Statement from the Clinical Effectiveness Unit

Sodium Valproate and Pregnancy Risks

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The Medicines and Healthcare products Regulatory Agency (MHRA) recently launched a toolkit for healthcare professionals (HCPs) regarding sodium valproate in order to communicate its teratogenic effects. Access the toolkit here.

The CEU recommends that all HCPs be prepared to provide information about and access to effective contraception for women who have undergone treatment with valproate-related medicines.

Sodium valproate is an antiepileptic drug used to treat bipolar disorder, all forms of epilepsy and migraine prophylaxis (off licence).[1]

According to the MHRA:

- *In utero* exposure puts children at a high risk of serious developmental disorders (30-40% of cases) and/or congenital malformations (10% of cases).
- When valproate is taken with other epilepsy medications, the risk of abnormal pregnancy outcomes is greater than when taken alone.
- Female children, female adolescents, women of childbearing age and pregnant women **should not** be prescribed valproate medicines unless there is no safer alternative.
- HCPs must ensure that all female patients understand the risks associated with valproate treatment and pregnancy, the need for effective contraception, the requirement for regular treatment reviews and the necessity of immediate consultation if planning or becoming pregnant.[2]

Data suggest that valproate carries a higher risk of adverse pregnancy outcomes than other epileptic medications.[3] Potential birth defects include spina bifida; facial and skull malformations; malformations of the heart, kidney and urinary tract and limb defects. Children exposed to valproate in utero have a higher risk of autism spectrum disorders, lower IQs and developmental delays.

Because of these risks, HCPs must discuss and provide effective contraception to women who are using a valproate medication. To be effective, contraception must be used correctly and consistently. Long-acting reversible contraception (LARC) (e.g. the progestogen-only implant, the progestogen-only injectable and intrauterine

contraceptives) is less user-dependent than other methods and provides the best protection with "typical use."[4] However, effective and continued use of contraception is directly related to its acceptability by the user, therefore HCPs should take individual preference into account when advising on contraception.

Valproate medicines do not interfere with or reduce the efficacy of any contraceptive method and contraception does not alter valproate function.[1] The UKMEC states that no form of contraception is contraindicated for women with epilepsy or depressive disorders. Therefore, most women using a valproate medicine can choose whichever contraceptive method they find most acceptable. However, HCPs should consult the UKMEC before prescribing contraception to women who are taking valproate medicines for migraines as some contraceptive methods are contraindicated for certain types of migraines.[4]

1. Joint Formulary Committee. *British National Formulary* (online) London: BMJ Group and Pharmaceutical Press. 2015. <www.medicinescomplete.com/mc/bnf/current/PHP2978-sodium-valproate.htm#PHP64779-pregnancy> [Accessed on 03/02/2016]
2. Medicine and Healthcare products Regulatory Agency. *Medicines related to valproate: risk of abnormal pregnancy outcomes*. 2015. <www.gov.uk/drug-safety-update/medicines-related-to-valproate-risk-of-abnormal-pregnancy-outcomes. [Accessed on 03/02/2016]
3. Patient Booklet—Valproate. 2015. <assets.digital.cabinet-office.gov.uk/media/54bd3a23e5274a15b3000009/Valproate_booklet_for_patients_Jan_2015.pdf> [Accessed on 03/02/2016]
4. Faculty of Sexual and Reproductive Healthcare. *UK Medical Eligibility Criteria for Contraceptive Use*. 2009. <www.fsrh.org/pdfs/UKMEC2009.pdf> [Accessed on 03/02/2016]