SAFETY ALERT

DRAP SAFTEY ALERT NO. 25

Risk of Severe Cutaneous Adverse Reactions (SCARs) with Atezolizumab

Date: 23rd of November, 2022

Target Audience:

- Manufacturers and importers of Atezolizumab;
- Healthcare Professionals; and
- Patients, consumers or caregivers.

Background: -

The National Pharmaceutical Regulatory Agency (NPRA) of Malaysia in April, 2021 announced that the product information for Atezolizumab (Tecentriq®) has been updated to include the risk of severe cutaneous adverse reactions (SCAR). Based on analysis from the company's global safety data of 99 cases of SCARs identified globally, of which 36 cases were confirmed by histopathology or specialist diagnosis.

Similarly, the Medicines and Healthcare Products Regulatory Agency (MHRA) in June, 2021 also announced that the product information for Atezolizumab (Tecentriq®) has been updated to include information about the risk of severe cutaneous adverse reactions (SCARs), which includes Stevens-Johnsons syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). SCARs were previously known to be potentially associated with the use of Atezolizumab. A review of safety data for Atezolizumab and the risk of SCARs was recently completed in Europe. Based on this review SCARs are an identified risk for Atezolizumab. Also, other products used for cancers in the same class as atezolizumab, including cemiplimab, ipilimumab, nivolumab and pembrolizumab list SCARs as possible adverse effects in the Summary of Product Characteristics (SmPC). In addition, Direct Healthcare Professional Communication (DHPC) were also issued by the manufacturers in

New Zealand and European Medicine Agency back in November, 2020.

SCARs are a heterogeneous group of delayed hypersensitivity reactions. These events mainly consist of acute generalised exanthematous pustulosis (AGEP), Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug rash with eosinophilia and systemic symptoms (DRESS) and can be potentially life-threatening, and lead to severe, potentially chronic sequelae.

Action in Pakistan:-

Accordingly, the case of risk of severe cutaneous adverse reactions (SCARs) with Atezolizumab was discussed in the 1st meeting of the Pharmacovigilance Risk Assessment Expert Committee (PRAEC) of the National Pharmacovigilance Centre (NPC), Division of Pharmacy Services, Drug Regulatory Authority of Pakistan (DRAP). The PRAEC after deliberation decided as per Rule 10 (1) (h) (iv) of Pharmacovigilance Rules, 2022 (reliance mechanism) to update prescribing information of Atezolizumab (Tecentriq®) to include the risk of severe cutaneous adverse reactions (SCAR) including Stevens-Johnsons Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). Furthermore, it was decided that registration holders should issue direct healthcare professional communication in this regard.

Therapeutic Goods Affected:-

Name: **Atezolizumab**

Atezolizumab is an immunostimulatory drug indicated to treat non-small cell lung cancer, small cell lung cancer, hepatocellular carcinoma, urothelial carcinoma and triple-negative breast cancer.

Advice for patients:-

Patients are advised to be vigilant for the signs of severe skin reactions with the use of Atezolizumab and to seek urgent medical advice if they occur.

Advice for healthcare professionals:-

Healthcare professionals are informed that severe cutaneous adverse reactions (SCARs), including cases of Steven-Johnsons Syndrome(SJS) and Toxic Epidermal Necrolysis (TEN), have been reported in patients treated with immune-stimulatory anti-cancer drugs including Atezolizumab. Advise patients to seek urgent medical assistance if severe skin reactions occur. Also, monitor patients for signs and symptoms of severe skin reactions and exclude other causes. If a SCAR is suspected, treatment should be withheld and patients should be referred to a specialist for diagnosis and treatment. If SJS or TEN is confirmed or in case of any grade 4 SCAR, permanently discontinue treatment with immune stimulatory drugs.

Guidelines for reporting of Adverse Drug Reactions (ADRs):

Both healthcare professionals and patients are requested to report any suspected adverse drug reaction (ADRs) with Atezolizumab to the National Pharmacovigilance Centre, Drug Regulatory Authority of Pakistan through Med Vigilance E-Reporting system available on the DRAP website. Similarly, ADRs can also be reported through Med Safety App which is available for download from App store (for iOS devices) and Google Play (for Android devices).

References:

1. Minutes of 1st meeting of Pharmacovigilance Risk Assessment Expert Committee of the DRAP.
2. MHRA update on Atezolizumab (Tecentriq▼) and other immune-stimulatory anti-cancer drugs: risk of severe cutaneous adverse reactions (SCARs).

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