SFDA SAFETY SIGNAL

"A signal is defined by the SFDA as reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously. Usually more than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the information. A signal is a hypothesis together with data and arguments and it is important to note that a signal is not only uncertain but also preliminary in nature"

16-5-2023

Saudi Food and Drug Authority (SFDA) – Safety Signal of Amlodipine and Risk of Hyperkalaemia

The Saudi Food and Drug Authority (SFDA) recommends all health care professionals to be aware of the safety signal of ***Hyperkalaemia*** *associated with the use of* ***Amlodipine****. The signal has been originated as a result of routine pharmacovigilance monitoring activities.*

Introduction

Amlodipine, initially approved by the FDA in 1987, is a popular antihypertensive drug belonging to the group of drugs called dihydropyridine calcium channel blockers. Due to their selectivity for the peripheral blood vessels, dihydropyridine calcium channel blockers are associated with a lower incidence of myocardial depression and cardiac conduction abnormalities than other calcium channel blockers.[1] Amlodipine is commonly used in the treatment of high blood pressure and angina. Amlodipine has antioxidant properties and an ability to enhance the production of nitric oxide (NO), an important vasodilator that decreases blood pressure.[2] Hyperkalemia is defined as a serum or plasma potassium level above the upper limits of normal, usually greater than 5.0 mEq/L to 5.5 mEq/L. While mild hyperkalemia is usually asymptomatic, high potassium levels may cause life-threatening cardiac arrhythmias, muscle weakness, or paralysis. Symptoms usually develop at higher levels, 6.5 mEq/L to 7 mEq/L, but the rate of change is more important than the numerical value. Patients with chronic hyperkalemia may be asymptomatic at increased levels, while patients with dramatic, acute potassium shifts may develop severe symptoms at lower ones. Infants have higher baseline levels than children and adults.[3] The aim of this review is to evaluate the risk of Hyperkalemia associated with the use of Amlodipine and to suggest regulatory recommendations if required.

Methodology

Signal Detection team at the National Pharmacovigilance Center (NPC) of Saudi Food and Drug Authority (SFDA) performed a comprehensive signal review using its national database as well as the World Health Organization (WHO) database (VigiBase), to retrieve related information for assessing the causality between Amlodipine and the risk of Hyperkalemia. [4][5] WHO-Uppsala Monitoring Centre (UMC) criteria have been used as standard for assessing the causality of the reported cases. [6]

Results

Case Review: The search in the local database resulted in one unassessable case. [4] The number of resulted cases for the combined drug/adverse drug reaction is 225 global ICSRs as of February 26th 2023. [5] The reviewers have extracted and assessed thirty cases with highest completeness score. The causality assessment resulted in two probable cases, sixteen possible cases, six unlikely case and six cases were not assessable.

Data Mining: The disproportionality of the observed and the expected reporting rate for drug/adverse drug reaction pair is estimated using information component (IC), a tool developed by WHO-UMC to measure the reporting ratio. Positive IC reflects higher statistical association while negative values indicates less statistical association. The result of (IC= 1.0) revealed a positive statistical association for the drug/ADR combination, which means "Hyperkalemia" with the use of "Amlodipine" have been observed more than expected when compared to other medications available in WHO database. [5]

Literature: A reported case of an 89-year-old female patient who presented to the emergency department with a medical history of essential hypertension treated with amlodipine 10 mg oral daily and furosemide 40 mg oral daily, type 2 diabetes mellitus treated with neutral protamine Hagedorn (NPH) insulin, paroxysmal atrial fibrillation (AF) anticoagulated with edoxaban 60 mg once daily, She had been previously hospitalized due to prostration and sinus bradycardia, the electrocardiogram (EKG) presenting a first-degree AV blockade and right bundle branch block (RBBB). Patient lab result was indicating, hyponatremia and hyperkalemia of were documented. [7]

Additional evidence: Hyperkalemia is mentioned in Saudi Drug Information System, Medicines and Healthcare products Regulatory Agency and European Medicines Agency in the Interaction section. [8] [9] [10]

Conclusion

The weighted cumulative evidences identified from causality assessment of the reported cases, and literature are sufficient to support a causal association between Amlodipine and the risk of Hyperkalemia . Health regulators and health care professionals must be aware of this potential risk and it is advisable to monitor any signs or symptoms in treated patients.

Report Adverse Drug Events (ADRs) to the SFDA

The SFDA urges both healthcare professionals and patients to continue reporting adverse drug reactions (ADRs) resulted from using any medications to the SFDA either online, by regular mail or by fax, using the following contact information:

National Pharmacovigilance Center (NPC)
Saudi Food and Drug Authority-Drug sector
4904 northern ring branch rd
Hittin District
Riyadh 13513 – 7148
Kingdom of Saudi Arabia
Toll free number: 19999
Email: NPC.Drug@sfda.gov.sa

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