Sodium valproate and women with epilepsy

British Pregnancy Advisory Service briefing

The British Pregnancy Advisory Service (BPAS) is a British reproductive healthcare charity that offers pregnancy counselling, abortion care, miscarriage management, contraception and STI testing to 85,000 women each year via our clinics in England, Wales, and Scotland.

We counsel and treat many women who are concerned about the impact their condition or prescription medication may have had on their pregnancy, and provide abortions for women whose doctors have advised them that continuing with their pregnancy poses a serious risk to their life or health.

We also advocate for women's reproductive choice and the right to make their own choices about their own bodies and treatments, with access to impartial, evidence-based information and services to support their decision making.

Overview

In 2018, new restrictions were introduced on the use of Sodium Valproate among women of childbearing age. Under the new rules, Sodium Valproate should not be used in girls and women of childbearing potential unless other treatments are ineffective or not tolerated, even if they have no intention of becoming pregnant. Valproate can only be initiated in girls and women of childbearing potential if the conditions of a "Pregnancy Prevention" scheme are fulfilled.

We believe **it is of paramount importance that women understand that Sodium Valproate poses risks in pregnancy**, and it is clear that there have been major shortcomings in the provision of this information to women historically.

However, sodium valproate may be the only effective medication for some women, and we believe **women should have the right to specialist information about the risks and benefits of Sodium Valproate and its alternatives to make their own choice**, based on their individual circumstances.

Key facts:

- Epilepsy affects around 600,000 people in the UK and 1200 people die every year due to epilepsy
- Sodium Valproate may be the only effective medication for some women who have particular epilepsies. The Government estimates that 27,000 women of childbearing age were prescribed Sodium Valproate in 2016.
- It raises serious ethical questions to deny a woman what may be the most effective medication to treat her serious medical condition based on her capacity for pregnancy
- Prescribing of Sodium Valproate in pregnancy fell by nearly 50% between 2010 and 2017, before the latest restrictions were announced.

Background

In women who take valproate while pregnant, around 1 in 10 babies will have a birth defect.

Birth defects seen when mothers take valproate during pregnancy include:

- spina bifida (where the bones of the spine do not develop properly)
- facial and skull malformations (including cleft lip and palate, where the upper lip or facial bones are split)
- malformations of the limbs, heart, kidney, urinary tract and sexual organs.

In women who take valproate while pregnant, about 3–4 children in every 10 may have developmental problems. The long-term effects are not known.

The effects on development can include:

- being late in learning to walk and talk
- lower intelligence than other children of the same age
- poor speech and language skills
- memory problems.

Children exposed to valproate in the womb are more likely to have autism or autistic spectrum disorders. There is also some evidence children may be more likely to be at risk of developing symptoms of attention deficit hyperactivity disorder (ADHD).

Outside sodium valproate, other AEDs also carry warnings for pregnant women, with recommendations to engage in pre-conception counselling and potentially reduce the dosage or change the type of medication they are prescribed during pregnancy.

New valproate guidance

The Medicines and Healthcare products Regulatory Agency (MHRA) announced on 24th April 2018 that they had amended the licence for the use of valproate medicines among women of childbearing age. This update is based on a European Medicines Agency agreement and the MHRA took an active role in developing the guidance.

Although the MHRA guidance is based on the European measures, the UK requirements have been significantly reworded.

<table>
<tr><th>European guidance</th><th>MHRA guidance</th></tr>
<tr><td>an assessment of each patient’s potential for becoming pregnant,</td><td rowspan="2">ensure the patient understands the need to comply with contraception throughout treatment and undergo pregnancy testing when required e.g. if there is any reason to suggest lack of compliance or effectiveness of contraception</td></tr>
<tr><td>pregnancy tests before starting and during treatment as needed,</td></tr>
<tr><td>counselling about the risks of valproate treatment and the need for effective contraception throughout treatment,</td><td>ensure the patient understands the risks to the unborn child of using valproate during pregnancy and provide patient guide</td></tr>
<tr><td>a review of ongoing treatment by a specialist at least annually,</td><td rowspan="2">complete and sign the acknowledgement of risk form (at every annual visit), give a copy to the patient and send one to the GP</td></tr>
<tr><td>introduction of a new risk acknowledgement form that patients and prescribers will go through at each such annual review to confirm that appropriate advice has been given and understood.</td></tr>
<tr><td></td><td>refer for contraception services as needed</td></tr>
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Care of pregnant women with epilepsy

The introduction of these guidelines comes at a time when deaths of pregnant women with epilepsy remain static – with several women a year dying either during pregnancy or in the post-partum period – and where concerns have been raised that the withdrawal of AEDs may have played a role in the deaths of women who stopped them as a result of their pregnancy.

One in 200 pregnant women have epilepsy. **Maternal mortality is almost 10 times greater for women with epilepsy** than for those without epilepsy (100 versus 11/100 000 pregnancies).

The 2017 national MBRRACE report on the surveillance of investigation of maternal deaths found that between 2013 and 2015, **eight women with epilepsy died during pregnancy or in the immediate post-partum period,** and there was **one additional pregnancy-related death between six weeks and one year after delivery**.

In the 2017 report, **5 of the 9 women whose deaths were considered had stopped their AED and were not taking any medication during pregnancy**. **Of these, 2 had previously been taking sodium valproate.** This compares to the 2014 report where only 2 out of 14 epileptic women who died were not taking any medication.

The same report found that **only 4% of women with severe morbidity from epilepsy received good maternity care**. Improvements in care may have made a difference to the care outcome of 52% of women with epilepsy.

The importance of messaging

The discussion around sodium valproate and the impact of other AEDs on pregnancies has focused overwhelmingly on the impact on 'unborn children' rather than on the health and care of women with epilepsy.

The evidence from MBRRACE that women are stopping their medication, sometimes in conjunction with advice from medical professionals, makes clear that the current discourse may endanger some women's health.

The decision-making around sodium valproate and other AEDs among women of childbearing age requires thorough and individualised discussions with patients, enabling women to make their own decisions. We should be prioritising information-sharing and informed consent – not the restriction of women's choices.

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