lamotrigine treatment is being commenced in: patients taking drugs known not to affect lamotrigine metabolism; patients taking valproate; or patients taking enzyme inducers (e.g. carbamazepine or phenytoin) and not taking valproate. If the effect of concomitant medications on lamotrigine metabolism is unknown, it is safest to use the regimen for patients taking valproate. Recommencement after an interruption to lamotrigine therapy may require re-titration according to the dosing guidelines. The greater the time interval that has elapsed since the previous dose, the more consideration should be given to this.

All patients treated with lamotrigine should be alerted to the risk of developing rash and should be advised to seek medical advice immediately on first sign of a rash or any skin reaction, or any sign of hypersensitivity, such as fever or lymphadenopathy.

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