



EPILEPSY



# NATIONAL CLINICAL PROGRAMME FOR EPILEPSY

## PRACTICE GUIDE FOR THE MANAGEMENT OF WOMEN WITH EPILEPSY



National Clinical  
& Integrated Care Programmes  
*Person-centred, co-ordinated care*



ROYAL COLLEGE OF  
PHYSICIANS OF IRELAND



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## Version Control

This Practice Guide is the work of a subgroup of the National Clinical Programme for Epilepsy initiated in 2012. Membership of this subgroup was wide including representatives from Medics including Consultant Neurologist and GP, CNS Epilepsy, Patient, CNS Neurology PAEDS and Consultant Physician ID. Consultant Obstetrician input was also achieved with significant input from Dr Mary Holohan, Rotunda Hospital and reviewed by Professor McAuliffe from the National Maternity Hospital.

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Version 0.6	Dec 2014	Amendments by working group following publication of international recommendations re: prescribing of Valproate.
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Version 0.9	Feb 2016	Resubmission to Clinical Advisory Group Leads for Consultation
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Version 0.13	Mar 2017	Review based on publication from FSRH UK
Version 0.14	Jan 2018	Approval of draft document by CSPD SMT
Version 0.15	May 2018	Update with HPRA recommendations re; pregnancy prevention programme
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Version 1.0	July 2018	Final Draft Published

*This practice guide will be reviewed in October 2019*

## FORWARD

**WOMEN WITH EPILEPSY** have particular issues in relation to cyclical impact on seizures, contraceptive choices, medication options and foetal development, pregnancy complications and adverse menopausal impact; such that Women with Epilepsy should receive care from informed health professionals who can minimise the risks faced by these women and their children. This guide sets out the Clinical Care Pathway that best addresses the needs of Women with Epilepsy in Ireland and identifies the responsibilities of the health care providers from whom these patients receive care. The objective of this practice guide is to achieve optimal seizure control on medication that has minimal foetal impact in pregnancy that is relatively complication free and supported throughout adult life in adopting positive lifestyle choices.

Dr Mary Holohan  
Consultant Obstetrician  
FRCOG, FRCPI, FFFFLM (RCP Lon).

## KEY RECOMMENDATIONS

- The diagnosis of epilepsy should be made by a medical practitioner with expertise in epilepsy, usually a neurologist.
- Women with epilepsy and those caring for them should be made aware of the different types of epilepsy and their seizure types in order to assess the individual risks to the mother and baby.
- Women with Epilepsy (WWE) should be encouraged to attend for preconception counseling with an epilepsy specialist at least 1 year prior to conception.
- Clinicians are encouraged to inform WWE of the most up to date information concerning the individual risk to the fetus exposed to AED medication.
- WWE should be informed that the risk of congenital abnormalities can be associated with the particular Anti-epileptic drug (AED) type and dose.
- The lowest effective dose of the most appropriate AED should be employed.
- Doctors in the EU are now advised not to prescribe valproate for epilepsy or bipolar disorder in pregnant women, in females unless other treatments are ineffective or not tolerated.<sup>1</sup>
- Valproate may be initiated in girls and women of childbearing potential only if the conditions of the valproate pregnancy prevention programme are fulfilled. Full details on the pregnancy prevention programme are available at <http://www.hpra.ie/docs/defaultsource/Valproate/pharmacy-poster.pdf?sfvrsn=0>
- Women on Valproate therapy must be reviewed annually by a specialist and the risk acknowledgment form completed annually.
- All WWE should be prescribed Folic Acid 5mg once an anti-seizure medication is commenced and should be continued until at least 3 months into the pregnancy; however the epilepsy service will recommend continuing the Folic Acid 5mg throughout the pregnancy<sup>23</sup>.
- WWE with an unplanned pregnancy should attend an epilepsy specialist once pregnancy is confirmed.
- WWE should never stop taking their AEDs without discussing it with their doctor/nurse first, even in the event of confirmation of a pregnancy.
- WWE should have baseline pre pregnancy AED levels for comparison in pregnancy and to monitor compliance for appropriate AED
- WWE on all AEDS should have a trough<sup>4</sup> levels taken to assess compliance.
- According to the Royal College of Obstetricians and Gynaecologists in the UK routine monitoring of serum AED levels in pregnancy is not recommended. Clinicians will need to take into account other features such as suspicion of non-adherence, toxicity and intractable

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1 Health Products Regulatory Authority 2014, <https://www.hpra.ie/docs/default-source/default-document-library/prac---valproate-art-31---dhcp-sanofi-ie-final-27nov2014.pdf?sfvrsn=0>

2 Crawford, P. Appleton, R. Betts, T. J. Duncan, J., Guthrie, E., & Morrow, J. (1999) Best practice guidelines for the management of women with epilepsy. *Seizure* 8: 201-217

3 Epilepsies: diagnosis and management. NICE guidelines [CG137] Published date: January 2012 at <https://www.nice.org.uk/guidance/cg137/chapter/1-guidance-> accessed on line April 2016

4 In medicine and pharmacology, a trough level or trough concentration is the lowest level (concentration) at which a medication is present in the body.

seizures in their decisions on therapeutic drug monitoring (RCOG 2016<sup>5</sup>). Concerns about routine AED levels in pregnancy should be discussed with the specialist involved in treating the WWE.

- There should be a minimum of 1 visit per trimester at either their primary neurology center or at a specialist nurse led clinic. The final prenatal visit should be scheduled for no later than a month before the EDD.
- Pregnant WWE who have experienced seizure activity within the last year should be closely monitored
- WWE with epilepsy can Breastfeed if they wish to do so.
- It is recommended that pregnant women taking antiepileptic drugs in general and valproate in particular, are enrolled in the Irish Epilepsy and Pregnancy Register ([www.epilepsypregnancyregister.ie](http://www.epilepsypregnancyregister.ie)). This should be done as early as possible in the pregnancy, before the outcome is known.

### 1.0. Purpose of Practice Guide

The purpose of this guide is to ensure that all medical/nursing staff are clear on their role in delivering a service to women with epilepsy.

### 2.0. Scope of Practice Guide

This guide applies to all female patients with epilepsy, Neurologists, GPs, Obstetricians, Nursing staff, Midwives, PHNs, Pharmacists and staff at Family Planning Clinics.

### 3.0. Definitions

AED	Anti-epileptic drug
Clinician	Any Doctor or nurse who reviews the patient
Dexa scan	Dual Energy Xray Absorbtiometry
EDD	Estimated Date of Delivery
EPR	Electronic Patient Record
GP	General Practitioner
IV	Intravenous
Monotherapy	Single Drug Plan
PHN	Public Health Nurse
PR	Per Rectum
RANP	Registered Advanced Nurse Practitioner
WWE	Women with Epilepsy

### 4.0. Responsibilities

For the purpose of this Practice Guide the delivery key aspects of service delivery requires separate responsibilities from different members of the Multidisciplinary team as outlined below.

- [Managing the care of WWE at the preconception stage](#), including those considering pregnancy (Responsibility of the Neurologist, RANP the GP, the patient and Family Planning Clinics)

- **Management by the epilepsy service of WWE who is pregnant** (Responsibility of the Clinician to include Neurologist, GP and RANP)
- **Management by the obstetric service of WWE who is pregnant** (Responsibility of the Neurologist, RANP and GP)
- **Managing the care of WWE who are in labour** (Responsibility of Obstetrician, Midwives, Maternity staff)
- **Managing the care of WWE with regard to post-natal care** (Responsibility of Obstetrician, Midwives, Maternity staff)
- Managing the care of WWE of menopausal age (Responsibility of Obstetrician, Midwives, Maternity staff, Neurologist, RANP and PHN)

The recommendations outlined in this document are pertinent to the total care of WWE with epilepsy in all health care settings. In the case of women attending maternity hospitals who are seen in the specialist obstetrical epilepsy clinics, which are nurse-led; this service is considered an outreach service from the specialist epilepsy centres.

## 5.0 Procedure

### The following steps are to be carried out in the overall management of WWE

#### 5.1 Managing the care of WWE at the preconception stage, including those considering pregnancy.

The Clinician/GP should identify women of appropriate age and invite them for a consultation to discuss contraception and family planning issues with them- see appendix 1.

Key issues to be discussed at the consultation include:

- Contraception
- Family planning
- Pregnancy, including risks of unplanned pregnancies to the woman, and the foetus and why WWE need to be plan their pregnancies.
- Doctors in the EU are now advised not to prescribe valproate for epilepsy or bipolar disorder in pregnant women, in women who can become pregnant or in girls unless other treatments are ineffective or not tolerated. Those for whom valproate is the only option for epilepsy or bipolar disorder should be advised on the use of effective contraception and treatment should be started and supervised by a doctor experienced in treating these conditions<sup>6</sup>. The conditions of the new Pregnancy Prevention Programme (HPRA, 2018) should also be met.

This includes;

- 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 patient about the risks of valproate treatment

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6 Adab N, Tudur SC, Vinten J, Williamson P, Winterbottom J. Common antiepileptic drugs in pregnancy in women with epilepsy. *Cochrane Database Syst Rev.* 2004;(3):CD004848. Review.



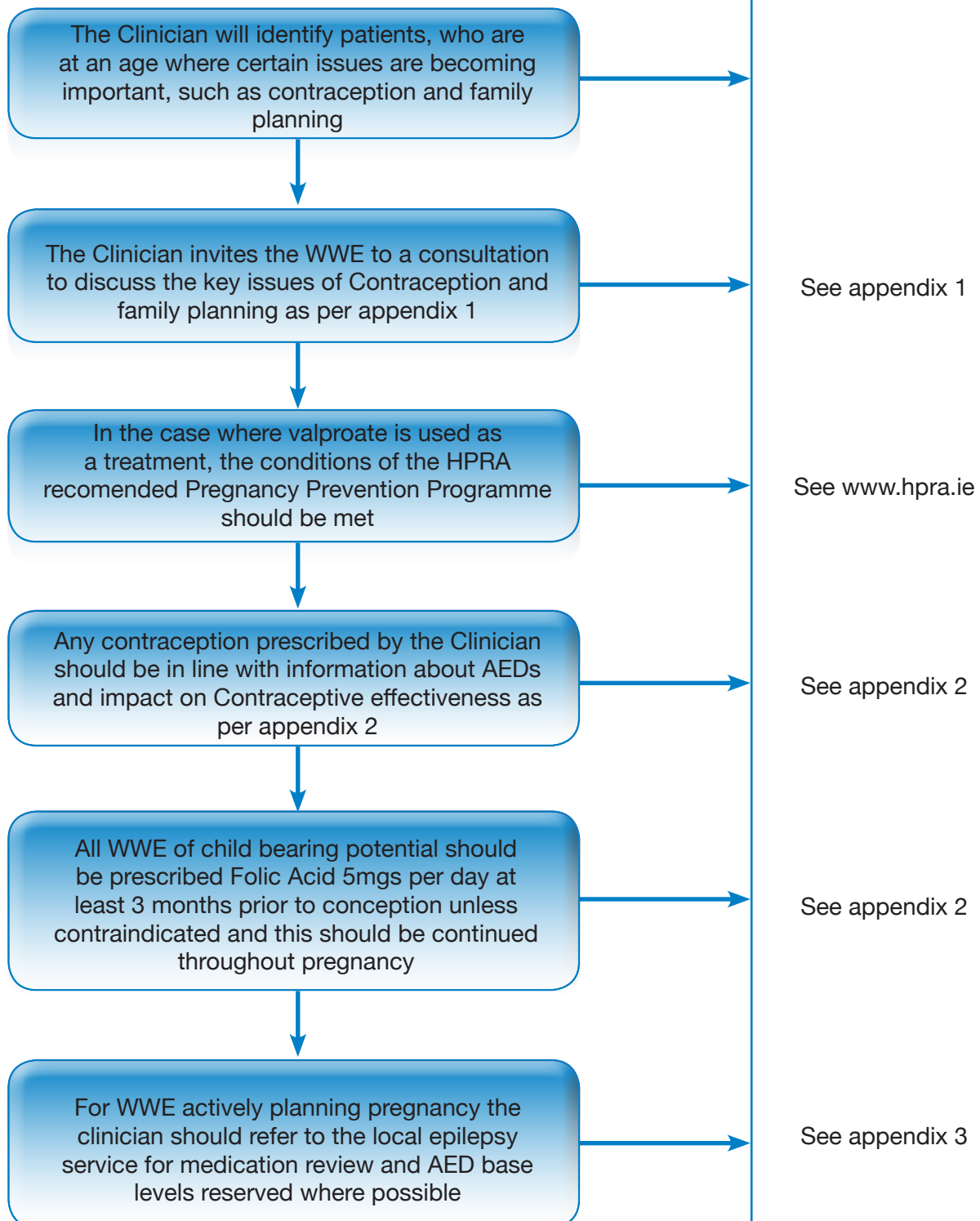
- Explaining the need for effective contraception through treatment
  - Carry out reviews of treatment by a specialist at least annually
  - Introduction of a new risk acknowledgement form that patients and prescribers will go through at each such review to confirm that appropriate advice has been given and understood
- WWE should be provided with a Patient Information Leaflet
  - Clinicians may wish to consider completing the checklist for prescribers and patients.
  - 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
  - WWE should be given written information concerning all aspects of pregnancy
  - All WWE of child bearing potential should be prescribed Folic Acid 5mgs per day at least 3 months prior to conception unless contraindicated and this should be continued throughout pregnancy. - see appendix 2.
- 5.1.2 In the management of WWE, where clinically relevant it is recommended to have baseline AED monitoring completed for the purpose of comparison during pregnancy.
- 5.1.3 If prescribing oral contraception to WWE it is important that the Clinician notes that the contraception effectiveness may be decreased due to enzyme inducing AEDS so a review of medication may be required see appendix 2. If a medication review is required, then the Clinician should refer the WWE to the relevant neurology service - see appendix 3.
- 5.1.4 For WWE actively planning pregnancy Clinician should consider monotherapy where possible and refer the woman to the local neurology service for medication review - see appendix 3.
- 5.1.5 Discussion regarding bone health on AED<sup>7</sup>s<sup>8</sup>.

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7 Crawford, P. Appleton, R. Betts, T. J. Duncan, J., Guthrie, E., & Morrow, J. (1999) Best practice guidelines for the management of women with epilepsy. *Seizure* 8: 201-217.

8 J. Liporace, A. D'Abreu Epilepsy and women's health: family planning, bone health, menopause, and menstrual-related seizures *Mayo Clin Proc*, 78 (2003), pp. 497-506

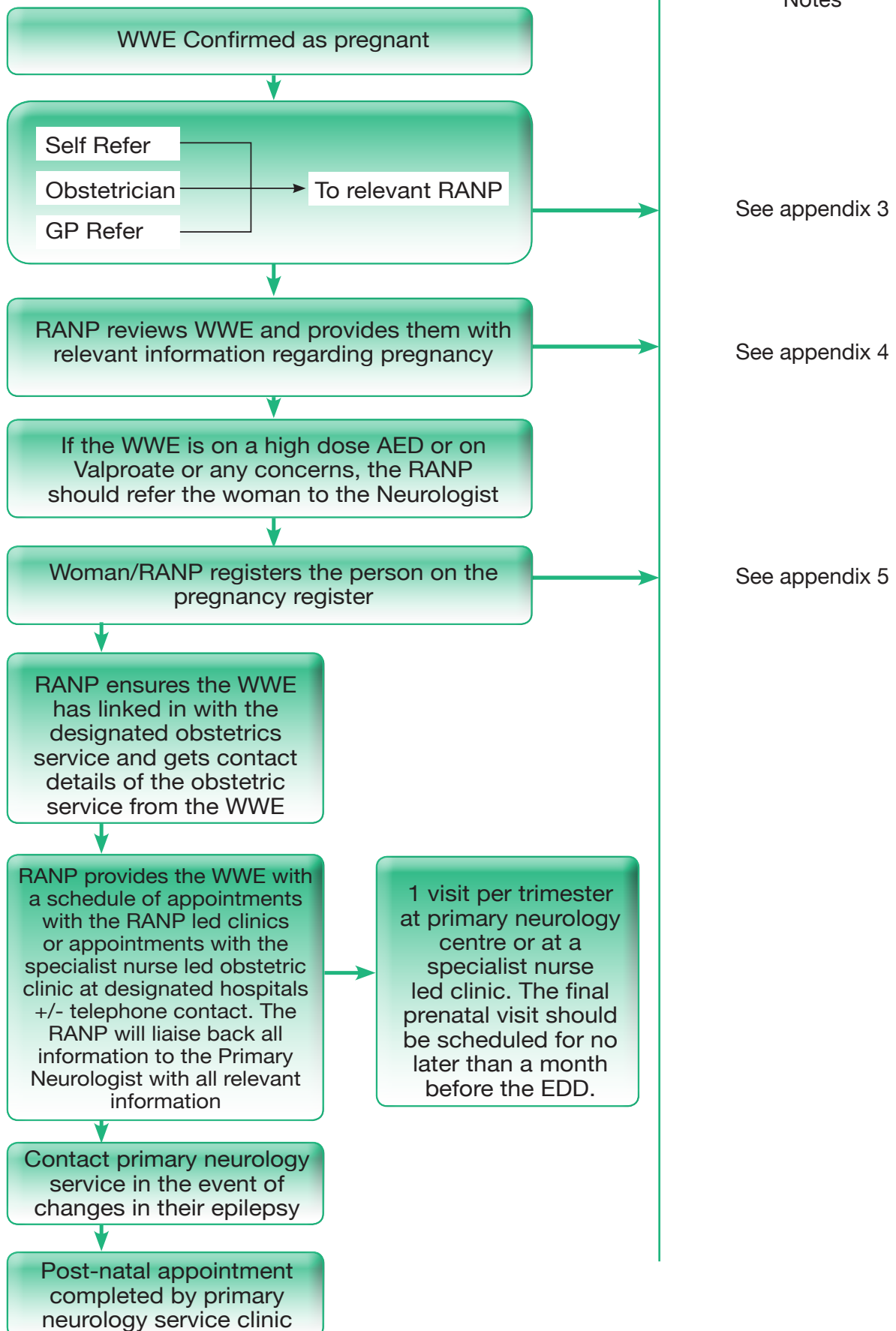
## 5.1 Managing the care of WWE at the preconception stage, including those considering pregnancy



## 5.2. Management by the epilepsy service of WWE who is pregnant

- 5.2.1 Woman with epilepsy is confirmed as pregnant.
- 5.2.2 The woman should attend the relevant RANP service. This can occur either as self-referral, Obstetrician referral or GP referral.
- 5.2.3 Registered Advanced Nurse Practitioner (RANP) should review the WWE and provide them with relevant information regarding pregnancy that the woman needs to consider - see appendix 4. If the RANP has any concerns about the WWE they should refer the WWE to the neurologist for a consultation.
- 5.2.4 If the WWE is on a high dose AED (see British National Formulary (BNF) Guidelines) or is on Valproate or any other concerns the RANP may have, then she should be referred for a consultation with the neurologist.
- 5.2.5 RANP should discuss the pregnancy register with the WWE and get their agreement to be registered on the register - see appendix 5.
- 5.2.6 RANP should ensure the WWE has linked in with the obstetrics service. The RANP should get the contact details of the obstetric service from the WWE to circulate any OPD correspondence to obstetrics service.
- 5.2.7 RANP should provide the WWE with a schedule of appointments with the epilepsy clinic or appointments with the specialist nurse led obstetric clinic at designated hospitals ensuring a minimum of 1 visit per trimester. The final visit should be scheduled for at least a month prior to the EDD of the woman. The RANP or the specialist nurse led obstetric clinic at designated hospitals should also schedule a clinic visit for after the expected delivery date.
- 5.2.8 The WWE should be encouraged to contact the epilepsy service in the event of changes to their epilepsy.
- 5.2.9 The EPR should be updated after each clinical interaction (where available).

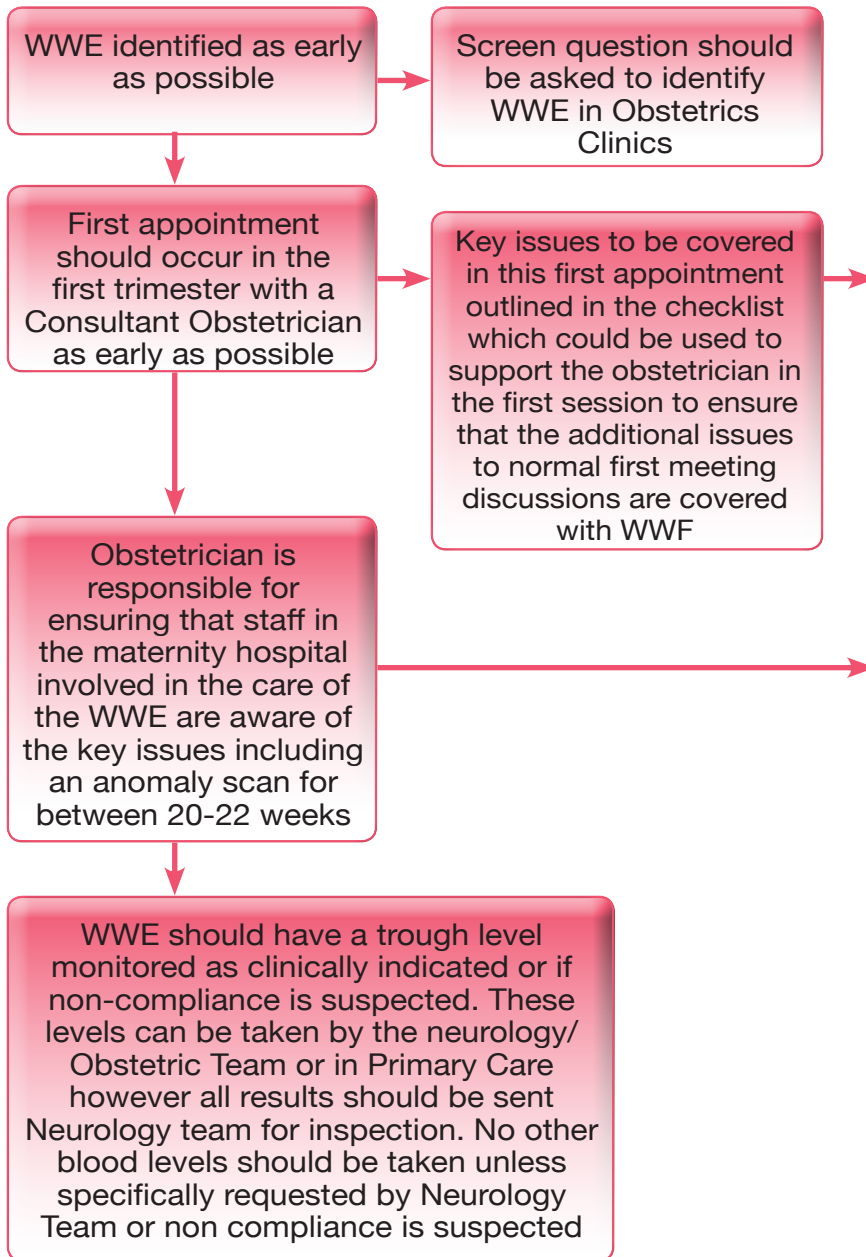
## 5.2 Management by the epilepsy service of WWE who is pregnant



### **5.3 Management by the obstetric service of WWE who is pregnant**

- 5.3.1 WWE should be identified by obstetric service as early as possible and referred to Neurology service if patient has not had a recent neurology consultation. Screen questions should be asked in obstetric clinics to ensure that WWE are identified as early as possible by the obstetric service.
- 5.3.2 The first appointment with the Obstetrician should be with a consultant obstetrician as early as possible in the first trimester.
- 5.3.3 A number of key issues should be discussed at this first meeting to ensure that the pregnancy and delivery is as safe as possible for the WWE and her child. The checklist see appendix 6 should be used to ensure that all critical issues are addressed in this first appointment.
- 5.3.4 Obstetrician is responsible for ensuring all staff in the maternity hospital involved in the care of the WWE are made aware of the key issues including an anomaly scan for between 20-22 weeks as per current Irish practice. There is therefore no evidence for routine antepartum foetal surveillance with cardiotocography in WWE taking AEDs (RCOG, 2016).
- 5.3.5 WWE with epilepsy should be encouraged to have a written care plan detailing medications to avoid and medications that can be given if the woman has a seizure while an in-patient at the maternity hospital. The care plan should include a written prescription for IV PRN Lorazepam/ Buccal Midazolam for use if the WWE has a seizure while in-patient. - see appendix 7.
- 5.3.6 WWE should have a trough level<sup>4</sup> monitored as clinically indicated or if non-compliance is suspected (RCOG, 2016). These levels can be taken by the neurology/Obstetric team or in Primary Care however all results should be sent to Neurology team for inspection.
- 5.3.7 If not already registered with the Irish Epilepsy and Pregnancy register the WWE should be encouraged to do so.

### 5.3 Management by the obstetric service of WWE who is pregnant



Reference Material/ Key Notes

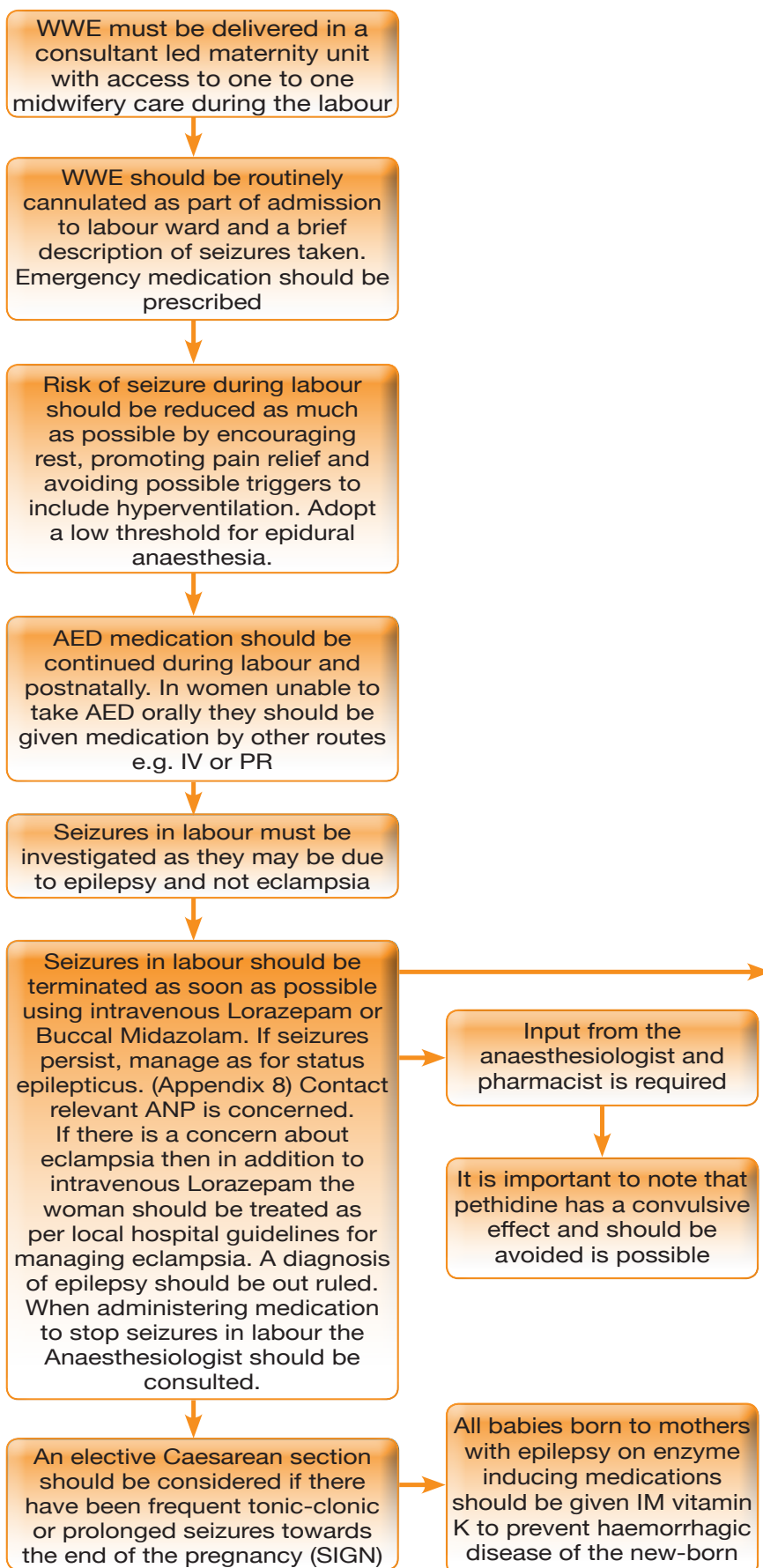
See appendix 6

See appendix 7

#### 5.4. Managing the care of WWE who are in labour

- 5.4.1 WWE should be delivered in a maternity unit with access to one to one midwifery care during the labour.
- 5.4.2 WWE should have an IV cannula inserted on admission to the labour ward to allow easy access for the administration of medication should it be required in the event of a seizure occurring during labour. Intravenous Lorazepam and/or Buccal Midazolam should be prescribed PRN on admission. A brief seizure history should be taken defining seizure type and be prominently placed in the case notes.
- 5.4.3 Factors that predispose WWE to increased seizures in labour, such as high levels of pain, sleep deprivation and hyperventilation should be prevented as much as possible. The use of epidural anaesthesia should be avoided.
- 5.4.4 The use of Pethidine should be avoided if possible in a WWE.
- 5.4.5 The WWE's usual oral AED medication should be continued during labour and post-natally. In women unable to tolerate oral medication, AEDs can be given by other routes to include IV and PR.
- 5.4.6 WWE should be counselled and reassured that the risk of seizures in labour is low.
- 5.4.7 Seizures in labour should be terminated as soon as possible using intravenous Lorazepam or Buccal Midazolam. If seizures persist, manage as for status epilepticus - see appendix 8. Maternal airway and oxygenation should be maintained at all times. If there is doubt whether a seizure in labour is due to eclampsia or epilepsy, then, in addition to intravenous Lorazepam, the woman should be treated as per local hospital guidelines for managing eclampsia. A diagnosis of epilepsy should be out ruled.
- 5.4.8 When administering medication to stop seizures in labour the Anaesthesiologist should be consulted.
- 5.4.9 An elective caesarean section should be considered and discussed with the treating epilepsy specialist if there have been frequent tonic-clonic or prolonged complex partial seizures towards the end of pregnancy
- 5.4.10 All babies born to mothers with epilepsy on enzyme inducing medications should be given IM vitamin K to prevent haemorrhagic disease of the new-born. (Phenytoin, phenobarbitone, Carbamazepine, Oxcarbazepine, Eslicarbazepine, Topiramate, Lacosamide).

### 5.4 Managing the care of WWE who are in labour



Reference Material/ Key Notes

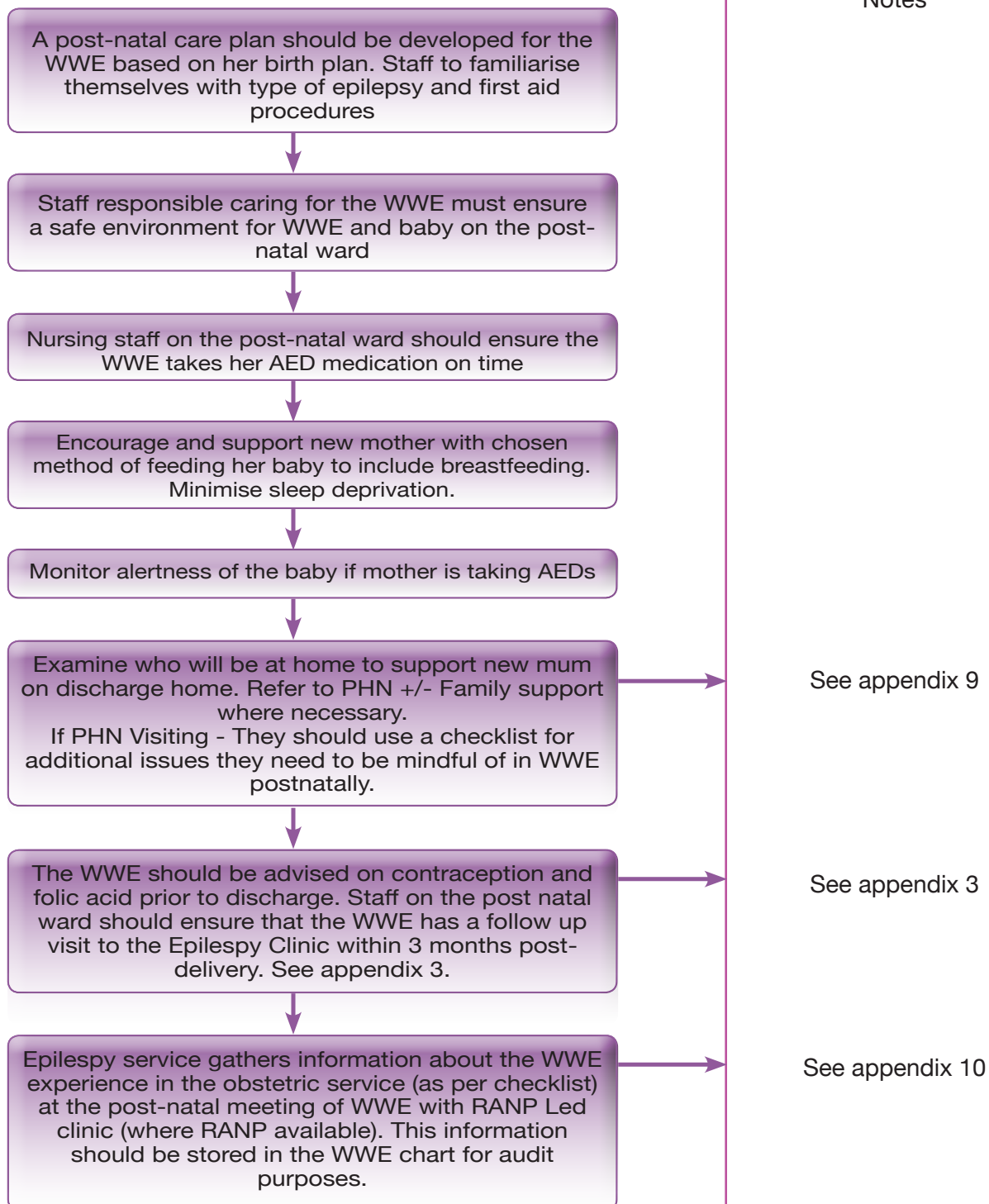
Appendix 8



## **5.5. Managing the care of WWE with regard to post-natal care**

- 5.5.1 A care plan should be developed for the WWE in the post-natal ward based on the birth plan developed.
- 5.5.2 Staff caring for the WWE should educate themselves on the type of epilepsy and the first aid of seizure management
- 5.5.3 Staff responsible for caring for the WWE must ensure a safe environment for WWE and the baby while in hospital.
- 5.5.4 Nursing Staff in the postnatal ward should ensure that WWE continue taking their AEDs on time and encourage the WWE to avoid any possible triggers, sleep deprivation and pain stimuli.
- 5.5.5 Compliance with medication should be emphasized and reinforced.
- 5.5.6 Any WWE who wishes to breastfeed should be encouraged to do so and support given to her with breastfeeding to minimise sleep deprivation.
- 5.5.7 Staff on the maternity unit (maternity staff doing home visits if the WWE has chosen the early discharge option) should monitor the alertness of the baby if the mother is taking AEDs.
- 5.5.8 Maternity staff should check who will be supporting the new mum on returning home and a PHN referral should be sent. The PHN should be aware of the special requirements that need to be considered when dealing with a WWE and her baby postnatally.- see Appendix 9.
- 5.5.9 The WWE should be advised on contraception and folic acid prior to discharge. Staff on the post natal ward should ensure that the WWE has a follow up visit to the Epilepsy Clinic within 3 months post-delivery. - see appendix 3.
- 5.5.10 If AED medications were increased during pregnancy the WWE should be advised to contact her local neurology service on discharge regarding the need to reduce the current dose of the medication to avoid any potential side effects due to toxicity.
- 5.5.11 At the follow up Epilepsy Clinic, the RANP should gather information about the WWE experience in the obstetric service as per checklist and file in the chart to be audited at a later date - see appendix 10.

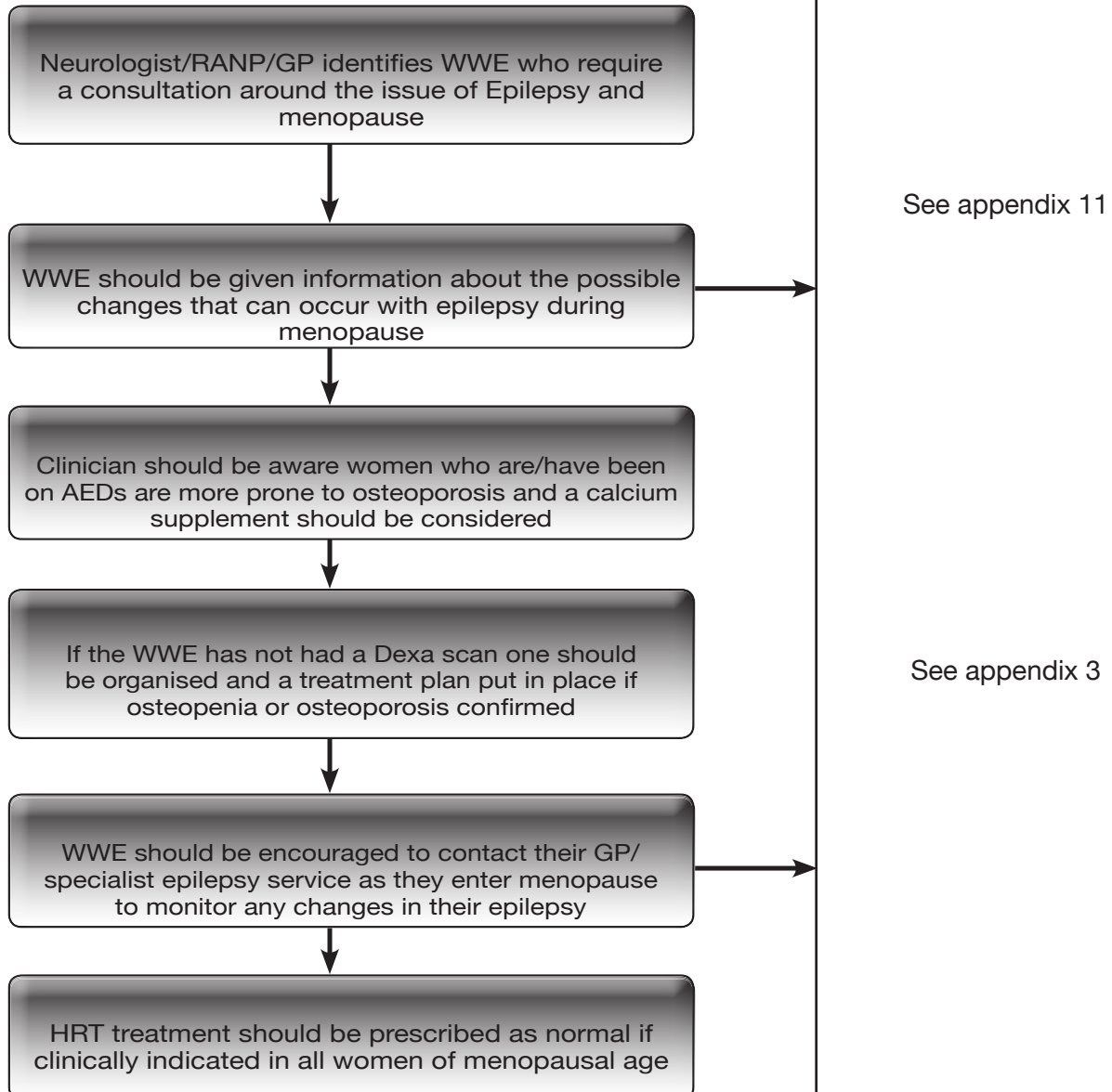
### 5.5. Managing the care of women with epilepsy in regard to post-natal care



## **5.6. Managing the care of WWE of menopausal age**

- 5.6.1 The Neurologist/RANP/GP will identify those patients attending their service who are potentially approaching menopause and discuss this at their next scheduled review.
- 5.6.2 The WWE should be given information about the possible changes to their epilepsy during menopause -see appendix 11 regarding the information on possible changes that can occur).
- 5.6.3 The Clinician should be aware that WWE who are on or have taken AEDs are more prone to osteoporosis and a calcium supplement should be considered.
- 5.6.4 If the WWE has not had a DEXA scan then the GP should organise a scan and initiate a plan to monitor the osteopenia or osteoporosis if DEXA scan shows a reduced bone density.
- 5.6.5 WWE should be encouraged to visit their local primary care or epilepsy service (see appendix 3) so that they can be monitored for any changes in epilepsy.
- 5.6.6 As with all women of menopausal age the WWE should be prescribed HRT if clinically indicated.

## 5.6 Managing the care of women with epilepsy of menopausal age



## 6.0 Evaluation Process (Audit Tool)

The audit tools are broken down in line with the six sections in the procedure.

### Audit tool in relation to section 5.1

	YES	NO	Other
WWE prescribed folic acid unless contraindicated			
Conditions of HPRA Pregnancy Prevention Programme met (appendix 1)			
Number of WWE who are actively considering becoming pregnant referred to neurologist for medication review.			
All WWE are provided with information related to contraception and family planning issues by their GPs.			
All education provided in line with appendix 2			

### Audit tool in relation to section 5.2

	YES	NO	Other
Source of referrals to RANP led clinics			
WWE is provided with a schedule of meetings, a minimum of one per trimester, with the final meeting scheduled for 4 weeks prior to woman's EDD			
% of WWE referred to neurologist from RANP led clinic			
All pregnancies are registered			

### Audit tool in relation to section 5.3

	YES	NO	Other
Date of first appointment with obstetric service			
Date of scan (in terms of number of weeks pregnant)			
Documented birth plan developed			

### Audit tool in relation to section 5.4

	YES	NO	Other
WWE was looked after on a 1to 1 basis by midwife			
WWE was delivered in a consultant led service			
% of maternity units that have signed up for the Epilepsy programme in their unit.			

**Audit tool in relation to section 5.5**

	YES	NO	Other
A care plan is developed for the WWE which includes a plan for dealing with seizures should they occur.			
WWE was provided with advice on contraception			
% of mother's with epilepsy breastfeeding.			
Information gathered at post-natal meeting by RANP on the obstetric experience of the WWE in line with the checklist.			

**Audit tool in relation to section 5.6**

			NO
How many WWE have had DEXA scans			
How many WWE on calcium			
How many women have been referred to the epilepsy service by GP for menopause related issues			

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## Appendix 1

### AEDs and Contraception – information leaflet for advice on contraception for women with epilepsy

#### Contraception advice for women with epilepsy

Interactions between antiepileptic drugs and contraceptive hormones are important due to the risks associated with contraceptive failure or reduced seizure control<sup>9</sup>.

#### 1. Effect of enzyme inducing AEDs on hormonal contraception

Some antiepileptic medicines have a drug-drug interaction with hormonal contraceptive pills which can increase the speed in which some contraceptive pills and injections are processed by the liver. (These medicines are known as liver enzyme inducers as they speed up metabolism in liver cells) (Walker et al 2009; Adab N 2004).

The following antiepileptic medicines are liver enzyme inducers:

Strong inducers	Less potent inducers
Carbamazepine	Rufinamide
Eslicarbazepine	Topiramate
Oxcarbazepine	
Phenobarbital	
Phenytoin	
Primidone	

*Reference; Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit. Antiepileptic drugs and contraception, Jan 2010*

Evidence would suggest that the impact on the effectiveness of the contraceptive pill is linked to the dose of hormone(s) and the route of administration (eg tablet or injection).

The effectiveness of the progesterone-only injectable, depot medroxyprogesterone acetate (DMPA) is not reduced by AEDs.

As the consequences of contraceptive failure is potentially very serious, the National Clinical Programme for Epilepsy advises the consistent use of barrier methods of contraception in women using any enzyme inducing AED with combined hormonal contraceptive (CHC), the progesterone-only pill (POP) or progesterone only implant. For women on long term enzyme inducing AEDs, alternative reliable contraceptive methods are recommended (eg DMPA or intrauterine methods).

Enzyme activity returns to normal within 28 days of stopping most enzyme inducing drugs, thus 28 days is sufficient for recovery of the contraceptive efficacy. For some drugs with associated risks for foetal abnormalities, barrier protection for longer than 28 days may be recommended.

<sup>9</sup> Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit. Antiepileptic drugs and contraception, Jan 2010. <http://www.fsrh.org/pdfs/CEUStatementADC0110.pdf>

The table below outlines specific advice for women using enzyme inducing AEDs;

Contraceptive method	Short-term use of enzyme-Inducing drugs ( $\leq 2$ months)	Long-term use of enzyme-Inducing drugs ( $> 2$ months) or difficulty using additional contraceptive precautions
<b>Combined hormonal contraception (CHC)</b> Combined oral contraception (COC) Combined transdermal patch Combined vaginal ring	<b>Recommended option</b>  Change to an alternative method unaffected by enzyme-inducing drugs. This could include temporarily stopping COC and having a one-off DMPA injection to cover the short-term treatment and 28 days after	Change to an alternative method unaffected by enzyme-inducing drugs
	<b>Alternative options</b> Use one COC pill daily (at least 30 $\mu\text{g}$ EE), one patch weekly or one ring 3-weekly and use an extended or tricycling regimen with a hormone-free interval of 4 days  <b>Plus</b> Additional contraceptive precautions (e.g. condoms) while taking and for 28 days after stopping the enzyme-inducing drug  <b>Or</b> Use two COC pills as per long-term treatment (see opposite). Not recommended if using the potent enzyme-inducers rifampicin or rifabutin	Use two COC pills containing at least 50 $\mu\text{g}$ EE (e.g. 20 and 30 $\mu\text{g}$ COCs). Use an extended or tricycling regimen with a pill-free interval of 4 days  <b>Note</b> Not recommended if using the potent enzyme-inducers rifampicin or rifabutin  Use of two patches or two rings not recommended
<b>Progestogen-only contraception</b> Progestogen-only pills (POPs) and progestogen-only implant	<b>Recommended option</b>  Change to an alternative method unaffected by enzyme-inducing drugs (including one-off dose of progestogen-only injectable to cover period of risk)	Change to an alternative method unaffected by enzyme-inducing drugs
	<b>Alternative option</b> Continue use of POP or implant  <b>Plus</b> Additional contraceptive precautions (e.g. condoms) while taking and for 28 days after stopping the enzyme-inducing drug	No alternative-change advised
<b>Progestogen-only injectable</b> Levonorgestrel-releasing intrauterine system (LNG-IUS)	<b>No change required</b> Efficacy of DMPA, NET-EN and LNG-IUS unaffected by enzyme-inducing drugs and women can continue with the usual dose and dosing/replacement interval of 12 weeks, 8 weeks or 5 years, respectively	
<b>Non-hormonal methods</b> Copper-bearing intrauterine device (Cu-IUD), barrier methods	<b>No change required</b> Efficacy unaffected	

Reference; Faculty of Sexual & Reproductive Healthcare & Clinical Guidance, Jan 2012<sup>10</sup>

The guidance above should also be noted by women taking the relatively new AEDs, Fycompa and Zebinix, both of which are enzyme inducing AEDs.

10 Faculty of Sexual & Reproductive Healthcare Clinical Guidance. Drug Interactions with Hormonal Contraception, Clinical Effectiveness Unit, Jan 2012. <http://www.fsrh.org/pdfs/CEUGuidanceDrugInteractionsHormonal.pdf>

Drug	Enzyme inducer	Summary of SPC advice for Fycompa® <sup>(1)</sup> and Zebinix® <sup>(2)</sup>	Faculty advice
Perampanel	Yes  (SPC indicates not considered a strong inducer or inhibitor of cytochrome P450)	At 12mg (not 4 or 8) concomitant use with COC containing ethinylestradiol and levonorgestrel resulted in a reduction in levonorgestrel exposure (mean peak serum concentration (C <sub>max</sub> ) and Area under the curve (AUC) values were each decreased by 40%). Ethinylestradiol AUC was not affected but C <sub>max</sub> was decreased by 18%.  In women using 12mg/day, there is a possibility of reduced contraceptive efficacy in women using progestogen containing oral contraceptives and an additional reliable method (intra-uterine device (IUD), condom) should be used	Efficacy of combined hormonal contraceptives and the progestogen-only implant may be reduced by enzyme inducers <sup>1</sup> .  The FSRH do not consider the efficacy of the progestogen-only injectable or intrauterine methods to be affected by enzyme inducing drugs and advise that ideally women using enzyme inducing drugs should switch to one of these methods.  If enzyme inducing drug use is short-term (<2months) and switching does not occur, additional precautions are required during treatment and for 28 days after stopping.
Eslicarbazepine acetate	Yes	Reduction (decrease of 37% and 42% in systemic exposure) in levonorgestrel and ethinylestradiol respectively in women using COC. Women of childbearing age should use adequate contraceptive protection during treatment and until the next menstrual period after stopping.	

Reference; Faculty of Sexual & Reproductive Healthcare, Clinical Effectiveness Unit Statement, August 2013<sup>11</sup>.

#### Quick reference for enzyme-inducing drugs and contraception

Drug type	CHC	POP	IMP	DMPA	LNG-IUS	Cu-IUD (EC)	LNG-EC	UPA-EC
Enzyme-inducers (during use and for 4 weeks afterwards)								

**Antiepileptics** carbamazepine, eslicarbazepine, oxcarbazepine, phenobarbital, phenytoin, primidone, rufinamide topiramate

**Known clinical interaction:**  
avoid use & advise alternative method

**Potential interaction:**  
caution required

**No clinical interaction:**  
method suitable

Contraceptive methods: CHC, combined hormonal contraception; Cu-IUD, copper intrauterine device; DMPA, progestogen-only injectable; depot medroxyprogesterone acetate; EC, emergency contraception; IMP, progestogen-only implant; LNG-IUS, levonorgestrel-releasing intrauterine system; POP, progestogen-only pill; UPA, ulipristal acetate.

Norethisterone enanthate (NET-EN) is rarely used in UK practice but should be considered as for DMPA.

Reference; Faculty of Sexual & Reproductive Healthcare January 2017

11 Faculty of Sexual & Reproductive Healthcare, Clinical Effectiveness Unit Statement, August 2013. Update on newer antiepileptic and antiretroviral drugs and interactions with hormonal contraceptives. <http://www.fsrh.org/pdfs/CEUstatementUpdateNewerAntiepilepticAntiretroviralDrugs.pdf>






## 2. Effect of non-enzyme inducing AEDs on hormonal contraception

Some of the other antiepileptic medicines, including sodium valproate (Epilim) and lamotrigine (Lamictal), are not considered to be liver enzyme inducers, however they do come with specific risks as outlined below;

- Lamotrigine (Lamictal).

While Lamictal does not have a direct effect on hormonal contraception, the hormonal contraceptive pill has a direct effect on the levels of lamictal in the body by increasing the rate at which the medication is cleared within the system.(FSRH 2010). This can lead to decreased seizure control in the active hormone phase and then increased lamotrigine exposure with a risk of toxicity in the hormone –free week (FSRH 2017<sup>12</sup>). The use of combined hormonal contraception when taking lamictal for seizure management is not recommended. It is considered UKMEX category 3 (risks generally outweigh the benefits). If it is being prescribed, the dose should be increased by 25% when an OCP is initiated.

### Use of contraceptive methods when woman is using lamotrigine

Method	Clinical recommendation
CHC	 Potential risk of reduced seizure control whilst taking CHC, and potential for toxicity in the CHC-free week. The risks of using CHC may outweigh the benefits and alternative methods should be considered.
POP	 <ul style="list-style-type: none"> <li>• May increase lamotrigine levels. Monitor for side effects.</li> <li>• No need for extra precaution.</li> </ul>
IMP	 <ul style="list-style-type: none"> <li>• No interaction.</li> <li>• No need for extra precautions.</li> </ul>
DMPA	
LNG-IUS	
Cu-IUD (EC)	 <ul style="list-style-type: none"> <li>• No interaction.</li> <li>• No need for extra precautions.</li> </ul> <ul style="list-style-type: none"> <li>• Most effective method of EC.</li> </ul>
LNG-EC	 <ul style="list-style-type: none"> <li>• No interaction.</li> <li>• No need for extra precautions.</li> </ul>
UPA-EC	

Reference; FSRH 2017

- Sodium Valproate (Epilim)

Taking Sodium Valproate during pregnancy can cause harm to the unborn baby including birth defects and problems with development and learning.

In women who take valproate while pregnant, around 10 babies in every 100 will have a birth defect.

Birth defects seen in children of mothers who take valproate during pregnancy include:

- Spina bifida (when the bones of the spine do not develop properly)
- Facial and skull malformations (including cleft lip and palate, where the upper lip or facial bones are split)
- Malformations of the limbs, heart, kidney, urinary tract and sexual organs.

In view of the risks associated with use during pregnancy, valproate and related substances should not be used in female children, women of childbearing potential and pregnant women unless alternative treatments are ineffective or not tolerated (EMA, 2014<sup>13</sup>)

12 Faculty of Sexual & Reproductive Healthcare January 2017. Clinical Guidance: drug interactions with hormonal contraception.

13 European Medicines Agency, Oct 2014. Pharmacovigilance Risk Assessment Committee (PRAC).

Effective methods of contraception are considered essential if taking this medication and should be discussed with Consultant Neurologist or Epilepsy Nurse Practitioner. (see appendix 13 for additional information including patient information leaflet)

### 3. Effect of AEDs and hormonal contraception on bone

The Medicines and Healthcare products and Regulatory Agency (MHRA) suggests that long term treatment with Carbamazepine, phenytoin, primidone and sodium valproate is associated with an decreased bone mineral density (BMD). This can increase the risk of developing osteopenia, osteoporosis and fractures in patients considered to be at-risk. 'At-risk' patients include those that;

- Are immobilised for long periods
- Have inadequate exposure to the sun
- Have inadequate daily calcium intake.

Those within the 'at-risk' group should be taking vitamin d supplementation.

While the progesterone only injectable (DMPA) is listed as an appropriate contraceptive for women with epilepsy on an AED, it should be noted that DMPA itself has been linked with loss of bone mineral density (BMD). The use of both AEDs and DMPA together is not currently associated with an additional higher risk (FSRH 2010).

Strategies which can help protect against BMD should be used by women on either AEDs or DMPA (or both). Such strategies include;

- Diet (calcium intake)
- Vitamin D supplements
- Exercise

### 4. Emergency Contraception

If you are taking liver enzyme-inducing drugs (or who have stopped taking this medication within the last 28 days) a copper-bearing intrauterine device (Cu-IUD) is the only method of emergency contraceptive not affected by these drugs (FSRH 2012)<sup>14</sup>.

If you choose not to use a Cu-ICD, a dose of 3mg LNG (2 levonelle tablets) can be taken as soon as possible. This is outside the product license and as such, is not available over the counter. It should be taken as soon as possible and within the first 72 hours of unprotected sexual intercourse (FSRH 2010). This is not however recommended for women using enzyme inducing AEDs.

The emergency contraceptive, ulipristal acetate (EllaOne) is not recommended (FSRH 2010).

### 5. Pregnancy

Most pregnant women with epilepsy have a normal pregnancy and childbirth. The frequency of seizures may increase in pregnancy in around 3 in 10 women with epilepsy. For women with epilepsy, the risk of complications during pregnancy and labour is slightly higher than for

14 Faculty of Sexual & Reproductive Healthcare. Clinical Guidance. Emergency Contraception. Clinical Effectiveness unit, Jan 2012) <http://www.fsrh.org/pdfs/CEUguidanceEmergencyContraception11.pdf>

15 Tomson T, Battino D. Pregnancy and epilepsy: what should we tell our patients? J Neurol. 2009 Jun;256(6):856-62. Epub 2009 Mar 1. Review.

women without epilepsy (Tomson et al 2009). The increase in risk is due to the risk of harm coming to a baby if you have a serious seizure whilst pregnant, and also the risk of harm to an unborn baby from some antiepileptic medicines (as discussed above). Note: The risk of complications to both mother and baby is greater with uncontrolled seizures compared to the risks of taking medication. It is not proven that uncontrolled seizures cause congenital abnormalities but there appears to be a risk of increased foetal loss and maternal mortality (Tomson et al 2009, Pennell et al 2009<sup>15</sup>).

## 6. Before becoming pregnant

Before becoming pregnant, it is best to seek advice from your doctor or epilepsy nurse. You should be seen by an epilepsy expert to discuss your treatment during your pregnancy in detail. The potential risks and benefits of adjusting your treatment, if necessary, can be discussed. If your pregnancy is planned carefully then any risk of complications may be minimised. Advice on diet, smoking, alcohol, avoiding infection, etc) will be the same for any woman planning pregnancy, however, other specific things that may be pertinent for women with epilepsy include:

In some cases it may be wise to change to a different medication, which is less likely to cause harm to a developing baby (depending on the medication you are already taking).

It may be an option to stop or reduce the dose of your treatment before you become pregnant if your seizures have been well controlled. However, deciding to come off antiepileptic medication can be a difficult decision. Factors such as the type of epilepsy that you have can be important. For example, if you have the type of epilepsy that causes severe tonic-clonic seizures, there is a risk that you could have a severe seizure when you are pregnant if you stop your medication.

Advice to take folic acid at strength of 5 mg a day. This should ideally be taken before you become pregnant and continued until you are 12 weeks pregnant. Although folic acid is recommended for all women who are pregnant, the dose for women taking antiepileptic medicines is higher than usual. Taking folic acid has been shown to reduce the risk of having a baby born with a spinal cord problem such as spina bifida. There is some evidence to suggest that Folic acid should be avoided in those with a history of bowel cancer due to the potential for tumour reactivation.

Advice to notify your pregnancy to the Irish Epilepsy and Pregnancy Register (Phone: 1800 320 820) this is to allow information to be gathered to improve the future management of pregnant women with epilepsy.

## 7. Breast-feeding

Breast-feeding for most women taking antiepileptic medicines is generally safe (Davanzo et al 2013<sup>16</sup>), however, each mother needs to be supported in the choice of feeding method that best suits her and her family.

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16 Riccardo Davanzo, Sara Dal Bo, Jenny Bua, Marco Copertino, Elisa Zanelli and Lorenza Matarazzo; Antiepileptic drugs and breastfeeding. Italian Journal of Paediatrics 2013; 39:50 <http://www.ijponline.net/content/39/1/50>

Prescribers should consult individual drug advice in the SPC and the BNF (available at) when prescribing AEDs for women and girls who are breastfeeding. The decision regarding AED therapy and breastfeeding should be made between the woman or girl and the prescriber, and be based on the risks and benefits of breastfeeding against the potential risks of the drug affecting the child.

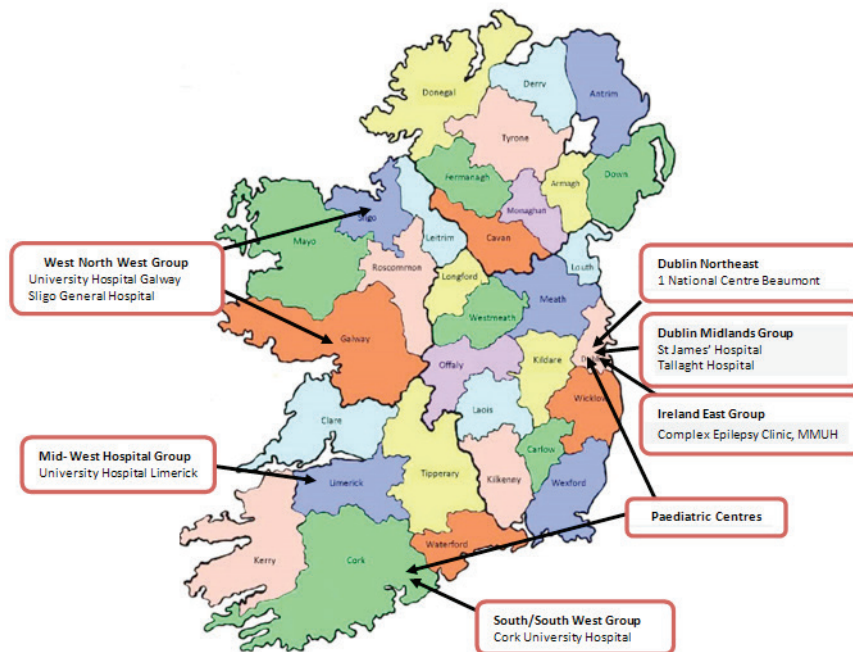
In addition some suggest that by continuing to breastfeed this is a good way to wean the baby off the medication that they have already been exposed to in utero, as exposure to medication through breast milk is lower than that occurring during pregnancy.

Any decision to limit or advise a woman with epilepsy against breastfeeding must be justified by confirmation that the risk to the baby clearly out ways all the known benefits breastfeeding. Your doctor, midwife or nurse specialist can advise you in more detail.

### **8. What are the risks that your child will also have epilepsy?**

In general, the probability is low that a child born to a parent with epilepsy will also have epilepsy. However, it can partly depend on your family history, as some types of epilepsy run in families. Therefore, genetic counselling may be an option to consider if you or your partner has epilepsy and also a family history of epilepsy.

## Appendix 2 National Epilepsy Services



### Neurology Centres

<p>Ireland East Mater Hospital St Vincent's University Hospital - Outreach to Cavan</p>	<p>Dublin Northeast Beaumont - Outreach to Drogheda</p>
<p>Mid-west University Hospital Limerick</p>	<p>Dublin Midlands St James Hospital Tallaght Hospital</p>
<p>West/Northwest University Hospital Galway Sligo General Hospital - Outreach to Letterkenny</p>	<p>South/southwest Cork University Hospital Mercy Hospital Wexford General - Outreach to Kilkenny Sessions to Kerry</p>



## Appendix 3

### Checklist of information to be discussed at first meeting with ANP and WWE who is pregnant



#### EPILEPSY

Information that needs to be gained from and imparted to the pregnant WWE by the ANP at their 1st visit to the epilepsy clinic

- All pregnant WWE should be encouraged to notify their pregnancy, or allow the ANP/Canp/ CNS E to notify the pregnancy to the Irish Epilepsy and Pregnancy Register (see appendix 6)
- Obtain EDD
- Advise obstetric appointment as soon as possible
- Discuss/prescribe folic acid 5mg
- Review Epilepsy history and seizure semiology and diagnosis
- Establish if patients epilepsy is stable/monitoring of seizure frequency
- Discuss risk of seizures in pregnancy and what to do if WWE has seizure in pregnancy
- Review and document what AEDs patient is on
- Discuss with epilepsy specialist if necessary
- If the WWE is prescribed Lamotrigine an AED level should be taken on confirmation of pregnancy and in every trimester or if seizures increase. A Carbamazepine level should only be reserved when clinically indicated.
- WWE should be encouraged to carry own supply of AEDS and to take as normal throughout antenatal appointments/labour/after birth. (This is to ensure consistency of supply, as changes in drug brand can potentially affect seizure control).
- Discuss any triggers for seizures which may be important in course of pregnancy – e.g. nausea & vomiting, changes in WWE metabolism due to pregnancy, sleep deprivation (maternal discomfort or active foetal movements), non-compliance with AEDs.
- Discuss risks to developing baby associated with taking AEDs in pregnancy
- Discuss risks associated with seizures in pregnancy
- Complete Obstetric Performa in Patients obstetric chart
- WWE should be delivered in a consultant led maternity unit and one to one midwifery care during labour
- Reassure that majority of mothers have uncomplicated pregnancies and normal deliveries
- Reassure that majority of mothers give birth to healthy babies and that AEDs should be taken as prescribed
- Discuss healthy lifestyle, cessation of smoking & alcohol
- Advise birth plan (appendix 7)

- Discuss labour -
  - Potential seizure triggers (e.g. stress, exhaustion, lack of sleep, inadequate pain relief, hyperventilation, forgetting to take AEDs on time, dehydration).
  - Risk of seizure in labour approx. 1 -4 %
  - Majority of WWE have normal vaginal deliveries (if foetal & maternal health uncompromised). Caesarean sections should be considered if increase in seizures towards end of pregnancy.
  - Pain relief – Avoid pethidine (when metabolised can convert to norpethidine which may be pro-convulsive) , all other pain relief acceptable (TENS machine, gas & air, epidural anaesthesia etc)
  - AEDs continued during labour and postnatally.
  - Discuss the risks and benefits of breastfeeding.
  - Discuss safety issues when baby arrives.

## Appendix 4

### Pregnancy register – guideline on how to register a WWE on the register

#### *How to register a WWE to the Irish Epilepsy and Pregnancy Register*

- Pregnant WWE may register their own pregnancy to the Register by contacting the free-phone line in confidence: 1800 320 820 to register.  
Or
- Pregnant WWE may also register their pregnancy via website [www.epilepsypregnancyregister.ie](http://www.epilepsypregnancyregister.ie)  
Or
- Health Professionals may also register a WWE pregnancy by contacting the free-phone advice line 1800 320 820 or by downloading the registration forms from the website [www.epilepsypregnancyregister.ie](http://www.epilepsypregnancyregister.ie)
  
- If voicemail obtained WWE are asked to leave their contact details on the Register voicemail system - name, contact number and reason for call. A return call will be made to the woman to enable full registration.  
Or
- If voicemail obtained the Health Professional is asked to leave the WWE contact details on the Register voicemail system - name, contact number and reason for call. A call will be made to the woman to enable full registration.

#### **The Role of the Register in completing patient's registration**

- The role of the Register with the aims and objectives will be explained to the woman at the time of registration. The reason for written consent as well as verbal consent will be explained. A questionnaire is then completed over the phone with the woman and then input into a Database and held in Clinical Research Centre, Beaumont Hospital, Dublin 9.
- When registering by phone, explanation that 3 consent forms will be mailed out to the woman's postal address and explanation to her that all 3 to be signed and dated and 2 returned back to the Register in an attached stamped addressed envelope. On receipt of the 2 signed and dated consent forms, this confirms fully informed consent for personal data to be held on database and held in Clinical Research Centre, Beaumont Hospital.
- If registering via the website [www.epilepsypregnancyregister.ie](http://www.epilepsypregnancyregister.ie) a questionnaire is printed off and completed. Three consent forms are printed off and signed and dated and 2 are returned back to the Register together with the completed questionnaire. Full information about the aims & objectives and running of the Register are available online. On receipt of completed questionnaire and consent forms the pregnant WWE is then registered and on receipt of the completed questionnaire and the 2 signed and dated consent forms, this confirms fully informed consent for personal data to be held on secure database and held in Clinical Research Centre, Beaumont Hospital.
- GP will be contacted by letter at the time of registration and 3 months post expected date of delivery (EDD) for outcome of pregnancy.
- The WWE can contact the Register on free-phone 1800 320 820 for any further questions related to the Register or women's issues questions.
- Additional written information on the Register and its functions and use of data will also be

posted out to the woman's postal address when registered.

- Over the phone, WWE may ask additional questions on the Register and/or questions on epilepsy and pregnancy.
- Written information on epilepsy and pregnancy/folic acid/contraception etc is offered to the woman and will be posted out.
- Letter confirming registration will be posted to the woman
- Additional information will be posted out to GP on issues relating to epilepsy and Pregnancy.
- The Irish Epilepsy and Pregnancy Register operational days and hours (which may vary) will be on voicemail at all times.
- Confidentiality of calls will be maintained at all times
- All phone-calls for registration of pregnancy will be documented and recorded into a phone log book
- Any queries or questions that need to be discussed with PI will be done in confidence and call returned to the person.
- If a currently registered woman contacts the registration with questions/issues/ difficulties with her epilepsy during pregnancy, a letter will be sent to their Neurologist (if attending a neurologist) or relevant health care provider during pregnancy informing the relevant health care provider of contact with Register. Consent from the registered pregnant woman will be obtained prior to sending the letter.
- Use of Data: The anonymised data from both Irish & UK Registers will be amalgamated every 6 months. This data may be presented at various conferences both national and international either platform or poster presentations. Irish data from the Irish Epilepsy and Pregnancy Register alone may also be presented individually as either platform or poster presentations. Anonymised data from the Irish Epilepsy and Pregnancy Register may also be viewed by pharmaceutical companies about their own licensed drug. This disclosure of this data in an anonymised way is referred to in patient information leaflet and consent form.

## Appendix 5

### Checklist of information to be discussed with WWE at first Obstetric meeting additional to the normal obstetric issues discussed.



#### EPILEPSY

Checklist of what should happen at 1st visit with WWE & the Obstetrician

In parallel with routine obstetric checks the following is a checklist for pregnant WWE:

- All pregnant WWE should be encouraged to notify their pregnancy, or allow their clinician to notify the pregnancy to the Irish Epilepsy and Pregnancy Register (see appendix 6)
- Establish if patients epilepsy is active and record seizure type and frequency
- Document what AEDs patient is taking
- Discuss any triggers for seizures which may be important in course of pregnancy
- Enzyme-inducer AEDs accelerate metabolism of steroids (if required to reduce the risk of respiratory distress in preterm infants)
- Any increase in seizure frequency in pregnancy should be monitored closely and referred urgently back to her epilepsy specialist
- Dose of AEDs should not be increased routinely but only on clinical grounds
- Lamotrigine and Levetiracetam levels per trimester minimum, Carbamazepine level reserved if clinically indicated, and no other AED levels required.
- Interpretation of AED blood levels is best done by epilepsy specialist
- Arrange anomaly scan for between 20-22 weeks.
- WWE should be encouraged to carry own supply of AEDS and to take as normal throughout antenatal appointments. (This is to ensure consistency of supply, as changes in drug brand can potentially affect seizure control).
- Advise birth plan (appendix 9)
- Discuss labour & advise risk of seizure in labour is low (approximately 1 – 2%)
- Document treatment plan if WWE has seizure while in hospital
- Discuss desired method of feeding the newborn and if the patient wishes to breastfeed
- Regular obstetric follow-up appointments and communication between epilepsy specialist and obstetrician.
- Advise that majority of mothers with epilepsy will continue to have good seizure control in pregnancy.

## Appendix 6

### Birth plan for WWE/Obstetric Plan

#### Birth Plan Sample for WWE

A birth plan is a document drawn up by the woman (with or without her partner) which enables her to express her wishes for labour and the immediate post partum period and to actively participate in the decision making when delivering her baby. It affords the woman an opportunity to discuss with the midwife on how she would like to be supported during this time.

A birth plan for women with epilepsy should include:

- Name and address
- Epilepsy Type
- Brief description of seizures
- Information on routine seizure medication and when it should be administered and by whom
- One to one midwifery care as per National Epilepsy Care Programme Standard Operating Procedure Guidelines
- Information from Neurologist/ ANP/cANP/ CNS E on how to manage each seizure type in labour; get emergency medication prescribed for the duration of this hospital admission
- Requests about Pain relief (Avoid Pethidine converts to pro convulsing agent)
- Requests about Vaginal Examinations, rupturing of membranes, using medication to accelerate labour , baby monitoring, delivery type where possible
- Labouring and delivery position preferred
- Preferred chosen method of feeding the new-born

#### After the birth

- Personal and baby safety (to include not to be left alone with baby in the bed beside mum, no bathing the baby alone; assess support available on discharge home)
- One to one midwifery care as per National Epilepsy Care Programme Standard Operating Procedure Guidelines
- Assistance and support with preferred chosen method of feeding the new-born
- Information on seizure types and how to manage each seizure postnatally; get emergency medication prescribed for the duration of this hospital admission
- Information on routine seizure medication and when it should be administered and by whom
- Prevent routine triggers such as sleep deprivation, missed medication and pain

## Appendix 7

### Protocol for managing Status Epilepticus

Guidelines for Administration of Buccal Midazolam.

What is the definition of a prolonged seizure?

A prolonged seizure is defined as a generalised tonic clonic (Grand-mal) seizure lasting 5 minutes or longer, or when there is successive seizures occurring which prevents the individual regaining consciousness fully. This should be considered an operational definition of Status Epilepticus (Lowenstein et al, 1999, Meldrum B, 1999)

Why intervention is required.

Prolonged seizures demand prompt medical treatment. Any seizure last  $\geq$  5 minutes has a 30% chance of lasting more than 30 minutes which is considered the biological threshold for seizure related brain damage (Lowenstein DH, 1999)

Information about Midazolam.

Midazolam is part of the Benzodiazepines group. Its mechanism of action is to promote the activity of GABA one of the inhibitory neurotransmitters in the Central Nervous System. Thus it has potent anxiolytic and seizure controlling activity. It works as effectively and reliably as rectal Diazepam (McMullan J, 2010).

Midazolam Brands

The midazolam should be stored in a cool cupboard, safely out of the reach of children. Each bottle of midazolam has its own shelf life of 2 years.

Buccal Midazolam (Epistatus) comes in a glass bottle containing 5mls of solution (10mg/ml) with a supply of 4 oral syringes or in 10mg/1ml prefilled syringes.

Buccal Midazolam (Buccalam) comes in age-specific, prefilled, needle-free oral syringes in 4 strengths 2.5 mgs in 0.5 ml, 5 mgs in 1ml, 7.5 mgs in 1.5 mls and 10 mgs in 2mls

Syringes are colour-coded according to the prescribed dose for a particular age range.

Procedure for administration:

In the event of a prolonged convulsion:

1. General management of the convulsion

- Make the patient safe and note the time the convulsion started.
- Place the patient on a flat surface
- Place something soft under the head to protect them from injury.
- Ensure the airway is not obstructed. Turn the patient to the recovery position

2. Administration of midazolam.

- If the convulsion lasts 5 minutes, or if the patient has one seizure after another (a cluster) lasting more than 5 minutes, then either an ambulance should be called or midazolam should be administered.
- The standard dose for an adult is 10mg and for children 6-12months (2.5mg)  
1-4years (5mg) 5-9years..... (7.5mg) 10years+ (10mg).

### 3. Directions for use.

- Check that midazolam is within expiry date.

#### For Epistatus

- Open the syringe and open the bottle of midazolam and put on gloves. (optional)
- Place the syringe into the bottle of midazolam until the end of the syringe is in the fluid.
- Draw up \_\_\_\_\_ml of the solution, ensuring that the dose is correct once the syringe is removed.

#### For Buccalam

Take one plastic tube, break the tamper proof seal and remove the syringe containing buccolam

#### For both brands of Buccal Midazolam

- Insert the syringe gently into the buccal cavity of the mouth. (inside the bottom of the cheek, outside of the teeth)
- Squirt the contents of the syringe into the mouth very slowly (a drop at a time, over 30-60seconds) then remove the syringe.
- Support the cheek/lips whilst giving the midazolam and afterwards to reduce the amount of leakage. Use gauze swabs to wipe mouth after.
- If the seizure lasts any more than five minutes after giving the midazolam then an ambulance needs to be called.

## References

1. Lowenstein DH, Bleck T, Macdonald RL. It's time to revise the definition of status epilepticus. *Epilepsia*. 1999 Jan;40(1):120-2.
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3. McMullan J, Sasson C, Pancioli A, Silbergleit R. Midazolam versus diazepam for the treatment of status epilepticus in children and young adults: a meta-analysis. *Acad Emerg Med*. 2010 Jun;17(6):575-82..
4. Meldrum B. The revised operational definition of generalised tonic-clonic (TC) status epilepticus in adults. *Epilepsia*. 1999 Jan;40(1):123-4.



## Appendix 8

### Checklist to guide PHN visits to WWE and their baby's post delivery



#### EPILEPSY

Guideline for PHN'S for looking after a WWE who has had a baby recently

In parallel with routine PHN checks the following is a checklist for WWE and baby postnatally:

- Discuss desired method of feeding the newborn and if the patient wishes to breastfeed. WWE should not be discouraged from breastfeeding because of epilepsy
- Discuss the risks and benefits of breastfeeding if taking AEDs
- Risks of breastfeeding while on AEDs - hypersensitivity in babies exposed to AEDs through mothers breast milk may develop
- Benefit of breastfeeding babies who were exposed to AEDs in utero - may help babies to wean off their mothers AEDs.
- Possibility of sedation should be considered if mothers taking older AEDs e.g. Phenobarbital and bottle feeding should be considered
- Monitor baby alertness and baby weight if mother taking AEDs
- To reduce the risk of accidents and minimise anxiety - Promote and reinforce baby/toddler safety in the home
  - If possible, share the care of baby at night (to reduce exhaustion/sleep deprivation) while mother gets alternate full night's sleep
  - Feeding and /or holding baby – sitting on the floor, on a rug or cushion (low to ground) may reduce the potential impact of dropping their child during a seizure.
  - Bathing baby – never alone, small amount of water in bath, in event of seizure baby wouldn't go under water.
  - A “top & tail” wash is a safer alternative than bathing baby while alone
  - Carrying baby – If stairs in house have all baby items downstairs so a not carrying baby up and down stairs; use carry cot/car seat up and down stairs to provide protection from a fall in the event of a seizure.
  - Where a parent's seizures affect just one side of their body, they should position their child on the non-affected side, to reduce the risk of falling onto the child.
  - Parents who fall over during a seizure (tonic clonic seizure) should be advised against the use of a baby sling.
  - Safety gates/ play pens in the home and child reins or wrist straps will prevent child wandering away if the parent has a seizure.
  - Pram with a brake that is automatically activated when the handle is released
- If using high chair – make sure can't knock over (in event of seizure); or use bouncer chair/car seat on floor

- Information regarding contraception with AEDs should be discussed with the WWE
  - Enzyme-inducing AEDs reduce the effectiveness of the combined oral contraceptive pill (COCP), progesterone only pill, progesterone implant and contraceptive patch.
  - Depot Provera, intrauterine device (IUD) and Mirena intrauterine system (IUS) provide effective contraception for women with epilepsy, as they are not affected by AEDs.
  - Women on the AED lamotrigine need to discuss contraception with their epilepsy specialist before prescribing COCP to allow adjustment of lamotrigine dose to be considered. Prescribing COCP can significantly reduce blood lamotrigine levels and may result in breakthrough seizures. Lamotrigine may also reduce the effectiveness of COCP
- Future pregnancies should be discussed/ planning next pregnancy and seeking pre-conceptual counselling prior to next pregnancy

## Appendix 9

### Post-natal RANP First Clinic with Women with Epilepsy, Information to be gathered by RANP



#### EPILEPSY

#### Information to be gathered at post-natal visit of WWE

Birth Type: Vaginal, Instrumental, C-Section

Were you offered pethidine for pain relief during labour?: Y/N

Did you experience seizures during labour?: Y/N

Did you experience seizures post nately?: Y/N

Were there cot sides in place while you were in hospital?: Y/N/Not known

Were your AED's administered on time?: Y/N

Did you have midazolam with you?: Y/N

Did you have assistance with the baby?: Y/N

Did you have assistance with feeding?: Y/N

Did a PHN visit you at home after discharge? Y/N

Information regarding contraception with AEDs should be discussed with the WWE at first post-natal meeting:

- Enzyme-inducing AEDs reduce the effectiveness of the combined oral contraceptive pill (COCP), progesterone only pill, progesterone implant and contraceptive patch.
- Depot Provera, intrauterine device (IUD) and Mirena intrauterine system (IUS) provide effective contraception for women with epilepsy, as they are not affected by AEDs.
- Women on the AED lamotrigine need to discuss contraception with their epilepsy specialist before prescribing COCP to allow adjustment of lamotrigine dose to be considered. Prescribing COCP can significantly reduce blood lamotrigine levels and may result in breakthrough seizures. Lamotrigine may also reduce the effectiveness of COCP
- Future pregnancies should be discussed/ planning next pregnancy and seeking pre-conceptual counselling prior to next pregnancy.
- Ensure compliance with Folic Acid 5mg.
- Ensure the WWE has a follow up OPD appointment at epilepsy clinic within 3 months post-delivery.

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## Appendix 10

### Review with WWE regarding Menopause and Epilepsy

Checklist for interaction with WWE and Menopause

The following issues should be discussed with a WWE regarding her epilepsy and menopause:

- Confirmation/diagnosis of menopause
- Possibility of change in seizure frequency
- Need for HRT
- DEXA scan
- +/- Calcium supplementation
- Mood Issues