Medicines & Healthcare products
Regulatory Agency

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[redacted]

30th May 2024

Dear [redacted]

FOI2024/00085

Thank you for your Freedom of Information requested dated Wednesday 1st May 2024 where you stated: "*I am writing to make a FOI request for the number of yellow card reports you have received on the Besins' pump action oestrogen gel that goes by the names of Oestrogel, Estrogel or Oestrodose.*

As you may be aware many women are being given different versions of the medications by their pharmacies as parallel imports or due to a change in branding but some are finding the products do not dispense correctly, the consistency is different and their symptoms return.

If you could let me know how many have been received over the past 12 and 24 months it would be greatly appreciated."

In response to your query, I can confirm that between 1st May 2022 up until the 30th April 2024, the MHRA has received **358** UK spontaneous suspected Adverse Drug Reaction (ADR) reports for Oestrogel, **25** concerning Oestrodose and **11** concerning Estrogel respectively. To note, these are total numbers of reports and have not been broken down by specific ADRs such as dispensing and consistency issues. Please see Table 1 below for a further breakdown of these reports by month and year received.

It is important to note that this data has been extracted based on the reported drug name and not the associated manufacturer. In many cases this is not provided and cannot be determined with the information included within the report.

Table 1: Number of UK spontaneous suspected ADR reports received for Oestrogel, Estrogel and Oestrodose between 1st May 2022 up to and including 30th April 2024, by month and year received.

Year	Month	Number of Reports		
		Oestrogel	Oestrodose	Estrogel
2022	May	18	0	0
	June	7	0	0
	July	3	0	3
	August	6	0	0
	September	4	1	0
	October	6	3	0
	November	12	2	1
	December	12	2	1
2023	January	11	2	0
	February	10	0	1
	March	11	1	0
	April	11	0	0
	May	5	1	1
	June	14	1	0
	July	22	1	1
	August	14	1	2
	September	33	0	0
	October	33	3	1
	November	26	2	0
	December	23	2	0
2024	January	37	1	0
	February	16	1	0
	March	18	0	0
	April	6	1	0

When considering the spontaneous ADR data within this response, it is important to be aware of the following points:

- A reported reaction does not necessarily mean it has been caused by the drug, only that the reporter had a suspicion it may have. The fact that symptoms occur after use of a drug, and are reported via the Yellow Card scheme, does not in itself mean that they are proven to have been caused by the drug. 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, and may be stimulated by promotion and publicity about a drug. 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 enclosed data should not be used as a basis for determining incidence of side effects.

Additionally, in response to your query, I can confirm that between 1st May 2022 up until the 30th April 2024, the MHRA has received **721** reports that relate to potential quality defects for Oestrogel, Estrogel and Oestrodose. Of the **721** reports, **67** are related to potential device failure, **4** are related to solubility, **15** are related to adverse drug reactions and **451** are related to lack of efficacy which could be related to the consideration that the products do not dispense correctly, the consistency is different and their symptoms return. To note, the remaining reports have not been broken down by other potential defect classifications and grouped within 'Other.'

Table 2: Number of reports received for Oestrogel, Estrogel and Oestrodose between 1st May 2022 up to and including 30th April 2024, and year received by the Defective Medicines Report Centre.

Year	Number of Reports	Potential Reported Defect Classification
2022	4	Device Failure
	57	Lack of Efficacy
2023	15	Adverse Drug Reaction
	49	Device Failure
	279	Lack of efficacy
	96	Other
	4	Solubility
2024	14	Device Failure
	115	Lack of efficacy
	88	Other

The MHRA, including the Defective Medicines Report Centre (DMRC), has been liaising with Besins Healthcare (UK) Ltd since we initially received a signal of potential quality issues with the product. The investigations to date have not identified any deficiencies regarding the ingredients, manufacturing process, or the equipment during testing. No quality deficiencies were found for batches specific to reports where it was stated that the product does not work. Additionally, whilst the MHRA have been investigating this issue with Besins Healthcare (UK) Ltd both the MHRA and Besins Healthcare (UK) Ltd have not identified any deviations during the manufacturing and packaging of product batches that could lead to an explanation for the reported defect of lack of effect.

The DMRC were informed of a potential quality issue that impacted two specific batches, and this information was assessed with Besins Healthcare (UK) Ltd which resulted in a recall due to a failure to dispense the product from the pump. The assessment and the information shared by Besins Healthcare (UK) Ltd indicated that this was only impacting two batches, batch number 74800 and batch number 74830. Further information can be found below:

Besins Healthcare (UK) Ltd has informed the MHRA that a defective pump system was detected in two batches of Oestrogel Pump-Pack 750 micrograms/actuation Gel. The product pumps are subject to mechanical faults which result in the failure to dispense the product and in some cases, the detachment of the pump from the container. It is estimated that 11% of units across the two batches could be affected by the defect. Where the pump is functioning, there is no impact on the quality or safety of the Gel and therefore this is not a

patient level recall. *https://www.gov.uk/drug-device-alerts/class-3-medicines-recall-besins-healthcare-uk-ltd-oestrogel-pump-pack-750-micrograms-slash-actuation-gel-estradiol-el-24-a-slash-09*

The MHRA have not conducted any independent testing of Oestrogel. In the first instance, the DMRC will ask the company to investigate the suspected defect. The company are best placed to review the records of manufacture and packaging and have the analytical methods and equipment in place to test the complaint sample and retained samples. The DMRC will critically review the company's investigation and testing results. If the investigation or testing are not satisfactory, then independent testing may be performed by the MHRA Laboratories. The product continues to meet the finished product specifications and therefore the DMRC have considered no further market action and the MHRA are not considering any further product testing at this stage.

I hope the information provided is helpful, but if you are dissatisfied with the handling of the part of your request handled under FOI, 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 and Healthcare products Regulatory Agency