Clozapine (Clozaril)

Clozapine (Clozaril) is an atypical antipsychotic agent (second-generation antipsychotic, SGA) that works by antagonizing serotonergic and dopaminergic receptors. It is indicated for treatment-resistant psychotic disorders such as Schizophrenia, especially in patients in whom other treatments have failed. In addition, patients who have Parkinson's disease can use this drug to manage levodopa-induced psychosis. Clozapine is known to induce multiple side effects like agranulocytosis, weight gain, and seizures; thus, weekly lab tests should be done. Patients may even complain of sedation and can experience myocarditis or orthostatic hypotension. Clozapine interacts with many drugs and should not be taken with alcohol, other CNS depressants, or drugs that suppress bone marrow function, such as anticancer drugs. Prescribers are required to be certified in the Risk Evaluation and Mitigation Strategy (REMS) mandated by the FDA prior to prescribing this medication due to its unique side effect profile.



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Mechanism

Atypical Antipsychotic
A-tipi Anti-tie-psychiatrist
Clozapine is a second-generation atypical antipsychotic drug given to patients who are unresponsive to other atypical medications for the treatment of psychosis. Atypical antipsychotics are less likely to cause extrapyramidal symptoms than typical antipsychotics, like Haloperidol.

Indications

Schizophrenia
Sketchy-fern
This medication is used in patients who are intolerant or unresponsive to other therapies for schizophrenia.

Levodopa-Induced Psychosis
Levitating L-Doberman and Psychic
Clozapine has been shown to be effective in treating the psychosis associated with Levodopa use in patients with Parkinson's disease. Furthermore, it can also diminish the tremor and dyskinesia associated with Parkinson's disease.

Side Effects

Weight Gain
Up-arrow Weight-scale
Clozapine causes significant weight gain and leads to other metabolic effects as well. Patients develop impaired glucose metabolism, leading to diabetes, along with dyslipidemias and metabolic syndrome.

Hypersalivation (Sialorrhea)
Hiker-salivating
A very common side effect of clozapine use is dose-dependent sialorrhea, or hypersalivation. Tolerance to this side effect typically does not develop, and this may persist for years. Risks of hypersalivation include aspiration, chronic cough, and hoarseness when speaking.

Myocarditis
Mayo-heart-card
Myocarditis can be a fatal side effect of this medication and is most likely seen in the first month of treatment. Thus, patients should have their C-reactive protein (CRP) and troponin levels monitored for the first four weeks of treatment in order to assess for possible cardiac damage.

Agranulocytosis
A-granny-side-toe
A major side effect that occurs with this medication is agranulocytosis, or a severe and dangerous decrease in white blood cell count. The cause is unknown and typically occurs with a gradual onset within the first six months of administration.

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Sedation

Sedation-dart

Due to dopaminergic blockade, this medication can lead to heavy sedation in patients.

Orthostatic Hypotension

Oar Hippo-BP

Clozapine may also cause orthostatic hypotension, with or without associated syncope. This side effect occurs because clozapine has anti-alpha-1 adrenergic effects, which may lead to decreased catecholamine release.

Constipation (Risk of Bowel Ileus)

Corked Con-toilet

Clozapine also binds and blocks cholinergic receptors, leading to various anticholinergic side effects, like constipation. It is important to note that sialorrhea, rather than dry mouth, is more commonly associated with this medication, as described in detail above. While patients may only complain of abdominal discomfort, this side effect can lead to more treacherous outcomes, such as bowel ileus, gastric outlet obstruction, and peritonitis with bowel infarction or perforation.

Considerations

Weekly Lab Tests

Weekly-newspaper with Lab-coat and Test-tubes

Because agranulocytosis is a common fatal side effect, blood lab values are checked often. For the first six months, white blood cell (WBC) levels and absolute neutrophil count (ANC) are checked weekly. For the second six months, they are checked every two weeks. They must continue to be checked for four weeks after discontinuing treatment with the medication. C-reactive protein (CRP) and troponins are also followed because of the risk of myocarditis.

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