Medicines & Healthcare products
Regulatory Agency

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[redacted]

7 March 2024

FOI 24/136

Dear [redacted]

Thank you for your information request, dated 8 February, where you asked for details associated with European Medicines Agency's (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) report "The Valporate - EMEA -H-A31-1454 - Assessment Report".

Background to Request 1

In section 6 of THE REPORT entitled "Conditions to the marketing authorisations", it stated that: "The MAHs of medicinal products with substances related to valproate shall conduct a retrospective observational study to investigate the association between paternal exposure to valproate and the risk of congenital anomalies and neurodevelopmental disorders including autism in offspring. Protocol to be submitted in accordance with Article 107n (1) of Directive 2001/83/EC within 6 months after Commission decision.
The first interim report shall be submitted to the PRAC within 12 months after endorsement of the study protocol.

a) Further interim reports should be submitted to the PRAC 6-monthly thereafter for the first 2 years
b) The final study report shall be submitted to the PRAC within 48 months after endorsement of the study protocol.

REQUEST 1:
Please provide copies of the reports as described in a), b) and c) above. In the event that you do not have these reports, please provide reports covering studies to investigate the association between paternal exposure to valproate and the risk of congenital anomalies and neurodevelopmental disorders including autism in offspring. In the event that you do not have similar reports, please advise if such studies are being commissioned by you or another UK Agency, and if so, when are the subsequent reports expected to be submitted?

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Background to Request 2

As set out in the last bullet point of section 7 of THE DOCUMENT entitled "Grounds for Recommendation", it stated that: "The PRAC also reviewed the available scientific evidence on the risk of malformations and neurodevelopmental disorders to offspring after paternal exposure, the risk of malformations and neurodevelopmental disorders to the third generation offspring and considered that further research is needed before conclusions can be drawn. The PRAC requested the conduct of post authorisation studies."

REQUEST 2:
Please provide copies of interim and final reports of these post authorisation studies where available. In the event that you do not have these reports, please provide reports covering studies commissioned by you or another UK agency to investigate the association between paternal exposure to valproate and the risk of malformations and neurodevelopmental disorders to the third generation offspring. In the event that you do not have similar reports, please advise if such studies are being commissioned, and if so, when are the subsequent reports expected to be submitted?

Unfortunately, the information is exempt from release under section 41:

Section 41 – Information provided in confidence: information provided to us in confidence, with the expectation that it will not be released, is exempt from disclosure under the FOI Act. Information will be covered by Section 41 if: it was obtained by the authority from any other person; its disclosure would constitute a breach of confidence; a person or organisation could bring a court action for that breach of confidence; and that court action would be likely to succeed.

Both request 1 and 2 relate to the same data set, as the grounds in section 7 are the basis for the conditions in section 6 of the PRAC report. The Marketing Authorisation Holders (MAHs) for valproate containing medicines initiated a post authorisation safety study (PASS) with the reference EMEA/H/N/PSP/J/0072 – Paternal exposure, to investigate the risk of malformations and neurodevelopmental disorders to offspring after paternal exposure using a retrospective observational study. The MHRA received copies of the interim report for this PASS in August 2021 and the final report which was subject to reanalysis and resubmitted in October 2023 at the same time these documents were submitted to the EMA.

In this case, we confirm that this exemption applies because this information was obtained by the authority (the MHRA) from another person. As described above, the information was provided to us by the MAHs as part of the Post Authorisation Safety Study commissioned by the EMA, therefore it has been supplied by a third party.

We consider that disclosure would constitute an actionable breach of confidence

because it meets the tests stated above; the information has the necessary quality of confidence because it is not trivial and is not otherwise accessible in the public domain, and it was imported to the MHRA with explicit conditions of confidentiality. Disclosure in this instance would therefore be an unauthorised use of the information which would cause detriment to the third-party providing the information to use. This detriment is associated with the regulatory requirements imposed on MAHs to provide data, and our independent advisory committees ability to provide unbiased advice which are used as the basis for regulatory action in the UK. In addition, release of the information may compromise future publication of the data by the third-party.

The data was provided to us in confidence, with the expectation that it will not be released. It is therefore considered that disclosure would be an actionable breach with the likelihood that this action would succeed, and Section 41(1) applies.

Although we are unable to release the documents submitted by the MAHs, you may be interested to know that MHRA have communicated to healthcare professionals in the UK on this issue via our bulletin Drug Safety Update in August 2023 and will issue further communications in due course.

If you have a query about the information provided, please reply to this email.

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 you receive this response and addressed to: info@mhra.gov.uk

Please remember to quote the reference number above in any future communications.

If you were to remain dissatisfied with the outcome of the internal review, you would have the right to apply directly to the Information Commissioner for a decision. Please bear in mind that the Information Commissioner will not normally review our handling of your request unless you have first contacted us to conduct an internal review. The Information Commissioner can be contacted at:

Information Commissioner's Office
Wycliffe House
Water Lane
Wilmslow
Cheshire
SK9 5AF

Yours sincerely,

Safety & Surveillance