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"

7-3-2021

Saudi Food and Drug Authority (SFDA) – Safety Signal of Teriparatide and the Risk of Shivering

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

Introduction Teriparatide is the active fragment of endogenous human parathyroid hormone which can cause a stimulation of bone formation by direct effects on bone forming cells (osteoblasts) indirectly increasing the intestinal absorption of calcium and increasing the tubular re-absorption of calcium and excretion of phosphate by the kidney. It is indicated to treat osteoporosis in postmenopausal women and in men at increased risk of fracture [1]. Shivering is form of chills and it is refers to a feeling of being cold without an apparent cause [2]. The aim of this review is to evaluate the risk of Shivering associated with the use of Teriparatide 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) [3], to retrieve related information for assessing the causality between Teriparatide and the Risk of Shivering. The WHO- Uppsala Monitoring Centre (UMC) criteria used as standard for assessing the causality of the reported cases.[4]

Results

Case Review: The number of resulted cases for the reported drug/adverse drug reaction are 1080 global ICSRs and one local case as of September 20, 2020. Well-documented global ICSRs with completeness scores of 1.0 and above have been selected for assessment (39 ICSRs). Among the 39 seven cases reported with positive dechallenge, and one with negative dechallenge. After applying WHO-UMC causality assessment, five cases resulted in probable association, thirteen cases with possible association, eighteen cases with unlikely association, and three cases resulted in unassessable association. For the local case, it was a possible association.

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, considering the null value equal to zero. The results of (IC= -0.6) revealed a negative statistical association for the drug/ADR combination, which means "Shivering" with the use of "Teriparatide " have been observed slightly less than expected when compared to other medications available in WHO database.

Literature: Multiple evidences have been found during the literature search, which are suggestive for the association between drug and the adverse event:

- In a post marketing observational study that aimed to reassess the safety and efficacy teriparatide in osteoporosis patients with a high fracture risk. Author listed all adverse drug reactions observed in the all 3573 patients, Chills has been reported in 20 patients [5].
- In a retrospective study was conducted to evaluate the effects of treatment interruption due to patient convenience on treatment of once a week teriparatide, and the author listed all the reported ADRs and "Chills" has been reported in one of the assessed cases [6].

Conclusion

The weighted cumulative evidences identified from global and local cases assessment and literature are sufficient to support a causal association between teriparatide and the risk of shivering. Health regulators and health care professionals must be aware for the 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

References:

1. Eurs Is Yours (2008). Forteo Saudi Summary of Product Characteristics. [Accessed 9/20/2020].
2. Maureen Donohue. (2019). What You Should Know About the Chills. Health line Retrieved from: https://www.healthline.com/symptom/chills [Accessed 9/23/2020].
3. Uppsala Monitoring Center (UMC) (2020), Vigilyze database; Available at: https://vigilyze.who-umc.org/ [Accessed 9/21/2020]
4. Uppsala Monitoring Center (UMC) (2020), The use of the WHO-UMC system for standardized case causality assessment; Available at https://www.who.int/medicines/areas/quality_safety/safety_efficacy/WHOcausality_assessment.pdf?ua=1 [Accessed 23/7/2020].

5. Ifuku, E. (2019). Safety and efficacy in actual clinical practice of once-weekly subcutaneous teriparatide for osteoporosis patients with a high fracture risk. ScienceDirect, 5(2), 44–50. https://www.sciencedirect.com/science/article/abs/pii/S2405525519300093#
6. Katahira, G. (2020). Effects of treatment interruption due to patient convenience on treatment of once a week teriparatide. ScienceDirect, 6(1), 8–14. https://www.sciencedirect.com/science/article/pii/S2405525519300330#