

# PRAC recommends new measures to avoid valproate exposure in pregnancy

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### New restrictions on use; pregnancy prevention programme to be put in place

The European Medicines Agency's experts in medicines safety, the Pharmacovigilance Risk Assessment Committee (PRAC) are recommending new measures to avoid exposure of babies to valproate medicines in the womb. Babies exposed are at risk of malformations and developmental problems.

#### What are the main measures recommended by the PRAC?

- Where licensed for **migraine** or **bipolar disorder**:
  - In *pregnancy* - valproate must not be used.
  - In *female patients from the time they become able to have children* – valproate must not be used unless the conditions of a new **pregnancy prevention programme** ([see below](#)) are met.
- For **epilepsy**:
  - In *pregnancy* - valproate must not be used. However it is recognised that for some women with epilepsy it may not be possible to stop valproate and they may have to continue treatment (with appropriate specialist care) in pregnancy.
  - In *female patients from the time they become able to have children* – valproate must not be used unless the conditions of the new **pregnancy prevention programme** are met.
- The PRAC has also recommended that the outer packaging of all valproate medicines must include a **visual warning** about the risks in pregnancy. In addition to boxed text, this may include a symbol/pictogram, with the details to be adapted at national level.
- A **patient reminder card** will also be attached to the outer package for pharmacists to discuss with the patient each time the medicine is dispensed.
- Companies that market valproate should also provide **updated educational materials** in the form of guides for healthcare professionals and patients.

#### What are the main points of the new valproate pregnancy prevention programme?

- **Assessing** patients for the potential of becoming pregnant, and involving the patient in evaluating her individual circumstances and supporting informed decision making,
- **pregnancy tests** before starting and during treatment as needed,
- **counselling** patients about the risks of valproate treatment,
- explaining the need for **effective contraception throughout treatment**,
- carrying out **reviews of treatment** by a specialist at least annually,
- introduction of a new **risk acknowledgement form** that patients and prescribers will go through at each such review to confirm that appropriate advice has been given and understood.

Medicines containing valproate have been approved nationally in the EU to treat epilepsy, bipolar disorder and in some countries for prevention of migraine. They are known to pose a considerable risk of malformations and developmental problems in babies who are exposed to valproate in the womb. An [earlier review](#) had recommended measures aimed at better informing women about these risks in order to reduce use of the medicine during pregnancy, and not starting treatment unless other options were ineffective or could not be used because of side effects. The current review was launched because of concerns that these measures had not been sufficiently effective.

The PRAC examined the available evidence and consulted widely with healthcare professionals and with patients, including women and their children who have been affected by valproate use during pregnancy, through written submissions, expert meetings, meetings with stakeholders including healthcare professionals, patients organisations, patients and their families, and via a [public hearing](#). The PRAC noted that women were still not always receiving the right information in a timely manner and that further measures were needed to help avoid use during pregnancy. However, it was also clear that for some women, such as those with particular forms of epilepsy, valproate is the only appropriate treatment and might be life-saving.

The PRAC therefore considered that the way the products are used should be changed. It recommended strengthening restrictions on their use and introducing new measures to require appropriate counselling and information for affected women.

The PRAC also recommended that the companies marketing these medicines carry out additional studies to further characterise the nature and extent of the risks posed by valproate and to monitor ongoing valproate use and the long-term effects from affected pregnancies.

Because valproate medicines are all licensed at national level, the PRAC recommendations will now be sent to Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human<sup>[1]</sup> (CMDh), which will adopt a position.

**In the meantime, women who have any concerns should consult their doctor. Women and girls who have been prescribed valproate should not stop taking their medicines without consulting their doctor as doing so could result in harm to themselves or to an unborn child.**

### More about the medicine

Valproate medicines are used to treat epilepsy and bipolar disorder. In some EU Member States they are also authorised to prevent migraine headaches.

The active ingredient in these medicines may be valproic acid, magnesium valproate, sodium valproate, valproate semisodium or valpromide.

Valproate medicines have been authorised via national procedures in all EU Member States and in Norway and Iceland. They are marketed under several brand names including: Absenor, Convival Chrono, Convulex, Delepsine, Depakin, Depakine, Depakote, Depamag, Depamide, Deprakine, Diplexil, Dipromal, Epilim, Episenta, Epival, Ergenyl, Espa-Valept, Hexaquin, Kentlim, Leptilan, Micropakine L.P., Orfiril, Petilin, Valepil, Valhel PR, Valpal, Valpro and Valprolek.

### More about the procedure

The review of valproate medicines 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 has been carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which has made a set of recommendations. The PRAC recommendations will now be sent to Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a position. The CMDh is responsible for ensuring harmonised safety standards for medicines authorised via national procedures across the EU.

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[1] The CMDh is a medicines regulatory body representing the European Union (EU) Member States, Iceland, Liechtenstein and Norway.

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