



SINGAPORE DENTAL COUNCIL

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All registered Dental Professionals

TESTING OF HLA-B*1502 allele prior to initiation of Carbamazepine in new patients

The Singapore Dental Council (SDC) would like to remind all dental professionals of the circular sent jointly by MOH and HSA dated 30 Apr 2013, recommending genotyping of the HLA-B*1502 allele prior to the initiation of **Carbamazepine (CBZ)** in new patients of Asian ancestry, as genotyping for this group of patients for all indications of the drug is now considered the standard of care.

To reiterate the pertinent points:

Carbamazepine (CBZ) has been registered in Singapore since 1988 and is currently available as Tegretol[®] (Novartis) and six generic products. It is indicated for the treatment of epilepsy and other conditions such as diabetic neuropathy, trigeminal neuralgia and bipolar disorders. While CBZ is an effective drug and is the drug of choice for several conditions, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) which are associated with significant mortality and long-term morbidity have been reported with its use.

Between 2003 and 2012, HSA received 131 local serious reports of CBZ-induced SJS/TEN (average of 15 reports per year). Since the beginning of this year, HSA has received four reports of CBZ-induced SJS/TEN. A one-time HLA-B*1502 genotyping test helps distinguish high-risk patients who should avoid CBZ from low-risk patients who are able to continue to use this low-cost yet effective medicine.

HSA is working with the product licence holders of CBZ products to strengthen the package inserts to reflect the new recommendation that testing for the presence of HLA-B*1502 allele is highly recommended in new patients with Asian ancestry.

All healthcare professionals are therefore advised on the following:

- CBZ should not be prescribed prior to the return of HLA-B*1502 test results. This is because of the possibility of development and progression of SJS/TEN in susceptible patients even after prompt discontinuation of the drug.
- The use of CBZ should be avoided and treatment alternatives are recommended in patients who are found to be positive for HLA-B*1502. Preliminary data have shown a suspected association between this allele and phenytoin-induced SJS/TEN, although the effect size is not as large. As a precaution, patients who are identified to be positive for the HLA-B*1502 allele should also not be prescribed phenytoin.

- Genetic testing should not substitute for appropriate clinical vigilance and patient management. Although rare, patients negative for HLA-B*1502 could still develop SJS/TEN as the role of other factors such as drug dose, concomitant medications and comorbidities have not been studied.

Testing facility

The HLA-B*1502 test is available at the NUH Molecular Diagnosis Centre (MDC). Each test costs \$187 (excluding GST) and the estimated turnaround time is two to four working days. All subsidised patients in the MOH-funded restructured hospitals and institutions will be subsidised for this test as detailed in a recent circular dated 15 April 2013 from MOH. Clinicians may send their patients' samples directly to NUH MDC, via the NUH Referral Laboratories (NRL), Tel: 6778 5171. For this test, 3 to 5ml of blood is to be collected in a 5-ml EDTA-anti-coagulated sample tube and kept at 4°C before despatch.

The Council would like to remind all dentists to adhere to the above recommendations.

Yours faithfully



Clin A/Prof Patrick Tseng
Registrar