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(來函請敍明此檔案號碼) DH DO DIMC/7-30/1
(IN REPLY PLEASE QUOTE THIS FILE REF.)

23 Mar 2026

Dear Healthcare Professionals,

FDA is Requiring Warning about Vitamin B6 Deficiency and Associated Seizures for Drug Products containing Carbidopa/Levodopa

Your attention is drawn to the United States Food and Drug Administration's (FDA) announcement requiring warning about Vitamin B6 deficiency and associated seizures for drug products containing carbidopa/levodopa.

FDA has notified application holders for all drug products containing carbidopa/levodopa that the Agency is requiring the addition of a warning, and corresponding revisions, to the prescribing information to state that these medications, approved to treat symptoms of Parkinson's disease, can cause vitamin B6 deficiency and vitamin B6 deficiency-associated seizures. The warning directs health care professionals to evaluate baseline vitamin B6 levels prior to starting patients on treatment with carbidopa/levodopa therapies and periodically while on treatment and to supplement with vitamin B6 as necessary.

What Are Drug Products Containing Carbidopa/Levodopa?

Drug products containing carbidopa/levodopa are approved to treat symptoms of Parkinson's disease, a progressive nervous system disorder. Levodopa is the metabolic precursor to dopamine, a neurotransmitter in the brain that declines in patients with Parkinson's disease, leading to motor symptoms such as tremors, rigidity and bradykinesia (slow movements). Carbidopa inhibits the decarboxylation of peripheral levodopa, making more levodopa available for delivery to the brain.

Drug products containing carbidopa/levodopa approved to treat symptoms of Parkinson's disease may contain both carbidopa and levodopa (trade names: Crexont, Dhivy, Duopa, Rytary, Sinemet, and Sinemet CR); carbidopa/levodopa/entacapone (trade name: Stalevo); or foscarbidopa/foslevodopa (trade name: Vyalev), which is converted to active carbidopa/levodopa in the body. These products are available in multiple formulations and may

be administered by several different routes, including oral tablets, an enteral (intestinal) suspension, and a subcutaneous injection for continuous infusion.

Drug products containing carbidopa/levodopa can deplete vitamin B6 levels during the process by which levodopa is converted to dopamine. Additionally, carbidopa binds to the active form of vitamin B6, which creates additional functional loss of vitamin B6.

What Should Patients and Caregivers Do?

Patients and caregivers should be aware that taking drug products containing carbidopa/levodopa can lead to vitamin B6 deficiency, which can increase the risk of seizures. To monitor for vitamin B6 deficiency, your health care professional should evaluate your vitamin B6 levels before starting treatment with a drug product containing carbidopa/levodopa, periodically during treatment, and if symptoms of vitamin B6 deficiency appear during treatment. These symptoms include seizures, as well as depression; confusion; inflammation of the lips, tongue, and skin; and nerve damage causing numbness, tingling, sharp pain, or muscle weakness. Patients should take vitamin B6 supplements as recommended in consultation with a health care professional.

Higher doses of carbidopa/levodopa may increase the risk of vitamin B6 deficiency. Many of the cases of seizures reported with carbidopa/levodopa use did not respond to traditional anti-seizure medications but resolved after vitamin B6 administration.

What Should Health Care Professionals Do?

Health care professionals should evaluate vitamin B6 levels before starting patients on treatment with drug products containing carbidopa/levodopa, periodically during treatment, and if symptoms of vitamin B6 deficiency appear during treatment. Health care professionals should consider whether vitamin B6 supplementation is necessary. Higher doses of carbidopa/levodopa may increase the risk of vitamin B6 deficiency.

Health care professionals should be aware that seizures associated with the use of a product containing carbidopa and levodopa do not respond to traditional anti-seizure medications but resolve after vitamin B6 administration. Furthermore, select anti-seizure medications may further worsen a vitamin B6 deficiency. Health care professionals should inform patients of these risks.

What Did FDA Find?

FDA conducted a safety review and identified 14 cases of seizures linked to vitamin B6 deficiency in patients using drug products containing carbidopa/levodopa. The 14 cases included postmarketing reports submitted to FDA (13 reports) or found in the medical literature (1 report), so there are likely additional cases about which we are unaware. All of the reviewed cases involved levodopa doses exceeding 1,000 mg daily, with higher doses (>1,500 mg levodopa) associated with shorter duration from treatment initiation to identification of vitamin

B6 deficiency. The seizure cases were split among oral formulations and an enteral suspension, with latency periods ranging from 23 to 132 months. The seizures have typically presented as focal onset seizures with secondary generalization, consistent with seizures observed with vitamin B6-dependent epilepsy, and progression to status epilepticus was observed in some cases, indicating an urgent need for rapid identification and treatment.

In these cases of reported seizures, there was additional clinical evidence supportive of vitamin B6 deficiency, including elevated homocysteine levels in four cases, microcytic or normocytic anemia in three cases, and neuropsychiatric symptoms in four cases. Of the 9 patients treated with vitamin B6 supplementation, all 9 had resolution of their seizures, despite the majority of these patients previously demonstrating a lack of response to multiple antiseizure medications. Two fatalities occurred, both with documented low vitamin B6 levels and poorly controlled seizures.

The review found no cases of vitamin B6-associated seizures associated with carbidopa/levodopa/entacapone products or with the injectable carbidopa/levodopa product, which may reflect lower usage patterns, more recent approval dates, and/or different dosing and administration requirements. However, biological plausibility suggests there may be a similar risk across all drug products containing carbidopa/levodopa, as vitamin B6 deficiency was also observed in the clinical trials that supported the original approval of the injectable carbidopa/levodopa product. Based on the available data, FDA concluded there is reasonable evidence of a causal association between drug products containing carbidopa/levodopa and vitamin B6 deficiency-associated seizures.

Please refer to the following website in FDA for details:
https://www.fda.gov/drugs/drug-safety-and-availability/fda-requiring-warning-about-vitamin-b6-deficiency-and-associated-seizures-drug-products-containing

In Hong Kong, Vyalev containing foscarbidopa/foslevodopa is not a registered pharmaceutical product, while there are registered pharmaceutical products containing carbidopa and levodopa including carbidopa/levodopa (8 products), carbidopa/levodopa/entacapone (8 products) and levodopa/benserazide (3 products). All products are prescription-only medicines. So far, the Department of Health (DH) has received one case of adverse drug reaction report with regard to carbidopa/levodopa and levodopa/benserazide; and one case with regard to levodopa/benserazide, but these cases were not reported as vitamin B6 deficiency or vitamin B6 deficiency-associated seizures. In light of the above FDA's announcement, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board of Hong Kong.

Please note that this letter serves as a means for the DH to communicate important new safety information about registered pharmaceutical products with healthcare professionals in Hong Kong and is not intended to serve as guidelines or to replace professional clinical judgement.

Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Clinical Trials and Pharmacovigilance Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,

(Clive CHAN)
for Assistant Director (Drug)