Department of Health & Social Care

NHS

Supply Disruption Alert

SDA/2020/002 Issued: 25 February 2020 Valid until: 19/06/2020

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

Summary

- Epanutin® (phenytoin) 30mg/5ml oral suspension will be out of stock from w/c 2nd March until late June 2020.
- The Canadian brand of phenytoin 30mg/5ml oral suspension - '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 which may require specialist advice, support, or referral.

Action

All healthcare organisations in primary, secondary or specialist healthcare services should work with clinicians including pharmacists to ensure the following actions are undertaken where relevant:

If a patient has exhausted their supplies of Epanutin® 30mg/5ml oral suspension during this out of stock period, the following advice should be followed by the General Practitioner (GP):

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, GPs should consider alternative formulations of phenytoin with support, where required, from secondary care specialists. Follow advice in later sections for monitoring requirements.
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 (including Dilantin® 30mg/5ml oral suspension), they should be switched back to Epanutin® 30mg/5ml oral suspension when supplies are back in stock, which is likely to be late June 2020.
v. Careful management of switching and monitoring may be required when switching back from a product other than Dilantin® 30mg/5ml oral suspension to licensed Epanutin® 30mg/5ml suspension, and prescribers and pharmacists should liaise to ensure this is done safely.
vi. Any decision to prescribe an unlicensed medicine should consider the relevant guidance about unlicensed medicines and NHS Trust or local governance procedures. Please see the links below for further information:
    - Prescribing unlicensed medicines, General Medical Council (GMC)

- The supply of unlicensed medicinal products, Medicines and Healthcare products Regulatory Agency (MHRA)
- Professional Guidance for the Procurement and Supply of Specials, Royal Pharmaceutical Society (RPS)

vii. When prescribing a product that is not licensed in the UK prescribers must indicate on the FP10 prescription that an unlicensed product is required. This can be done by annotating the prescription with the following wording: "**special order**".

viii. 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 late June 2020.

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:	on receipt of this alert
Actions completed:	19/06/2020

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 quality issue resulting in 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 2nd March 2020. Further deliveries are currently anticipated late June 2020, 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 Medicines and Healthcare Regulatory Agency (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 Dilantin® 30mg/5ml oral suspension in the first instance. If a patient is considered for this switch, prescribers should be aware of the following:

Prescribing:

- All available alternative phenytoin oral suspensions are considered unlicensed in the UK.
- Use of unlicensed products should be in line with agreed policies and guidance.
- Any decision to prescribe an unlicensed medicine must take into account the relevant GMC guidance and NHS/ local governance procedures. See links above.

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.

Different formulations and manufacturer's products of phenytoin may not be bioequivalent. If patients are switched to anything other than Dilantin® 30mg/5ml oral suspension, careful management of switching and monitoring is required, and the following advice should be followed:

Switching to formulations other than Dilantin® 30mg/5ml oral suspension

Prescribers in primary care should ensure appropriate monitoring is carried out for all patients' undergoing switches from their regular phenytoin product.

- Patients should be monitored closely for toxic effects and changes in seizure frequency. Patients should be referred to a specialist for review if there are changes in seizure control or the product is not tolerated.
- Monitoring of plasma trough levels of phenytoin should be carried out before a patient is switched and checked again two weeks after. The brand switch should not be deferred whilst awaiting the pre-switch result.
- If the blood level has changed, the phenytoin dose should be adjusted – this is usually in 25mg increments for adults but may be lower in children. The blood level should be repeated every 3 weeks until the pre-change phenytoin plasma level is achieved
- Phenytoin Therapeutic Drug Monitoring services are routinely available but local neurology services should be contacted for assistance if required.
- Patients should continue to have their routine checks for renal function and albumin level.

Dose equivalence and conversion

Dilantin® 30mg/5ml oral suspension can be considered equivalent to the UK brand ***'Epanutin®'*** 30mg/5ml oral suspension (both contain phenytoin base) and no dosing adjustments should be required.
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 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 if 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

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 out of stock 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

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 regional offices

For onward distribution to all relevant staff including:

- Community pharmacists
- GP Practices not yet registered with CAS

General practice

For onward distribution to all relevant staff including:

- 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

Enquiries

England

Send enquiries about this notice to the DHSC Supply Resilience Team, quoting reference number SDA/2020/002.

Email: supplyresiliencemd@dhsc.gov.uk

Addressees may take copies for distribution within their own organisations