Department of Health & Social Care

Supply Disruption Alert

SDA/2018/002 Issued: 22nd October 2018 at 14:30 Valid until: 10th December 2018

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

Summary

Pfizer will be out of stock of Epanutin (phenytoin) 30mg/5ml oral suspension from w/c 29th October until early December 2018.

Pfizer are the sole licensed UK supplier of this product and alternative phenytoin formulations are not directly interchangeable; switching to alternative formulations may require specialist advice, support, or referral.

For action by

Care Trusts, Mental Health Trusts, Learning Disabilities Trusts, Mental Health & Social Care Trusts, Specialist Trusts, Ambulance Trusts, Acute Trusts, Mental Health & Learning Disabilities, NHS Regional Offices, Community Trust

Action start date: 22/10/2018

Action

Different formulations of phenytoin are not interchangeable and careful management of switching and monitoring is required. All health care professionals in primary, secondary or specialist healthcare services who prescribe, dispense or administer Epanutin oral suspension, should be aware of the following advice:

All Patients

- 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 the stocks at home will last until early December, or if any switches are likely to be required during the next 7-8 weeks.
- If the patient has sufficient supplies to last them until early December 2018, then no further action is required. These patients should **not** be issued with a repeat prescription during this period.

If a patient does not have sufficient supplies to last until early December, the following advice should be followed:

Paediatric Patients (<18 years of age)

- The patient should be referred to their specialist prescriber. Switching to alternative formulations should be undertaken by specialist prescribers only

Adult Patients (>18 years of age)

- Switching some patients to alternative formulations may be managed in the community with the support of a clinical specialist
- General Practitioners should make early contact with secondary care or tertiary care to seek support on the most suitable management plan for the patient and monitoring requirements if needed
- Prescribers may wish to use advice in later sections of this alert when switching patients to alternative products

Prescribers should work in close collaboration with their pharmacists to understand which phenytoin formulations are available. Prescribers and pharmacists should work together to ensure correct calculation of dosing and monitoring of plasma levels are undertaken when patients are switched to alternative formulations.

Patients should revert to Epanutin 30mg/5ml oral suspension when supplies are back in stock and prescribers should liaise with their pharmacists to be alerted to this.

Deadlines for actions

Actions initiated:	22/10/2018
Actions completed:	10/12/2018

Product details

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

Background

There is a global short-term supply issue affecting Epanutin suspension due to global manufacturing delays. Pfizer are the sole licensed UK supplier of phenytoin 30mg/5ml oral suspension.

It is anticipated that current stock will be depleted week commencing 29th October 2018. Further deliveries are currently anticipated early December, 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. 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 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:

- Although phenytoin alternative oral suspensions are unlicensed, expert clinical advice is that it is preferable, where possible, to switch patients to these products.
- The alternative oral suspension may be of a different strength to Epanutin
- As Epanutin oral suspension contains phenytoin **base**, patients switching product should be prescribed an oral suspension containing phenytoin **base**
- Any decision to prescribe an unlicensed medicine must take into account the relevant GMC guidance and NHS Trust 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

Information on other preparations are discussed below.

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]

Alternative formulations

Licensed preparation

There are a number of alternative licensed phenytoin preparations available (see table). However please note that none of the licensed alternatives are in the form of suspension.

Formulation	**Strength**	**Presentation**	**Phenytoin sodium OR base**
Phenytoin Capsules	25, 50, 100 and 300mg	Oral Capsules	Phenytoin sodium
Phenytoin Tablets	100mg	Oral Tablets	Phenytoin sodium
*Epanutin Infatabs	50mg	Chewable Tablets	Phenytoin base

*please be aware that supplies of Epanutin Infatabs are only available to meet normal market demand**,** as such **patients should not be switched to Epanutin Infatabs as this may precipitate a shortage of this presentation,**

In the case of the alternative suspensions not being suitable, advice can be sought from pharmacy on emptying out 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.

Unlicensed Preparations

To help mitigate the shortage, Pfizer has obtained approval from the Medicines and Healthcare Regulatory Agency (MHRA) to import stock of phenytoin oral suspension from Canada. This stock is considered an unlicensed preparation in the UK. It is important to note that supplies of this product are very limited and therefore it may not be possible to access for all patients. The bottle size of this product is half that of Epanutin oral suspension. Further details on Epanutin and Dilantin-30 are below and copies of the Patient Information Leaflet and product monograph have been included with this alert on the CAS website.

Name	**Strength**	**Presentation**	**Bottle Size**	**Phenytoin sodium OR base**
Epanutin	30mg/5ml	Oral Suspension	500ml	Phenytoin base
*Dilantin-30	30mg/5ml	Oral Suspension	250ml	Phenytoin base

*please be aware that there are some differences in excipients to that in Epanutin

Unlicensed phenytoin suspensions are available from a number of specials manufacturers. In addition, unlicensed specialist importers may be able to source phenytoin oral suspension from abroad. Pharmacists will know how to source these unlicensed and specials products and should be able to advise you further. Before prescribing, you should liaise with your pharmacist to clarify local availability of products.

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

- Ensure patient consent has been sought for use of an unlicensed preparation
- It should be confirmed whether the unlicensed phenytoin oral suspension contains phenytoin **sodium** or phenytoin **base** (Epanutin oral suspension contains phenytoin **base**)
- If a switch is made to a different strength suspension, prescribers, carers and patients must be made aware of the change in strength and ensure the correct dose is being taken
- Patients are supplied sufficient quantity of a specific unlicensed preparation to cover until Epanutin returns in stock in early December 2018

Monitoring Patients After Switching

- A change in formulation should 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
- Patients who have switched to another product should be referred to a specialist for review if there are changes in seizure control or the product is not tolerated

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; however, each organisation needs to ensure a senior clinician takes responsibility for coordinating all actions that need to be taken.

- General practitioners
- Practice nurses
- Chief pharmacist
- Allergy specialists/allergy teams
- School nursing/medical services
- Emergency Preparedness and Response officer
- Medical directors
- Pharmacists
- Paediatricians
- Paediatrics departments

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 Medicines and Healthcare products Regulatory Agency's Central Alerting System (CAS) by sending an email to: safetyalerts@mhra.gov.uk and requesting this facility.

Enquiries

Send enquiries about this notice to the DH Supply Resilience Team, quoting reference number SDA/2018/002.

Email: supplyresiliencemd@dh.gsi.gov.uk

Addressees may take copies for distribution within their own organisations