SAFETY ALERT

DRAP SAFTEY ALERT NO. 21

Risk of Infusion-Related Hypersensitivity Reactions with Remdesivir

Update from Pharmacovigilance Risk Assessment Expert Committee of Pakistan.

Date: 18th of November, 2022.

Target Audience:

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

Problem or Issue:

The National Pharmacovigilance Centre (NPC), Division of Pharmacy Services, Drug Regulatory Authority of Pakistan (DRAP) received a cluster of three serious (life-threatening) adverse drug reaction reports from a hospital with Inj Remdesivir (100mg/20ml). The events of tachycardia, dyspnoea, chills and pyrexia were noted after the use of Remdesivir through an intravenous drip for COVID-19 Pneumonia, with a time to onset of 0 days. The causality assessment of all three cases was performed by the Causality Assessment Group of the NPC and classified that all three cases have a possible relationship with drug intake. However, at the same time, the NPC also carried out the quality testing of the suspected batch of Remdesivir, which was declared of standard quality with regard to the tests performed by the Central Drugs Laboratory, DRAP, Karachi. The NPC accordingly labelled it as a potential signal of infusion-related hypersensitivity reactions with the injection of Remdesivir.

Further assessment was also carried out at NPC-DRAP, where the signal was confirmed from the approved label of the United States Food and Drugs Administration (US-FDA) and Summary of Product Characteristics (SmPC) of Medicine and Health Products Agency (MHRA) of the United Kingdom. There was also significant disproportionality and potential association of Remdesivir with infusion-related hypersensitivity reactions as per the statistical tools available in VigiLyze of the Uppsala Monitoring Centre.

The case was, therefore, discussed in the 1st meeting of the Pharmacovigilance Risk Assessment Expert Committee (PRAEC) of the NPC, DRAP which after detailed deliberation and discussion

decided to update the prescribing information/ safety specification/ label of Remdesivir injection with the inclusion of information related to infusion-related hypersensitivity reactions and its monitoring in the warning and precaution sections. Furthermore, it was also decided that all registration holders should introduce educational training for healthcare professionals on proper preparation, administration and flow rate of Remdesivir, and monitoring of patients.

Therapeutic Goods Affected.

Name: **Remdesivir injection.**

Remdesivir is a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleotide analog RNA polymerase inhibitor indicated for the treatment of coronavirus disease 2019 (COVID-19) in adults and pediatric patients (28 days of age and older and weighing at least 3 kg) with positive results of direct SARS-CoV-2 viral testing, who are: hospitalized, or not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death.

Advice/directions for Registration Holders:

Registration holders of Remdesivir injection are hereby advised/directed to update the prescribing information/safety specification/ label of Remdesivir with the inclusion of information related to infusion-related hypersensitivity reactions and its monitoring in the warning and precaution sections. Furthermore, registration holders should also introduce educational training for healthcare professionals on proper preparation, administration and flow rate of Remdesivir, and monitoring of patients.

Advice for patients.

Patients are informed that hypersensitivity reactions including infusion-related reactions have been observed during and following the administration of Remdesivir injection. Immediately call your doctor if you experience signs and symptoms such as hypotension, hypertension, tachycardia, bradycardia, hypoxia, fever, dyspnea, wheezing, angioedema, rash, nausea, diaphoresis, and shivering after administration of Remdesivir injection.

Advice for healthcare professionals.

Healthcare professionals are informed that the Pharmacovigilance Risk Assessment Expert Committee (PRAEC) of the DRAP has recommended updating the prescribing information/ safety specification/ label of Remdesivir injection with the inclusion of information related to infusion-related hypersensitivity reactions and its monitoring in the warning and precaution sections, and is working with registration holders in this regard.

Healthcare professionals are also informed that the signs and symptoms of infusion-related

hypersensitivity reactions may include hypotension, hypertension, tachycardia, bradycardia, hypoxia, fever, dyspnea, wheezing, angioedema, rash, nausea, diaphoresis, and shivering, which have been observed during and following administration of Remdesivir injection which mostly occurred within one hour. Therefore, slower infusion rates with a maximum infusion time of up to 120 minutes should be considered to potentially prevent these signs and symptoms. Furthermore, monitor patients during infusion and observe patients for at least one hour after the infusion is completed for signs and symptoms of hypersensitivity as clinically appropriate. If signs and symptoms of a clinically significant hypersensitivity reaction occur, immediately discontinue the administration of Remdesivir injection and initiate appropriate treatment.

Guidelines for reporting of Adverse Drug Reactions (ADRs):

Both healthcare professionals and patients are requested to report any suspected adverse drug reaction (ADRs) with Remdesivir injection 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 MedSafety 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.
2. Approved label of Veklury (Remdesivir) of US-FDA.