Supply Disruption Alert

SDA/2019/001 Issued: 06 June 2019 at 15:30 Valid until: 31/07/2019

Epanutin® (phenytoin) 30mg/5ml Oral Suspension – Supply Disruption

Summary

- Epanutin® (phenytoin) 30mg/5ml oral suspension will be out of stock from w/c 10th June for 6-8 weeks.
- The Canadian brand of Epanutin® 'Dilantin-30®' is equivalent to Epanutin® 30mg/5ml oral suspension and supplies are available on an 'unlicensed' basis.
- Different formulations of phenytoin (other than Dilantin® 30mg/5ml oral suspension) are not interchangeable and if patients are switched to anything other than 'Dilantin® (phenytoin) 30mg/5mL oral suspension' careful management of switching and monitoring is required.

Action

Alternative phenytoin formulations (other than Dilantin® 30mg/5ml oral suspension) are not directly interchangeable; switching to alternative formulations may require specialist advice, support, or referral. Health care professionals in primary, secondary or specialist healthcare services who prescribe, dispense or administer Epanutin® oral suspension, should take the following action:

1. General Practitioners should identify all patients currently prescribed Epanutin® 30mg/5ml oral suspension. Early contact should be made with the patient or patient's parent/carer to determine if they have enough Epanutin® 30mg/5ml oral suspension to last until end of July.
2. If the patient has sufficient supplies to last them until end of July, then no further action is required.
3. If a patient does not have sufficient supplies to last until end of July, the following advice should be followed.
    i. Switch suitable patients to the unlicensed Canadian brand, ***'Dilantin®'*** (phenytoin) 30mg/5ml oral suspension. This can be considered equivalent to the UK brand ***'Epanutin®'*** (phenytoin) 30mg/5ml oral suspension and no dosing adjustments should be required.
    ii. If Dilantin® (phenytoin) 30mg/5ml oral suspension is not considered suitable then General Practitioners should make early contact with secondary care or tertiary care specialists to seek support regarding the most suitable management plan for the patient and monitoring requirements if needed.
    iii. If patients are switched to alternative formulations, other than Dilantin® 30mg/5ml oral suspension, prescribers and pharmacists should work together to ensure the patient receives the correct dose of the alternative product and that monitoring of plasma levels are undertaken.
    iv. Patients should be prescribed a licensed product if available, therefore if it is necessary to switch a patient to an unlicensed preparation they should be switched back to Epanutin® 30mg/5ml oral suspension when supplies are back in stock, which is likely to be by the end of July 2019. Careful management of switching and monitoring may be required when switching back to licensed Epanutin® 30mg/5ml suspension, and prescribers and pharmacists should liaise to ensure this is done safely.

If prescribers have any concerns about switching a patients' medication, or reverting back to Epanutin®, they should consult the patient's specialist prescriber to seek support.

Action, to be taken by

- NHS Regional Offices
- Community pharmacists
- General practitioners
- General practice nurses
- Hospitals in the independent sector
- Independent treatment centres
- Private medical practitioners
- Paediatrics departments
- Paediatric nurse specialists
- Pharmaceutical advisors
- Pharmacists
- Hospital pharmacies
- Hospital pharmacists
- Community nurses
- District nurses

Please also send on to others you feel may need to take actions.

Deadlines for actions

Actions underway:	11/06/2019
Actions completed:	31/07/2019

Product details

Pfizer Epanutin® (phenytoin) 30mg/5ml Oral Suspension 500ml bottle.

Problem / background

There is a short-term supply issue affecting Epanutin® suspension due to a manufacturing delay of UK licensed stock. Pfizer are the sole licensed UK supplier of phenytoin 30mg/5ml oral suspension.
It is anticipated that current stock will be depleted week commencing 10th June. Further deliveries are currently anticipated at the end of July, however exact dates have not been confirmed.

Epanutin® oral suspension is licensed for the control of tonic-clonic seizures, partial seizures or a combination of these, and for the prevention and treatment of seizures occurring during or following neurosurgery and/or severe head injury. It has also been employed in the treatment of trigeminal neuralgia as second line therapy if carbamazepine is ineffective or patients are intolerant to carbamazepine. Dosage is individualised as there may be wide interpatient variability in phenytoin serum levels with equivalent dosage. In some cases serum level determinations may be necessary for optimal dosage adjustments.[1]

The MHRA has classified phenytoin as a Category 1 antiepileptic drug, which means there are clear indications that clinically relevant differences between different manufacturers' products might occur, even when the pharmaceutical forms are the same and bioequivalence has been shown. Therefore, the patient should be maintained on a specific manufacturer's product.[2]

However, in the event of a shortage of a product, it may not be possible to maintain the patient on their previous preparation, and therefore all product switches should be carried out with care and close monitoring.[3]

Advice on switching and monitoring patients

It is recommended that patients who require switching should be prescribed an alternative phenytoin oral suspension in the first instance. If a patient is considered for this switch, prescribers should be aware of the following:

Prescribing:

- All other available alternative phenytoin oral suspensions are considered unlicensed in the UK.
- Any decision to prescribe an unlicensed medicine must take into account the relevant GMC guidance and NHS Trust or local governance procedures. Please see link to GMC guidance:

https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/prescribing-and-managing-medicines-and-devices/prescribing-unlicensed-medicines

Switching to Dilantin® 30mg/5ml oral suspension

- Pfizer have obtained permission from the MHRA to import Canadian stock as an unlicensed product, Dilantin® (phenytoin) 30mg/5ml oral suspension.
- Both Epanutin® oral suspension and Dilantin® 30mg/5ml oral suspension contain phenytoin **base** and can be considered equivalent in dosing, therefore changes in dosing should not be required.

Switching to other formulations

- Different formulations of phenytoin (other than Dilantin® 30mg/5ml oral suspension) are not interchangeable. If patients are switched to anything other than Dilantin® 30mg/5ml oral suspension, careful management of switching and monitoring is required, and the switch should therefore always be overseen by a specialist.
- As different formulations of phenytoin may not be bioequivalent, monitoring of plasma levels of phenytoin is advisable before and one week after any phenytoin product switch. GPs may need to seek local advice on how to do this and access Therapeutic Drug Monitoring services.

Dose equivalence and conversion

Doses of the phenytoin base preparations (suspension and Infatabs) require dose conversion when switching formulation from or to the sodium salt preparations (capsules, injection, tablets).[3]

Although 100mg of phenytoin sodium is equivalent to 92mg of phenytoin base on a molecular weight basis, these molecular equivalents are not necessarily biologically equivalent. Thus, care should be taken where it is necessary to change the dosage form and serum level monitoring is advised.[1] In practice, the conversion used is, phenytoin sodium 100mg is equivalent to phenytoin base 90mg therefore 45mg of suspension (7.5ml of 30mg/5ml) is equivalent to a 50mg capsule.[4]

Dilantin® (phenytoin) 30mg/5ml Oral Suspension

Unlicensed Preparations – Pfizer product imported from Canada

To help mitigate the shortage, Pfizer has obtained approval from the Medicines and Healthcare Regulatory Agency (MHRA) to import stock of phenytoin oral suspension, Dilantin-30®, from Canada. This stock is considered an unlicensed preparation in the UK. Dilantin-30® can be considered equivalent to Epanutin® 30mg/5ml suspension and therefore no dosing adjustments should be required. Pfizer have confirmed they can import sufficient quantities of this stock to support the whole UK market during this period of short supply. Details on Epanutin® and Dilantin-30® are below and copies of the Patient Information Leaflet (PIL), product monograph and Dear Healthcare Professional Letter have been included with this alert on the CAS website. The Dilantin-30® PIL contains different dosing information compared to the Epanutin® PIL. Therefore, patients should be made aware of this and will need to be counselled to always remain on their prescribed regimen and consult their prescriber is they are unsure.

Name	Strength	Presentation	Bottle Size	Excipients	Phenytoin sodium OR base
Epanutin®	30mg/5ml	Oral Suspension	500ml	Carmoisine (E122)	Phenytoin base
*Dilantin-30®	30mg/5ml	Oral Suspension	250ml	Amaranth (E123)	Phenytoin base

When prescribing and dispensing unlicensed preparations, prescribers and pharmacists should always ensure the following:

- Patient consent has been sought for use of an unlicensed preparation.
- Patients are supplied sufficient quantity of a specific unlicensed preparation to cover until Epanutin® returns into stock end of July 2019.

Alternative Phenytoin Preparations

There are a number of alternative licensed and unlicensed phenytoin preparations available. However please note that none of the licensed alternatives are in the form of suspension.

Please be aware that supplies of Epanutin® Infatabs are currently in short supply and patients have been required to switch to unlicensed Canadian stock, Dilantin® 50mg Chewable tablets. As such, **patients should not be switched to Epanutin® Infatabs.**

In the case of the alternative suspensions not being suitable, advice can be sought from pharmacy on emptying out phenytoin capsules for dispersion[3,5] (unlicensed use). It should be noted that as the capsule contents do not dissolve, they cannot be used for withdrawal of part doses.

References

1. Pfizer Limited. Epanutin 30mg/5ml oral Suspension. SPC; date of revision of the text, 09/2018: https://www.medicines.org.uk/emc/product/2257/smpc
2. MHRA. Antiepileptic drugs: updated advice on switching between different manufacturers' products, Published 24 November 2017: https://www.gov.uk/drug-safety-update/antiepileptic-drugs-updated-advice-on-switching-between-different-manufacturers-products
3. The NEWT Guidelines. Phenytoin monograph updated October 2017 http://www.newtguidelines.com/
4. Evelina London Paediatric Formulary. Phenytoin monograph, last published on 03 October, 2014: http://cms.ubqo.com/public/d2595446-ce3c-47ff-9dcc-63167d9f4b80/content/99e5ed1f-8143-453e-a8ea-45984597e32a
5. Handbook of Drug Administration via Enteral Feeding Tube: https://about.medicinescomplete.com/publication/drug-administration-via-enteral-feeding-tubes/

Distribution

- Care Quality Commission (CQC) (headquarters) for information
- Directors of public health
- Health and Safety Executive
- OFSTED (directors of children's services) for information
- Public Health England (for information)
- Social services in England (directors)
- MHRA
- NHS England Patient Safety
- NHS England EPRR
- Chief Medical Officer
- NHS England – National Clinical Director
- NHS Supply Chain

- Wholesalers and Distributors
- Directors of Procurement – Devolved Authorities

If you are responsible for cascading these alerts in your organisation, these are our suggested distribution lists.

Trusts (NHS boards in Scotland)

CAS and SABS (NI) liaison officers for onward distribution to all relevant staff including:

- A&E consultants
- A&E departments
- A&E directors
- A&E nurses
- Chief pharmacists
- Clinical governance leads
- Clinical Procurement Specialists
- Community hospitals
- Community nurses
- District nurses
- Hospital pharmacies
- Hospital pharmacists
- Intensive care medical staff/paediatrics
- Intensive care nursing staff (adult)
- Intensive care nursing staff (paediatric)
- Intensive care units
- Intensive care, directors of
- Medical directors
- Neonatal nurse specialists
- Neonatology departments
- Neonatology directors
- NHS walk-in centres
- Paediatric intensive care units
- Paediatric medicine, directors of
- Paediatric nurse specialists
- Paediatric wards
- Paediatricians
- Paediatrics departments
- Pharmaceutical advisors
- Pharmacists
- School nurses
- Special care baby units
- Walk-in centres

NHS England area teams

CAS liaison officers for onward distribution to all relevant staff including:

- Community pharmacists
- General practitioners
- General practice managers
- General practice nurses

Independent distribution

Establishments registered with the Care Quality Commission (CQC) (England only)

- Care homes providing nursing care (adults)
- Hospitals in the independent sector
- Independent treatment centres
- Private medical practitioners

Establishments registered with OFSTED

- Children's services
- Educational establishments with beds for children
- Residential special schools

Please note: CQC and OFSTED do not distribute these alerts. Independent healthcare providers and social care providers can sign up to receive Supply Disruption Alerts directly from the Medicine and Healthcare Regulatory Agency's Central Alerting System (CAS) by sending an email to: safetyalerts@mhra.gov.uk and requesting this facility.

Enquiries

England
Send enquiries about this notice to the DHSC Supply Resilience Team, quoting reference number SDA/2019/001 or email: supplyresiliencemd@dhsc.gov.uk

Addressees may take copies for distribution within their own organisations