Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

[redacted]

MHRA

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www.gov.uk/mhra

2nd April 2024

Dear [redacted]

FOI 24/222

Thank you for your email dated 03 March 2024 where you requested the following information:

"Medications of interest
- *Denosumab*
- *Zoledronate/Zolendronic acid*
- *Alendronic Acid*
- *Risedronate/Risedronic Acid*
- *Bevicazumab*
- *Aflibercept*
- *Palbociclib*

I've looked through the data on the website and at the number of reports of these drugs relating to MRONJ in 2023. It would be good to know where the reports for these drugs came through, whether it was patients reporting or pharmaceutical companies or medical professionals and which region they were reported in.

Our project is aiming to improve reporting relating to MRONJ both locally at our hospital and hopefully more regionally also. We were surprised by the low number of reports in particularly in drugs such as denosumab and zoledronate- is this because it is now a known side effect and people don't see the point in reporting? And further to that is there a point in reporting if it is already a recognised side effect? And are official reports of incidence/prevalence taken from this data or from other sources?"

It may be helpful to firstly provide some background information to allow interpretation of this data. The Yellow Card scheme is the UK system for collecting and monitoring information on suspected adverse drug reactions (ADRs). The scheme is run by the MHRA and currently relies on voluntary reporting of suspected ADRs by health professionals and patients. There is also a legal obligation for pharmaceutical companies to report serious ADR reports to their drugs. All reports, including from patients, are reviewed through a signal detection process to identify previously unrecognised concerns about medicines and consider if further action is necessary.

As you are aware we have published data on our website as iDAPs. These have filters down the left of the webpage that allow users to view the data that they are interested in more easily. The "report submission" filter will allow you to view reports submitted directly to the Yellow Card scheme from healthcare professionals and patients, or report received directly via pharmaceutical

companies. Further to this you are also able to filter using “reporter” to view reports submitted via healthcare professional or patients only.

To be helpful we have provided this information for you below, please see table 1 for the total number of UK suspected spontaneous ADR reports associated with Osteonecrosis of the Jaw received between 01 January 2023 and 31 December 2023, from patients, healthcare professionals and pharmaceutical companies.

Table 1: Total number of UK suspected spontaneous ADR reports for Osteonecrosis of the Jaw received in 2023.

	Patients	Healthcare Professionals	Pharmaceutical companies	Total number of reports
Denosumab	1	3	30	34
Zoledronic Acid	0	3	15	18
Alendronic Acid	0	6	7	13
Risedronic Acid	0	0	0	0
Bevacizumab	0	0	0	0
Aflibercept	0	0	0	0
Palbociclib	0	0	0	0

Please note that a single Yellow Card report may contain multiple suspect drugs. As such the total number of reports for these drugs cannot be calculated from the information available for each individual drug.

Additional please see table 2 below which displays the number of UK suspected spontaneous reports received by region for those reports which have been submitted directly to the MHRA from healthcare professionals and patients, i.e. this will not include reports received from pharmaceutical companies due to limited information held on the original reporter.

Table 2: Total number of UK suspected spontaneous ADR reports from healthcare professionals and patients for Osteonecrosis of the Jaw received directly in 2023 by region.

	Region	Number of reports
Denosumab	North England (Yorkshire and Humber)	2
	East England and Midlands (East)	1
	South West England (South West North)	1
Zoledronic Acid	England (London)	1
	North England (Yorkshire and Humber)	1
	East England and Midlands (West Midlands)	1
Alendronic Acid	England (London)	2
	East England and Midlands (West Midlands)	1
	North England (Cheshire and Merseyside)	3

A reported reaction does not necessarily mean it has been caused by the medicine or vaccine, only that the reporter had a suspicion it may have. The fact that symptoms or events occur after use of a medicine 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 medicine or vaccines. Underlying or concurrent illnesses may be responsible and such events can also be coincidental.

You have asked about the number of reports in relation to osteonecrosis being a known side effect. As you will know the scheme is voluntary and many factors influence the number of reports that we receive in the UK meaning volumes of reporting can be variable. Reporting rates are influenced by the seriousness of the adverse drug reactions, their ease of recognition, the extent of use of a particular product, and may also be stimulated by promotion and publicity about a product. Reporting rates tend to be highest when a product is first put on the market. Our Yellow Card strategy aims to publicise the importance of reporting to the scheme and raise awareness amongst healthcare professionals and patients. Alongside this we are improving the ease of reporting, for example with mobile apps, and increasing transparency through publishing our data.

The MHRA monitors all reports of adverse reactions associated with all medicines or vaccines regardless of whether information on the suspected adverse reaction is already present in product information. This information may be used to further characterise adverse reactions listed in the product information and can inform regulatory actions to minimize risk such as restricting use in particular patient populations and under specific clinical circumstances.

Further to your last question, the number of reports received cannot be used as a basis for determining the incidence of a reaction as neither the total number of reactions occurring, nor the number of patients using the drug is known.

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 this response's date and can be addressed to this email address.

Yours sincerely,

FOI Team,
Safety and Surveillance Division

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