檔　　號:
保存年限:

衛生福利部食品藥物管理署 函

地址：115209 臺北市南港區昆陽街161-2號
聯絡人：詹筑雅
聯絡電話：2787-7418
傳真：(02)26532073
電子郵件：y821105@fda.gov.tw

受文者：中華民國藥師公會全國聯合會

發文日期：中華民國112年3月30日
發文字號：FDA藥字第1121402174A號
速別：普通件
密等及解密條件或保密期限：
附件：歐洲藥品管理局EMA警訊乙份 (A21020000I_1121402174A_doc3_Attach1.pdf)

主旨：有關本署擬啟動含infliximab成分藥品之臨床效益及風險再評估一案，詳如說明段，請查照。

說明：

一、因含infliximab成分藥品可穿過胎盤，倘女性病人於懷孕或哺乳期間使用含infliximab成分藥品，其嬰兒體內尚殘留該成分藥品時又接種活性疫苗，恐發生感染之風險（包含致命性嚴重瀰漫性感染），故本署啟動該成分藥品之臨床效益及風險再評估。另歐洲藥品管理局(EMA)於111年2月14日及同年3月7日發布安全警訊（警訊內容如附件），建議懷孕期間曾使用infliximab之病人，其嬰兒於出生後12個月內不應接種活性疫苗，並修訂仿單中針對嬰兒暴露於infliximab成分藥品之安全資訊以及其接種活性疫苗之適當時機與施打建議。

二、為進行含infliximab成分藥品之臨床效益及風險再評估，貴會倘有相關意見或下列相關研究文獻等資料，請於112年4月30日前檢送至本署，逾期未提具資料者，視同無意

見：

(一)針對旨揭成分藥品用於特殊族群（孕婦、哺乳婦女）之臨床風險效益見解，另就需長期使用該成分藥品之該等特殊族群，其所產之嬰兒或接受其哺乳之嬰兒是否需監測infliximab血中濃度，以避免體內尚殘留該成分藥品時又接種活性疫苗而增加感染風險，以及臨床實務於嬰兒血清中仍可測得其濃度之殘留時間為何？

(二)臨床上是否有孕婦、哺乳婦女因使用旨揭成分藥品，導致其所產之嬰兒或接受其哺乳之嬰兒後續接種活性疫苗疑似發生不良反應之案例或國內相關統計數據？

(三)是否同意於「警語及注意事項」、「交互作用」與「特定族群注意事項」處修訂有關懷孕期間使用infliximab治療而暴露該成分之嬰兒，建議出生後至少12個月的等待期再給予任何活性減毒疫苗，除非於嬰兒血中已檢測不出infliximab，或暴露時間僅限於第一孕期，則其可評估於更早的時間點接種活性疫苗，且不建議哺乳期間接受 infliximab治療之女性讓其嬰兒接種活性疫苗等內容，若否，建議等待期至少多久或嬰兒血中infliximab濃度低於多少，較可使哺乳及接種疫苗對嬰兒的健康需求及疾病預防，與嬰兒暴露於該成分藥品而接種疫苗可能導致不良反應之發生間，取得風險效益之平衡？敬請說明理由。

(四)承上題，是否同意一併修訂卡介苗及輪狀病毒疫苗之中文仿單有關嬰兒暴露於infliximab成分藥品之安全資訊及其接種之適當時機與施打建議。

(五)其他意見或建議。

正本：中華民國醫師公會全國聯合會、中華民國藥師公會全國聯合會、中華民國藥劑生公會全國聯合會、台灣製藥工業同業公會、中華民國製藥發展協會、中華民國學名藥協會、中華民國西藥商業同業公會全國聯合會、中華民國西藥代理商業同業公會、台北市西藥代理商業同業公會、中華民國基層醫療協會、中華民國免疫學會、中華民國風濕病醫學會、台灣消化系醫學會、台灣兒科醫學會、台灣婦產科醫學會、台灣母胎醫學會、台灣周產期醫學會、台灣新生兒科醫學會、台灣母乳哺育聯合學會、台灣家庭醫學醫學會、台灣內科醫學會、台灣藥品行銷暨管理協會、台灣社區醫院協會、台灣醫院協會、台灣藥物臨床研究協會、社團法人臺灣臨床藥學會、財團法人醫院評鑑暨醫療品質策進會

副本：全國藥物不良反應通報中心、衛生福利部疾病管制署、衛生福利部中央健康保險署、財團法人醫藥品查驗中心、衛生福利部國民健康署 電子公文交換章 2023/03/31 09:48:43

裝 訂 線

Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 7 - 10 February 2022

News 11/02/2022

PRAC recommends suspending hydroxyethyl-starch solutions for infusion from the market

EMA's safety committee (PRAC) has recommended that marketing authorisations for hydroxyethyl-starch (HES) solutions for infusion should be suspended across the European Union (EU). These products were authorised as an addition to other treatments for plasma volume replacements following acute (sudden) blood loss.

The safety of HES solutions for infusion was reviewed in two separate procedures in 2013, and a number of restrictions and measures to minimise the risk of kidney injury and death in certain patients (those critically ill, with burn injuries or with sepsis, i.e. a bacterial infection in the blood) were put in place at the time.

As a result of a third review conducted in 2018, the use of HES solutions for infusion was further restricted to accredited hospitals, and healthcare professionals prescribing or administering the medicines had to be trained in their appropriate use. Companies marketing HES solutions for infusion were also requested to conduct a drug utilisation study to check that the restrictions were adhered to in clinical practice, and to submit the results of this study to EMA.

The PRAC has now reviewed the results from this study, which show that HES solutions for infusion are still being used outside the recommendations included in the product information. In view of the serious risks that certain patient populations are still exposed to, the PRAC has therefore recommended the suspension of the marketing authorisations for HES solutions for infusion in the EU.

More information is available in EMA's public health communication.

EMA starts safety review of Janus kinase inhibitors for inflammatory disorders

The PRAC has started a review of the safety of Janus kinase (JAK) inhibitors used to treat several chronic inflammatory disorders (rheumatoid arthritis, psoriatic arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, ulcerative colitis and atopic dermatitis).

The review was prompted by the final results from a clinical trial (study A3921133) of the JAK inhibitor Xeljanz (tofacitinib). The results showed that patients taking Xeljanz for rheumatoid arthritis and who were at risk of heart disease were more likely to experience a major cardiovascular problem (such as heart attack, stroke or death due to cardiovascular disease) and had a higher risk of developing cancer than those treated with medicines belonging to the class of TNF-alpha inhibitors. The study also showed that compared with TNF-alpha inhibitors, Xeljanz was associated with a higher risk of death due to any cause, serious infections and blood clots in the lungs and in deep veins (venous thromboembolism VTE).

In addition, preliminary findings from an observational study involving another JAK inhibitor, Olumiant (baricitinib), also suggest an increased risk of major cardiovascular problems and VTE in patients with rheumatoid arthritis treated with Olumiant compared with those treated with TNF-alpha inhibitors.

In the treatment of inflammatory disorders, Olumiant and other JAK inhibitors work in a similar way to Xeljanz. PRAC will therefore carry out a review to determine whether these risks are associated with all JAK inhibitors authorised in the EU for the treatment of inflammatory disorders[1] and whether the marketing authorisations for these medicines should be amended.

Some measures to minimise these risks are already in place for Xeljanz as a result of a review finalised in 2020, which analysed the interim results of study A3921133. In addition, the product information for Xeljanz was further updated in 2021 to reflect the increased risk of major cardiovascular problems and cancer observed after the release of additional data from this study.

More information is available in EMA's public health communication.

PRAC reviewing cases of period irregularities with mRNA COVID-19 vaccines

The PRAC is assessing reported cases of heavy menstrual bleeding (heavy periods) and absence of menstruation (amenorrhea) with the COVID-19 vaccines Comirnaty and Spikevax.

The Committee had previously analysed reports of menstrual (period) disorders in the context of the safety summary reports for COVID-19 vaccines approved in the EU and concluded at the time that the evidence did not support a causal link between these vaccines and menstrual disorders.

In view of spontaneous reports of menstrual disorders with both vaccines and of findings from the literature, the PRAC decided to further assess occurrences of heavy periods or amenorrhea following vaccination.

Menstrual disorders are very common and can occur with a wide range of underlying medical conditions as well as from stress and tiredness. Cases of these disorders have also been reported following COVID-19 infection.

Heavy periods may be defined as bleeding characterised by a volume, which may interfere with the person's physical, social, emotional and material quality of life. Amenorrhea may be defined as the absence of menstrual bleeding for three or more months in a row.

After reviewing the available evidence, the PRAC decided to request an in-depth evaluation of all available data, including reports from spontaneous reporting systems, clinical trials and the published literature.

At this stage, it is not yet clear whether there is a causal link between the COVID-19 vaccines and the reports of heavy periods or amenorrhea. There is also no evidence to suggest that COVID-19 vaccines affect fertility.

EMA will communicate further when more information becomes available.

Updated guidance on core requirements for risk management plans of COVID-19 vaccines

The PRAC has adopted updated guidance on core requirements for risk management plans (RMPs) of COVID-19 vaccines.

As for any medicinal product that is authorised in the EU, companies need to submit their RMP when applying for a marketing authorisation to detail their plan for the post-marketing surveillance and what measures they must put in place to further characterise and manage risks. In the context of the pandemic, EMA adopted specific RMP guidance for COVID-19 vaccines, which complements the existing guidelines on the RMP format in the EU and guidance on good pharmacovigilance practices.

Following discussion at the PRAC, this guidance has been updated in light of the experience accrued during the pandemic to include specific considerations on:

- content requirements for summary safety reports (formerly 'Monthly summary safety reports') to be submitted to EMA by marketing authorisation holders of newly authorised COVID-19 vaccines, and

details on safety topics for which monitoring with the usual periodic safety update reports (PSURs) is more appropriate;
- considerations for summary safety reports' frequency changes and when it is appropriate to remove the requirement to submit such safety reports.

The new version of the guidance is available on EMA's website.

New safety information for healthcare professionals

As part of its advice on safety-related aspects to other EMA committees, the PRAC discussed a direct healthcare professional communication (DHPC) containing important safety information for infliximab.

Advice to postpone use of live vaccines in infants exposed to infliximab during pregnancy or via breastfeeding

This DHPC informs healthcare professionals on the need to postpone the use of live vaccines in infants who are exposed to infliximab during pregnancy or via breastfeeding.

Infliximab is an anti-inflammatory medicine authorised for the treatment of adults with rheumatoid arthritis (an immune system disease causing inflammation of the joints), Crohn's disease (a disease causing inflammation of the digestive tract), ulcerative colitis (a disease causing inflammation and ulcers in the lining of the gut), ankylosing spondylitis (a disease causing inflammation and pain in the joints of the spine), psoriatic arthritis (a disease causing red, scaly patches on the skin and inflammation of the joints) or psoriasis (a disease causing red, scaly patches on the skin). Infliximab is also authorised in patients aged between 6 and 17 years with severe, active Crohn's disease or severely active ulcerative colitis, when they have not responded to or cannot take other medicines or treatments.

Following treatment during pregnancy, it has been reported that infliximab crosses the placenta and it has been detected in infants up to 12 months after birth. Live vaccines should not be given to infants for 12 months after birth if they have been exposed to infliximab during pregnancy. If infant infliximab serum levels are undetectable or infliximab administration was limited to the first trimester of pregnancy, administration of a live vaccine might be considered at an earlier time point if there is a clear clinical benefit for the individual infant.

Infliximab has also been detected at low levels in breast milk, therefore, administration of a live vaccine to a breastfed infant while the mother is receiving the medicine is not recommended unless infant infliximab serum levels are undetectable.

It is important that women treated with infliximab who become pregnant or who breastfeed their infant inform the healthcare professional responsible for vaccination of their infant about their treatment with infliximab.

The DHPC for infliximab will be forwarded to EMA's human medicines committee, the CHMP.

Following the CHMP decision, the DHPC will be disseminated to healthcare professionals by the marketing authorisation holders according to an agreed communication plan, and published on the Direct healthcare professional communications page and in national registers in the EU Member States.

---

[1] Cibinqo (abrocitinib), Jyseleca (filgotinib), Olumiant (baricitinib), Rinvoq (upadacitinib) and Xeljanz (tofacitinib).

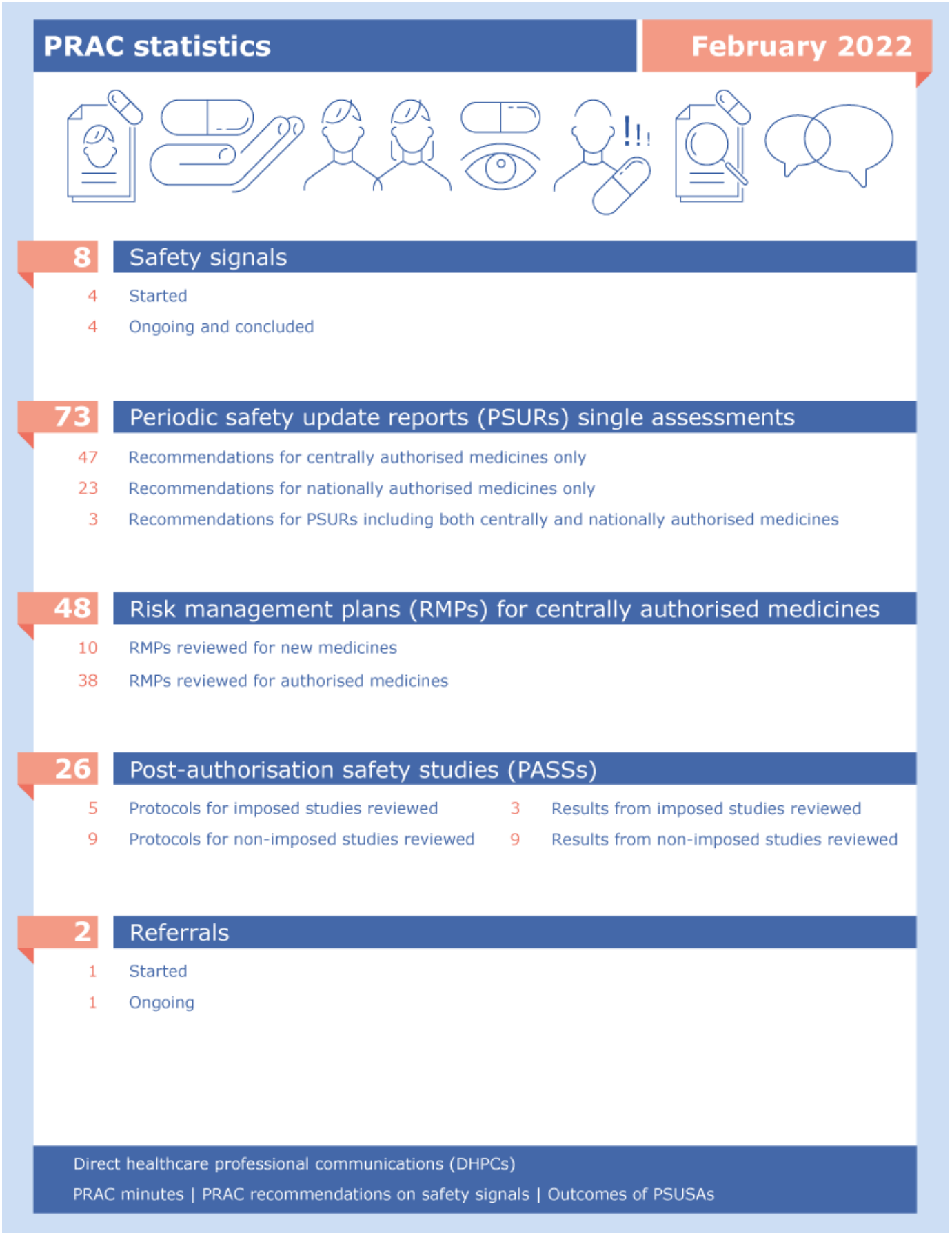
Agenda

Agenda of the PRAC meeting 7-10 February 2022 (PDF/601.84 KB)

Draft

First published: 08/02/2022
EMA/PRAC/76191/2022

PRAC statistics: February 2022



PRAC statistics: February 2022 (PDF/567.47 KB)

First published: 11/02/2022

Glossary:

- **Safety signal assessments**. A safety signal is information which suggests a new potentially causal association, or a new aspect of a known association between a medicine and an adverse event that warrants further investigation. Safety signals are generated from several sources such as spontaneous reports, clinical studies and the scientific literature. More information can be found under 'Signal management'.
- **Periodic safety update reports**, abbreviated as PSURs, are reports prepared by the marketing authorisation holder to describe the worldwide safety experience with a medicine in a defined period after its authorisation. PSURs for medicinal products that contain the same active substance or the same combination of active substances but have different marketing authorisations and are authorised in different EU Member States, are jointly assessed in a single assessment procedure. More information can be found under 'Periodic safety update reports: questions and answers'.
- **Risk management plans**, abbreviated as RMPs, are detailed descriptions of the activities and interventions designed to identify, characterise, prevent or minimise risks relating to medicines. Companies are required to submit an RMP to EMA when applying for a marketing authorisation. RMPs are continually updated throughout the lifetime of the medicine as new information becomes available. More information is available under 'Risk-management plans'.
- **Post-authorisation safety studies**, abbreviated as PASSs, are studies carried out after a medicine has been authorised to obtain further information on its safety, or to measure the effectiveness of risk-management measures. The PRAC assesses the protocols (aspects related to the organisation of a study) and the results of PASSs. More information can be found under 'Post-authorisation safety studies'.
- **Referrals** are procedures used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral related to safety of medicines, the PRAC is requested by a Member State or the European Commission to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the EU. More information can be found under referral procedures.
- **Summary safety reports** have been introduced as part of the enhanced safety monitoring of COVID-19 vaccines. Marketing authorisation holders are required to submit these reports to EMA, starting on a monthly basis. Their submission complements the submission of PSURs. For more information see EMA's pharmacovigilance plan for COVID-19 vaccines.

Ongoing referrals

Amfepramone-containing medicinal products - Article - 31 Referral
Under evaluation
PRAC continued its assessment.
Nomegestrol and chlormadinone - Article - 31 Referral
Under evaluation
PRAC continued its assessment.
Terlipressin-containing medicinal products-Article 31 Referral
Under evaluation
PRAC continued its assessment.

Related content

- Cibinqo: EPAR
- Comirnaty: EPAR
- Jyseleca: EPAR
- Olumiant: EPAR
- Rinvoq: EPAR
- Spikevax (previously COVID-19 Vaccine Moderna): EPAR
- Comirnaty: Pending EC decision
- Rinvoq: Pending EC decision
- Olumiant: Withdrawn application
- Olumiant: Paediatric investigation plan
- Olumiant: Paediatric investigation plan
- Olumiant: Paediatric investigation plan
- Olumiant: Paediatric investigation plan
- Olumiant: Paediatric investigation plan
- Rinvoq: Paediatric investigation plan
- Rinvoq: Paediatric investigation plan
- Comirnaty: Paediatric investigation plan
- Spikevax (previously COVID-19 Vaccine Moderna): Paediatric investigation plan
- Janus kinase inhibitors (JAKi): Article 20 procedures
- Janus kinase inhibitors (JAKi): Article 20 procedures
- Xeljanz: Article 20 procedures

- PRAC recommends suspending hydroxyethyl-starch solutions for infusion from the market (11/02/2022)
- EMA starts safety review of Janus kinase inhibitors for inflammatory disorders (11/02/2022)
- Safety of COVID-19 vaccines
- COVID-19 vaccines: authorised
- PRAC: Agendas, minutes and highlights
- Pharmacovigilance Risk Assessment Committee (PRAC): 7-10 February 2022

Related documents

Acronyms and abbreviations used in PRAC minutes (PDF/223.84 KB)

First published: 05/10/2012
Last updated: 22/07/2014
EMA/645658/2012 Rev. 2

Contact point

Media enquiries
Tel. +31 (0)88 781 8427
E-mail: press@ema.europa.eu

All other enquiries
please submit your request via the online form
Follow us on Twitter @EMA_News

European Medicines Agency
Domenico Scarlattilaan 6
1083 HS Amsterdam
The Netherlands

Tel: +31 (0)88 781 6000

How to find us

Postal address and deliveries

Business hours and holidays

For the United Kingdom, as of 1 January 2021, European Union law applies only to the territory of Northern Ireland (NI) to the extent foreseen in the Protocol on Ireland / NI.

European Union agencies network

An agency of the European Union

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

Table of contents

About

This direct healthcare professional communication (DHPC) contains important information for healthcare professionals prescribing, dispensing or administering the medicine(s). It also includes a communication plan with details of intended recipients and the dissemination date.

Documents

Direct healthcare professional communication (DHPC): Infliximab (Remicade, Flixabi, Inflectra, Remsima and Zessly): Use of live vaccines in infants exposed in utero or during breastfeeding
(PDF/252.37 KB)

First published: 07/03/2022

Key facts

Medicine name

- Remicade
- Flixabi
- Inflectra
- Remsima
- Zessly

Active substance

infliximab

Therapeutic area (MeSH)

- Spondylitis, Ankylosing
- Arthritis, Rheumatoid
- Psoriasis
- Crohn Disease
- Arthritis, Psoriatic

- Colitis, Ulcerative

Procedure number
EMEA/H/C/000240/IB/233
Regulatory outcome
Variation
DHPC type
New contraindication
Human ATC code
L04AB02
Dissemination date
07/03/2022

Related content

- Remicade
- Flixabi
- Inflectra
- Remsima
- Zessly
- Direct healthcare professional communications

European Medicines Agency
Domenico Scarlattilaan 6
1083 HS Amsterdam
The Netherlands

Tel: +31 (0)88 781 6000

How to find us

Postal address and deliveries

Business hours and holidays