



## SAFETY ALERT

DRAP SAFETY ALERT NO. 22

### **Risk of Serious Bowel Complications with Clozapine**

**Date:** 18<sup>th</sup> of November, 2022

**Target Audience:**

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

**Background:**

The Therapeutic Goods Administration (TGA) of Australia on 22<sup>nd</sup>, April 2022 through a safety advisory informed that Product Information (PI) and Consumer Medicine Information (CMI) for Clozapine have been updated to strengthen warnings about potential severe gastrointestinal side effects, including constipation. It was informed that Clozapine may also affect the bowels by slowing them down and can cause severe constipation, the condition known as clozapine-induced gastrointestinal hypomotility. If untreated, it can lead to serious problems. Consumers who were using clozapine were informed to look out for changes in their bowel function and to contact their health professionals if they develop any of the symptoms.

On 14<sup>th</sup> January 2022, the United States Food and Drug Administration (US-FDA) through Drug Safety Podcast referred to the already issued communication dated 18<sup>th</sup> of February, 2020 where the FDA strengthens the existing warning that untreated constipation caused by schizophrenia medicine clozapine (Clozaril®) can lead to serious bowel problems. It was informed that serious bowel complications can lead to hospitalization or even death if constipation is not diagnosed and treated quickly.





## Action in Pakistan:

Accordingly, the case of risk of serious bowel complications with Clozapine was discussed in the 1<sup>st</sup> 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) which after detailed deliberation and discussion decided to update and strengthen the warning section of Clozapine with gastrointestinal side effects, including constipation and severe bowel problem in light of Rule 10 (1) (h) (iv) of Pharmacovigilance Rules, 2022 as a part of reliance mechanism on stringent regulatory authorities.

## Therapeutic Goods Affected.

Name: **Clozapine**

Clozapine is a medicine that has been used for more than 40 years to treat schizophrenia in patients whose symptoms are not controlled with standard treatment.

## Advice for patients.

Patients are advised to contact their healthcare professionals if they have symptoms that can be associated with serious bowel problems such as nausea, vomiting or stomach pain. To prevent constipation, they should eat more fruits, vegetables, and grains that are high in fibre; drink plenty of water and other liquids, and get enough exercise.

## Advice for healthcare professionals.

Healthcare professionals are advised the following: to evaluate bowel function before starting a patient on clozapine and avoid co-prescribing clozapine with other anticholinergic medicines that can cause gastrointestinal hypomotility; advise patients frequently of the significant risk of constipation and life-threatening bowel issues and the need to stay hydrated to prevent constipation; advise patients to contact a healthcare professional right away if they have difficulty having a bowel movement or passing stools, do not have a bowel movement at least three times a week or less than their normal frequency.





## **Guidelines for reporting of Adverse Drug Reactions (ADRs):**

Both healthcare professionals and patients are requested to report any suspected adverse drug reaction (ADRs) with Clozapine 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 1<sup>st</sup> meeting of Pharmacovigilance Risk Assessment Expert Committee.](#)
2. [Safety Advisory- constipation: a potentially serious side effect issued by the Therapeutic Goods Administration of Australia.](#)
3. [Drug safety podcast of the United States Food and Drug Administration \(US-FDA\) regarding constipation caused by schizophrenia medicine clozapine.](#)

