MCAZ Medicines Control Authority of Zimbabwe

106 Baines Avenue
Tel: +263 242 736 981-7
708 255 / 792 165 / 0772 145 191/2/3
Email: mcaz@mcaz.co.zw
Website: www.mcaz.co.zw

P.O. Box 10559
Harare
Zimbabwe

REF: B/279/35/15/2022

CIRCULAR 15 of 2022

Date: 11/07/2022

To:

1) Retail and Hospital Pharmacies
2) Zimbabwe Medical Association (ZiMA)
3) Medical and Dental Practitioners Council of Zimbabwe
4) Pharmaceutical Society of Zimbabwe (PSZ)
5) Community Pharmacists Association (CPA)
6) Nurses Association of Zimbabwe
7) National Medicine and Therapeutics Policy Advisory Committee (NMTPAC)
8) Provincial Medical Directors (PMDs)
9) Provincial Nursing Officers (PNOs)
10) Provincial Pharmacists

RE: Safety measures for sodium valproate and the risk of congenital malformation in neonates and neurodevelopmental problems in children exposed to sodium valproate during pregnancy

Background of Safety Issue

A recent newspaper article by the Daily mail UK, highlighted concerns around the use of sodium valproate/ valproic acid products by pregnant women and women of child-bearing age. Sodium Valproate is indicated for the treatment of epilepsy (complex partial seizures and /or simple and complex absence seizures, among others), bipolar disorder and rarely in migraines.

Sodium valproate has been known to cause congenital malformations in neonates (approximately 10% of cases), and serious developmental problems among children in up to 30-40% of cases whose mothers were exposed to sodium valproate during pregnancy (1). Examples of congenital malformations include neural tube defects, facial dysmorphism, cleft lip and palate, and multiple anomalies involving various body systems. Available data showed that children with a history of sodium valproate exposure in utero may experience delays in their early development and had increased risk of developmental disorders compared to the general study population. The product is contraindicated in in girls and women of childbearing potential unless other treatments are ineffective or not tolerated. The Authority wishes to advise health care professionals as follows;

Advice for Healthcare Professionals

1. The product is contraindicated in in girls and women of childbearing potential unless other treatments are ineffective or not tolerated.

2. **All female patients who are considering sodium valproate therapy must be informed on the following points:**
   - There is a risk of congenital malformation and neurodevelopmental problems in children whose mothers were exposed to sodium valproate during pregnancy.
   - Pregnancy testing is required before starting sodium valproate and throughout treatment, as necessary.
   - The use of effective contraception during the entire duration of treatment is important.
   - Patients to consult their doctor if they are planning for pregnancy.

3. **If sodium valproate is required for the patient and other treatment options are ineffective or not tolerated, please ensure the following:**
   - Treatment should only be initiated after pregnancy has been excluded (negative pregnancy test).
   - Annual review should be carried out, and ad-hoc treatment review conducted when required. The benefit and risk should be carefully reconsidered during every treatment review.
   - When patient is planning for pregnancy, all efforts should be made to switch to appropriate alternative treatment prior to conception, if possible.
   - In the case where sodium valproate must be used during pregnancy, prenatal monitoring is recommended to detect any malformations.

References

1. Valproate medicines (Epilim▼, Depakote▼): contraindicated in women and girls of childbearing potential unless conditions of Pregnancy Prevention Programme are met - GOV.UK (www.gov.uk)
2. https://www.dailymail.co.uk/news/article-10725253/NHS-faces-thalidomide-stylescandal-doctors-gave-pregnant-women-drug-known-cause-birth-defects.html

MEDICINES CONTROL AUTHORITY OF ZIMBABWE

.....Ayambaye.....

pp R. T. Rukwata (Mr.)
ACTING DIRECTOR-GENERAL