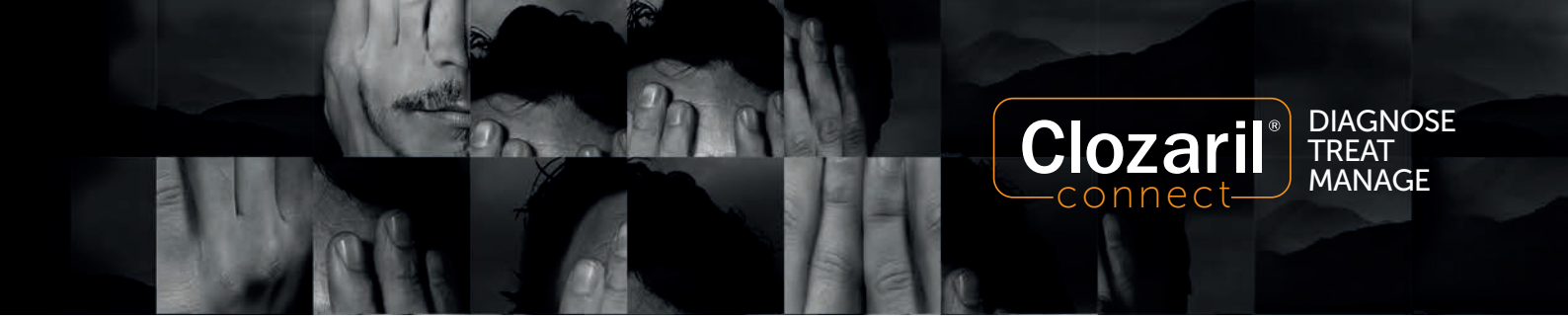


Clozapine and eosinophilia

The information in this document is not intended as a definitive treatment strategy, but as a suggested approach for clinicians. It is based on previous successful experience. Each case should, of course, be considered individually.

This information is provided for healthcare professionals and should not be used as a patient information leaflet.

Background

Eosinophilia is a common (≥1/100 but <1/10) side-effect of Clozaril® (clozapine).[1,2]

Eosinophils are a type of white blood cell involved mainly in immune and allergic responses and parasitic infections.[3] The normal range for eosinophils varies according to the haematology laboratory which analyses the blood sample.

Common causes of eosinophilia are parasitic infections such as hookworms or tapeworms, and allergic syndromes such as asthma.[3]

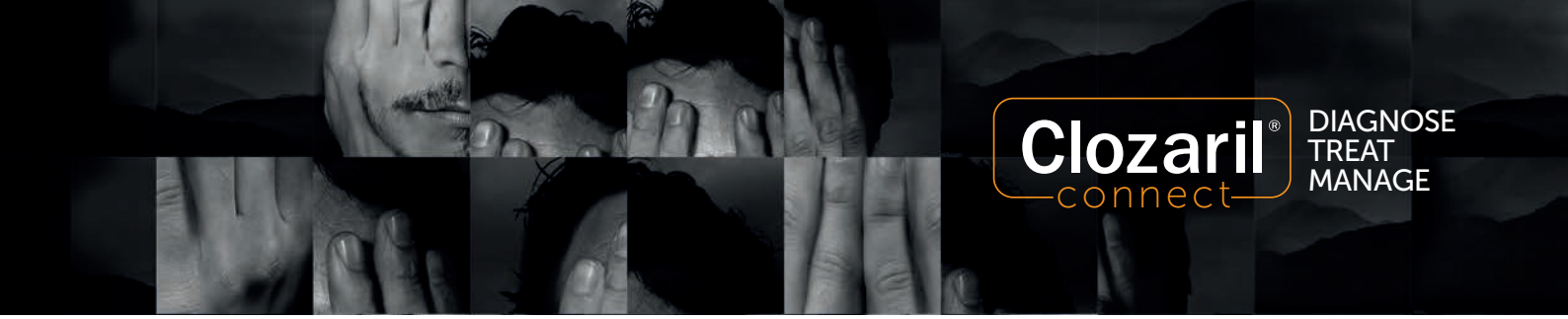
Eosinophilia has also been reported in association with serious disorders such as myocarditis.[4,5]

In addition, it is a common allergic symptom of many drugs (for example, non-steroidal anti-inflammatory drugs, anticonvulsants and some antibiotics) and usually disappears when the drug is stopped.[6] As well as clozapine, eosinophilia has been reported in association with other antipsychotics including haloperidol,[7] olanzapine[8] and quetiapine.[9]

Eosinophils may also play a role in the regulation of granulopoiesis and an association between eosinophilia and neutropenia has been reported in several conditions,[10] however, no strong evidence has been identified for a link between neutropenia or agranulocytosis and eosinophilia in patients on clozapine.[7,11]

The incidence of eosinophilia in clozapine-treated patients reported in the literature varies enormously from 0.2%[12] up to as much as 62%.[13] Banov *et al* (1993) conducted a review of 118 patients treated with clozapine over a 1-year period.[14] Eosinophilia developed in 14% of their patients, and a higher incidence was seen in women (23%) compared to men (7%), although a study by Ames *et al* (1996) did not confirm this gender difference.[7] No association with age has emerged from the literature.

Eosinophilia, in patients on clozapine, is usually transient and generally occurs in the first 3-6 weeks of treatment,[4,8] resolving spontaneously over a few weeks.[13,14] It is usually asymptomatic although it may be associated with a transient rise in temperature.[15] As noted above, there is no strong evidence at present to link eosinophilia with agranulocytosis, and eosinophilia is not believed to be of any value in predicting the onset of agranulocytosis.



Clozaril® connect

DIAGNOSE
TREAT
MANAGE

Association with myocarditis

Eosinophilia has been co-reported in approximately 14% of cases of myocarditis occurring in Clozaril®-treated patients, as well as some cases of pericarditis/pericardial effusion.[1,2] However, since many patients develop eosinophilia and do not develop subsequent myocarditis or pericardial disorder it is not known whether eosinophilia is a reliable predictor of carditis.

Management

In most cases the eosinophilia will resolve spontaneously without the need for dose alteration or discontinuation, but due to the possible association between myocarditis and eosinophilia it is recommended that Clozaril® should be discontinued if the eosinophil count rises above 3.0 x 10^9/L and should not be restarted until the eosinophil count has fallen below 1.0 x 10^9/L.[1,2] If myocarditis or cardiomyopathy is suspected, Clozaril® treatment should be stopped immediately and the patient should be referred to a cardiologist urgently.

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Adverse events should be reported.
For the UK, reporting forms and information can be found at www.mhra.gov.uk/yellowcard.
For Ireland, report adverse events via HPRA Pharmacovigilance medsafety@hpra.ie.
Adverse events should also be reported to Mylan via cpms@mylan.co.uk

Clozaril® (clozapine)

CLOZARIL® Clozapine PATIENT MONITORING SERVICE

NON 2018 0770 Date of preparation: May 2018

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