COMMISSION ON HUMAN MEDICINES
CHAIRMAN: Professor Stuart Ralston

11 November 2013

Antiepileptic drugs: new advice on switching between different manufacturers' products for a particular drug

Dear healthcare professional

I am writing to inform you about new advice about oral antiepileptic drugs (AEDs) and switching between different manufacturers' products of a particular drug.

Background

When a generic medicinal product is shown to be bioequivalent to the originator ('reference') product, as defined by the relevant regulations and guidelines, it follows that the products can be considered to be clinically equivalent. However, concerns about switching between different manufacturers' products of AEDs have been raised by patients and prescribers. These include switching between branded originator and generic products, and between different generic products of a particular drug. The main reasons for these concerns are the narrow therapeutic index of some AEDs and the potentially serious consequences of therapeutic failure. Drug-drug interactions and the relatively low solubility or bioavailability (or both) of some AEDs are other important factors.

Potential risk from switching between different manufacturers' products

The Commission on Human Medicines (CHM) reviewed spontaneous adverse reactions received by MHRA and publications that reported potential harm arising from generic switching of AEDs in patients previously stabilised on a branded product. Following this review, CHM concluded that reports of loss of seizure control and/or worsening of side effects around the time of switching between products could be explained as chance associations, but that a causal role of switching could not be ruled out in all cases.

New categorisation to help minimise risk

CHM considered the characteristics of AEDs and advised that they could be classified into three categories based on therapeutic index, solubility and absorption to help prescribers and patients decide whether it was necessary to maintain continuity of supply of a specific manufacturer's product. These categories are listed below:

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Category 1 – Phenytoin, carbamazepine, phenobarbital, primidone.
For these drugs doctors are advised to ensure that their patient is maintained on a specific manufacturer's product.

Category 2 – Valproate, lamotrigine, perampanel, retigabine, rufinamide, clobazam, clonazepam, oxcarbazepine, eslicarbazepine, zonisamide, topiramate
For these drugs the need for continued supply of a particular manufacturer's product should be based on clinical judgement and consultation with patient and/or carer taking into account factors such as seizure frequency and treatment history.

Category 3 - Levetiracetam, lacosamide, tiagabine, gabapentin, pregabalin, ethosuximide, vigabatrin
For these drugs it is usually unnecessary to ensure that patients are maintained on a specific manufacturer's product unless there are specific concerns such as patient anxiety, and risk of confusion or dosing errors.

Advice for healthcare professionals:

- Different AEDs vary considerably in their characteristics, which influence the risk of whether or not switching between different manufacturers' products of a particular drug may cause adverse effects or loss of seizure control.
- Antiepileptic drugs have been divided into three categories to help healthcare professionals decide upon whether it is necessary to maintain continuity of supply of a specific manufacturer's product.
- If it is felt desirable for a patient to be maintained on a specific manufacturer's product this should be prescribed either by specifying a brand name or by using the generic drug name and name of the manufacturer (otherwise known as the 'Marketing Authorisation Holder')
- This advice relates only to AED used for treatment of epilepsy and does not apply to the use of AED for indications such as mood stabilisation or neuropathic pain.

Additional advice for pharmacists:

- Dispensing pharmacists should ensure the continuity of supply of a particular product when the prescription specifies it. If the prescribed product is unavailable, it may be necessary to dispense a product from a different manufacturer to maintain continuity of treatment of that AED. Such cases should be discussed and agreed with both the prescriber and patient (or carer)
- Usual dispensing practice can be followed when a specific product is not stated

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Yours faithfully,

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