Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

[redacted]

**MHRA**

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**11th April 2024**

Dear [redacted]

**FOI 24/308**

Thank you for your FOI request dated 30th March 2024, where you requested the following information:

*"Please could you tell me the total number of adverse drug reactions (ADRs) reported to you through the Yellow Card scheme in the 2023 calendar year?*

*In relation to the figures for 2023 could you also provide (i) the number of UK suspected ADR reports received with a fatal outcome, (ii) number of ADR reports received which resulted in prolonged hospitalisation and (iii) the number of reports received which resulted in prolonged hospitalisation AND had a fatal outcome?*

*In relation to the fatal outcomes could you please provide a table showing the ten drugs that were most frequently recorded as having caused such a reaction along with the number of times each one was recorded as having a fatal outcome."*

As mentioned in our previous FOI responses (FOI 21/313, FOI 22/584 and FOI 23/247), the MHRA continuously monitors the safety of medicines and vaccines through a variety of pharmacovigilance processes including the Yellow Card scheme. As part of our signal detection processes each fatal adverse drug reaction report received by the Yellow Card scheme is individually assessed and cumulative fatal information reviewed at regular intervals.

As with any serious suspected ADR, reports with a fatal outcome are fully evaluated by the MHRA, including an assessment of post-mortem details if available, to consider whether the medicine (or vaccine) may have caused the event, or whether the event and fatal outcome were likely to be purely coincidental and due to underlying illness. We hold weekly signal meetings in which drug/vaccine-reaction combinations which meet defined criteria are assessed by a group of scientists, physicians and pharmacists to determine if risk-minimisation measures need to be implemented. This includes potentially unrecognised drug interactions. Any emerging evidence relating to possible risks associated with medicines and vaccines, would be carefully reviewed and, if appropriate, regulatory action would be taken if any serious risks were confirmed.

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I can confirm that the MHRA has received a total of 86,578 UK spontaneous suspected ADR reports between 01/01/2023 and 31/12/2023 (data extracted 09/04/2024). Table 1 below shows the number of these reports that indicate a fatal outcome as well as the number considered serious due to the selection of hospitalisation or prolonged inpatient hospitalisation from the 6 serious categories[1] available.

**Table 1 – UK spontaneous suspected ADR reports received by the MHRA in 2023 (01/01/2023– 31/12/2023 inclusive)**

| | Fatal outcome | Hospitalised | Hospitalised with fatal outcome |
|---|---|---|---|
| **Number of reports** | 2280 | 10,071 | 377 |

As requested, please see Table 2 below of the ten most frequently reported drug substances that report a fatal outcome in the spontaneous ADR reports received in 2023.

**Table 2 – Drug substances most frequently reported in UK spontaneous suspected ADR reports with a fatal outcome received in 2023 (01/01/2023– 31/12/2023 inclusive)***

| Drug name | Number of ADR reports with a fatal outcome |
|---|---|
| CLOZAPINE | 338 |
| DARBEPOETIN ALFA | 256 |
| TOZINAMERAN | 96 |
| CHADOX1 NCOV-19 | 77 |
| METHOTREXATE | 65 |
| TACROLIMUS | 60 |
| RILTOZINAMERAN | 41 |
| GOLIMUMAB | 38 |
| RISPERIDONE | 35 |
| APIXABAN | 34 |

*Please note that the sum of reports in the table will not be equal to the total number of unique reports with a fatal outcome as one report may contain more than one suspect drug.

As mentioned in our previous FOI responses (FOI 20/165, FOI 22/584 and FOI 23/247), Yellow Card data for clozapine is subject to reporting bias which results in an unusually high number of reports compared to other medicines. This is because people treated with clozapine in the UK are required to undergo weekly, 2-weekly or monthly blood monitoring and are monitored more closely in clinical practice than patients receiving most other medicines. This in turn increases the likelihood that adverse reactions, as well as co-incidental medical events, are detected and reported to us.

[1] The seriousness criteria for ADR reporting were determined by a working group of the Council for International Organizations of Medical Sciences (CIOMS) and are defined as 6 possible categories which are documented on the Yellow Card. Reporters can select one or more of the following criteria by ticking the appropriate box on the Yellow Card. The criteria are: (1) patient died due to reaction (2) life threatening (3) resulted in hospitalisation or prolonged inpatient hospitalisation (4) congenital abnormality and (5) involved persistent or significant disability or incapacity or (6) if the reaction was deemed medically significant.

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Darbepoetin alfa is used in anaemia associated with chronic kidney disease and some cancer treatments. These patients are at a higher risk of death due to their underlying condition, this does not mean that there is a link between the medication and the fatalities reported.

Similarly, COVID-19 vaccines are subject to high number of reports compared to other products, due to public awareness of the pandemic and patient information encouraging reporting of all events relating to COVID-19 vaccines. The data provided above regarding COVID-19 vaccines should be viewed in light of the very large numbers of people who have received COVID-19 vaccine doses. The majority of reports of suspected ADRs to the COVID-19 vaccines in which the patient died shortly after vaccination were in elderly people or people with underlying illness. However, this does not mean that there is a link between vaccination and the fatalities reported. Review of specific groups of fatal reports is provided within the analysis of reports section of our coronavirus vaccine - weekly summary of Yellow Card reporting.

When considering the above information, it is important to note that an ADR report is not proof of a side effect occurring but a suspicion by the reporter that the drug may have caused the side effect. The fact that symptoms occur after a drug is given does not mean that they are caused by the drug itself as underlying or undiagnosed illnesses and other factors may be responsible.

Furthermore, the number of reports received via the Yellow Card Scheme does not directly equate to the number of people who suffer adverse reactions to drugs for a number of reasons. ADR reporting rates may be influenced by the seriousness of reactions, their ease of recognition, extent of use of a particular drug or vaccine and promotion and publicity about a drug or vaccine.

I hope the information provided is helpful. The MHRA encourages the use of Yellow Card data. However, we seek to ensure that the data is studied and applied appropriately, and any conclusions/interpretations consider the above information. For this reason, if you wish to use this information for a publication, we request that you engage with the MHRA during this process and provide a copy of the report. 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



If you have a query about this email, please contact us. If you are unhappy with our decision, you may ask for it to be reviewed. That review will be undertaken by a senior member of the Agency who has not previously been involved in your request. If you wish to pursue that option please write to the Communications Directorate, 4-T, Medicines and Healthcare products Regulatory Agency, (via this email address). After that, if you remain dissatisfied, you may ask the Information Commissioner at:

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