ADDENDUM TO NOTIFICATION TO THE PRAC/EMA SECRETARIAT OF A REFERRAL UNDER ARTICLE 20 OF REGULATION (EC) 726/2004 (procedure number EMEA/H/A-20/1517)

This is an addendum to the 28 January 2022 notification by the European Commission of a referral under Article 20 of Regulation (EC) 726/2004 to the Pharmacovigilance Risk Assessment Committee (PRAC) concerning the following medicinal products:

Product(s) Name(s)	Olumiant Xeljanz Rinvoq Jyseleca Cibinqo
Active Substance(s)	Baricitinib Tofacitinib Upadicitinib Filgotinib Abrocitinib
Pharmaceutical form(s)	All
Strength(s)	All
Route(s) of administration	All
Marketing Authorisation Holder(s)	Eli Lilly Nederland B.V. Pfizer Europe MA EEIG AbbVie Deutschland GmbH & Co. KG Galapagos NV

On 28 January 2022, the European Commission requested the European Medicines Agency (the Agency) to perform a safety review on the risks of major cardiovascular events (MACEs), venous thromboembolisms (VTEs), serious infections, malignancies and mortality with all Janus Kinase Inhibitors (JAKis) used in inflammatory disorders (Xeljanz, Rinvoq, Olumiant, Jyseleca, Cibinqo) and their impact on the benefit-risk balance of the products. The European Commission requested the Agency to give its opinion under Article 20 of Regulation (EC) No 726/2004 on whether a regulatory action with regard to the marketing authorisation for these products is necessary.

JAKis included in the referral are authorised in the chronic treatment of inflammatory disorders (rheumatoid arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, psoriatic arthritis, ulcerative colitis and atopic dermatitis). Since the submission of the above mentioned notification new indications have been recommended for approval by the Committee for Medicinal Products for Human Use (CHMP) in the treatment of ulcerative colitis for Rinvoq and of alopecia aerata for Olumiant. In addition, extensions of indications are under review by the CHMP in treatment of non-radiographic axial spondyloarthritis for Rinvoq and in treatment of COVID-19 for Olumiant.

The PRAC has indicated that the possible class effect of the safety concerns from long-term use of JAKis under review in the ongoing Article 20 referral may also impact the new indications for chronic treatments i.e. non-radiographic axial spondyloarthritis, and alopecia aerata that have been recommended or are under review by CHMP. Whereas PRAC does not expect that the ongoing safety review would impact the indication of COVID-19 since a short-term use of the product is foreseen for this indication.

In view of the above, the European Commission extends the scope of the ongoing referral under Article 20 of Regulation (EC) No 726/2004 to include the indications for the chronic treatment of inflammatory disorders reviewed by the CHMP and requests the Agency to assess the impact of the safety concerns under review on the benefit-risk balance of Rinvoq in the treatment of non-radiographic axial spondyloarthritis and ulcerative colitis, and the benefit-risk of Olumiant in the treatment of alopecia aerata.

The European Commission requests the Agency to give its opinion by 25 November 2022.

Signed Date

Olga Solomon
Head of Unit - Medicines: policy, authorisation and monitoring
Health and Food Safety Directorate General