Medicines & Healthcare products Regulatory Agency

MHRA

Ms Joanna Wood
Review Team
Independent Medicines and Medical Devices Safety Review
King's College,
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Dear Ms Wood

Thank you for your letter of 4 June providing the opportunity to respond to the transcript of the oral hearing with Clare Pelham, Chief Executive of the Epilepsy Society, and Simon Wigglesworth, Deputy Chief Executive of Epilepsy Action.

**Accountability of the MHRA**
The MHRA is an Executive Agency of the Department of Health and Social Care. As Civil Servants, we are accountable to Ministers and we work in accordance with the Civil Service Code. The Department of Health and Social Care holds the Agency to account and provides assurance via formal sponsorship arrangements, which include publishing minutes of an annual accountability meeting between the Minister and the Agency Chair and CEO. Along with ongoing public communication about our work, the Agency publishes details of how we are scrutinised and our KPI performance via a variety of online corporate documents (including an annual business plan, a five-year corporate plan and an annual report and accounts which are laid before Parliament). The Agency Board publishes meeting minutes and holds public sessions every two months. The Agency is subject to the Freedom of Information Act like any other public body. Transcripts of parliamentary activity on Agency matters and answers to every Parliamentary Question are freely available in Hansard.

**Confidentiality of ongoing discussions of the Expert Working Groups of the Commission on Human Medicines**
Under the Human Medicines Regulations 2012, restrictions are expressly placed on the disclosure of any information by a person who obtains it by virtue of those Regulations. This includes those participating in meetings of the CHM and its Expert Working Groups. The purpose is to ensure that the regulatory process can proceed without bias or interruption resulting from media or other external influence. Following completion of a safety review, the Agency's policy is for the minutes of the discussions of Expert Working Groups to be published, together with the minutes of the CHM.

**Use of the term 'pregnancy prevention programme'; 'informed choice'**
For medicines known to be teratogenic, it is standard practice for regulators in the European system and internationally to implement and monitor compliance with a Pregnancy Prevention Plan or Programme. During discussions at the Expert Working Group on Sodium Valproate Ms Pelham expressed her concern about the term 'pregnancy prevention programme' and asked that it only be used in expert circumstances. We took this on board and asked the originator company, Sanofi, to

develop a 'brand' for the patient and healthcare materials which would be more accessible than the term 'pregnancy prevention programme'. The materials to support the valproate pregnancy prevention programme therefore have the 'Prevent' branding.

The role of the regulator is to describe the conditions in the marketing authorisation under which the benefits of a medicine are considered to outweigh its risks. Given the magnitude and nature of the harm caused when valproate is taken in pregnancy, the regulatory position is that valproate is contraindicated in women of childbearing potential unless they comply with the conditions of a pregnancy prevention programme. This is in line with other major teratogens such as thalidomide and isotretinoin. The use of valproate by a woman who wishes to become pregnant (and therefore is openly, to the knowledge of the treating clinician, not following the pregnancy prevention programme) would be outside the terms of the medicine's licence. Any such decision would be a matter for an individual patient and their specialist(s). As an off-label prescription, the prescriber would need to take responsibility for, and record the reasons for, that decision: in this regard, there is relevant GMC guidance on any clinical decision to prescribe medicines outside the terms of the product licence. Such a decision may well give rise to a risk of liability issues for the prescriber in the event of an adverse outcome, the nature of which would depend in particular on the individual circumstances of the patient and the reasons for the prescriber's decision.

The goal of risk minimisation for sodium valproate, as set out by Ministers, given the high incidence of serious and permanent disability of children exposed in utero, is to rapidly reduce and eventually eliminate exposed pregnancies. It is therefore anticipated that women on valproate who wish to become pregnant will be supported by their healthcare professionals either to use alternative antiepileptic medicines or to choose other ways of parenting. Our responses to the transcripts of the evidence given to the IMMDS review by Dr Jim Morrow and the APPG for Valproate and Other Anti-epileptic Drugs outline our ongoing work to ensure that decisions on alternative antiepileptics are informed by the most up to date data on their safety in pregnancy.

I would be happy to provide any further clarification, and once again my thanks for the opportunity to respond on these important matters.

Yours sincerely

**Dr June Raine**
**Director – Vigilance and Risk Management of Medicines**

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