

SFDA Drug Safety communication

[26/11/2024]

Potential Risk of Overlap Syndrome of (Myocarditis, Myositis, and Myasthenia Gravis) Associated with Immune Checkpoint Inhibitors

The Saudi Food and Drug Authority (SFDA) would like to notify healthcare professionals about the potential association between immune checkpoint inhibitors and a rare but serious overlap syndrome of myocarditis, myositis, and myasthenia gravis (neuromuscular disorder characterized by muscle weakness and muscle fatigue). This condition is called “triple M overlap syndrome”.

The SFDA conducted a comprehensive safety review of available data, including published literature and cases retrieved from post-marketing databases. This review identified one observational study and 60 reported cases of myocarditis with myositis and/or myasthenia gravis in the literature supporting the potential association between immune checkpoint inhibitors and the potential risk of triple M overlap syndrome. Additionally, 103 global cases of triple M overlap syndrome associated with immune checkpoint inhibitors were reported in the World Health Organization's database.

The available evidence suggests that the likelihood of developing this overlap syndrome is higher among older adults, and who receiving a combination therapy of immune checkpoint inhibitors.

Advice for Healthcare Professionals

Given the severity and potentially fatal outcome of triple M overlap syndrome, the SFDA strongly advises healthcare professionals to take the following measures:

- Monitor patients receiving immune checkpoint inhibitors for signs and symptoms of triple M overlap syndrome, particularly those at higher risk.
- If triple M overlap syndrome is suspected, close monitoring should be initiated immediately.
- Refer patients to a specialist for evaluation and treatment without delay.
- Educate patients on the early signs and symptoms of triple M overlap syndrome.
- Encourage patients to report symptoms such as muscle pain, stiffness, weakness, chest pain, or severe fatigue and seek medical attention promptly.

Table 1: List of brand names of immune checkpoint inhibitors that are registered in Saudi Arabia [[Drugs List](#)]

Drug Name	Trade Name	Strength	Dosage Form	Marketing Company
ATEZOLIZUMAB	TECENTRIQ®	60 mg/mL	Injection	Roche
DURVALUMAB	IMFINZI®	50 mg/mL	Solution for infusion	AstraZeneca
AVELUMAB	BAVENCIO®	20 m g/ml	Solution for infusion	Merck Europe BV
IPILIMUMAB	YERVOY®	5 mg/ml	Solution for infusion	Bristol-Myers Squibb
PEMBROLIZUMAB	KEYTRUDA®	25 mg/mL	Concentrate for solution for infusion	Merck Sharp & Dohme
NIVOLUMAB	OPDIVO®	10 mg/mL	Solution for injection	Bristol-Myers Squibb

Call for reporting:

The SFDA urges both healthcare professionals and patients to report ADRs related to use of any medication to the SFDA using the following contact information:

The National Pharmacovigilance Centre (NPC):

Call Center: 19999

Website: <https://ade.sfda.gov.sa>

RMMs:

