Response to “The proposals to implement 'generic substitution' in primary care, further to the Pharmaceutical Price Regulation Scheme (PPRS) 2009” consultation, March 2010.

**Question 1**

a) In general do you think that the preferable implementation approach is indeed Option 3, with opt-out endorsement, i.e. allowing the dispenser flexibility as to which manufacturer’s product to supply if a product is listed unless the prescriber specifically opts out?

(b) If so, do you have any particular comments regarding its workability for patients, prescribers and dispensers?

(c) If not, why not – what is your preferred approach – Option 1/2/3, opt-in/opt-out, tickbox/endorsement or other?

Epilepsy Action does not believe Option 3 is the preferable approach.

Epilepsy Action strongly favours Option 2, provided anti-epileptic drugs (AEDs) are on the associated list of drugs not to be substituted. This option would be best to ensure that people with epilepsy are not put at unnecessary risk.

Epilepsy Action strongly believes AEDs should be excluded from any automatic generic substitution. There is strong evidence that brand switching for many people with epilepsy has caused breakthrough seizures, worsening of their seizure control or worsening of side-effects.

These are major issues for many people with epilepsy, and can affect employment, education, and social life. For example a single seizure can cause the loss of a driving licence for a year, and this may impact on a person’s quality of life.

We have attached a more detailed document explaining why AEDs should be excluded.

It is pleasing that epilepsy is specifically mentioned as one condition where substitution may not be suitable, on page 8 of the consultation document.
Epilepsy Action believes Option 3 of the proposals would be acceptable provided two changes are made to the proposals. Without these changes (or, as a minimum, the second proposed change), Epilepsy Action opposes Option 3.

1. There should be a second list to accompany the substitution list. This list should be of drug groups that cannot be added to the substitution list under any circumstance. We would expect this to include AEDs for the reasons outlined above.

2. There should be a formal consultation mechanism for any drugs that are to be added to the flexible dispensing list – see answer to question 5.

We are not supportive of Option 1, as maintaining the status quo would not be beneficial to people with epilepsy. If Option 1 is pursued by the Department of Health, there are major issues with the current prescribing system that require attention for the safety and quality of treatment for people with epilepsy.

Although currently generic prescribing is not permitted, there is nothing to prevent drug switching if the generic name is prescribed, or foreign produced versions of brands are available on the wholesale market. These factors affect consistency of supply, and are as threatening to good epilepsy treatment as including anti-epileptic drugs in any generic substitution scheme.

If Option 1 is chosen, this would represent an ideal opportunity for the Department of Health to help reinforce the message to prescribers and dispensers that brand switching for certain conditions, including epilepsy, can have serious consequences, and best practice is to ensure consistency of supply.

Epilepsy Action would like to stress that we are not opposed to generic drugs and many people with epilepsy are successfully treated by generic drugs. Epilepsy Action promotes the importance of ‘consistency of supply’, receiving the same version of an AED each time when a successful treatment plan has been found. It is the switching of versions which could endanger a person’s control of their epilepsy.

We are not opposed to people with epilepsy receiving ‘generically substituted’ drugs for other conditions or ailments, where no questions of patient safety have arisen. However AEDs should be excluded on clinical and safety grounds. Actively exempting AEDs from generic substitution would reaffirm the important message of consistency to GPs and prescribers.

Epilepsy Action has concerns about the proposal to allow a tick box or an endorsement to enable the prescriber to opt out of the substitution proposal.

Evidence from an Epilepsy Action survey in 2009 showed that when responding to patients queries about alternative versions of AEDs many doctors (16 per cent) were not aware of the issues until they were raised by the patient; 30 per cent said there was nothing to worry about, 22 per cent said all brands were the same and 11 per cent were uninterested or dismissive.
While, after discussion, an encouraging 85 per cent did listen to their patients concerns, this is putting the onus on the patient to be aware of and prepared to challenge their doctor over a clinical issue.

It is clear that many people with epilepsy will not be aware of the issues, nor necessarily be in a position to understand them if they were made aware.

Epilepsy Action strongly feels that neither the opt out tick box or endorsement provides a satisfactory solution to protecting people with epilepsy from the potential impact of brand substitution.

**Question 2**

Do you agree that using rINNs and BANs, and requiring the generic to be in the same pharmaceutical form as the named product, is the best way to identify products that are subject to the arrangements?

Epilepsy Action believes that drugs subject to the arrangements should be shown to be therapeutically equivalent to the original brand. Epilepsy Action is not aware that the proposals satisfactorily demonstrate therapeutic equivalence.

Epilepsy Action is not qualified to comment on the detailed definitions but understands that generic forms of AEDs may satisfy the proposed definitions. We believe strongly, as evidenced in the supporting documentation, that generic versions of AEDs are not all therapeutically equivalent. That being the case Epilepsy Action does not believe the proposed definitions provide adequate safeguards for patients.

**Question 3**

a) Do you agree with the proposed scope of the definition of “generic equivalent”, to allow for different salts?

b) Do you think that the proposed wording (see paragraph 56b) to be included within the rubric of NHS prescriptions (electronic as well as manual) delivers the definition effectively?

See answer to question 2.

**Question 4**

a) Do you think a select list of just under 40 rINNs and BANs, plus permitted alternative salts, that is amended via additions and deletions, which in practice will be made no more than four times a year, is an appropriate balance between being flexible enough to reflect changes in the market, while still being workable for prescribers and dispensers?

b) Do you think it is appropriate for this list and the notice of its amendments to be published in the Drug Tariff?

Epilepsy Action is concerned that AEDs could be added to a substitution list without warning or further discussion (clause 60 on page 18).
This would be a particular concern to us if the initial drug list does not provide the anticipated financial savings. AEDs could meet three of the Department of Health’s other criteria for being added to the list (page 18, clause 57). While in our opinion AEDs do not meet the criteria in relation to patient safety there is no indication as to how the criteria will be applied as the consultation only refers to “take account” of the criteria. As such there is nothing to prevent AEDs being added to this list at a later date. We are therefore calling on the Department of Health to put in place a formal process for adding drugs to this list.

Epilepsy Action further believes that refusing consultation on additions to the list would directly contravene the requirement in clause 4 of the NHS constitution. NHS services must reflect the needs and preferences of patients, their families and their carers.

“Patients, with their families and carers, where appropriate, will be involved in and consulted on all decisions about their care and treatment.”

It has been suggested at the consultation events that a limited list of drugs (under Option 3) would be easier to remember (by prescribers and pharmacists) than a longer list of exclusions under Option 2. Since there isn’t a proposed list of exclusions under Option 2, it cannot be said which will initially, or in the future, be the longer list. Under current proposals, either list can be added to at any time and without consultation.

In any instance, excluding drugs by their therapeutic area may be more practical than a list of individual products. Doing this would avoid an extensive list of drugs, and would prevent any confusion regarding the status of drugs newly off-patent. We recommend that the Department of Health look into this alternative way of preparing a list.

As prescribers and pharmacists use standard electronic systems and any included/excluded drugs will be flagged up at the point of prescribing/dispensing, we do not believe the relative size of any list should have any bearing on a policy which is essentially one of patient safety and treatment.

We call on the Department of Health to clarify at what intervals any prospective list will be reviewed and changed. Although the consultation states that “in practice” any list would be updated no more than four times a year, at a consultation event in York it was conceded that the list could be changed more regularly than this.

If the Department of Health’s preferred option is introduced as proposed, to which we object, we as a patient body would have the perpetual task of monitoring the list for updates and defending the rights of our members. We believe this would be an unfair and unnecessary demand of our time and resources.

We believe that notification of any proposed changes, with acceptable time for patient consultation, is not only desirable but essential.
We express some concern over the four criteria for selecting drugs to be added to the substitution list, and ask the Department of Health to make this list more robust in light of this consultation.

Epilepsy Action believes that “general clinical or patient safety concerns with regard to interchange between different manufacturer’s products” is the most important of the criteria. We believe it should have the power to mean a drug is not added to the list, even if the drug meets the other three criteria (see page 18).

If, as the Department of Health has inferred in the consultation document, AEDs are not to be included in the generic substitution scheme, and would not be added in the future (on clinical grounds), we would welcome legal protection to guarantee this.

A recent survey by Epilepsy Action of more than 1,400 people with epilepsy revealed that 43 per cent had been given different versions of their prescribed AEDs in the past year. Of these, 25 per cent felt that their epilepsy had got worse. In other words approximately 10 per cent of all respondents (144 out of 1,483) had received alternative medication and their epilepsy got worse.

Breakthrough seizures, worsening of their seizure control or worsening of side effects can have a major impact on an individual’s life. A breakthrough seizure can mean the loss of an individual’s driving licence for a year, which can lead to loss of employment. Seizures carry a risk of injury and can, in some cases, be fatal. Side effects of AEDs include cognitive impairment, weight gain or loss, loss of hair or growth of body hair, bone damage, psychiatric disorders and potentially life-threatening rashes.

In a study of AED ‘topiramate’, the risk of head injury or fracture was found to be three times greater following a generic-to-generic switch compared to brand use.\(^1\)

There are no Random Controlled Trials studying the effects of AED switching that we are aware of, largely due to lack of funding and the ethical implications of putting individuals at potential risk of breakthrough seizures. However, numerous reviews and scientific papers have been written on anti-epileptic drug switching, and none that we have read equivocally state that brand switching for anti-epileptic drugs is safe. All caution against brand switching.

The National Institute for Health and Clinical Excellence epilepsies guideline states that changing anti-epileptic drugs is not recommended. In addition, the NHS Choices

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website states that switching AEDs does make a difference and that they should be prescribed by brand to ensure patients receive the same version and preparation each time.

In the Appendix 4 of the consultation response we have included an analysis of the slow-release version of the AED ‘carbamazepine’, prepared for us by a practicing pharmacist. This demonstrates each drug’s differing excipients, and illustrates the variances between different versions of the drug available on the UK market.

**Question 6**

*Do you have any comments on the proposed initial select list in Annex A?*

We are pleased to note that no anti-epileptic drugs are listed in the initial select list in Annex A, for the reasons outlined in previous questions. We hope that the Department of Health has taken notice of the information provided to them by epilepsy professionals and organisations about the potential risks.

**Question 7**

*Do you have any comments on the proposed scope of the arrangements, namely that dispensing by both appliance contractors and dispensing doctors is out of scope?*

We believe that any introduction of generic substitution should apply to all prescribers in primary care, and dispensing doctors should be included in the scheme in the interest of patient safety for people with epilepsy and equality.

This scheme has the ability to improve patient safety for people with epilepsy exempting AEDs from the substitution rules and therefore help ensure a consistent supply of AED brand. This safety net of avoiding generic substitution would not be available to patients of dispensing doctors if they are excluded from the scheme.

It should be noted that patients with epilepsy could experience generic substitution (if introduced and dispensing doctors are exempt) and they occasionally choose to use a pharmacist other than their dispensing doctor’s in-house service.

**Question 8**

*Do you agree with our estimate of the likely benefits and costs? If not, please indicate and provide evidence, where possible, of any areas of disagreement.*

The cost-benefit analysis accompanying the consultation document does not take into account the impact of adding other drugs to the list in the future.

Epilepsy Action feels the cost-benefit analysis would be no longer be correct if AEDs were added to the list of drugs allowable under flexible prescribing.

It is accepted that substitution of named brand AEDs by generics may have an immediate cost saving to the NHS. However we suggest there are potential long term costs from substituting AEDs that have not been taken into account.
It must be noted that the government has not undertaken a full cost-benefit analysis, estimation of possible numbers of patients affected by or calculation of the potential savings from the implementation of generic substitution in relation to anti-epileptic drugs.\(^2\)

Proposed savings could be outweighed by the additional costs of treating and supporting people with epilepsy whose condition has been made worse by AED substitution. No such calculation of costs has been included in the Department of Health’s cost-benefit analysis and it is clear however that any adverse clinical effect on the patient will also have a cost impact, both on the NHS, the individual and society.

Any breakthrough seizure (loss of seizure control in a person previously seizure free for 12 months) will result in:

i. Costs to the NHS from:
   1. Possible A & E admission.
   2. GP consultation – at least one – probably more than one.
   3. Referral to an epilepsy specialist or indeed tertiary centre, (If seizures are not controlled and/or there is diagnostic uncertainty or treatment failure, should be referred to tertiary services soon for further assessment. NICE).

ii. Costs to society from:
   1. Possible loss of productivity at work or school.
   2. Possible loss of employment resulting in higher benefit costs and lower tax revenue.

iii. Costs to the individual from:
   1. Bodily injury
   2. Death
   3. Loss of driving licence
   4. Loss of employment
   5. Missed educational opportunities
   6. Loss (or lowering) of self esteem

Any worsening of seizure control (in a person who is having seizures) will result in:

iv. Costs to the NHS from:
   1. Possible increased A & E admissions.
   2. Possible increased GP consultation – at least one – probably more than one.
   3. Possible referral to an epilepsy specialist or indeed tertiary centre, (If seizures are not controlled and/or there is diagnostic uncertainty or treatment failure, should be referred to tertiary services soon for further assessment. NICE).

v. Costs to society from:
   1. Possible loss of productivity at work or school.

\(^2\) Mike O’Brien MP, Health Minister, House of Commons written answer, 13 July 2009
2. Possible loss of employment resulting in higher benefit costs and lower tax revenue.

vi. Cost to the individual from:
   1. Bodily injury
   2. Death
   3. Loss of employment
   4. Missed educational opportunities
   5. Loss (or lowering) of self esteem

Any worsening of side-effects will result in:

vii. Costs to the NHS from:
   1. Possible increased A & E admissions.
   2. Possible increased GP consultation.
   3. Possible referral to an epilepsy specialist or indeed tertiary centre, (If seizures are not controlled and/or there is diagnostic uncertainty or treatment failure, should be referred to tertiary services soon for further assessment. NICE).

viii. Costs to society from:
   1. Possible loss of productivity at work or school.

ix. Costs to the individual from:
   1. cognitive impairment
   2. weight gain or loss
   3. loss of hair or growth of body hair, bone damage, psychiatric disorders and potentially life-threatening rashes.

If generic substitution of AEDs is at some point introduced, consultants and GPs would have a duty to both inform patients and closely monitor their epilepsy once any switching had taken place. Given the large number of people with epilepsy in the UK, this could lead to hundreds of thousands of additional consultant or GP appointments.

**Question 9**

a) Do you think any of the options present any risks to equality for particular groups of people, people from minority ethnic groups, disabled people, older people, men women and transgender people and people from different faith groups? If so, what are they and what do you think needs to be done to address these risks?

b) Do you think there are opportunities to promote equality in any of the three options? If so, what are these?

Any introduction of generic substitution that does not explicitly exclude AEDs could discriminate against people with epilepsy classed as disabled under the Disability Discrimination Act. This is because successful drug treatments, in other words consistent supply of brand of AED, could not be safeguarded for the future. We would like to see an exclusion for AEDs guaranteed in the secondary legislation when it passes through parliament.
There are vulnerable groups within the epilepsy community for whom generic substitution could disproportionately impact. These include children and young people, people with learning disabilities, women and older adults.

In the UK, 60,000 children under 18 years have epilepsy, as do over 100,000 people over the age of 65. More than one in five people with epilepsy has learning difficulties. To help these special groups, we recommend simple drug regimes to aid concordance. Switching AEDs resulting in different size, shape, colour and possible number of tablets, can cause confusion and affect compliance. This is a particular worry these groups where co-morbidities (and multiple drug therapies) are more likely and understanding may be less.

In addition, if multiple generic substitutions for multiple conditions has occurred, and seizure control is lost, the ineffective drug may be very difficult to identify, and regaining control a difficult task.

Certain formulations are prepared for the benefit of people with epilepsy with different needs, such as liquids or chewable tablets, and concordance on these preparations is vitally important. Generic substitution should not cause a substitution of formulations, and this is a concern.

For people with certain difficult to control epilepsies, there are modified release versions of drugs which carefully balance the bioavailability of a drug in the bloodstream. People who take these versions are in a volatile position as not only is their epilepsy control more precarious, but there is the added concern that their drug could be substituted for a non-modified release version.

For these people with additional needs, changing version of AEDs may bring confusion, worry (a possible trigger for seizures) and practical obstacles to drug adherence. And these issues are of a greater risk to the more vulnerable people with the condition.

We have been told by many of our members that it is important we emphasise that the obligation to monitor this scheme should not be placed on the patient. By this we mean that no individual patient should have to ensure their drug has not been substituted, or to explain why this is important. Epilepsy Action would expect the administration to be carried out and followed up by the Department of Health. From our research we know that not all people with epilepsy are aware of the potential problems. They rely upon the advice and guidance of their prescriber and dispenser when receiving their medication.

We are aware that some people, although a small minority, have been misinformed about the risks of drug switching when they have approached medical professionals (see survey results). It is crucial to remember that some people who take anti-epileptic medication are not able to question medical staff or ‘speak up’ for themselves. They should not experience worse health outcomes as a result.

However, adopting Option 2 with anti-epileptic drugs on an exclusion list has the potential to improve the healthcare of some people with epilepsy. Currently many prescribers and pharmacists are ignorant to the problems that can occur when a
patient switching between versions of an AED. Including AEDs on an exemption list would reinforce the message that consistently receiving the same AED is of clinical importance, and may lead to more secure treatment regimes for large numbers of people with epilepsy. This would be a clear promotion of equality, ensuring that people with epilepsy receive the best available treatment.

**Question 10**

**Do you have any additional comments on any aspect of this consultation?**

Please see the attached document for more information why anti-epileptic drugs should not be substituted.

For people with epilepsy, drug treatments are a key component of their condition management, and many are understandably concerned about any plans which affect this. These concerns have been raised to us and we call on the Department of Health to ensure that after the close of the consultation there is a thorough strategy in place to inform and educate all stakeholders affected by any change, with special consideration given to patients.

Patients should be at the forefront of any policy change, and are kept adequately informed. There should be specific information written for patients, in clear and accessible ways, which address their concerns and tackle any misconceptions which exist.

**Epilepsy Action**

**March 2010.**