This document is approved by The Executive Directorate of Pharmacovigilance, at SFDA

Annual Risk Acknowledgement Form for Epival® (Sodium Valproate) VALPROATE HAS RISKS IN PREGNANCY

- **Name of valproate user:**
- **Date of birth:**
- **Identification number:**
- **Name and role of specialist:**
- **Signature of specialist and date:**
- **Name of valproate user's GP:**

Children exposed to valproate in utero have a very high risk for congenital malformations and neurodevelopmental disorders. Valproate is therefore contraindicated in women of childbearing potential unless the conditions of "prevent", the pregnancy prevention programme are fulfilled.

The specialist must provide this form to girls and women of childbearing potential treated with valproate – or to their "responsible person": a parent/legal guardian or person capable of giving consent on behalf of patients who are minors or without the capacity to make an informed decision or person acknowledging that the treatment is in the best interests of the patient.

There are three steps needed to complete this form:

Step 1 – Decide if the patient needs to be on "prevent" – the valproate pregnancy prevention programme

Step 2 – "prevent" applies to this patient- she is of childbearing potential and at risk of pregnancy

Step 3 – Your patient needs to complete this section to confirm they understand the risks of valproate in pregnancy

WARNING: Prescribing valproate to a woman of childbearing potential without the pregnancy prevention programme conditions being fulfilled is contraindicated and represents an unlicensed use of the drug. Use of valproate during pregnancy for epilepsy (unless there is no suitable alternative treatment), isunlicensed. This is the case even when treatment is based on an informed choice made by the patient.

As a prescriber you must document in the patient's clinical record your reason for unlicensed use, that you have informed the patient of the unlicensed use and its associated risk.

This form expires on _____ (12 months after completion).
Complete a new form at each annual review.

Step 1 – Decide if the patient needs to be on "prevent" – the valproate pregnancy prevention programme

- Women of childbearing potential (from menarche to menopause) who are taking any medicine containing valproate, regardless of the indication, should fulfil all the requirements of "prevent".
- The only exception is when you (the specialist) consider that there are compelling reasons to indicate that there is no risk of pregnancy.
- The absence of risk of pregnancy may be permanent (e.g., post-menopausal patients or those after hysterectomy) and in this case the risk does not need to be discussed in the next annual review and the requirements of "prevent" do not apply.
- If the absence of risk is subject to change (e.g., the patient is pre-menarchal), the date for the next annual discussion of the risks must be documented and the patient or the patient's family/carers asked to contact you rapidly if the situation changes before the next annual review in order to bring this review forward.
- Girls who have not yet reached menarche DO NOT need to be on "prevent", but they and their responsible person need to be aware of the risks for the future. You should provide a copy of the Patient Guide, and remind the responsible person to contact the specialist or GP to arrange for review of treatment as soon as menarche occurs.

If you consider there is a compelling reason that indicates there is no risk of pregnancy, record this here. **If appropriate, you and your patient should still complete the rest of the form** so that your patient and/or their responsible person is aware of the risks if their situation were to change in the future.

To be completed by the specialist when they consider a Pregnancy Prevention Programme (PPP) is not needed

The requirements of **"prevent"**, the valproate pregnancy prevention programme, are not necessary because there are compelling reasons to indicate that there is no risk of pregnancy, because (*tick* which applies):

☐ the patient has not yet reached menarche. I have informed the patient and family to inform me if this changes before the next annual review which is due on *(insert date)*:

☐ the absence of pregnancy risk is permanent for the following reason (insert reason):

☐ I consider that sexual activity that could lead to pregnancy will not occur before the next annual review because (insert reason):

☐ I have given the patient or responsible person a copy of the Patient Guide

Signature of patient or responsible person to confirm:

Step 2 – "prevent" applies to this patient- she is of childbearing potential and at risk of pregnancy

This form confirms that you have discussed the risks with girls, women of childbearing potential and their responsible person (if applicable), and you are acting in compliance with the pregnancy prevention programme.

You need to:

- Explain the risks of valproate in pregnancy and ensure these are understood.
- Give your patient (or their responsible person) a copy of the Patient Guide.
- Complete all parts of this form, keep the original in the patient record and provide a copy to the patient, her responsible person (if appropriate), and to her GP.

Arrange a follow-up appointment at least every year to review the need for continued treatment with valproate and compliance with **"prevent"**.

To be completed and initialed by the specialist	**Initials**
I confirm that the patient needs valproate because: ▪ her condition does not respond adequately to other treatments, or ▪ she does not tolerate other treatments, or **I confirm I have discussed the following with the patient:**	
Valproate must not be used during pregnancy (except in rare situations in epilepsy for patients who are resistant or intolerant to other treatments)	
The overall risks in children exposed to valproate during pregnancy are: ▪ an approximately 10% chance of birth defects ▪ a 30% to 40% chance of a wide range of early developmental problems that can lead to learning disabilities.	
The conditions of the pregnancy prevention programme must be fulfilled	
The need for regular (at least annual) review of the need to continue valproate treatment by a specialist	
The need for effective contraception, without interruption, throughout treatment with valproate	
The need to arrange an appointment with her specialist as soon as she is planning pregnancy to ensure timely discussion, and a timely switch to an alternative treatment before stopping contraception and conception occurring.	
The need to contact her GP immediately for an **urgent** review of her treatment in case of suspected or inadvertent pregnancy.	
The need for a negative (ideally serum) pregnancy test result at start and if needed thereafter	
I confirm I have given the patient or responsible person a copy of the Patient Guide	
In case of pregnancy, I confirm that:	
▪ We have discussed options for switching treatment	
▪ She is fully aware of the risks of pregnancy, and has had the opportunity for counselling about the risks	
▪ I have given the patient or responsible person a copy of the Patient Guide	

Step 3 – Your patient needs to complete this section to confirm they understand the risks of valproate in pregnancy

If you use valproate while you are pregnant, your future child has significant risk of serious harm.

Completing this form confirms that you (or your responsible person) understand the risks of using valproate during pregnancy, and what method of contraception you will use to prevent becoming pregnant during treatment.

To be completed and signed by the patient or their responsible person	Initials
I have discussed the following with my specialist, and I understand:	
√ Why I need valproate rather than another medicine	
√ That I should visit a specialist regularly (at least once a year) to review whether valproate remains the best option for me	
√ The risks in children whose mothers took valproate during pregnancy are: ♦ 1 out of 10 children will have physical birth defects ♦ 3 to 4 out of 10 children will have early developmental problems that can lead to significant learning disabilities	
√ That I have had a negative pregnancy test (if advised by my doctor/specialist)	
√ Why I must use effective contraception, without stopping or interruption, at all times while taking valproate	
√ The options for effective long-term contraception (or a consultation has been planned with a professional who can give me advice)	
√ The need to consult my specialist or GP as soon as I start thinking about becoming pregnant. This is to make sure I have time to switch to another treatment before I come off contraception	
√ The need for regular (at least annually) review and the need to continue valproate treatment by a consultant	
√ That I should request an **urgent** GP appointment if I think I am pregnant	
√ I have been given a copy of the Valproate Patient Guide and know where to find more information	
In case of pregnancy, I confirm that: √ Options for switching treatment have been considered √ I am fully aware of the risks and have had the opportunity to have counselling about the risks √ The need to appropriate monitoring of my baby if I am pregnant	

Name of patient: _____

Name of responsible person (if applicable): _____

Signature of patient (or responsible person) and date: _____

Effective contraception is essential while taking valproate.

At least one highly effective method of contraception (preferably a user independent form such as an intrauterine device or implant) or two complementary forms of contraception including a barrier method should be used. Individual circumstances should be evaluated in each case. When choosing the contraception method involve the patient in the discussion to guarantee her engagement and compliance with the chosen measures. Even if she has amenorrhoea she must follow all the advice on highly effective contraception.

Call for reporting

Report suspected adverse drug reactions associated with Epival® (Sodium Valproate) by contacting:

Local representative / Cigalah Group

Sharafiyyah District - Al Yousfia Building

P.O. Box 19435 - Ali Bin Abi Taleb Street, Jeddah, 21435 Saudi Arabia

Tel: +966-12-6148259 - Mob: +966-539455825 - Fax: +966-12-6148458

Email: drug-safety@cigalah.com.sa - moghamdi@cigalah.com.sa

The National Pharmacovigilance Centre (NPC) Saudi Food and Drug Authority (SFDA)

SFDA call center: 19999

Toll free phone: 8002490000 - Fax: +966-11-2057662

E-mail: npc.drug@sfda.gov.sa - Website: http://ade.sfda.gov.sa/

References

1. Epival® Leaflet