Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

[redacted]

MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

www.gov.uk/mhra

17th August 2023

Dear [redacted]

FOI 23/533

Thank you for your email dated the 24th July 2023 where you requested;

1. How many cases of active tuberculosis related to the use of anti-tumour necrosis factor drugs (specifically etanercept, infliximab, adalimumab, golimumab and certolizumab pegol) have been made in the last 5 years?
2. How many of these cases of tuberculosis were reported to be fatal?

Apologies for any difficulties that you have experienced when navigating our website. In answer to your first question, please be aware that you can stay up to date on the number of reports and the adverse drug reactions (ADRs) submitted within those reports through our interactive drug analysis profiles (iDAPs). Please see below links to the iDAPs for the anti-tumour necrosis factor drugs you are interested in.

- Etanercept
- Infliximab
- Adalimumab
- Golimumab
- Certolizumab

It may be helpful to provide some information on the dictionary that we use when classifying ADR reports. MedDRA (Medical Dictionary for Regulatory Activities) is a clinically validated international medical terminology dictionary. It's organised by System Organ Class (SOC), divided into High-Level Group Terms (HLGT), High-Level Terms (HLT), Preferred Terms (PT) and finally into Lowest Level Terms (LLT). We use this to code our ADR reports within our database.

Please be aware that the iDAPs use PT terms and the LLTs 'Active Tuberculosis' and 'Tuberculosis' map to the same PT of 'Tuberculosis'. To view how many reports we have of tuberculosis on the iDAPs, on the profile for the selected drug, scroll down to the 'Reactions by MedDRA' section and expand the 'Infections and infestations' tab. Further expand 'Mycobacterial infectious disorders', and then 'Tuberculosis infections' to view the number of reports we have received where the PT

'Tuberculosis' was reported. To view the number of reports that we have received in the last five years, you can filter for the year received on the lefthand side of the iDAP.

In answer to your second question of how many of these cases were reported to be fatal, you can filter on the lefthand side of the iDAP for seriousness to see the number of reports with a fatal outcome that we have received. To do this, deselect 'Serious (excluding fatal)' and 'Non-Serious' to view only reports where a fatal outcome was reported.

When considering the provided spontaneous Adverse Drug Reaction (ADR) data, it is important to be aware of the following points:

- A reported reaction does not necessarily mean it has been caused by the drug or vaccine, only that the reporter had a suspicion it may have. The fact that symptoms occur after use of a drug or vaccine, and are reported via the Yellow Card scheme, does not in itself mean that they are proven to have been caused by the drug or vaccine. Underlying or concurrent illnesses may be responsible and such events can also be coincidental.

- It is also important to note that the number of reports received via the Yellow Card scheme does not directly equate to the number of people who suffer adverse reactions and therefore cannot be used to determine the incidence of a reaction. ADR reporting rates are influenced by the seriousness of ADRs, their ease of recognition, the extent of use of a particular drug or vaccine and may be stimulated by promotion and publicity about a drug or vaccine. Reporting tends to be highest for newly introduced medicines during the first one to two years on the market and then falls over time. For these reasons the above data should not be used as a basis for determining incidence of side effects. During assessment we take into account of the variable levels of reporting as part of our monitoring procedures.

I hope the information provided is helpful, but if you are dissatisfied with the handling of your request, you have the right to ask for an internal review. Internal review requests should be submitted within two months of the date of this response; and can be addressed to this email address.

Yours sincerely,

FOI Team,
Safety and Surveillance

Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

Water Lane
Wilmslow
Cheshire
SK9 5AF