IMPORTANT MEDICINE SAFETY INFORMATION

17 November 2020

Dear Healthcare Professional

Re: Tecentriq® (atezolizumab): Risk of Severe Cutaneous Adverse Reactions (SCARs) and Immune-related myositis

In collaboration with the South African Health Products Regulatory Authority (SAHPRA), Roche Products (Pty) Ltd would like to inform you of the risk of Severe Cutaneous Adverse Reactions (SCARs) and immune-related myositis associated with the use of Tecentriq® (azeolizumab).

The Professional Information and Patient Information Leaflet will be updated in line with this new safety information.

1. SEVERE CUTANEOUS ADVERSE REACTIONS (SCARS)

Summary

- Severe Cutaneous Adverse Reactions (SCARs) are potentially fatal skin toxicities frequently associated with drug use including immune checkpoint inhibitors, as a class. A comprehensive analysis of the data available across the Tecentriq® (atezolizumab) program has identified cases of SCARs following atezolizumab use.
- SCARs were previously known to be potentially associated with the use of atezolizumab, and have been monitored continuously. Based upon the totality of evidence in a recent analysis, SCARs are now considered to be an identified risk for atezolizumab.

Background on the safety concern

SCARs are a heterogeneous group of immunologically mediated drug eruptions. Although rare, these events are potentially fatal, and are mainly constituted by acute generalised exanthematous pustulosis, Stevens-Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN) and drug rash with eosinophilia and systemic symptoms (DRESS).

A cumulative analysis of the company safety database across the Tecentriq® (atezolizumab) program identified 99 cases, of which 36 cases of SCARs were confirmed by histopathology or specialist diagnosis. In clinical studies, incidence rates of SCARs, from pooled atezolizumab monotherapy and combination therapy was 0.7% and 0.6%, respectively. One fatal case of TEN was reported in a 77 year old female patient who received atezolizumab monotherapy.

Advice to healthcare professionals

- Patients suspected of having SCARs should be referred to a dermatologist for further diagnosis and management.
- Treatment with Tecentriq® should be suspended for patients with suspected SJS or TEN and permanently withdrawn for any grade confirmed SJS or TEN.
- Caution should be taken when considering the use of Tecentriq® in a patient who has previously experienced a severe or life-threatening skin adverse reaction on prior treatment with other immune-stimulatory anticancer agents.

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2. IMMUNE-RELATED MYOSITIS

Summary on the background on the safety concern

Myositis or inflammatory myopathies are a group of disorders sharing the common feature of inflammatory muscle injury; dermatomyositis and polymyositis are amongst the most common disorders. Diagnosis is based on clinical (muscle weakness, muscle pain, skin rash in dermatomyositis), biochemical (serum creatine-kinase increase), and imaging (electromyography/MRI) features, and is confirmed with a muscle-biopsy. Immune-related myositis has now been added as a new important identified risk associated with the use of Tecentirq® (atezolizumab).

A comprehensive analysis was performed across the Tecentriq® program and identified cases of immune-related myositis, including biopsy-confirmed cases, in patients that have received atezolizumab. There were 4 cases of myositis with a fatal outcome with some cases suggestive of cardiac involvement (myocarditis or AV blocks). The incidence of myositis, including related terms of dermatomyositis, polymyositis and rhabdomyolysis, observed across the atezolizumab monotherapy clinical programme was <0.1%.

Advice to healthcare professionals

- It is recommended that Tecentriq® (atezolizumab) should be suspended for moderate or severe (Grade 2 or 3) immune-related myositis and permanently discontinued for recurrent severe or life-threatening myositis (recurrent Grade 3 and Grade 4).
- Healthcare providers are advised to refer the patient to a rheumatologist and/or neurologist and consider muscle biopsy and supportive measures as clinically indicated.
- Corticosteroids treatment with 1-2 mg/kg/day IV methylprednisolone or higher-dose bolus if severely compromised (weakness severely limiting mobility, cardiac function, respiratory function, dysphagia) and/or additional immunosuppressive agents should be administered for > grade 2 events or if event does not improve after initial corticosteroids.

Call for reporting

Healthcare professionals are urged to report any adverse drug reactions (ADRs) or product quality issues associated with the use of Tecentriq® (atezolizumab) to Roche Products (Pty) Ltd, or to SAHPRA via the eReporting link available on the SAHPRA website (www.sahpra.org.za). Alternatively, please complete the ADR reporting form accessible via the SAHPRA website at https://www.sahpra.org.za/documents/12e54dcaADRForms.pdf and email it to adr@sahpra.org.za or fax to (021) 448 6181.

For further information, kindly contact Roche Products (Pty Ltd as indicated below:

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References:

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Yours sincerely,

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