Department of Health & Social Care

NHS

Supply Disruption Alert

SDA/2020/001 Issued: 10 January 2020 Valid until: 08 May 2020

Phenytoin Sodium NRIM 100mg capsules – Supply Disruption Alert

Summary

Accord will be out of stock of phenytoin sodium 100mg capsules from 4th January 2020 until early May 2020.

Phenytoin is classified by the Medicines and Healthcare products Regulatory Agency (MHRA) as a Category 1 anti-epileptic drug; for these drugs, prescribers are advised to ensure that their patient is maintained on a specific manufacturer's product.

An alternative phenytoin sodium 100mg capsules manufactured by Flynn Pharma is available, however switching to an alternative formulation requires monitoring and may also require specialist support, advice or referral.

Action

Healthcare professionals in primary care who prescribe and dispense phenytoin 100mg capsules, should take the following actions:

1. identify all patients currently prescribed phenytoin sodium 100mg capsules. Early contact should be made by the prescriber with the patient or patient's parent/carer to determine the brand of phenytoin 100mg capsules the patient takes;
2. if the patient is prescribed or takes a phenytoin 100mg capsule which is not manufactured by Accord, ensure MHRA guidance is adhered to and patients are maintained on the same product; or
3. if the patient is prescribed or takes a phenytoin sodium 100mg capsule which is manufactured by Accord, the following advice should be followed:
    I. switch patients to phenytoin sodium 100mg capsules manufactured by Flynn Pharma, where clinically appropriate and follow advice in later sections of this alert to monitor patients.
    II. if phenytoin sodium 100mg capsules manufactured by Flynn Pharma are not clinically appropriate then alternative phenytoin formulations should be considered. Prescribers and pharmacists should then work together to understand which formulations are available and ensure the patient receives the correct dose of the alternative product and
    III. for all switches, prescribers and pharmacists should work together to ensure monitoring requirements are undertaken as per guidance in later sections of this alert.
4. prescribers should make early contact with secondary care or tertiary care specialists if specialist support is required for specific patients and ensure that any patient whose epilepsy is unstable is referred to specialist care for management;
5. prescribers should read the latest MHRA guidance (link below) and ensure that patients are maintained on the same manufacturers brand of phenytoin preparation going forward and that the brand is clearly stated on the prescription.

Deadlines for actions

Actions initiated: on receipt of this alert
Actions completed: 08 May 2020

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Product details

Phenytoin Sodium NRIM 100mg capsules (Accord)

Background

Due to a regulatory change at their manufacturing site, Accord are expected to be out of stock of phenytoin sodium 100mg capsules until early May 2020.

Phenytoin sodium 100mg capsules are 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]. Further information can be found at: https://www.gov.uk/drug-safety-update/antiepileptic-drugs-updated-advice-on-switching-between-different-manufacturers-products

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 and dose equivalence

Switching to alternative phenytoin sodium 100mg capsule preparation

- It is recommended that patients who require switching should be prescribed an alternative manufacturers' phenytoin sodium 100mg capsule in the first instance. Phenytoin 100mg capsules are available from Flynn Pharma and therefore, prescribers should prescribe **'Phenytoin sodium 100mg capsules (Flynn Pharma Ltd)'**, where clinically appropriate.
- When switching a patient from phenytoin sodium 100mg capsules manufactured by Accord to phenytoin 100mg capsules manufactured by Flynn Pharma, no initial dosing adjustments are required. Both preparations contain phenytoin sodium.
- Nevertheless, as this is a Category 1 anti-epileptic drug, patients should be monitored closely during the switching period (see monitoring section).

Switching to alternative formulations

- For patients considered not suitable for this switch to the Flynn Pharma capsules, there are a number of alternative licensed phenytoin preparations available.
- For such patients, it is important to note that doses of sodium salt preparations (capsules, tablets, injection) require dose conversion when switching formulations from and to phenytoin base preparations (suspension and Infatabs)[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
- In practice, the conversion used is, phenytoin sodium 100mg is equivalent to phenytoin base 90mg therefore 100mg capsule is equivalent to 90mg suspension[4].

- Prior to undertaking any formulation switch, prescribers should work in close collaboration with their pharmacists to understand which phenytoin formulations are available and ensure patients are monitored appropriate (see monitoring section).

Monitoring Patients After Switching

As different formulations and manufacturer's products of phenytoin may not be bioequivalent, prescribers in primary care should ensure appropriate monitoring is carried out for all patients' undergoing switches from their regular phenytoin product.

The following advice should be followed:

- 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 (usually in 25 mg increments) and the blood level 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.

References

1. Accord. Phenytoin Sodium NRIM 100mg Capsules. SPC; date of revision of the text, 06/11/2019: https://www.medicines.org.uk/emc/product/5046/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-updatedadvice-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-8143-453ea8ea-45984597e32a

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England
Send enquiries about this notice to the DHSC Supply Resilience Team, quoting reference number **SDA/2020/001**

Email: supplyresiliencemd@dhsc.gov.uk