HOUSE OF COMMONS LIBRARY

DEBATE PACK

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Valproate and Fetal Anti-Convulsant Syndrome

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This pack has been produced ahead of the general debate to be held in the Commons Chamber on Thursday 19 October 2017 on Valproate and Fetal Anti-Convulsant Syndrome. The debate was scheduled by the Backbench Business Committee following a representation from Norman Lamb MP.

Contents

1. Valproate and Fetal Anti-Convulsant Syndrome

Summary

A Backbench Business Committee debate, led by Norman Lamb on 19 October 2017 will focus on Fetal Anti-convulsant syndrome and sodium valproate. MPs and charities have raised concerns about the risks of fetal abnormalities and child developmental problems associated with the use of this drug in pregnancy, and women's awareness of these risks.

There is a small risk of birth defects in any pregnancy. Generally, some anti-epileptic drugs (AEDs) may increase this risk, but there is also a risk from uncontrolled seizures in pregnancy. Medical organisations stress that women should not stop/alter their epilepsy medication without discussing this with their doctor.

Sodium Valproate is an anti-epileptic drug (AED) that is associated with greater risks in pregnancy than other AEDs (there are also other valproate drugs, for example valproic acid and valproate semisodium). The Medicines and Healthcare products Regulatory Agency (MHRA) report that whilst the general risk of a fetal abnormality is 2-3%, in women taking sodium valproate the risk is around 10%. Birth defects can include spina bifida, malformation of limbs and facial and skull malformations. It also states that the use of sodium valproate in pregnancy can affect a child's development, about 30-40 children in 100 may have developmental problems such as delays in learning to walk and talk, lower intelligence than children of the same age and poor speech and language skills.

A concern raised by epilepsy charities and patient groups is that there has been a lack of information for women about the risks associated with sodium valproate. A 2016 survey of 2,788 women, showed that 20% of those who were taking sodium valproate for their epilepsy were not aware of the risks in pregnancy. This survey was repeated in 2017, when responses were very similar.

In 2016, the MHRA produced a valproate toolkit. This provides guidance for clinicians, and patient information on sodium valproate. This includes that:

- Women and girls of child bearing potential should not be prescribed valproate unless other treatments are ineffective or not tolerated;
- No one should stop taking valproate without discussing this with their doctor. The benefits and risks of the treatment need to be carefully balanced; and
- If valproate is the only option, women should be given effective contraception, and should have regular reviews of treatment.

There have been similar concerns about this drug internationally. In 2016, following a report that estimated that about 450 children in France had been affected by sodium valproate between 2006 and 2014, the French Parliament voted to establish a compensation fund for those affected. A class action legal case has also been recently launched against the company that manufacture the medicine in France, Sanofi. In the past there has also been legal action launched on this subject in the UK. In 2004, a class action was brought by a group of families under the *Consumer Protection Act 1987*. The case was expected to go to trial in 2011, but the litigation was discontinued prior to this after the Legal Services Commission withdrew funding.

In March 2017, the European Medicines Agency launched a review of the safety of using valproate-containing medicines in women and girls who are pregnant or of childbearing age. This has included the first public hearing on a medicine safety review. The Pharmacovigilance and Risk Assessment Committee heard evidence from patients and patient representatives, healthcare professionals, academics and pharmaceutical industry representatives.

In Parliament, the Government have highlighted the MHRA's work with a range of stakeholders to raise awareness of the risks of this medicine. They have said that there was no current plans to introduce a compensation fund similar to that in France, but there is support available through local authorities and CCGs for families with children born with a disability.

Epilepsy charities are calling on the Government to change the way prescribing is undertaken for sodium valproate. They suggest that repeat prescriptions should not be routinely renewed for this drug for longer than 12 months without a face to face consultation with a health professional.

1.1 Epilepsy and pregnancy

There is a small risk of birth defects in any pregnancy. Generally, some anti-epileptic drugs (AEDs) may increase this risk, but there is also a risk from uncontrolled seizures in pregnancy.

More information about the risks with AEDs in pregnancy are provided on the NHS choices website:

> Many women with epilepsy use AEDs to keep their seizures under control. Research has shown that there may be an increased risk of foetal anti-convulsant syndrome (FACS) in children born to mothers who have taken some AEDs during pregnancy. A child with FACS may have a number of physical or brain development (neurodevelopmental) difficulties, including the ones listed below.
>
> These drugs may increase the risk of physical defects such as spina bifida, heart abnormalities and cleft lip. Depending on the type of drug and the dose you are taking, there may also be an increased risk of developmental problems in the baby, such as:
>
> - lower intellectual abilities
> - poor language skills (speaking and understanding)
> - memory problems
> - autistic spectrum disorders
> - delayed walking and talking

The webpage goes on to state that women should seek advice from their doctor on this, and stresses that women should not alter or stop taking their medication without specialist advice (bold retained from original):

> Before you get pregnant (or you think you might be pregnant unexpectedly, or are planning to get pregnant) discuss your treatment with an obstetrician and a neurologist who knows about **your** epilepsy. They may want to consider an alternative treatment. It is usually better to make any changes to drug treatment before rather than during pregnancy.
>
> If you get pregnant while you are taking an AED, **continue to take your medication and contact your specialist immediately to discuss your drug treatment. Do not alter your drug treatment or stop taking your medication without specialist advice, especially during pregnancy**. This is because a severe seizure in pregnancy could result in harm or injury, or possibly even death, to you or your baby.

For general information on pregnancy and epilepsy, and the risks associated with AEDs (including sodium valproate), as well as guidance on preconception counselling, the following webpages may be useful:

- NHS Choices, Epilepsy and pregnancy, 2015
- Epilepsy Action, During pregnancy

- Epilepsy Society, Pregnancy and epilepsy

1.2 Sodium valproate

Sodium valproate is an anti-epileptic drug (AED) that is associated with greater risks in pregnancy than other AEDs. There are also other valproate drugs, for example valproic acid and valproate semisodium. Valproate medicines can also be used to treat bipolar disorder, and to prevent migraines.

The Medicines and Healthcare Products Regulatory Agency (MHRA) produced guidance in 2016 on the prescribing of valproate. This reports that the product information for this medicine has included a warning about the possible risk of birth defects since 1974. It states that the MHRA has worked with healthcare professionals and patient groups to ensure that female patients are better informed about the risks. The document provides the following advice:

> Valproate should not be used in female children, in female adolescents, in women of childbearing potential and in pregnant women unless other treatments are ineffective or not tolerated. Women of childbearing potential must use effective contraception during treatment.
>
> No-one should stop taking valproate without discussing it first with their doctor and the benefits of valproate treatment must be carefully balanced against the risks.
>
> If valproate is the only option, women of childbearing age should be given effective contraception. Women taking valproate must have regular reviews of their treatment.[1]

The MHRA patient's guide, published at the same time provides information about the risks associated with taking sodium valproate (bold retained from original):

> **Taking valproate whilst pregnant can cause serious birth defects.**
>
> In women who take valproate while pregnant, around 10 babies in every 100 will have a birth defect.
>
> In women who don't have epilepsy, 2-3 babies in every 100 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.
>
> […]

[1] MHRA, Guidance: Toolkit on the risks of valproate medicines in female patients, February 2016

If you take valproate while you are pregnant, it could affect your child's development as they grow up.

In women who take valproate while pregnant, about 30–40 children in every 100 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).

The National Institute for Health and Care Excellence (NICE) has also updated its guidelines on the diagnosis and management of epilepsy in February 2016 to link to the new MHRA toolkit.

In April 2017, the MHRA and NHS Improvement sent a new Patient Safety Alert through the NHS Central Alerting System to further highlight the risks involved in the use of sodium valproate in pregnancy.[2] It asks all health organisations to identify women and girls taking valproate and to use the MHRA information to help them make informed choices about their treatment.

Recent figures published by NHS England report that of 173,787 patients taking sodium valproate in England, around 10% of these are women aged 14-45 (17,848).[3]

Concerns about patient awareness

There has been long standing knowledge of the risks associated with AEDs in pregnancy. Since the introduction of valproate medicines in the 1970s the product information for doctors has included a warning about the possible risk of birth defects.[4]

However, epilepsy charities and patient groups report that women are not aware of the potential risks when taking the drug in pregnancy.

In October 2016, a group of epilepsy charities reported that a survey of 2,788 women, had shown that 20% of those who were taking sodium valproate for their epilepsy were not aware of the risks in pregnancy.[5]

This survey has been repeated in 2017, when it was found that 18% of women taking the epilepsy medicine sodium valproate didn't know the risks this medicine can pose during pregnancy and 28% of women said that they had not been informed of the risks of this medicine in

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2 MHRA, Valproate and developmental disorders: new alert asking for patient review and further consideration of risk minimisation measures, 24 April 2017

3 NHS England, Sodium Valproate Prescribing, April 2017

4 MHRA, Guidance: Toolkit on the risks of valproate medicines in female patients, February 2016

5 Epilepsy Action, Women with epilepsy should be better informed about the risks of taking sodium valproate during pregnancy, survey shows, 31 October 2016

pregnancy.[6] Epilepsy Action highlighted that awareness of the toolkit was low but that the MHRA were working to ensure all women had access to the information:

> This lack of change has come despite efforts by the Medicines and Healthcare products Regulatory Agency (MHRA) to improve the situation. In February 2016, the MHRA released a valproate toolkit to help healthcare professionals talk to women with epilepsy about the risks of taking this medicine during pregnancy.
>
> However, according to the 2017 survey, more than two-thirds of women (68%) taking sodium valproate said they have not received any materials from the MHRA toolkit.
>
> A spokesperson from the MHRA explained that the agency had worked with the charities on the latest survey. The MHRA said: "The results of the survey are important in helping us understand the effectiveness of the measures taken to date in the UK. We want to encourage all women to have access to the valproate toolkit materials that we made available in February 2016.
>
> "We constantly monitor the safe use of valproate and support this latest review by the European Medicines Agency (EMA) on the use in pregnancy and women of childbearing age."

Epilepsy charities are calling on the Government to make sure that all GPs discuss the risks of valproate with patients. They have suggested that the process for repeat prescriptions for valproate be changed so that they are not routinely renewed for longer than 12 months without a face to face consultation with a doctor or a nurse. More information on this campaign is provided on the Epilepsy Action website:

> Philip Lee, chief executive at Epilepsy Action, said: "It is vital that women with epilepsy get the right information about their care and treatment to ensure a healthy pregnancy and minimise the risks associated with sodium valproate.
>
> "Yet these figures suggest that information is not filtering down to women and that conversations about the potential risks are not always happening. Discussions with a health professional about these risks should be a mandatory part of care for all women with epilepsy so they can make informed choices, ideally before they conceive."
>
> Dr Rhys Thomas, honorary consultant in epilepsy at the Royal Victoria Infirmary in Newcastle, said: "This is a dramatic and important survey focusing on a crucial area for women with epilepsy. As a medical community, we clearly could be doing more, and should be doing more.
>
> "Even if women are being told of the risks, this may be at the wrong time for them – or in the wrong way. The conversation needs to be had and repeated.
>
> "Women who want to know more about their medication should ask to speak to their GP, epilepsy specialist nurse or neurologist. I would advise anyone who is taking medicines for their epilepsy not to change their tablets or dose without the support of their doctor."[7]

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6 Epilepsy Action, Almost one-fifth of women taking sodium valproate for epilepsy still not aware of risks in pregnancy, survey shows, 22 September 2017

7 Epilepsy Action, Almost one-fifth of women taking sodium valproate for epilepsy still not aware of risks in pregnancy, survey shows, 22 September 2017

1.3 European Medicines Agency review

The Pharmacovigilance and Risk Assessment Committee at the European Medicines Agency is responsible for work assessing the safety of medicines across Europe.

In 2014, the European Medicines Agency (EMA) recommended a strengthening of measures to reduce the risk of harm to babies born to mothers taking valproate medicines.[8] Following a review of the evidence in this area, the Pharmacovigilance and Risk Assessment Committee[9] (PRAC) recommended that:

> Valproate should not be used to treat epilepsy or bipolar disorder in girls and in women who are pregnant or who can become pregnant unless other treatments are ineffective or not tolerated. Women for whom valproate is the only option after trying other treatments, should use effective contraception and treatment should be started and supervised by a doctor experienced in treating these conditions.
>
> Women who have been prescribed valproate should not stop taking their medicine without first consulting their doctor.
>
> In countries where valproate medicines are authorised for the prevention of migraine, women must not use valproate for preventing migraine when they are pregnant. Pregnancy should be excluded before starting treatment for migraine, and women should use effective contraception.
>
> The PRAC also recommended that doctors who prescribe valproate provide women with full information to ensure understanding of the risks and to support their decisions.[10]

In 2017, The EMA were asked to look again at the safety of valproate by the French medicines regulator ANSM (L'Agence nationale de sécurité du médicament et des produits de santé). The review was set up in March 2017 and seeks to "review the effectiveness of the measures and to consider whether further EU-wide action should be recommended to minimise the risks in women who are pregnant or of childbearing age."

As part of this review, the PRAC held a public hearing in London on 26 September 2017. The PRAC heard evidence from patients and patient representatives, healthcare professionals, academics and pharmaceutical industry representatives. A summary document of the public hearing provides an overview and a video of the hearing is available on the EMA website.

The contributors at the public hearing were asked to provide views on the evidence on the risks of valproate in pregnancy, on the current measures in place to reduce the risks, and what other measures may be introduced.

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8 EMA, Valproate and related substances, 2014

9 The committee that is responsible for assessing all aspects of the risk management of medicines for human use

10 EMA, PRAC recommends strengthening the restrictions on the use of valproate in women and girls, October 2014

The summary reports that there was a general consensus that whilst information had improved after the recommendations in 2014, these were not reaching the right people at the right time:

> Pretty much every speaker had confirmed that while much improved information resources had been developed in some member states after the PRAC's previous recommendations, these were simply not reaching the right people at the right time. Dissemination, implementation and acceptance of the need for change had not happened as had been intended, and so the hoped-for strengthening of risk minimisation had not been seen. As well as communication and knowledge there was a need to think about other ways to effect change. Things could not remain the same and it was clear that things can be done better.[11]

A number of suggestions were made about what further measures could be introduced. These included calls for risks to be shown on the outside of medicine packaging, regular reviews for women on valproate and prompts to be used in prescribing software so the prescription can be accompanied by appropriate information for women.

The PRAC will continue its review and publish a report with conclusions when this is complete.

1.4 French compensation fund and legal case

A health authorities report, published in France in early 2016, estimated that between 425 and 450 children were affected by birth defects attributable to valproate from 2006-2014.[12] This estimate was extrapolated from data from a particular region in France- the Rhone-Alpes region.

Following the publication of the report changes were made to the labelling of the exterior packaging of valproate medicines to include a warning for pregnant women (as well as the leaflet inside).

In August 2016 Marisol Touraine, the Minister at the Department of Social Affairs and Health, announced that the Government would be responsible for all medical costs of those identified as being affected, and that a compensation fund would be established. More information about the fund is provided in a Reuters news article:

> The French parliament voted to create a nationwide compensation fund and amended the 2017 budget bill late on Tuesday to set aside an initial 10 million euros ($10.7 million) for claims relating to Depakine, a brand name for valproate, which is also used to treat bipolar disorder.
>
> Parents of those affected say the French state and Sanofi were too slow to warn of the side effects of the drug, which has been used to successfully treat epilepsy since 1967, after the risks to fetuses became clear by the early 1980s.
>
> More than 14,000 women were prescribed Depakine despite the potential risks in pregnant women, authorities say, while an

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11 EMA, Summary of the EMA public hearing on valproate in pregnancy, 4 October 2017

12 Common epilepsy drug investigated in 450 cases of birth defects in France, The Guardian, February 2016

> association representing victims says it could have affected more than 50,000 people in France over the years.
>
> "The 10 million euros are a starting point," Health Minister Marisol Touraine told lawmakers in the lower house of parliament. "In future years, the sums should be much higher."
>
> Touraine told parliament later on Wednesday that compensation would ultimately be paid by "those deemed responsible" without giving details.
>
> "I regret that Sanofi didn't seek an amicable settlement as a matter of principle. I hope (Sanofi) will change its position," she said.
>
> A Sanofi spokeswoman had no comment on the minister's remarks and referred to a statement earlier on Wednesday in response to the vote to set up the fund.
>
> "The text of the amendment adopted by the National Assembly does not draw any conclusions ... as to the responsibilities of the various actors that may be involved," the Sanofi spokeswoman said in the emailed statement. [13]

This was passed as part of the budget provisions in May 2017, €10million was assigned for the fund in 2017 while an expert committee examines liability. It should be noted that international health systems and approaches to support can vary significantly.

A July 2017 article in the Lancet journal provides further information about action in France, which has included a ban on the use of valproate in women and girls of childbearing potential to treat Bipolar disorder.[14]

A class action has also been brought by the French association for people affected by sodium valproate (Association d'Aide aux Parents d'Enfants souffrant du Syndrome de l'Anti-Convulsivant) against the manufacturer Sanofi.

In the past there has also been legal action launched on this subject in the UK. In 2004, a class action was brought by a group of families under the *Consumer Protection Act 1987* . The case was expected to go to trial in 2011, but the litigation was discontinued prior to this after the Legal Services Commission withdrew funding.[15]

1.5 Government response

There has been growing interest on this issue in Parliament, with a number of recent Parliamentary Questions.

The most recent Government response on this subject was on 16 October 2017. The Under-Secretary of State for Health, Steve Brine, explained that Valproate is an effective treatment but should not be prescribed in women of child bearing potential unless other treatments

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13 Reuters, France sets up fund for Sanofi epilepsy drug victims, 16 November 2016

14 France bans sodium valproate use in case of pregnancy, The Lancet, Vol 390 July 15, 2017

15 The Guardian, Families devastated after legal aid withdrawn for birth defects case, 28 January 2011

are ineffective or intolerable. He set out the work ongoing to ensure awareness of the risks in pregnancy:

> Valproate is an effective treatment for epilepsy and bipolar disorder but should only be used in girls and women of childbearing potential if other treatments are ineffective or not tolerated. For some women there may be no other treatment option. Because of ongoing concerns about women's awareness of the risks, the Medicines and Healthcare products Regulatory Agency (MHRA) has worked with professional bodies, voluntary organisations and patient groups to develop a set of materials to aid communication between health professionals and women and girls.
>
> The valproate toolkit comprises booklets for healthcare professionals, a reminder card and a guide for women, a checklist for prescribers and clear package labelling carrying a prominent warning about use in pregnancy. The MHRA continues to work with stakeholders to disseminate information and ensure compliance with the statutory advice. On 6 April 2017, NHS Improvement and MHRA sent a Patient Safety Alert through the NHS Central Alerting System to further highlight risks to the unborn child and support the safety of girls and women taking valproate. The alert directs organisations to undertake systematic identification of women and girls taking valproate and to use the MHRA resources to support them to make informed choices. Consistent action was taken in Scotland, Wales, and Northern Ireland.[16]

Mr Brine reported that there had been a steady decline in prescribing of this medicine to women:

> The impact of the measures taken is being monitored and studies show a steady decline in prescribing to women in childbearing potential. The adequacy of measures taken to date across Europe is being reviewed in a Europe-wide review that started in March 2017. There are ongoing discussions at official level as the review progresses. An expert working group of the Commission on Human Medicines has been convened to inform the United Kingdom position during the ongoing European Union review and consider other measures which may be required across the healthcare system to ensure compliance with the regulatory position in clinical practice.[17]

He went on to state that there is currently no plans to set up a compensation fund similar to that in France, but there is support available through local authorities and CCGs for families with children born with a disability:

> France has its own legislation that allows for a state funded compensation scheme for medical accidents and they have amended this to include claims from those affected by valproate. We understand that this has been operational from June 2017. We are monitoring developments in France and do not feel that commissioning research is necessary at this time. We are not aware of similar action in other member states. There is currently no proposal to establish a care compensation plan specifically for those affected by valproate in the UK. However, the Government has great sympathy for those families who have been affected by

16 HC Written Question 106362: Pregnancy: Sodium Valproate, 16 October 2017
17 Ibid

the use of valproate in pregnancy. There is support available for families with children born with a disability. The Children and Families Act 2014 introduced a new statutory framework for local authorities and clinical commissioning groups (CCGs) to work together to secure educational, health and social care services for children and young people up to the age of 25 who have special educational needs or a disability (SEND).

Local authorities and CCGs must commission services jointly around a set of locally agreed outcomes to ensure that the needs of children and young people with SEND are met. Local authorities must also publish a clear, transparent 'local offer' of services available which has been developed for, and with, parents and young people. The reforms introduced by the Act are designed to reduce health inequalities, improve the experiences of children and young people with SEND, and their families, and deliver integrated services to achieve improved outcomes.

The Parliamentary Under Secretary of State for Health (Lord O'Shaughnessy) is meeting with the Chair of the All-Party Parliamentary Group on Anti-epileptic Drugs in Pregnancy to discuss these issues later this year; members of the Independent Fetal Anti Convulsant Trust may wish to attend also.[18]

[18] Ibid

2. Press Articles

The Times

Women demand stronger warnings on epilepsy drug sodium valproate

Chris Smyth, 27 September 2017

https://www.thetimes.co.uk/article/women-demand-stronger-warnings-on-epilepsy-drug-sodium-valproate-d0t737f7q

BBC News

We've had no help – epilepsy drug victims

Nick Triggle, 26 September 2017

http://www.bbc.co.uk/news/health-41399848

Guardian

Birth defect risks of sodium valproate 'known 40 years ago'

Sarah Boseley, 26 September 2017

https://www.theguardian.com/society/2017/sep/26/sodium-valproate-birth-defect-risks-known-40-years-ago-campaigners

Daily Telegraph

Medical experts 'complicit' over drug which caused deformities

Laura Donnelly, 26 September 2017

http://www.telegraph.co.uk/news/2017/09/26/medical-experts-complicit-letting-20000-children-develop-deformities/

Daily Telegraph

Epilepsy drug 'responsible for up to 4,100 severe birth defects' in France

David Chazan, 20 April 2017

http://www.telegraph.co.uk/news/2017/04/20/epilepsy-drug-responsible-4100-severe-birth-defects-france/

Financial Times

Sanofi epilepsy drug linked to birth defects in up to 4,100 children

Harriet Agnew, 20 April 2017

https://www.ft.com/content/1a682e88-25d1-11e7-8691-d5f7e0cd0a16

3. Press releases

European Medicines Agency

EMA takes yet another step in public engagement with its first public hearing

5 October 2017

Summary report now published

Patients, carers, doctors, pharmacists and academia shared their experience with valproate - a medicine that treats epilepsy, bipolar disorder and migraine - at the first public hearing held by the European Medicines Agency (EMA) at its offices in London on 26 September 2017.

"The European Parliament insisted on including public hearings in the EU law on medicines safety," said Linda McAvan, Member of the European Parliament. "The positive experience from EMA's first public hearing confirms that giving patients a platform to tell their story was the right thing to do."

The hearing gave an opportunity to EU citizens representing a wide range of groups to make their voices heard to complement the available scientific evidence in the evaluation of this medicine. The total number of attendees was 65, including 28 patients and patient representatives, 19 healthcare professionals and academics, 11 from pharmaceutical industry and 7 from media. There were a total of 25 speaker contributions, grouped into 16 speaker slots.

"The hearing today went absolutely well, beyond expectations. There was an open, non-judgemental atmosphere that allowed all participants to talk with equal credibility," explained François Houÿez from EURORDIS. "The hearing was carried out in a special ambiance characterised by solemnity, seriousness, and openness."

The public hearing is part of a review of the safety of using valproate-containing medicines in women and girls who are pregnant or of childbearing age by EMA's Pharmacovigilance Risk Assessment Committee (PRAC). There is a risk of malformations and neurodevelopmental problems in babies who are exposed to valproate in the womb, and the review follows concerns that European Union (EU)-wide risk minimisation measures currently in place do not seem to be sufficiently effective.

"The public hearing was a great opportunity to hear many different views in a relatively short time on a problem of high complexity," stressed Martin Brodie from the International Bureau for Epilepsy. "Discrepancies in the healthcare systems between EU countries and huge challenges that lie ahead when it comes to restrictions in the use of valproate make this topic a wise choice for a first hearing in Europe."

"I very much welcome EMA's efforts to engage with the 'real world' when making regulatory decisions. It was a great opportunity to share experience and ideas with PRAC members on how community

pharmacists could play an increased role in raising awareness about the risks of valproate in women of childbearing age," added Jūratė Švarcaitė, Pharmaceutical Group of the European Union (PGEU).

There was agreement among the participants on the undeniable risks of valproate to unborn babies, if used during pregnancy. Many speakers confirmed that the improved information resources that had been developed in some Member States after PRAC's previous recommendations were not reaching the targeted audiences, and the importance of the dissemination, implementation and acceptance of this information was stressed.

In response to the question of what other measures should be taken to reduce the risks of using valproate during pregnancy, the speakers provided important ideas such as including visual reminders of the risks on the outer packaging of valproate medicines and the need for regular reviews for all women receiving valproate long-term, to ensure that, in future, no woman taking this medicine is unaware of the risks.

More information on the deliberations made during the hearing can be found in the summary report.

The PRAC will take into account every single input received during the hearing. It will also consult two EMA scientific advisory groups (12 October 2017) and a stakeholder forum (13 October 2017) to further discuss these proposals. At the end of this review, the Committee will publish an assessment report on measures to reduce the risk of valproate-containing medicines during pregnancy and in women of childbearing potential, in accordance with the published timetable.

Notes

- The review of valproate was initiated on 9 March 2017 at the request of the French medicines regulator ANSM, under Article 31 of Directive 2001/83/EC.
- The review will be carried out by the Pharmacovigilance Risk Assessment Committee(PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which will make recommendations. The PRAC recommendations will then be sent to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a position. The CMDh is a body representing EU Member States as well as Iceland, Liechtenstein and Norway. It is responsible for ensuring harmonised safety standards for medicines authorised via national procedures across the EU.
- The public hearing follows the adoption of rules of procedure on the organisation and conduct of public hearings and a simulation training in 2016.

Organisation for Anti-Convulsant Syndrome

Valproate Review : New review of valproate use in pregnancy and women of childbearing age

EMA to consider if risks of these medicines require further restrictions

The European Medicines Agency (EMA) has started a review looking at the use of valproate-containing medicines in the treatment of women and girls who are pregnant or of childbearing age. These medicines are approved nationally in the EU to treat epilepsy, bipolar disorder and in some countries, migraine, and have been previously reviewed by the Agency

An EMA review in 20141 resulted in measures to strengthen the warnings and restrictions on the use of valproate medicines in women and girls, due to the risk of malformations and developmental problems in babies who are exposed to valproate in the womb. Although sometimes there may be no alternative to using valproate, these measures aimed to ensure that patients are aware of the risks of doing so, and that they take valproate only when clearly necessary. The 2014 review also recommended studies at EU level to measure how effective the proposed measures were.

The French medicines regulator, ANSM, has done recent assessment the result of which has meant that they have asked EMA to review the effectiveness of the measures and to consider whether further EU-wide action should be recommended to minimise the risks in women who are pregnant or of childbearing age.

For More information

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Valproate_and_related_substances/human_referral_prac_000066.jsp&mid=WC0b01ac05805c516f

Epilepsy Action

Almost one-fifth of women taking sodium valproate for epilepsy still not aware of risks in pregnancy, survey shows

22 September 2017

Almost one-fifth (18%) of women taking the epilepsy medicine sodium valproate don't know the risks this medicine can pose during pregnancy, according to the results of a new survey.

More than a quarter (28%) of the women currently taking sodium valproate said in the survey that they had not been informed of the risks of this medicine in pregnancy.

The survey of over 2,000 women with epilepsy, aged 16-50, was carried out by charities Epilepsy Action, Epilepsy Society and Young Epilepsy between August and September 2017. It aimed to look into the awareness among women taking sodium valproate of the risks this medicine can pose during pregnancy.

Sodium valproate is prescribed in the UK under the brand names Epilim, Epilim Chrono, Epilim Chronosphere, Episenta and Epival. For some people with epilepsy, it is a very effective medicine to control seizures, and, in some cases, may be the only medicine that works.

However, sodium valproate is also linked to an increased risk of birth defects and developmental problems in babies born to mothers taking

this medicine. The risk of physical disabilities in babies born to women taking sodium valproate is estimated to be around 1 in 10 (10%). The risk of developmental problems, which can lead to learning difficulties, is around 2 in 5 (40%).

Epilepsy Action advises that women do not stop taking their epilepsy medicines or change their dose without speaking to their doctor, as this could lead to breakthrough seizures.

Improving safety information

The charities carried out a similar survey in 2016. The results from this were very similar to the results of the 2017 survey. Of the women taking sodium valproate 1 in 5 (20%) said they didn't know the risks of taking this medicine during pregnancy. Over a quarter (27%) of women taking sodium valproate said they had not had a discussion with their healthcare professional about the risks in pregnancy.

This lack of change has come despite efforts by the Medicines and Healthcare products Regulatory Agency (MHRA) to improve the situation. In February 2016, the MHRA released a valproate toolkit to help healthcare professionals talk to women with epilepsy about the risks of taking this medicine during pregnancy.

However, according to the 2017 survey, more than two-thirds of women (68%) taking sodium valproate said they have not received any materials from the MHRA toolkit.

A spokesperson from the MHRA explained that the agency had worked with the charities on the latest survey. The MHRA said: "The results of the survey are important in helping us understand the effectiveness of the measures taken to date in the UK. We want to encourage all women to have access to the valproate toolkit materials that we made available in February 2016.

"We constantly monitor the safe use of valproate and support this latest review by the European Medicines Agency (EMA) on the use in pregnancy and women of childbearing age."

The results of the survey will be presented at the EMA's public hearing on sodium valproate on Tuesday 26 September. The hearing, in London, will be the first time the EMA has held a public hearing as part of the safety review of a medicine.

Ensuring conversations happen

The charities are calling on the government to change the way repeat prescriptions of sodium valproate are made for women and girls of childbearing age. They are asking that repeat prescriptions are not routinely renewed for more than 12 months without a face-to-face consultation with a doctor or nurse. They say this consultation must include personal and tailored information about the risks around sodium valproate during pregnancy, and should also be provided in written format.

Philip Lee, chief executive at Epilepsy Action, said: "It is vital that women with epilepsy get the right information about their care and

treatment to ensure a healthy pregnancy and minimise the risks associated with sodium valproate.

"Yet these figures suggest that information is not filtering down to women and that conversations about the potential risks are not always happening. Discussions with a health professional about these risks should be a mandatory part of care for all women with epilepsy so they can make informed choices, ideally before they conceive."

Dr Rhys Thomas, honorary consultant in epilepsy at the Royal Victoria Infirmary in Newcastle, said: "This is a dramatic and important survey focusing on a crucial area for women with epilepsy. As a medical community, we clearly could be doing more, and should be doing more.

"Even if women are being told of the risks, this may be at the wrong time for them – or in the wrong way. The conversation needs to be had and repeated.

"Women who want to know more about their medication should ask to speak to their GP, epilepsy specialist nurse or neurologist. I would advise anyone who is taking medicines for their epilepsy not to change their tablets or dose without the support of their doctor."

European Medical Agency

New review of valproate use in pregnancy and women of childbearing age

EMA to consider if risks of these medicines require further restrictions of use

3 April 2017

The European Medicines Agency (EMA) has started a review looking at the use of valproate-containing medicines in the treatment of women and girls who are pregnant or of childbearing age. These medicines are approved nationally in the EU to treat epilepsy, bipolar disorder and in some countries, migraine, and have been previously reviewed by the Agency.

An EMA review in 20141 resulted in measures to strengthen the warnings and restrictions on the use of valproate medicines in women and girls, due to the risk of malformations and developmental problems in babies who are exposed to valproate in the womb. Although sometimes there may be no alternative to using valproate, these measures aimed to ensure that patients are aware of the risks of doing so, and that they take valproate only when clearly necessary. The 2014 review also recommended studies at EU level to measure how effective the proposed measures were.

Some EU member states have since carried out additional assessments of the impact of the measures at national level and concerns have been raised about how effective the measures have been in increasing awareness and reducing valproate use appropriately in its various indications. The French medicines regulator, ANSM, therefore

asked EMA to review the effectiveness of the measures and to consider whether further EU-wide action should be recommended to minimise the risks in women who are pregnant or of childbearing age.

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) will examine the available evidence and will consult with relevant stakeholder groups. This will include holding a public hearing about their concerns. While the review is ongoing, patients prescribed valproate who have any concerns about their medication should discuss them with their healthcare professionals.

1Valproate and related substances

New toolkit supports better understanding of the risks of valproate and pregnancy

Medicines and Healthcare products Regulatory Agency

8 February 2016

A toolkit to ensure female patients are better informed about the risks of taking valproate medicines during pregnancy has been launched.

The Medicines and Healthcare products Regulatory Agency (MHRA) today welcomed the launch of a new toolkit to ensure female patients are better informed about the risks of taking valproate medicines during pregnancy.

Valproate (Epilim, Depakote and other generic brands) is a treatment for epilepsy and bipolar disorder and is prescribed to thousands of women. It is associated with a risk of birth defects and developmental disorders in children born to women who take valproate during pregnancy.

MHRA strengthened warnings on the risks of valproate in pregnancy last year, as understanding of the extent of these risks had increased. Up to 4 in 10 babies are at risk of developmental disorders, and approximately 1 in 10 are at risk of birth defects, if valproate is taken during pregnancy. The new toolkit addresses concerns that the risks of valproate are not being adequately explained to female patients.

Developed in consultation with stakeholders including healthcare professional and patient groups, the toolkit includes a credit card sized patient card to be issued by pharmacists, booklets for healthcare professionals and for patients together with a checklist of important questions and discussion points to be kept with the patient's file. Warnings will appear on the medicine's packaging later this year.

The MHRA is asking GPs, pharmacists, neurologists, psychiatrists, and other relevant healthcare and mental health professionals to use the toolkit to help facilitate discussion of the risks with their patients.

Dr Sarah Branch, Deputy Director of MHRA's Vigilance and Risk Management of Medicines Division said:

The warnings on the risks of valproate in pregnancy were strengthened last year. We want to ensure that women and girls have the latest information about the risks of developmental disorders and birth defects

in children exposed to valproate during pregnancy. This new toolkit supports healthcare professionals to give that advice to their patients.

It is important no-one should stop taking valproate without discussing it first with their doctor. If valproate is the only treatment option, women of childbearing age should be given effective contraception. Women taking valproate must have regular reviews of their treatment.

Anyone with questions or concerns about the risks associated with valproate and pregnancy should speak to their doctor, pharmacist or other healthcare professional.

Anyone who has experienced any side effects to this medicine can report these to the MHRA using the Yellow Card Scheme.

Louise Cousins, campaigns manager at Epilepsy Action, said:

The new toolkit is an invaluable resource for women with epilepsy to better understand all aspects of pregnancy and the risks of taking valproate. By being fully informed, women can work together with health professionals to make the right choices for them and properly manage their care before, during and after pregnancy. This will help reduce the risk of malformations in babies born to women with epilepsy.

Suzanne Hudson, Chief Executive, Bipolar UK, said:

Valproate can be used to treat bipolar and other mental health conditions but it's vital that women and girls are aware of the risks surrounding this medication. After working alongside the MHRA and other organisations, we welcome the launch of the new communications toolkit, which will provide women with the knowledge they need to make an informed decision with their doctor or psychiatrist.

Stephen Buckley, Head of Information at Mind, the mental health charity, said:

We welcome this toolkit, which will help health professionals have a vital conversation with women and girls taking valproate for their mental health problem. It's really important that women are aware of the risks of taking valproate during pregnancy so that they can make an informed choice about their medication.

Trustees of the Organisation for Anti Convulsant Syndrome said:

The Organisation for Anticonvulsant Syndrome fully supports the MHRAand their development of the valproate tool kit, it is an invaluable contribution to the welfare of those taking valproate. Medicine safety is of paramount importance in this organisation; we believe that valproate is a beacon, an opportunity, in the field of medicine development.

Janet Williams, CEO INFACT, said:

INFACT welcome and appreciate the new communication and toolkit which should ensure all female patients prescribed valproate during their child bearing years are informed of the dangers. INFACT also

appreciate the input we have been able to give to the new toolkit and hope that all healthcare professionals use it to the full, allowing every woman the opportunity to make the informed choice when planning her pregnancy. INFACT look forward to the future of valproate, understanding the fact that this essential medication can be prescribed with the knowledge of its dangers and in the hope that further casualties can be avoided.

Matthew Sowemimo, Director of External Affairs, Epilepsy Society, said:

Epilepsy Society welcomes the MHRA's launch of a new toolkit, which will help to better inform female patients about the risks of taking valproate during pregnancy.

This toolkit should help to ensure that awareness of the conception-related risks of taking valproate is heightened among women with epilepsy, while reinforcing to healthcare professionals that pre-conception counseling is an essential part of their treatment.
The MHRA has worked with a number of stakeholders to create detailed guidance for healthcare professionals and their patients, while confirming that valproate remains a very effective medication for a number of people with epilepsy. Epilepsy Society will continue to work with MHRA to ensure that every woman who is prescribed valproate as an anti-epileptic drug is fully aware of the risks involved.

Emma Friedmann, #FACSaware Campaign Director at the Fetal Anti-Convulsant Trust, said:

I have epilepsy and a child with Fetal Valproate Syndrome. Parents are delighted with the MHRA toolkit as it will enable girls to make an informed choice about parenting options and their future. The #FACSaware campaign has been a great success. We look forward to continuing our work with the MHRA to promote the Yellow Card and would like to thank all involved.

Young Epilepsy's Acting Director of Development, Emma Tingley, said:

Young Epilepsy is welcoming this new toolkit from MHRA. It will be an invaluable resource for women living with epilepsy when they come to making decisions about pregnancy and starting a family. The more informed women and their health professionals are, the safer the choices that will be made surrounding their care, throughout pregnancy.

Dr Asha Kasliwal, Vice President, Faculty of Sexual and Reproductive Healthcare said:

The Faculty of Sexual and Reproductive Healthcare (FSRH) welcomes the launch of the valproate toolkit for healthcare professionals and patients. As the representative body for a large number of the UK's contraceptive providers, we believe this toolkit will strongly highlight the risks associated with taking valproate during pregnancy. It will encourage clinicians to raise the subject proactively and give the best possible advice regarding highly effective contraception to women taking valproate so that they can avoid unintended pregnancy.

Sandra Gidley, RPS Engand Board Chair, said:

We welcome this new resource for patients. The Royal Pharmaceutical Society will be raising awareness of the toolkit with our members as well as providing them with our new support guidance. We will be urging pharmacists to use the toolkit as a way of facilitating conversations they have with patients about the risks of taking valproate medicines during pregnancy.

4. Parliamentary material

4.1 PQs

Pregnancy: Sodium Valproate

Asked by: Gwynne, Andrew | **Party:** Labour

To ask the Secretary of State for Health, what support the Government plans to provide to children and young adults affected by valproate after their birth (a) now and (b) over the next 10 years.

Answering Member: Steve Brine | **Party:** Conservative Party |

Department: Department of Health

Valproate is an effective treatment for epilepsy and bipolar disorder but should only be used in girls and women of childbearing potential if other treatments are ineffective or not tolerated. For some women there may be no other treatment option. Because of ongoing concerns about women's awareness of the risks, the Medicines and Healthcare products Regulatory Agency (MHRA) has worked with professional bodies, voluntary organisations and patient groups to develop a set of materials to aid communication between health professionals and women and girls.

The valproate toolkit comprises booklets for healthcare professionals, a reminder card and a guide for women, a checklist for prescribers and clear package labelling carrying a prominent warning about use in pregnancy. The MHRA continues to work with stakeholders to disseminate information and ensure compliance with the statutory advice. On 6 April 2017, NHS Improvement and MHRA sent a Patient Safety Alert through the NHS Central Alerting System to further highlight risks to the unborn child and support the safety of girls and women taking valproate. The alert directs organisations to undertake systematic identification of women and girls taking valproate and to use the MHRA resources to support them to make informed choices. Consistent action was taken in Scotland, Wales, and Northern Ireland.

The impact of the measures taken is being monitored and studies show a steady decline in prescribing to women in childbearing potential. The adequacy of measures taken to date across Europe is being reviewed in a Europe-wide review that started in March 2017. There are ongoing discussions at official level as the review progresses. An expert working group of the Commission on Human Medicines has been convened to inform the United Kingdom position during the ongoing European Union review and consider other measures which may be required across the healthcare system to ensure compliance with the regulatory position in clinical practice.

France has its own legislation that allows for a state funded compensation scheme for medical accidents and they have amended this to include claims from those affected by valproate. We understand

that this has been operational from June 2017. We are monitoring developments in France and do not feel that commissioning research is necessary at this time. We are not aware of similar action in other member states. There is currently no proposal to establish a care compensation plan specifically for those affected by valproate in the UK. However, the Government has great sympathy for those families who have been affected by the use of valproate in pregnancy. There is support available for families with children born with a disability. The Children and Families Act 2014 introduced a new statutory framework for local authorities and clinical commissioning groups (CCGs) to work together to secure educational, health and social care services for children and young people up to the age of 25 who have special educational needs or a disability (SEND).

Local authorities and CCGs must commission services jointly around a set of locally agreed outcomes to ensure that the needs of children and young people with SEND are met. Local authorities must also publish a clear, transparent 'local offer' of services available which has been developed for, and with, parents and young people. The reforms introduced by the Act are designed to reduce health inequalities, improve the experiences of children and young people with SEND, and their families, and deliver integrated services to achieve improved outcomes.

The Parliamentary Under Secretary of State for Health (Lord O'Shaughnessy) is meeting with the Chair of the All-Party Parliamentary Group on Anti-epileptic Drugs in Pregnancy to discuss these issues later this year; members of the Independent Fetal Anti Convulsant Trust may wish to attend also.

HC Deb 16 Oct 2017 | PQ 106362

Pregnancy: Sodium Valproate

Asked by: Gwynne, Andrew | **Party:** Labour Party

To ask the Secretary of State for Health, how (a) his Department and (b) the Medicines and Healthcare Products Regulatory Agency will be alerted when all concerned women have been warned of the dangers of prescribed Valproate.

Answering member: Nicola Blackwood | **Party:** Conservative Party | **Department:** Department of Health

Valproate is an effective treatment for epilepsy and bipolar disorder but should only be used in girls and women of childbearing potential if other treatments are ineffective or not tolerated. For some women there may be no other treatment option. When it was authorised, valproate was known to have risks in pregnancy. The statutory Patient Information Leaflet which accompanies the medicine provides up-to-date detailed information on the risks of valproate in pregnancy. Because of ongoing concerns about women's awareness of the risks, the Medicines and Healthcare products Regulatory Agency (MHRA) has worked with professional bodies, voluntary organisations and patient groups to

develop a set of materials to aid communication between health professionals and women and girls.

The valproate toolkit comprises booklets for healthcare professionals and a checklist for prescribers; a reminder card to be provided by pharmacists to patients when the product is dispensed; a guide for women; and clear package labelling carrying a prominent warning about use in pregnancy. It was widely disseminated to relevant healthcare professionals from February 2016 including through a Central Alerting System (a web based cascade system for issuing alerts to the National Health Service), the MHRA's Drug Safety Update bulletin and in hard copy from the marketing authorisation holders. Electronic copies of the toolkit are hosted on several websites, including the Electronic Medicines Compendium.

In addition the MHRA has worked, and continues to work with, a coalition of stakeholders including Royal Colleges, professional bodies, patient groups, relevant charities and health system organisations, including clinical commissioning groups, to increase awareness of the toolkit among general practitioners, pharmacists and patients, through a variety of communication channels.

In order to monitor the effectiveness of the valproate toolkit, the MHRA continues to work with all stakeholders to gather feedback that demonstrates the toolkit materials are being used. This includes working with voluntary organisations and patient groups to produce online patient surveys to measure awareness of the risks among patients. Furthermore, the MHRA is conducting a study using the Clinical Practice Research Datalink to track changes in prescribing of valproate to women and girls following the communications to healthcare professionals and patients on the risks of valproate in pregnancy. The marketing authorisation holder is conducting Europe-wide studies to measure the changes in patterns of prescribing and the awareness of healthcare professionals of the risks. The available data will be brought together in a regularly updated dashboard that will be used to track the impact of the communications on patient and professional awareness over time.

All doctors are expected to comply with good practice set out in General Medical Council (GMC) guidance. The GMC prescribing guidance states that doctors should reach agreement with the patient on the treatment proposed, explaining the likely benefits, risks and burdens, including serious and common side effects. Doctors should report any adverse reactions to medicines through the Yellow Card Scheme.

HC Deb 23 Jan 2017 | PQ 60691

Pregnancy: Sodium Valproate

Asked by: Lamb, Norman | **Party:** Liberal Democrats

To ask the Secretary of State for Health, what the implications are for his policies of the decision by the French parliament to establish a

national compensation fund for people affected by the teratogenic effects of sodium valproate.

Answering member: Nicola Blackwood | **Party:** Conservative Party | **Department:** Department of Health

Valproate is an effective treatment for epilepsy and bipolar disorder but should only be used in girls and women of childbearing potential if other treatments are ineffective or not tolerated. For some women there may be no other treatment option. Since it was authorised, valproate was known to have risks in pregnancy. Because of ongoing concerns about women's awareness of the risks, the Medicines and Healthcare products Regulatory Agency (MHRA) has worked with professional bodies, voluntary organisations and patient groups to develop a set of materials to aid communication between health professionals and women and girls. The valproate toolkit comprises booklets for healthcare professionals, a reminder card and a guide for women, a checklist for prescribers and clear package labelling carrying a prominent warning about use in pregnancy.

In order to monitor the effectiveness of the valproate toolkit, the MHRA has sought feedback from all stakeholders and will continue to work with the Royal Colleges, professional bodies, patient groups and relevant charities to increase awareness of the toolkit among general practitioners, pharmacists and patients. The MHRA's current priority is working to ensure that women taking valproate are fully aware of the risks in pregnancy. Once this is achieved we will look back and see what lessons have been or could be usefully learnt by examining events.

HC Deb 30 Nov 2016 | PQ 54957

Epilepsy: Drugs

Asked by: Bruce, Fiona | **Party:** Conservative Party

To ask the Secretary of State for Health, what assessment he has made of the clarity and accuracy of warnings on anti-convulsant drugs for women with epilepsy who are also pregnant on the risk of developmental disorders and birth defects associated with the use of such drugs.

Answering member: George Freeman | **Party:** Conservative Party | **Department:** Department of Health

In 2013 the Medicines and Healthcare products Regulatory Agency (MHRA) initiated a Europe-wide review of the risk of developmental problems in children born to mothers who take the anticonvulsant drug valproate in pregnancy. This followed the publication of new studies providing further clarity and accuracy on the risk of neurodevelopmental disorders in children of mothers who took valproate in pregnancy.

As a result of this assessment the MHRA has better defined the size and nature of the risk of developmental disorders in updated product information for healthcare professionals and patients. The MHRA recommend that valproate should not be used in girls, women who can

become pregnant or pregnant women unless other treatments are ineffective or not tolerated and that the need for continued treatment should be reviewed regularly.

There is now a mandatory requirement for all manufacturers to include the very latest information about the known risks of sodium valproate to the unborn child. The product information for healthcare professionals and patients has been updated to contain strengthened warnings about use in pregnancy and in women of child bearing age. New educational materials have been produced for use by healthcare professionals and patients that further highlight warnings of the risk of sodium valproate to the unborn child.

HC Deb 22 Jun 2015 | PQ 2376

Sodium Valproate

Asked by: Green, Kate

To ask the Secretary of State for Health, what information he holds on what knowledge his Department had of the emergence of risks associated with sodium valproate within the first five years following first prescription of that drug.

Answering member: George Freeman | **Party:** Conservative Party | **Department:** Department of Health

Sodium valproate was licensed in the United Kingdom in 1972 as a treatment for epilepsy and was marketed in 1974 for general prescription. The risks known to be associated with sodium valproate at that time were described in the data sheet first published in 1975 in the Association of British Pharmaceutical Industry (ABPI) Data Sheet Compendium. A copy is attached.

The safety of sodium valproate was monitored after licensing using data from the Yellow Card Scheme, which was set up in 1964 to collect reports of suspected adverse reactions to medicines. The data sheet published in the 1980-81 ABPI Data Sheet Compendium reflects the safety profile of sodium valproate following five years of availability on general prescription. A copy is attached.

HC Deb 19 Jun 2015 | PQ 2077

Attachment: ABPI Datasheet for Epilim - 1975; ABPI Datasheet for Epilim - 1980-81

Pregnancy: Sodium Valproate

Asked by: Pickles, Sir Eric | **Party:** Conservative Party

To ask the Secretary of State for Health, what steps he is taking to ensure that every pregnant women prescribed the anti-epilepsy drug sodium valproate is warned of the risk to her unborn child.

Answering member: George Freeman | **Party:** Conservative Party | **Department:** Department of Health

After completion of a United Kingdom-led European review in 2014, the Department worked with the Medicines and Healthcare products Regulatory Agency, healthcare professionals and patient groups to raise awareness and encourage discussion about the risks and benefits of sodium valproate between healthcare professionals and their patients.

Several measures were put in place to minimise the prescribing of sodium valproate to women of childbearing potential (except where other drugs are ineffective or not tolerated) and to communicate the warnings around the drug sodium valproate to healthcare professionals and patients (particularly women of child bearing potential).

There is now a mandatory requirement for all manufacturers to include the very latest information about the known risks of sodium valproate to the unborn child. The product information for healthcare professionals and patients has been updated to contain strengthened warnings about use in pregnancy and in women of child bearing age. New educational materials have been produced for use by healthcare professionals and patients that further highlight warnings of the risk of sodium valproate to the unborn child. Other actions include:

- working with the Health and Social Care Information Centre on introducing red-flag warnings on general practitioner and community pharmacy IT systems;
- updating the British National Formulary (BNF) and BNF for children; and
- using existing Departmental and National Health Service communication channels to raise awareness and provide information to patients.

HC Deb 12 Jun 2015 | PQ 989

4.2 Early Day Motion

Valproate Toolkit

Primary sponsor: Norman Lamb MP

EDM 83 Session 2016-17

24 May 2016

That this House notes with concern that the medicine valproate, which is used for the treatment of epilepsy and bipolar disorder, can seriously harm an unborn child when taken during pregnancy, including increased risk of malformations and developmental disorders; welcomes the development of a valproate toolkit to aid communication of the risks of valproate in pregnancy, including a warning on package labelling, a checklist for discussion between prescribers and patients, a reminder card and information booklet for women, and a booklet for healthcare professionals; further notes that the toolkit was disseminated by the Medicines and Healthcare products Regulatory Agency (MHRA) and the valproate manufacturer, Sanofi, in February 2016; expresses concern at reports that many pharmacists and clinicians have not received the toolkit, potentially leaving many women ill-informed of the

severe risks of the medicine; and urgently calls on the Government, the MHRA and NHS England to work together to ensure that the toolkit is effectively disseminated and utilised across the country so that all women being prescribed valproate are fully informed of the risks to an unborn child.

5. Useful links and further reading

European Medicines Agency: *EMA seeks views of public during its safety review of valproate* 11 July 2017

http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2017/07/WC500231106.pdf

NHS England *Sodium Valproate Prescribing* 18 April 2017

https://www.england.nhs.uk/publication/prescribing-for-sodium-valproate/

MHRA, *Guidance: Toolkit on the risks of valproate medicines in female patients* 18 February 2016

https://www.gov.uk/government/publications/toolkit-on-the-risks-of-valproate-medicines-in-female-patients

European Medicines Agency: *Valproate and related substances* 9 March 2017

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Valproate_and_related_substances/human_referral_prac_000066.jsp&mid=WC0b01ac05805c516f

Epilepsy Society

https://www.epilepsysociety.org.uk/

Epilepsy Action

https://www.epilepsy.org.uk/

Organisations for Anti-Convulsant Syndrome

https://www.oacscharity.org/about-fetal-anti-convulsant-syndromes

FACSAWARE

http://www.facsaware.net/

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