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Direct Healthcare Professional Communication

Infliximab (Remicade, Inflectra, and Remsima): Use of live vaccines in infants exposed *in utero* or during breastfeeding

Dear Healthcare professional,

The marketing authorization holders of infliximab, in agreement with the European Medicines Agency and the Maltese Medicines Authority, would like to inform you about the following:

Summary

Infants exposed to infliximab *in utero* (i.e., during pregnancy)

- **Infliximab crosses the placenta and has been detected in infant serum up to 12 months after birth. After *in utero* exposure, infants may be at increased risk of infection, including serious disseminated infection that can become fatal.**
- **Live vaccines (e.g., BCG vaccine) should not be given to infants after *in utero* exposure to infliximab for 12 months after birth.**
- **If there is a clear clinical benefit for the individual infant, administration of a live vaccine might be considered at an earlier timepoint if infant infliximab serum levels are undetectable or if infliximab administration was limited to the first trimester of pregnancy.**

Infants exposed to infliximab via breast milk

- **Infliximab has been detected at low levels in breast milk. It has also been detected in infant serum after exposure to infliximab via breast milk.**
- **Administration of a live vaccine to a breastfed infant, while the mother is receiving infliximab, is not recommended unless infant infliximab serum levels are undetectable.**

Background on the safety concern

Infliximab is a chimeric human-murine immunoglobulin G1 (IgG1) monoclonal antibody that specifically binds to human TNFα. In the European Union, it is indicated for the treatment of rheumatoid arthritis, Crohn's disease (adult and pediatric), ulcerative colitis (adult and pediatric), ankylosing spondylitis, psoriatic arthritis, and psoriasis.

Administration of live vaccines to infants exposed to infliximab *in utero*

Infliximab crosses the placenta and has been detected in the serum of infants exposed to infliximab *in utero* for up to 12 months after birth (Julsgaard et al, 2016). These infants may be at increased risk of infection, including serious disseminated infection that can become fatal. This includes disseminated Bacillus Calmette Guérin (BCG) infection which has been reported following administration of BCG live vaccine after birth.

A 12-month waiting period starting at birth is therefore recommended before live vaccines are administered to infants who have been exposed to infliximab *in utero*. If there is a clear clinical benefit for the individual infant, administration of a live vaccine might be considered earlier if infant infliximab serum levels are undetectable or if infliximab administration was limited to the first trimester of pregnancy (when placental transfer of IgG is considered minimal).

Administration of live vaccines to infants exposed to infliximab via breast milk

Limited data from published literature indicate that infliximab has been detected at low levels in breast milk at concentrations up to 5% of the maternal serum level (Fritzsche et al, 2012).

Infliximab has also been detected in infant serum after exposure to infliximab via breast milk. Systemic exposure in a breastfed infant is expected to be low because infliximab is largely degraded in the gastrointestinal tract.

Administration of live vaccines to a breastfed infant when the mother is receiving infliximab is not recommended unless infant infliximab serum levels are undetectable.

Product information

The infliximab SmPC, patient leaflets and patient reminder cards are being updated to reflect the current recommendations on live vaccination of infants following *in utero* exposure or whilst breastfeeding. Patients treated with infliximab should be given the package leaflet and the patient reminder card. Women treated with infliximab should be educated on the importance of discussing (live) vaccines with their infants' physicians, should they become pregnant or choose to breastfeed while using infliximab.

Call for reporting

Healthcare professionals should report any suspected adverse reactions associated with the use of infliximab in accordance with the national spontaneous reporting system ADR Reporting at. Report forms can be downloaded at www.medicinesauthority.gov.mt/adrportal and sent to ADR reporting/Post-Licensing Directorate/Medicines Authority, Sir Temi Zammit Buildings, Malta Life Sciences Park, San Gwann, Malta, or sent by email to: Postlicensing.medicinesauthority@gov.mt Please report the product name and batch details.

Company contact points

MAH	Local Representative in Malta	Product name	Email	Phone
Janssen Biologics B.V.	Merck Sharp & Dohme Cyprus Ltd	Remicade	malta_info@merck.com	8007 4433 (+356 99917558)
Pfizer Europe MA EEIG	Drugsales Ltd	Inflectra	GRC.AEReporting@pfizer.com	+356 21419070/1/2 +30 2106785800
Celltrion Healthcare Hungary Kft.	Mint Health Ltd.	Remsima	pharmacovigilancemt@mint.com.mt	+356 2093 9800

Yours faithfully,

Post-Licensing Directorate

Medicines Authority

Disclaimer

This Direct Healthcare Professional Communication has been submitted to you on behalf of Janssen Biologics B.V., Pfizer Europe MA EEIG, and Celltrion Healthcare Hungary Kft.

References

Fritzsche J, Pilch A, Mury D et al. Infliximab and adalimumab use during breastfeeding. J Clin Gastroenterol. 2012;46:718-9. doi: 10.1097/MCG.0b013e31825f2807. PMID: 22858514.

Julsgaard M, Christensen LA, Gibson PR, et al. Concentrations of adalimumab and infliximab in mothers and newborns, and effects on infection. Gastroenterology. 2016;151:110-119. doi: 10.1053/j.gastro.2016.04.002. Epub 2016 Apr 8. PMID: 27063728.