Australian Government
Department of Health
Therapeutic Goods Administration

Advisory Committee on Medicines

Meeting Statement 9, Thursday 31 May and Friday 1 June 2018

Section A: Submissions for registration

The committee's advice was sought on nine new pre-market applications for prescription medicines, and one application for changes to the Product Information of a prescription medicine, as tabulated below.

Number of applications	Application Type	Main consideration by ACM (among other items)
2	Type A - New Chemical /Biological Entity/Biosimilar	For general consideration
1	Type B – New Fixed Combination	For general consideration
3	Type C - Extension of Indications	For consideration of broader indication with or without substantiating supportive evidence
3	Type F – Major Variation (New Dose Regimen, or New formulation)	For general consideration
1	Type J – Changes to Product Information	For consideration of Use in Pregnancy category

Further details of the ACM discussions and advice associated with pre-market items are released within the Australian Public Assessment Reports (AusPARs) for each new active. Please note that there is a delay from when an application was considered at ACM and the publication of the AusPAR. To browse all AusPARs see: <https://www.tga.gov.au/browse-auspars-active-ingredient>

Section B: Post-Market items referred for advice

The committee's advice was sought on one item.

Sodium valproate and use in pregnancy and women of child-bearing age

The ACM was asked to provide advice on the safety of sodium valproate in pregnancy and in women of child-bearing age. The ACM noted ongoing review in Europe on the effectiveness of risk mitigation activities to inform patients and health professionals of the considerable risk of malformations and developmental problems following exposure to valproate before birth.

Sodium valproate has been available for use in Australia since the 1960s and is available under several brand names. The approved indications are for epilepsy (including petit mal absences, various forms of myoclonic epilepsy, tonic-clonic grand mal seizures and partial (focal) epilepsy) and for mania in patients with bipolar disorder.

A broad range of congenital malformations can occur in babies born to women who take sodium valproate during pregnancy, and the risk of malformations increases with increasing dose of valproate.

Prescribing information for sodium valproate includes:

- the medicine is contraindicated during pregnancy
- the medicine should not be used in female children, in female adolescents, in women of childbearing potential and pregnant women unless alternative treatments are ineffective or not tolerated, because of the high risk of malformation and risk of developmental disorders in infants exposed to valproate before birth.
- patients and prescribers should reconsider benefit and risk at regular treatment reviews, at puberty and urgently when a woman of child bearing potential treated with valproate plans a pregnancy or becomes pregnant.

To date, activities to minimise the use of valproate by pregnant women and women of child-bearing age include:

- a patient card provided by the pharmacist at each dispensing of the product (not all brands)
- a pregnancy pictogram warning on the outer packaging (not all brands)
- information booklets for patients and healthcare providers.

The ACM noted that there is little evidence from Australian drug usage data that actions taken to date (such as including pictograms on packaging) have made a significant difference to prescribing patterns. However, in the absence of demonstrated differences in safe use between brands, visual warnings should be used consistently across all brands and patients should be provided with comparable information.

The ACM advised that it is more appropriate to educate prescribers (particularly psychiatrists) and undertake other risk communications than to introduce a pregnancy prevention program. The key messages to communicate are:

- avoid use of valproate in women of child-bearing age for all non-seizure indications
- for seizure indications, consider alternatives if they exist
- always use the lowest effective dose.

The ACM suggested that consideration could be given to implementing mechanisms that could reduce inappropriate prescribing in female patients between 14 and 50 years of age and use for non-seizure related indications.

The effect of any actions taken should be reviewed after two years.

Further information

For further information on the ACM, please visit Advisory Committee on Medicines

or contact the ACM Secretary by email ACM@health.gov.au.