Antiepileptic Drugs (AEDs) - Appropriate switching to generics

Over £429 million is spent annually on all antiepileptic drugs (AEDs) nationally (ePACT March 2014). QIPP projects in this area focus on reducing any unnecessary expenditure on AEDs, but within the current guidance on switching from branded to generic AEDs.

Recommendations

- Only consider switching brands of AEDs which the Medicines and Healthcare Products Regulatory Agency (MHRA) and Commission on Human Medicines (CHM) advise are suitable for switching where practical. See table 1 for details of the three categories, where category 1 is the highest risk.¹²
- All AEDs in category 3 should be prescribed generically when initiated to maximise savings available. Consider initiating category 2 AEDs on generic prescriptions.
- Category 1 AEDs must always be prescribed as a specific manufacturer's product (by brand name and formulation) to ensure that the patient is maintained on the same brand.
- Consider a generic switch for all AEDs prescribed for indications other than epilepsy (e.g. neuropathic pain).
- When considering switching appropriate patients to generic AEDs, ensure all patient factors are considered. Only switch suitable patients, not those with any contraindications. See principles for switching in the evidence base section (page 4).³
- Consider the impact. A brand-to-generic switch is likely to cause increased anxiety for many patients (with epilepsy), which may be a reason for increased clinic visits (possibly undue concern).⁴ Stress may also trigger a seizure⁵ increasing the disease burden to the patient/carer and costs to the NHS. Suitable patient information and support from the community pharmacist may help patients with any concerns, who are prone to these issues.¹
- Following recent loss of seizure control where extra (adjunctive therapy) or a new AED will be prescribed, even those where a switch is not recommended, consider initiating a generic version if felt appropriate.³

Background

Disease burden

In 2010 the neurological disease burden from epilepsy was higher than for Alzheimer's disease, other dementias, multiple sclerosis and Parkinson's disease combined. Epilepsy imposes a large economic burden on patients and their families. Discrimination against patients and their families, social isolation, emotional distress, dependence on family, poor employment prospects and personal injury add to the suffering. Epilepsy is often suboptimally diagnosed and managed, even in developed countries.⁶
The incidence of seizure recurrence in previously seizure-free patients has been reported as 30% with no known cause. Another 10% has an identifiable cause, such as omission of doses, sleep deprivation or fever. This confuses the picture regarding the impact of brand to generic switching and makes recommendations problematic.³

**Selecting AEDS**

Ideally, AEDs should fully control seizures and be well tolerated with no long term safety problems. Sodium valproate appears to be the most teratogenic AED. The newer drugs gabapentin and levetiracetam cause far fewer dermatological hypersensitivity reactions. AEDs should be easy to prescribe and for patients to take (once or twice daily, no drug interactions and no need for serum monitoring). It is difficult, even for epilepsy specialists to select the optimum drug for individual patients.⁶

**Brand to generic switching concerns**

Concerns about switching between different manufacturers’ products of AEDs have been raised by patients, patient organisations and prescribers. These include switching between branded and generic products and between different generics. The main 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.² Different AEDs vary considerably in their characteristics. This influences the risk of whether switching between different manufacturer’s products of a particular drug may cause adverse effects, or loss of seizure control. There is little good quality evidence to support any type of therapeutic policy in this area. AEDs have been divided into three risk-based categories to help healthcare professionals decide whether it is necessary to maintain continuity of supply of a specific manufacturer’s product.⁷

**National guidance**

The CHM reviewed spontaneous adverse reactions received by the MHRA (yellow cards). The CHM also reviewed publications reporting potential harm from generic switching of AEDs in patients previously stabilised on a branded product. Following this review, the CHM concluded that reports of loss of seizure control and/or worsening side-effects around the time of switching could be explained as chance, but that a causal link could not be ruled out.²

The CHM considered the characteristics of AEDs. They advised that AEDs could be classified into 3 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.² These 3 categories are shown in Table 1, along with advice to the doctor prescribing AEDs.

<table>
<thead>
<tr>
<th>Category</th>
<th>Advice for doctors</th>
<th>AEDs in category</th>
</tr>
</thead>
</table>
| 1        | Doctors are advised to ensure that their patient is maintained on a specific manufacturer’s product. | • Phenytoin  
• Carbamazepine  
• Phenobarbital  
• Primidone |
<table>
<thead>
<tr>
<th>Category</th>
<th>Advice for doctors</th>
<th>AEDs in category</th>
</tr>
</thead>
</table>
| 2        | Doctors are advised to use their clinical judgement (in consultation with their patient and/or their carer) to determine whether it would be advisable for them to be maintained on a specific manufacturer’s product, taking into account factors such as seizure frequency and treatment history. | • Valproate  
• Lamotrigine  
• Perampanel  
• Retigabine  
• Rufinamide  
• Clobazam  
• Clonazepam  
• Oxcarbazepine  
• Eslicarbazepine  
• Zonisamide  
• Topiramate |
| 3        | Doctors are advised that it is usually unnecessary to ensure that their patients are maintained on a specific manufacturer’s product, unless there are specific concerns such as patient anxiety or risk of confusion or dosing errors (from having several packs of different appearance). | • Levetiracetam  
• Lacosamide  
• Tiagabine  
• Gabapentin  
• Pregabalin  
• Ethosuximide  
• Vigabatrin |

The NICE evidence update on epilepsy stated a cross reference to the CHM advice had been added to NICE CG137. The MHRA classifications can help healthcare professionals decide whether it is necessary to maintain continuity of supply of a specific manufacturer’s product. The MHRA advice has been incorporated into NICE CG137 as a footnote.8

NICE has published a statement on AEDs which states: “Consistent supply to the child, young person or adult of a particular manufacturer’s AED preparation is recommended, unless the prescriber, in consultation with the child, young person, adult and their family and/or carers as appropriate, considers that this is not a concern. Different preparations of some AEDs may vary in bioavailability or pharmacokinetic profiles and care needs to be taken to avoid reduced effect or excessive side effects. Consult the summary of product characteristics (SPC) and British National Formulary (BNF) on the bioavailability and pharmacokinetic profiles of individual AEDs, but note that these do not give information on comparing bioavailability of different generic preparations.” 3,9

Healthcare professionals must be able to prescribe accordingly to maintain a consistent supply. Prescriptions will need to reflect this so that the appropriate product is dispensed.10 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 name and name of the manufacturer (otherwise known as the Marketing Authorisation Holder). This advice relates only to antiepileptic drugs used for treatment of epilepsy. It does not apply to their use in other indications (e.g. mood stabilisation, neuropathic pain). 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 antiepileptic drug. Such cases should be discussed and agreed with the both the prescriber and patient (or carer).11
Evidence base

Approval of generic AEDs

Normally if a generic product is shown to be bioequivalent to the originator or ‘reference’ product then they can be considered to be clinically equivalent. This is the basis for approval of generic products. The conventional bioequivalence criteria require the 90% confidence interval for the generic/reference product ratio for the mean area under the curve (AUC) [plasma drug concentration time] and maximum plasma concentration (Cmax) to lie within the range 80% to 125%. In specific cases of products with a narrow therapeutic index, the acceptance interval for AUC should be tightened to 90% to 111%. This acceptance interval also applies to Cmax where it is of particular importance for safety, efficacy or drug level monitoring. It is not possible to define a set of criteria to categorise drugs as narrow therapeutic index drugs (NTIDs) and it must be decided case by case if an active substance is an NTID based on clinical considerations. Some, but not all, AEDs are considered to be NTIDs.¹

Concerns have been raised by some patients and prescribers that bioequivalence criteria might not always be sufficient to ensure equivalent safety and efficacy when switching between different marketed antiepileptic products.¹

CHM review of switching AEDs

The CHM reviewed a number of published studies investigating potential harm from generic substitution of AEDs. These did not show clear evidence of harm due to switching formulations. However, the lack of robust evidence does not exclude the possibility that significant harm may sometimes occur. This is because of inherent limitations in the design of the studies, which were mostly observational. This is already reflected in the BNF with regard to phenytoin and carbamazepine, and more generally in the NICE AED guidance. In general terms, the CHM expert group decided that there was a need to maintain continuity of supply of a specific product for certain AEDs. The specific product could be either a branded product or a generic. Continuity of supply from the same manufacturer was the key issue, rather than whether the product was branded or a generic.¹⁰

Systematic reviews

There is little good quality evidence to support switching. In response to increasing cost pressures, healthcare systems are encouraging the use of generic medicines. A systematic review by Crawford et al published in 2006 explored the potential problems with generic substitution of AEDs, as it is important to ensure that patient health is not compromised. Potential problems included:¹²

- Bioequivalence as defined by regulatory bodies may not correspond to therapeutic equivalence for AEDs, because of the permitted range of bioavailability for generics, evaluation methods that use small numbers of healthy volunteers and individual variation.
- Potential problems from poor continuity of supply.
- Cost savings may be outweighed by the cost of adverse consequences.
- Potential medico-legal consequences in patients who did not give informed consent to switching of AEDs.
- The limited evidence, mainly case reports with some pharmacokinetic studies, appears to support these concerns for older AEDs. As a result restrictions on use of specific generic AEDs are in place in some countries and recommended by some lay epilepsy organisations.
- As more AEDs lose patent protection, it is important to examine the question of whether generic substitution may pose problems for patients with epilepsy and whether there should be safeguards to ensure that both physician and patient are informed when generic substitution occurs.
Crawford et al note that very few articles describe RCTs comparing generic and branded products. Avoidance of seizures is the primary goal, while keeping adverse effects to a minimum. When long-term remission has been achieved it becomes important to avoid even a single breakthrough seizure. Just one seizure after a period control can have major implications, e.g. loss of driving licence, loss of employment, risk of injury, loss of self-esteem. There may even be fatal consequences – the risk of death in patients with uncontrolled seizures is higher than in seizure-free patients. Therefore considerably more is at stake when treating epilepsy than with many other conditions. Many patients with epilepsy are on a daily regimen of multiple treatments that has been carefully adjusted to obtain the optimal response. Consequently there is great reluctance from physicians and patients to change therapeutic agents particularly once stability has been achieved.12

The true cost of generic prescribing must also include the cost of additional visits to a physician or the hospital if the substitution causes problems. Also the cost of treatment failure must be taken into account if a seizure occurs. The cost of one breakthrough seizure in a previously stable patient is so high that it could offset the savings from generics.12

The systematic review concludes that as other AEDs lose patent protection, it is important to ensure that patients, pharmacists, prescribers and decision-makers are all aware of the issues to consider. Although newer AEDs such as lamotrigine, gabapentin, topiramate and levetiracetam are not considered to have a narrow therapeutic range like carbamazepine or valproate some of the issues of concern still apply. Like the older AEDs they still need titration and the consequences of a breakthrough seizure are still the same. Therefore it is prudent for patients, neurologists and pharmacists to be aware of the issues and to approve generic prescribing of AEDs for certain high-risk patients prior to it being switched. However, it should make little difference to a patient if the initial titration of therapy is with a specific generic product.12

Another systematic review assessed seizure outcomes following the use of generic vs. branded AEDs. The authors (Kesselheim et al) identified 9 RCTs, 1 prospective non-randomised trial and 6 observational studies. Most of the RCTs were short-term evaluations, but the available evidence does not suggest an association between loss of seizure control and generic substitution of at least 3 types of AEDs (phenytoin, carbamazepine and valproic acid). The observational study data came to conclusions at odds with the RCTs about the safety of brand-to-generic switches. It may be explained by factors such as undue concern from patients or physicians about the effectiveness of generic AEDs after a recent switch. Patients with epilepsy can experience significant anxiety with any change to their AEDs. A brand-to-generic switch is likely to cause increased anxiety or worry for many of these patients, which may be a reason for increased clinic visits. Switchback rates may indicate high levels of concern with the perceived problem of switching even in the absence of a true clinical problem. The prescriber may also have requested more frequent visits in the initial post-switch period to monitor for adverse events or epilepsy symptoms.4

In the absence of better data, physicians may want to consider more intensive monitoring of high-risk patients taking AEDs when any switch occurs. The Kesselheim et al systematic review had several limitations, reflected by the underlying literature. Most trials identified by the search were short-term evaluations, included small populations and were powered to assess differences in pharmacokinetic parameters rather than clinical outcomes. Some clinical trial circumstances and patients were heterogeneous: studies included patients with uncontrolled epilepsy and those whose epilepsy was controlled also patients who were exposed to different formulations of the same active ingredient.4

The RCTs in the Kesselheim et al systematic review involved three older AEDs while the observational studies included a wide range of AEDs, some with newer products. The systematic review concludes that additional prospective studies with NTIDs may help clarify whether there are high-risk patients in whom switching between versions of a particular AED may be dangerous. If possible, such studies should examine the effect of brand-to-generic switches as well as seemingly minor alterations in a branded AEDs manufacturing process or switches between products originating from a company’s different factories. Better trial data is awaited.4
Another systematic review by Yamada et al concludes that there is inconsistency between retrospective and prospective studies of generic AED substitution. The highest levels of evidence indicate that there should not be a problem with generic substitution, although some patients are more prone to problems with generic products. Some evidence suggests that switches between multiple generic AED products in certain individuals may be problematic - there may be increased use of healthcare resources. On an individual basis, failure of a generic product and the resulting seizure or toxicity has a major effect on quality of life and could even cause injury or death. For these reasons, it is critical to carefully evaluate substitution of AEDs.¹³

In a fourth review by Desmarais et al, the authors note that generic medications do not undergo the rigorous approval process required of original medications. Their effectiveness and safety is expected to be equal to that of their more expensive counterparts. However, several case reports and studies describe clinical deterioration and decreased tolerability with generic substitution. Generics do not always lead to the anticipated monetary savings and also raise compliance issues. Although this systematic review is limited by publication bias and heterogeneity of studies the authors believe there is enough concern to advise generic switching on an individual basis, with close monitoring throughout the transition. Harmful effects of switching patients with epilepsy to generic AEDs have been described especially with valproate, phenytoin, carbamazepine and primidone. Consequently several European countries have announced policies forbidding substitution of anticonvulsant medications.¹⁴

The London New Drugs Group (LNDG) and the UK Clinical Pharmacy Association (UKCPA) have developed a consensus view on principles for switching between branded and generic AEDs:³

- Identify suitable patients for switching from brand to generic AEDS. Firstly these are patients who agree to try a generic version. The patient must not have any contraindications to switching such as sensitivity to small dose changes (other contraindications are listed below).
- Only consider if there is a significant clinical, logistical (i.e. stock shortages) or financial benefit. Risks involved in switching AEDs should be minimised.
- Patients should be asked if they previously experienced problems, or if they were told by their doctor that they must not switch between brands or generics.
- Patients should not routinely be switched from existing medicines without their consent, unless urgent treatment is needed.
- Sustained or modified release products present a greater risk and should not be considered generic.
- Patients with constantly changing seizure control should not be switched to generics. They should be maintained on their usual branded or generic AED.
- Maintain patients with optimal seizure control on their usual branded or generic AED. This is important in a history of good seizure control and where seizure recurrence could have severe consequences, e.g. loss of a driving licence.
- Following recent loss of seizure control and additional or alternative AEDs are to be prescribed, even where products are not recommended to be switched, this is an opportunity to move to a generic version where this is considered to be appropriate.
- Patients with allergies to certain excipients must only switch if the generic product does not contain those ingredients.
- Epileptic patients on a ketogenic diet should not be switched to generics unless agreed by the patient’s healthcare team, due to varying carbohydrate content.
Switching category 2 AEDs

Table 2 below shows category 2 AED branded products where no generic of these formulations are available.\textsuperscript{12,15} Patent expiry is shown where this information is available.\textsuperscript{3} The most costly price is shown for each of the branded products (usually the highest strength).

Table 2: Category 2 AED brands with no generic available\textsuperscript{3,12,15}

<table>
<thead>
<tr>
<th>Branded product</th>
<th>Generic name</th>
<th>Cost (quantity)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Convulex® capsules</td>
<td>Valproic acid</td>
<td>£12.25 (100)</td>
</tr>
<tr>
<td>Epilim Chrono®</td>
<td>Sodium valproate MR</td>
<td>£29.10 (100)</td>
</tr>
<tr>
<td>Epilim Chronosphere® MR granules</td>
<td>Sodium valproate MR</td>
<td>£30.00 (30)</td>
</tr>
<tr>
<td>Fycompa® tablets</td>
<td>Perampanel</td>
<td>£140 (28)</td>
</tr>
<tr>
<td>Inovelon® tablets (patent expiry 2022)</td>
<td>Rufinamide</td>
<td>£102.96 (60)</td>
</tr>
<tr>
<td>Lamictal® 2mg dispersible tablets</td>
<td>Lamotrigine</td>
<td>£10.45 (60)</td>
</tr>
<tr>
<td>Tapclob® suspension</td>
<td>Clobazam, special order</td>
<td>£120.25 (150ml)</td>
</tr>
<tr>
<td>Trileptal® suspension</td>
<td>Oxcarbazepine</td>
<td>£40.80 (250ml)</td>
</tr>
<tr>
<td>Trobalt® tablets</td>
<td>Retigabine</td>
<td>£126.78 (84)</td>
</tr>
<tr>
<td>Zebinix® tablets (patent expiry 2021)</td>
<td>Eslicabazepine</td>
<td>£136 (30)</td>
</tr>
<tr>
<td>Zonegran® capsules</td>
<td>Zonisamide</td>
<td>£62.72 (56)</td>
</tr>
</tbody>
</table>

Charts 1 to 5 below show cost comparisons of generic with branded products. This is where generic versions are available in the same formulation as the brand. There are a number of branded products which are not due to come off patent for many years, so a switch to a generic is not yet possible. For all switches, the general principles for switching from branded to generic AEDs suggested by the UKCPA consensus document will apply.\textsuperscript{3} Please note that price comparisons are based on pack sizes and may not directly equate to prescribed doses which are variable. The prices are a guide to potential cost differences between different formulations of the same product.

Chart 1 below shows a cost comparison of generic lamotrigine with branded Lamictal®. The London New Drug Group (LNDG)/UKCPA consensus document states that there is lots of evidence to support switching and some countries have mandatory switching programmes. In 2005 the Department for Health issued a statement supporting switching in the UK. The largest cost saving is £94.02 which is achieved by switching from Lamictal® 56 x 200mg tablets to generic lamotrigine 56 x 200mg tablets.\textsuperscript{15}

Chart 1: Comparing costs of generic and branded lamotrigine\textsuperscript{15}
Chart 2 below shows a cost comparison of generic sodium valproate with branded Epilim® preparations. The LNDG/UKCPA consensus document states that a cautious switching policy (within the salt) is supported by scanty evidence. The largest cost saving of £11.18 is achieved by switching from Epilim® 500mg enteric coated tablets to generic sodium valproate 500mg enteric coated tablets, per pack of 100 tablets.15

Chart 2: Comparing costs of generic and branded sodium valproate (category 2 AED)15

<table>
<thead>
<tr>
<th>Product</th>
<th>Generic Price</th>
<th>Branded Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium Valproate 200mg tabs e/c</td>
<td>£4.13</td>
<td></td>
</tr>
<tr>
<td>Sodium Valproate 200mg/5ml sugar-free oral solution</td>
<td>£5.66</td>
<td></td>
</tr>
<tr>
<td>Epilim® 200mg tabs e/c</td>
<td></td>
<td>£7.70</td>
</tr>
<tr>
<td>Epilim® Liquid 200mg/5ml sugar-free</td>
<td></td>
<td>£7.78</td>
</tr>
<tr>
<td>Sodium Valproate 500mg tabs e/c</td>
<td></td>
<td>£8.07</td>
</tr>
<tr>
<td>Epilim® 500mg tabs e/c</td>
<td></td>
<td>£19.25</td>
</tr>
</tbody>
</table>

Chart 3 below shows a cost comparison of generic topiramate with branded Topamax® preparations. The LNDG/UKCPA consensus document states that limited evidence would suggest cautious switching in appropriate patients. The largest cost saving of £94.50 is achieved by switching from Topamax® 200mg tablets to generic topiramate 200mg tablets, per pack of 60 tablets.15

Chart 3: Comparing 28 day costs of generic and branded topiramate (category 2 AED)15

<table>
<thead>
<tr>
<th>Product</th>
<th>Generic Price</th>
<th>Branded Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topiramate 25mg tabs</td>
<td>£2.77</td>
<td></td>
</tr>
<tr>
<td>Topiramate 50mg tabs</td>
<td>£3.11</td>
<td></td>
</tr>
<tr>
<td>Topiramate 100mg tabs</td>
<td>£3.16</td>
<td></td>
</tr>
<tr>
<td>Topiramate 200mg tabs</td>
<td></td>
<td>£15.73</td>
</tr>
<tr>
<td>Topamax® 25mg tabs</td>
<td></td>
<td>£19.29</td>
</tr>
<tr>
<td>Topamax® 50tabs</td>
<td></td>
<td>£31.69</td>
</tr>
<tr>
<td>Topamax® 100mg tabs</td>
<td></td>
<td>£56.76</td>
</tr>
<tr>
<td>Topamax® 200mg tabs</td>
<td></td>
<td>£110.23</td>
</tr>
</tbody>
</table>

Oxcarbazepine - switch not supported

Switching from Trileptal® to the generic AED oxcarbazepine is not supported. The limited studies indicate a greater variability in blood levels with this agent.3 Also the branded product is more cost-effective across all three strengths in comparison to the generic version. There is currently no financial advantage to switching.15

Switching category 3 AEDs

Table 3 on the following page shows category 3 AED branded products where no generics are available.12,15 Patent expiry is shown where this information is available.3 The highest listed price is shown for each of the branded products (usually the highest strength, but sometimes applies to several strengths).15 For all switches, the general principles for switching from branded to generic AEDs suggested by the LNDG/UKCPA consensus document will apply.3
Table 3: Category 3 AED brands with no generic available

<table>
<thead>
<tr>
<th>Branded product</th>
<th>Medicine</th>
<th>Cost (quantity)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lyrica® capsules/solution (patent expiry 2018)</td>
<td>pregabalin</td>
<td>£96.60 (84)</td>
</tr>
<tr>
<td>Sabril® tablets/powder</td>
<td>vigabatrin</td>
<td>£37.01 (100)</td>
</tr>
<tr>
<td>Gabitril® tablets</td>
<td>tiagabine</td>
<td>£156.13 (100)</td>
</tr>
<tr>
<td>Vimpat® tablets/syrup (patent expiry 2023)</td>
<td>lacosamide</td>
<td>£144.16 (56)</td>
</tr>
</tbody>
</table>

Chart 4 below shows a cost comparison of generic levetiracetam with branded Keppra® preparations. The UKCPA consensus summarises that there is no specific evidence to suggest switching causes problems. However, there is some anecdotal data in the form of healthcare professional letters that switching has caused issues in some patients in their clinics. It is advisable to consult with the neurologist/prescriber and patient before making the switch in this instance. The largest cost saving of £95.28 is achieved by switching from Keppra® 1g tablets to generic levetiracetam 1g tablets, per pack of 60 tablets. 

Chart 4: Comparing costs of generic and branded levetiracetam

Chart 5 below shows a cost comparison of generic gabapentin with branded Neurontin® preparations. The UKCPA consensus summarises that there is no specific evidence to suggest switching causes problems in clinical practice. There is no consistent evidence to suggest that switching to a generic is any worse that switching within brand so switching can be sanctioned with this medicine. Most gabapentin use is for neurological pain so the dose is not critical. The largest cost saving of £44.29 is achieved by switching from to branded Neurontin® 400mg capsules to generic gabapentin 400mg capsules, per pack of 100.

Chart 5: Comparing costs of generic and branded gabapentin
**Ethosuximide – no financial advantage in switching**

In the case of ethosuximide, only 250mg capsules are available generically at £48.20 for 56. The branded products are only available in a syrup formulation and are listed at much lower prices. Zarontin® 250mg/ml syrup is £4.22 (200ml). Emeside® 250mg/ml syrup is £6.60 (200ml). Ethosuximide is mostly used in paediatrics. No specific data suggests switching causes problems in clinical practice. It seems reasonable to allow switching for most patients. However, there is no financial advantage in doing this.

**Savings available for each group**

Currently over £429 million is spent annually on all AEDs nationally. The cost per 1000 patients for all AEDs is £1,899 (ePACT March 14). There are significant savings that can be made by reviewing prescribing of these products, especially when AEDs are initiated.

Table 4 below shows the total annual costs and costs per 1000 patients for each category of AEDs nationally (ePACT March 2014).

**Table 4: Costs of AEDs by category**

<table>
<thead>
<tr>
<th>Category 1</th>
<th>Category 2</th>
<th>Category 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cost</td>
<td>Cost/1000 patients</td>
<td>Total cost</td>
</tr>
<tr>
<td>£71.9 million</td>
<td>£318</td>
<td>£72.7 million</td>
</tr>
</tbody>
</table>

**Savings available**

The savings discussed below use calculations which are based on average costs across the range of products within each category and exclude branded products where no generic equivalent is available. These figures are an estimate of the maximum savings available but may not be fully achievable.

If 50% of products in category 2 (where a generic is available) were switched to generic, the total national savings available would be **over £12.4 million, this is equivalent to £21,992 per 100,000 patients.**

The switch amount of 50% is an estimate and may not all be achievable. Switching in this category would depend on whether the prescriber and patient think it is suitable to switch to generic products based on seizure frequency and treatment history.

If 100% of products in category 3 (where a generic is available) were switched to generic, the total national savings would be **over £13.7 million, this is equivalent to £24,219 per 100,000 patients.**

The switch amount of 100% is again an estimate. For category 3 AEDs, it is usually unnecessary to ensure that patients are maintained on a specific manufacturer’s product. However, a switch would still not be appropriate if the prescriber has any specific concerns such as:

- Patient anxiety, which may trigger a seizure.
- Risk of confusion or dosing errors, from having several packs at home of a different appearance.

Considerable savings can be released by appropriate switching from branded to generic AEDs in Categories 2 and 3, where seizure control can be maintained.

In practice the switch percentage may be lower than those suggested above. If there is any doubt, always consult the patient’s neurology consultant before suggesting any generic switches. The costs of treatment failure outweigh any cost savings in switching to generics and therefore patients should be carefully selected and counselled. Also therapy failure resulting in seizures or toxicity has a major impact on the patient’s quality of life, so initial cost savings on branded products must not be the only consideration.
Summary

- Category 1 AEDs must always be prescribed as a specific manufacturer’s product (by brand name and formulation) to ensure that the patient is maintained on the same brand.
- Careful consideration should be given before initiating AEDs by brand to patients with epilepsy.
- Identify suitable patients for switching from brand to generic AEDs.
- All patients taking AEDs for indications other than epilepsy can be considered for a switch.
- Patients should be fully informed and agree to try a generic version.
- The generic should be less costly than the brand if considering a switch.
- The patient must not have any contraindications to switching. These include:
  » Sensitivity to small dose changes
  » Past unsuccessful switch attempts
  » Currently taking an SR preparation
  » Good seizure control
  » Serious consequences from a change in seizure control (e.g. loss of driving licence)
  » Allergies to generic excipients
  » Ketogenic diet
- Ensure close monitoring throughout the transition.

References


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www.mhra.gov.uk/home/groups/comms-ic/documents/websiteresources/con335046.pdf

Additional PrescQIPP resources

Available here:  
http://www.prescqipp.info/resources/viewcategory/243-appropriately-switching-anti-epileptic-drugs

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