



Direct Healthcare Professional Communication

June 2022

Methotrexate - Risk of Progressive Multifocal Leukoencephalopathy (PML)

Dear Healthcare Professional,

The Egyptian Pharmaceutical Vigilance Center of the Central Administration for Pharmaceutical Care at The Egyptian Drug Authority would like to inform you of the following:

Summary

- Cases of progressive multifocal leukoencephalopathy (PML) have been reported in patients receiving Methotrexate, mostly in combination with other immunosuppressive medication.
- PML can be fatal and should be considered in the differential diagnosis in immunosuppressed patients with new onset or worsening neurological symptoms.
- If the patient, the partner, or the caregiver notice new onset or worsening of neurological symptoms including general muscle weakness, disturbance of vision, changes in thinking, memory and orientation leading to confusion and personality changes contact your doctor immediately because these may be symptoms of a very rare, serious brain infection called progressive multifocal leukoencephalopathy (PML).

Background information on the security concerns

Methotrexate is indicated for the treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriasis, psoriatic arthritis and Crohn's disease and often prescribed in combination with other immunosuppressants

PML is a serious, life-threatening demyelinating brain disease potentially leading to disability or death, if detected with delay. It is thought to occur following reactivation of John Cunningham virus (JCV) in the setting of profound suppression of cell-mediated immunity associated with disease or treatment.

Cases of PML have been reported in patients receiving methotrexate, mostly in combination with other immunosuppressive medication, e.g. corticosteroids with mainly prednisolone or monoclonal antibodies. A definite causality between methotrexate and PML has not been established, however, a contributory role of methotrexate in development of PML cannot be excluded either.

PML is characterized by new onset or worsening neurological symptoms. Patients may present with disturbance of vision, confusion, personality changes, muscle weakness and other neurological or psychiatric symptoms.





Data suggest an increased risk of PML in patients with rheumatic diseases, e.g. rheumatoid arthritis, as well as patients with systemic lupus erythematosus (SLE) and patients receiving multiple immunosuppressive medication.

While there is no specific anti-JCV-treatment, the mainstay of PML management is prompt diagnosis and restoration of the immune function including discontinuation of the inciting agent.

The Summary of Product Characteristics (SmPC) and the package leaflet of Methotrexate containing products, will be updated to include a warning on the risk of PML in order to raise awareness of healthcare professionals and to advise patients accordingly.

References

https://www.ema.europa.eu/en/documents/prac-recommendation/prac-recommendations-signals-adopted-30-august-2-september-2021-prac-meeting_en.pdf

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2605770/>

Call for reporting

Healthcare professionals are asked to report any suspected adverse reactions via the Egyptian reporting system:

Name: Egyptian Pharmaceutical Vigilance Center

Address: 21 Abd El Aziz Al Soud Street, El-Manial, Cairo, Egypt, And PO Box: 11451 Telephone: +202-25354100, Extension: 1470 Fax: +202 – 23610497

Email: pv.followup@edaegypt.gov.eg

Online reporting: <https://primaryreporting.who-umc.org/EG>

QR Code:

Hotline: 15301

