SAFETY ALERT

SUBCUTANEOUS VASCULITIS ASSOCIATED WITH METFORMIN & VILDAGLIPTIN

Subcutaneous vasculitis is a condition characterized by inflammation of the walls of the blood vessels. This may compromise or lead to destruction of affected blood vessels resulting in hemorrhagic and ischemic events. Subcutaneous vasculitis is caused by several factors which include primary factors such as idiopathic cutaneous leukocytoclastic angiitis or Wegener granulomatosis and secondary disorders (connective tissue disease, infections, or adverse drug eruption-associated vasculitis).[1,2] Some of the other medicines like beta lactam antibiotics, sulphonamides, non-steroidal anti-inflammatory drugs, retinoids, thiazides, insulin, and quinolone group antibiotics are also associated with subcutaneous vasculitis.[3,4]

Subcutaneous vasculitis is a new safety signal identified and is associated with the use of Dipeptidyl peptidase-4 (DPP-4) inhibitors and metformin.[3,4] As of the 15th of March 2021, globally there are eight (8) cases of subcutaneous vasculitis associated with metformin & vildagliptin combination, and seven (7) cases associated with vildagliptin only. Novartis Pharma AG has informed Botswana Medicines Regulatory Authority (BoMRA) of subcutaneous vasculitis, as a new safety signal for their products Galvus® (vildagliptin) and Eucreas® (vildagliptin & metformin).

This safety communication is applicable to all DPP-4 inhibitors and metformin combination products. Tragenta (Linagliptin), Jentadueto (Linagliptin and metformin), Onglyza (Saxagliptin), Junuvia (Sitagliptin) and Gulvas (Vildagliptin), Gulvas Met (Vildagliptin and metformin) are the DPP-4 inhibitors and DPP-4 inhibitors and metformin combinations registered in Botswana for the treatment of Diabetes Mellitus Type 2. To date, BoMRA through its National Pharmacovigilance Program, has not received any reports of subcutaneous vasculitis associated with the use of DPP-4 inhibitors and metformin.

Based on current evidence, incidence of subcutaneous vasculitis reports associated with DPP-4 inhibitors and metformin is very rare. As a result, the potential benefits of using DPP-4 inhibitors and metformin for treating diabetes mellitus type 2 outweighs the potential risk.

Healthcare professionals are encouraged to actively look for any such reactions in their patients receiving DPP-4 inhibitors and metformin. In addition, HCPs should advise the patients or caregivers to report any signs and symptoms of subcutaneous vasculitis which includes skin rash, with tender, purple or reddish-brown spots covering large areas especially the legs, buttocks or torso or upper body, blisters, hives, and open sores (ulcers) with dead tissue.

Reporting of Adverse Drug Reactions (ADRs)

HCPs should encourage patients or caregivers to visit their nearest healthcare facility if they experience any ADRs or any discomfort after they take any medication.

Reporting of ADRs can be done through:

1. ADR reporting forms available in your health facility. You may download the forms from BoMRA website **www.bomra.co.bw.**
2. MedSafety App, an ADR reporting App, available in apple store or google store for smart phones
3. E reporting by following the link **Primary eReporting (who-umc.org)** available on BoMRA website
4. Through e-mail at **reportadr@bomra.co.bw**
5. Through telephone – 373 1788/1771; 3620912

For more information about any medicine/vaccine safety contact BoMRA **National Medicines Information Centre** at 3731788/71 or email **nmic@bomra.co.bw**

REFERENCES

1. Chen, K. R., & Carlson, J. A. (2008). Clinical approach to cutaneous vasculitis. *American journal of clinical dermatology*, 9(2), 71-92.
2. Vaskülit, L. (2020). Sitagliptin/Metformin Related Cutaneous Leukocytoclastic Vasculitis in a Patient with Type-2 Diabetes Mellitus.
3. Beltrani, V. S. (1998). Cutaneous manifestations of adverse drug reactions. Immunology and allergy clinics of North America, 18(4), 867-895.'
4. Sayin, S., Omeroglu, E., & Bilgin, S. A. Vildagliptin induced cutaneous leukocytoclastic vasculitis: A case report.

Plot 112, International Finance Park, Gaborone
Private Bag 2, Gaborone Station, Botswana
+267 373 1727/20
Toll Free : 0800 600 216
info@bomra.co.bw
Botswana Medicines Regulatory Authority
www.bomra.co.bw