PHA – 6020Y

Person centered medicine from bench to bedside

Epilepsy workshop

Student Name

Answers

Learning Outcomes

By the end of this workshop you will be able to:

- To recall and understand the classification of seizures, including factors that increase the risk of a seizure
- To apply knowledge about AED therapy to understand the management of chronic epilepsy to include:
  - Appropriate choice of therapy
  - Special care group patients
  - Monitoring of efficacy and toxicity
  - Drug interactions with antiepileptic drug therapy
- To discuss and compare three different scenarios and their relevant counselling points

Method

This workshop consists of the following tasks:

Task 1: Risks of seizures and seizure classification (10mins)

Task 2: Management of epilepsy (20mins)

Task 3: Monitoring of therapy and management of drug interactions (45mins)

Task 4: Three scenarios around a patient and their prescription (30mins)

Task 1 - Risks of seizures and seizure classification

Consider what factors may increase the risk of seizures in a patient or trigger a seizure?

Head trauma
Stroke
Brain tumours
Infection e.g. meningitis
Multiple sclerosis – degenerative brain disorders

Triggers
Flickering lights
Sleep deprivation
Alcohol, recreational drugs
Drugs – common drugs that lower seizure threshold – tramadol, Quinolones and Carbapenems

Complete the following table with the classification of seizures.

Generalised seizures		
Motor	Tonic seizures	Stiffness and extension of limbs Consciousness is impaired Seizures are brief lasting only seconds
	Atonic seizures	Sudden loss of muscle tone Seizures are brief
	Myoclonic seizures	Abrupt muscle jerks affecting upper limbs Do not affect consciousness
	Clonic seizures	Loss of consciousness and rhythmic symmetrical shaking of limbs, face and neck due to rapidly alternating muscle contraction and relaxation
	Tonic-clonic seizures	Initial tonic phase – person loses consciousness, becomes rigid and falls to ground Clonic phase – jerking of muscles Convulsions last 2-3 minutes, person remains unconscious for up to a few hours
Non-motor	Absence seizures	Person will stop moving and have a fixated stare, usually lasts for about 10 seconds
Focal Seizures		
Simple focal seizures (awareness)	Motor onset	Change in muscle activity of some sort, such as jerking (clonic), stiffness (tonic), loss of muscle tone (atonic), automatisms (repeated or automatic movements e.g. lip smacking, repetition of words/phrases, pacing), irregular big movements like jumping/thrashing/rocking movements (hyperkinetic), Sudden flexing and/or extending of the muscles in the trunk and close to the trunk of the body (epileptic spasms). Quick, involuntary muscle jerk (Myoclonic)
	Non-motor onset	can include changes in heart rate, breathing, or color (autonomic); blank stare, stop talking or stop moving (behavioural arrest): confusion, slowed thinking, or& problems talking and understanding (cognitive changes); sudden fear, dread, anxiety/pleasure (emotional); or changes in hearing, vision, taste, tingling, or pain (sensory).

Complex focal seizures (impaired awareness)	Motor onset	Change in muscle activity of some sort, such as jerking (clonic), stiffness (tonic), loss of muscle tone (atonic), automatisms (repeated or automatic movements e.g. lip smacking, repetition of words/phrases, pacing), irregular big movements like jumping/thrashing/rocking movements (hyperkinetic), Sudden flexing and/or extending of the muscles in the trunk and close to the trunk of the body (epileptic spasms). Quick, involuntary muscle jerk (Myoclonic)
	Non-motor onset	Changes in heart rate, breathing, or colour (autonomic); blank stare, stop talking or stop moving (behavioural arrest): confusion, slowed thinking, or& problems talking and understanding (cognitive changes); sudden fear, dread, anxiety/pleasure (emotional); or changes in hearing, vision, taste, tingling, or pain (sensory).

Task 2 Management of epilepsy

Miss PT, a 27 year old woman has been newly diagnosed with focal seizures and the epilepsy consultant is considering prescribing Zonisamide 100mg once daily.
You are a hospital pharmacist reviewing the patient's notes, and can see is not on any regular medication:

1) Is the choice of therapy appropriate, if not what would you recommend?

No this is not appropriate as Zonisamide is 2nd line monotherapy option. This should only be considered if 1st line monotherapy options are not successful or not tolerated.
More appropriate first line choice would be levetiracetam or lamotrigine – also safe in patients in child-bearing potential in case they get pregnant whilst on it.

Other issue to consider – Zonisamide requires women to be on highly effective contraception (e.g. intrauterine devices – copper coil, levonorgesterol IUD or progesterone implant).
NOTE – it is 'non-enzyme inducer' AED so the drug does not alter the efficacy of the contraception. It is its teragenic effects that require the need for highly effective contraception

Also side effects of Zonisamide– risk of heat stroke (need to counsel about adequate hydration), hypersensitivity reactions, blood disorders, etc.

2) After a few months, Miss PT's therapy changes and is stabilised on carbamazepine 100mg TWICE daily. What counselling points would you cover with the patient?

- Not stopping the medication abruptly,
- Needs to stay on the same brand of medication (category 1 AED) – discuss supply of medication
- Potential side effects of medication –see BNF, SPC (drowsiness, fatigue, GI discomfort, leucopenia, eosinophilia, thrombocytopenia, etc)
- Risk of hypersensitivity syndrome (look out for rashes), also monitor for blood dyscrasias – to seek medical attention if they experience a fever, rash, mouth ulcers, bruising or bleeding develop

3) What additional non-pharmaceutical advice would you give Miss PT?

- Driving -Need to inform the DVLA. Also - need to be seizure free for at least 1 year before being able to drive. If weaned off antiepileptics then the patient should not drive during that period or for a further 6 months.
- Consider situations that may provoke a seizure and avoid e.g. sleep deprivation, alcohol, contact sports.
- Consider risk of seizures at home e.g. having baths (risk of seizure while in bath), any risk of hitting windows/glass panes during seizure
- Consider age – check to see if patient needs:

1) Contraceptive advice (types of contraception she could have are progesterone-only injection, Levongesterol IUD, and Cu-IUD)
2) Or if patient has plans to have a baby – advice that she needs to discuss with consultant a plan. Potential she may need to change AED

Task 3 Monitoring of therapy and management of drug interactions

1) Mr PS, a 55 year old man who takes carbamazepine 400mg BD, presents to your pharmacy with a prescription for ciprofloxacin 500mg BD 7/7 for a UTI. Is the prescription appropriate?

- There is an interaction between carbamazepine and ciprofloxacin – ciprofloxacin can lower the seizure threshold and therefore should be avoided in patients with epilepsy.

NOTE – it will not appear in as an interaction in the online BNF. It is a drug-disease interaction. Stockleys mentions that quinolones in general are known to induce seizures and therefore are generally not recommended in pts with epilepsy.

- As carbamazepine can be used for neuropathic pain as well as epilepsy then need to establish if the patient is taking carbamazepine for epilepsy, consider if patient has cultures and sensitivities/allergies but
- If alternative antibiotic therapy available would consider switching - possibly Trimethoprim but that causes hyponatraemia with carbamazepine; nitrofurantoin may be the best alternative depending on pt's renal function.
- Key message – you have drug-drug interactions AND drug-condition interactions

2) Mr HG has recently started on lamotrigine therapy and tells you that he has developed a severe rash over his trunk of his body. What would you advise?

- Check if anything else new has started/changed – i.e. any other possible causes of the rash
- But rash is a rare but reported ADR of lamotrigine – would need to see GP urgently as would need to stop but need to consider an alternative therapy as well

3) Mr TB has been admitted to hospital with uncontrolled seizures, he has had 2 seizures in the past month. He is taking phenytoin 300mg OD and has been on phenytoin for the past year. His phenytoin level is checked and the level is 10mg/L (10-20mg/L)

a) What would you want to check before interpreting his phenytoin level?

- Dose changes - check if there has been a recent dose change – can take 5-14 days to reach steady state after dose changes
- Other interactions - As phenytoin interacts with other drugs has any new drugs been recently started? Albumin levels – as phenytoin is highly protein bound – then if the patient has low albumin then the level will not reflect the true free concentration
- Adherence - Has the patient been taking their medication?

- Time of level – should be pre- dose trough level (because of long half-life and helps ensure measurements are taken consistently at the same time when the serum concentrations are least likely to vary). Usually within 1 hour of the dose being due.
- Formulation – check if patient is taking tablets or capsules – difference in phenytoin base levels

b) The doctor tells you he wants to increase the patient's dose to 500mg OD, what would you expect to happen to the therapeutic drug level?

Phenytoin doesn't display linear pharmacokinetics therefore would not expect a dose increase to result in a predictable increase in the therapeutic level – it also displays saturable (zero order) pharmacokinetics.

4) Mr CT is nil by mouth and is currently unable to take his medication, he is taking carbamazepine m/r 200mg BD. What would you recommend?

Carbamazepine is available as a suppository though not dose equivalent –

100mg tablet = 125mg suppository [stated in the BNF in indication section]

Therefore would need to give 125mg FOUR times a day – but would need to monitor clinical response

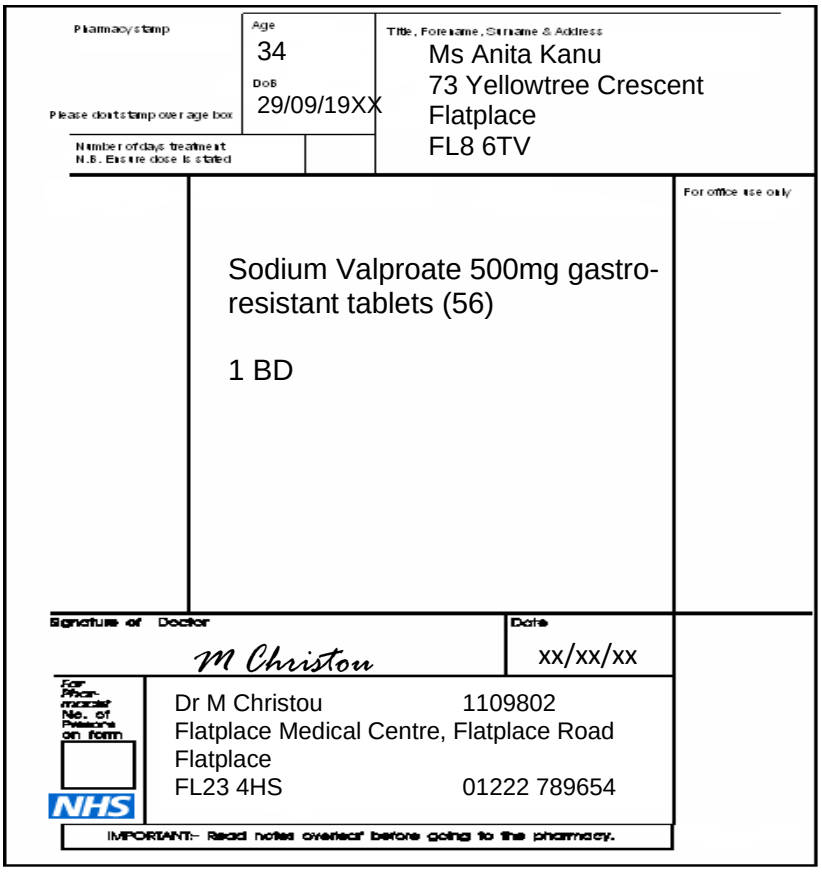
5) Mr SY has been taking sodium valproate 1g TWICE daily for generalised tonic-clonic seizures, but he is not achieving seizure control and the consultant decides to add in lamotrigine, what factors do you need to consider when you adding in another antiepileptic?

- Higher risk of liver toxicity when more than one antiepileptic used with valproate
- Is it appropriate for the seizure type the patient has? Don't want to exacerbate seizures
- Valporate can increase plasma concentration of lamotrigine therefore need to consider dose titration.
- Is the sodium valproate to be discontinued? will then need to consider reducing valproate slowly.

Task 4 Patient scenarios

In this task you will be assigned one out of the three scenarios to work through and prepare to feedback to the rest of the group. Please assign a spokesperson from your group to provide feedback.

You are the responsible pharmacist of a community pharmacy, and a patient has presented the prescription below to be dispensed and collected. They are a regular patient and you recognise them. Please assume the prescription is both legally and clinically correct.:



Pharmacy stamp

Age 34

DoB 29/09/19XX

Please don't stamp over age box

Number of days treatment
N.B. Ensure dose is stated

Title, Forename, Surname & Address
Ms Anita Kanu
73 Yellowtree Crescent
Flatplace
FL8 6TV

For office use only

Sodium Valproate 500mg gastro-resistant tablets (56)

1 BD

Signature of Doctor: M Christou

Date: xx/xx/xx

For Pharmacist No. of Patient's on form

NHS

Dr M Christou 1109802
Flatplace Medical Centre, Flatplace Road
Flatplace
FL23 4HS 01222 789654

IMPORTANT:- Read notes overleaf before going to the pharmacy.

Scenario 1: You have taken in the prescription, and as per your pharmacy SOP have checked her PMR record and seen she usually has Epilim© brand of Sodium Valproate dispensed. Unfortunately, this is currently out of stock with your supplier, and you only have the generic version in stock. Discuss in your groups:

- What things do you need to consider in order to dispense this prescription safely?
- What additional counselling points (if any) would you need to discuss with the patient

Things to discuss

Sodium valproate is a MHRA category 2 medicine, and the Epilepsy summary section of the BNF advises the following:

"For these drugs, the need for continued supply of a particular manufacturer's product should be based on clinical judgement and consultation with the patient and/or carer taking into account factors such as seizure frequency, treatment history, and potential implications to the patient of having a breakthrough seizure. Non-clinical factors as for Category 3 drugs should also be considered - differences between alternative products (e.g. product name, packaging, appearance, and taste) may be perceived negatively by patients and/or carers, and may lead to dissatisfaction, anxiety, confusion, dosing errors, and reduced adherence. In addition, difficulties for patients with co-morbid autism, mental health problems, or learning disability should also be considered."

So, check with the patient:
Have they had the generic brand ever in the past?
How controlled is their epilepsy? When was the last time they had a seizure?
How confident are they with their medication? Will a difference in colour, shape or taste of the tablet cause any issues? (potentially show the patient the tablets)

Do they have any concerns about having a generic brand?

If all the above are ok – dispense the medication, make a note on the patient's PMR and consider letting the GP know that a different brand has been dispensed due to lack of stock so that they are aware.

Additional counselling points:
Reassure the patient that the generic and branded version of the medication have the same drug in it, but the appearance is different

If they do start experiencing change in their seizures – frequency, duration, symptoms, to contact their GP/Epilepsy specialist asap

If they do find after a a few days/weeks they are getting confused about how to take their medicine because of the difference in the brand to contact the pharmacy so you can support them.

Scenario 2: You have taken in the prescription, and followed your pharmacy SOP in relation to dispensing, labelling and checking the prescription. As part of your SOP for processing prescriptions for Sodium Valproate you are required to talk to patients of child-bearing potential every time they present a prescription. Discuss in your groups:

- What are the key points that should be discussed with the patient?
- What materials/information must be provided to the patient with every prescription?

Things to discuss with the patient:
Check the patient is taking the medication ok and have no adherence problems

Check the patient has a signed and up to date Acknowledgement of Risk form (should be done annually). Also new regulations state the 2 prescriber need to sign off in relation to continued use of this in patients under 55 yrs.

If child-bearing potential (pt is 34 so there is the potential of this) - counsel patient about the risks in pregnancy while taking the medication and on a pregnancy prevention programme as they need to be on adequate contraception (barrier method like condoms are not enough) – need to be only **HIGHLY EFFECTIVE contraception** e.g. IUD (Cu or LNG), implant, female sterilisation. Pill/patch/vaginal rings can be used but condoms must be used alongside them as not classed as 'highly effective'.

If patient is not aware of the need for adequate contraception and has not seen their doctor in the last year, the patient must not stop taking the drug, and the drug must be dispensed as normal but refer them for a review with their doctor

If the patient wants to become pregnant refer patient urgently to their GP and/or specialist for a review.

Remind the patient they should have a review with their specialist every year

Note: The prescription is for 56 – how many would be supplied to the patient?
Sodium valproate (all tablet forms) is now a special container (the whole box now not just the strips). Therefore you would supply 60 against this prescription.

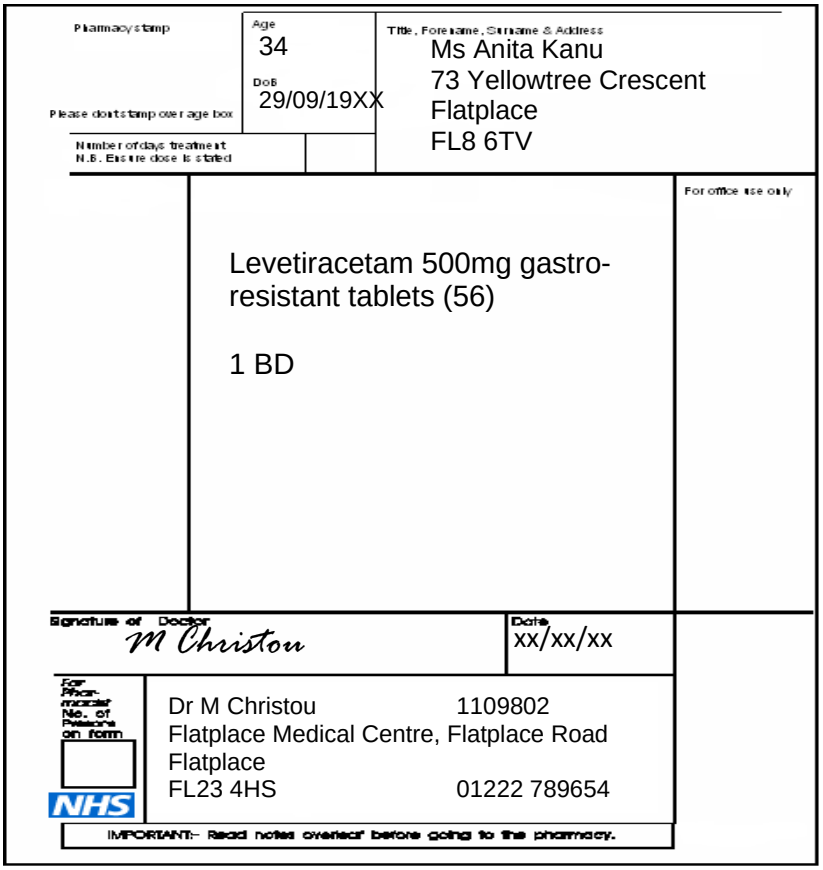
Same principle apply for pts taking valproic acid for bipolar disorder.

Other resources to provide to patient:

Patients must be provided with a patient alert card every time they have the medicine dispensed.

Also patient information leaflet (this is a standard for all medicines)

Scenario 3: The patient explains that they are no longer on Sodium valproate (so no longer need the previous prescription) and have recently had a baby. She asks you to dispense the new prescription (see below) and wants some advice around whether it is safe to breastfeed. She is also worried about having a seizure while looking after the baby.



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Please don't stamp over age box

Age 34

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Title, Forename, Surname & Address
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Flatplace
FL8 6TV

Number of days treatment
N.B. Ensure dose is stated

For office use only

Levetiracetam 500mg gastro-resistant tablets (56)

1 BD

Signature of Doctor M Christou

Date xx/xx/xx

For Pharmacist No. of Pieces on form

NHS

Dr M Christou 1109802
Flatplace Medical Centre, Flatplace Road
Flatplace
FL23 4HS 01222 789654

IMPORTANT:- Read notes overleaf before going to the pharmacy.

Discuss in your groups:

- What information would you discuss with the patient around breastfeeding whilst taking Levetiracetam?
- What additional information and precautionary measures would you need to advise the patient on in relation to looking after the baby?

Breastfeeding whilst on Levetiracetam

Looking at the SPC for Levetiracetaam it says:

"Levetiracetam is excreted in human breast milk. Therefore, breast-feeding is not recommended.

However, if levetiracetam treatment is needed during breastfeeding, the benefit/risk of the treatment should be weighed considering the importance of breastfeeding".
(https://www.medicines.org.uk/emc/product/2293/smpc#PREGNANCY)

So make sure patient is aware of the risks, check if she has discussed it with her epilepsy specialist and midwife. If needed refer patient back to epilepsy specialist if no discussion has been carried out.

Additional information

- Bathing - the N+N hospital recommend patients shower if washing alone. If taking a bath, it is recommended they have someone else with them(9).
  - This is because if they were to have a seizure whilst in the bath they could potentially drown, and therefore showers are preferred.
- Feeding – sitting on the floor when feeding, with the mother's back against the wall for support, and using cushions either side reduce risk of the child falling onto hard floor if the mother was to have a seizure
- Changing nappies – changing the baby on the floor not using a changing unit or the bed
- Going outside – having a length of cord attached to the wrist that will stop the pram from running away if the mother was to have a seizure.

Useful resources and extra information

- MHRA pregnancy testing and contraception for pregnancy prevention during treatment with medicines of teratogenic potential. Version 1 Published 2019. Accessed 09/01/20223) Available at: https://assets.publishing.service.gov.uk/media/5c936a4840f0b633f5bfd895/pregnancy_testing_and_contraception_table_for_medicines_with_teratogenic_potential_final.pdf
- MHRA guidance on Valproate use by women and girls. Published on 23/03/2018 and updated 11/02/21. Accessed on 09/01/23. Available at: https://www.gov.uk/guidance/valproate-use-by-women-and-girls
- MHRA guide for Healthcare professionals: Information on risks of Valproate use in girls (of any age) and women of childbearing potential. Accessed on 09/01/2023. Available at https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/950802/107995_Valproate_HCP_Booklet_DR15_v07_DS_07-01-2021.pdf
- Press release: MHRA instructs health organisations to prepare now for new measures to reduce ongoing serious harms of valproate. Accessed 0n 11/1/24 https://www.gov.uk/government/news/mhra-instructs-health-organisations-to-prepare-now-for-new-measures-to-reduce-ongoing-serious-harms-of-valproate
- Information for pregnant women who have epilepsy from the NNUH. Published 06/01/2017, updated 06/2019. Accessed on 09/01/2023 and available at: Information-for-pregnant-women-who-have-epilepsy (1).pdf
- Specialist Pharmacy Service: Switching between liquid and tablet/capsule formulations. Published 13/09/2023. Accessed on 11/01/2024 and available at https://www.sps.nhs.uk/articles/specific-medicine-switches-for-solid-dose-and-liquid-formulations/