The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care (partial update of NICE clinical guideline 20)

Costing statement
Implementing NICE guidance

January 2012
1 Introduction

1.1.1 NICE clinical guideline 137 is an update of the pharmacological recommendations in ‘The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care’ (NICE clinical guideline 20).

1.1.2 Costing work has focused on those recommendations that are new for 2012. A costing statement has been produced because there is uncertainty around current practice for pharmacological treatment of epilepsy and how clinicians will respond to the recommendations. Therefore it has not been possible to predict whether implementation of the new recommendations will have a significant national resource impact. This costing statement highlights recommended drugs that are potentially high cost and may have local resource implications. Organisations should estimate the resource impact locally.

1.1.3 The report ‘Wasted money wasted lives’ published in 2007 by the All Party Parliamentary Group on Epilepsy\(^1\) states that there is evidence of non-implementation of NICE clinical guideline 20. The report says that a much improved service can be delivered at the same time as making significant cost savings.

1.1.4 The report states that there are potential savings from reducing misdiagnosis. Many people are wrongly diagnosed with epilepsy or have been diagnosed with the wrong type of epilepsy, with misdiagnosis rates in England of between 20% and 31%. An unknown number of people also have a missed diagnosis, where they have got epilepsy but it has been diagnosed as something else. The clinical guideline estimates that due to misdiagnosis,

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around 124,500 people without the condition in England alone have a diagnosis of epilepsy and are receiving treatment for it.

1.1.5 The report also states that surgery should be made available to all people with epilepsy for whom it is indicated and that there could be long term savings, as the costs of a lifetime of medical support are far greater than the costs of surgery.

1.1.6 In addition, the report suggests that 70% of the population with epilepsy in the UK could be seizure-free with optimal treatment but that this is achieved for only 52% of people with epilepsy currently. This means that between 65,160 and 74,700 (see paragraph 2.1.1 for prevalence estimates) of those experiencing seizures in England could be seizure-free with optimal treatment. This has potential to result in reduced payments of Disability Living Allowance and improved quality of life for people with epilepsy that remain seizure-free.

1.1.7 Feedback received during development suggests that it is still the case that the original NICE clinical guideline has not been fully implemented. If so there will be an additional resource impact, which will need to be assessed locally. Commissioners are encouraged to assess current practice in line with recommendations in the guideline (NICE has produced a baseline assessment tool for this topic which can be accessed from http://guidance.nice.org.uk.CG137) and liaise with clinicians to predict how practice might change following implementation of the guideline.

1.1.8 Other NICE implementation tools may help organisations review the appropriate diagnosis, management and treatment of epilepsy. These include NICE support for commissioners using the quality standards for the epilepsies in adults and the epilepsies in children and young people, the epilepsies in adults commissioning and
budgeting tool and the epilepsies in children and young people commissioning and budgeting tool.

1.1.9 In addition to responding to the updated pharmacological recommendations, reviewing the original guidance and improving diagnosis may free up some resources to be redirected to the more expensive pharmacological management.

2 Background

2.1.1 Epilepsy has been estimated to affect between 362,000 and 415,000 people in England. In addition, there will be a further 124,500 people who have been diagnosed with epilepsy, but in whom the diagnosis is incorrect. There may be around 60,000 children in the UK with epilepsy. Incidence is estimated to be 50 per 100,000 per year and the prevalence of active epilepsy in the UK is estimated to be 5–10 cases per 1000. ‘The epilepsies’ (NICE clinical guideline 20) stated that the annual estimated cost of established epilepsies was £2 billion (direct and indirect costs).

3 Recommended drugs that may have a cost impact locally

3.1 First-line treatment in children, young people and adults with prolonged or repeated seizures

Recommendations

3.1.1 Only prescribe buccal midazolam or rectal diazepam\(^2\) for use in the community for children, young people and adults who have had a previous episode of prolonged or serial convulsive seizures.

[Recommendation 1.14.1.2]

\(^2\) At the time of publication (January 2012), this drug did not have UK marketing authorisation for this indication and/or population (see appendix E of the NICE guideline for details). Informed consent should be obtained and documented in line with normal standards in emergency care.
3.1.2 Administer buccal midazolam as first-line treatment in children, young people and adults with prolonged or repeated seizures in the community. Administer rectal diazepam\(^2\) if preferred or if buccal midazolam is not available. If intravenous access is already established and resuscitation facilities are available, administer intravenous lorazepam. [Recommendation 1.14.1.3]

Potential cost impact

3.1.3 According to clinical opinion, rectal diazepam is currently widely used for adults, with buccal midazolam being used more often for children because it is more socially acceptable. A form of buccal midazolam (ViroPharma Limited, Buccolam) has recently been licensed for children. It is likely that buccal midazolam will be used more widely after publication of the guideline.

3.1.4 Table 1 shows the estimated cost of each drug per administration.

**Table 1 Estimated drug cost per administration**

<table>
<thead>
<tr>
<th></th>
<th>Midazolam (ViroPharma Limited, Buccolam)(^a)</th>
<th>Midazolam (Epistatus, Special Products Limited)(^b)</th>
<th>Rectal diazepam(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated drug cost per adult or child over 12 years (£)(^d)</td>
<td>20.50</td>
<td>24.38</td>
<td>2.98</td>
</tr>
<tr>
<td>VAT at 20% (£)</td>
<td>4.10</td>
<td>4.88</td>
<td>0.60</td>
</tr>
<tr>
<td>Total cost (£)</td>
<td>24.60</td>
<td>29.25</td>
<td>3.58</td>
</tr>
</tbody>
</table>

\(^a\) According to the manufacturer, the hospital price of four pre-filled syringes of Buccolam is £73.50 for 2.5 mg doses, £76.50 for 5 mg doses, £80 for 7.5 mg doses and £82 for 10 mg doses.

\(^b\) According to the electronic drugs tariff (November 2011), the cost of Epistatus is £97.51 for 5 ml (10 mg/ml). This is sufficient to deliver 4 x 1 ml doses. There is a fee for sourcing unlicensed specials, this is currently £20.

\(^c\) According to the British national formulary (edition 62), the net price for Rectal tubes (rectal solution) is: £0.90 for a 1.25 ml (2.5 mg) tube, £1.27 for a 2.5 ml (5 mg) tube, and £1.71 for a 2.5 ml (10 mg) tube.

\(^d\) The dosages have been taken from the British national formulary (edition 62). Midazolam by buccal administration for adults and children over 10 years is 10 mg. Rectal diazepam is 10–20 mg for adults and children over 12 years (assumed to be 15mg).
3.1.5 Expert opinion is that approximately 5% of people with epilepsy may have prolonged seizures on a regular basis, which could equate to approximately 19,500 people in England. Exploring assumptions about the switch between medicines, the proportion of people who change and the average number of administrations in a simple sensitivity analysis\(^3\) resulted in a national cost impact of between £5838 and £9,839,232. The range of costs is shown in table 2.

### Table 2 Simple sensitivity analysis

<table>
<thead>
<tr>
<th>Change in drug</th>
<th>Number of administrations per person per year</th>
<th>Proportion of people that change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>25%</td>
</tr>
<tr>
<td>Person changes from Epistatus to Buccolam</td>
<td>1</td>
<td>£5,838</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>£35,030</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>£70,060</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>£140,119</td>
</tr>
<tr>
<td>Person changes from rectal diazepam to Epistatus</td>
<td>1</td>
<td>£96,654</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>£579,922</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>£1,159,844</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>£2,319,689</td>
</tr>
<tr>
<td>Person changes from rectal diazepam to Buccolam</td>
<td>1</td>
<td>£102,492</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>£614,952</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>£1,229,904</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>£2,459,808</td>
</tr>
</tbody>
</table>

3.1.6 The use of buccal midazolam should be limited to people who have had a previous episode of prolonged or repeated seizures because the drug can be costly. Targeting its usage in the community to those people who have a known risk of prolonged or repeated convulsive seizures has the potential to save NHS resources.

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\(^3\) It was assumed that 25–100% of people who experience prolonged seizures on a regular basis change drug, that they all change from rectal diazepam to Epistatus, from rectal diazepam to Buccolam and from Epistatus to Buccolam; and that there are 1–24 administrations per person per year.
3.2 *Ethosuximide*

**Recommendations**

3.2.1 Offer ethosuximide or sodium valproate as first-line treatment to children, young people and adults with absence seizures.....

[Recommendation 1.9.5.1]

3.2.2 If two first-line anti-epileptic drugs (AEDs)... are ineffective in children, young people and adults with absence seizures, consider a combination of two of these three AEDs as adjunctive treatment: ethosuximide, lamotrigine⁴ or sodium valproate..... [Recommendation 1.9.5.3]

3.2.3 Offer ethosuximide or sodium valproate as first-line treatment to children, young people and adults with absence syndromes.... [Recommendation 1.9.15.1]

3.2.4 If two first-line AEDs .... are ineffective in children, young people and adults with absence epilepsy syndromes, consider a combination of two of these three AEDs as adjunctive treatment: ethosuximide, lamotrigine⁴ or sodium valproate..... [Recommendation 1.9.15.3]

**Potential cost impact**

3.2.5 Ethosuximide comes in two different forms: syrup and tablet. Commissioners and providers should be aware that the tablet form of ethosuximide is more expensive (at £0.27 per mg) than the syrup form (which is normally prescribed by doctors at £0.04 per mg), and a switch to tablets would have a cost impact⁵.

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⁴ At the time of publication (January 2012), this drug did not have UK marketing authorisation for this indication and/or population (see appendix E of the NICE guideline for details). Informed consent should be obtained and documented in line with normal standards in emergency care.

⁵ Capsules, ethosuximide 250 mg, net price 56-cap pack = £38.23. Zarontin, ethosuximide oral solution, 250 mg/5 ml, net price 200 ml pack = £4.22. (Costs taken from the Electronic drugs tariff, November 2011).
3.3 Adjunctive first-line treatment for children, young people and adults with Dravet syndrome

Recommendation

3.3.1 Discuss with a tertiary epilepsy specialist if first-line treatments... in children, young people and adults with Dravet syndrome are ineffective or not tolerated, and consider clobazam\(^6\) or stiripentol as adjunctive treatment. [Recommendation 1.9.9.3]

Potential cost impact

3.3.2 The precise prevalence of genetically-proven Dravet syndrome is not known, however it is estimated to be only a small number of people. It is considered that stiripentol is already part of current practice in some areas.

3.3.3 Stiripentol is an expensive drug and commissioners may want to ensure that it is only prescribed in line with NICE guidance. It is difficult to give an average cost because this drug can be administered from the age of 3 and the recommended dosage depends on weight. For a 3-year-old child weighing 16.5 kg, the daily drug cost would be £13.56 or £4948 per year. Whereas, the daily drug cost for an adult weighing 70 kg would be £57.52 or £20,994 per year\(^7\). Clobazam is estimated to cost £267 per year for a child and £534 per year for an adult\(^8\).

\(^6\) At the time of publication (January 2012), this drug did not have UK marketing authorisation for this indication and/or population (see appendix E of the NICE guideline for details). Informed consent should be obtained and documented in line with normal standards in emergency care.

\(^7\) The recommended dosage and the cost of stiripentol have been taken from the British national formulary for children 2011/12.

\(^8\) Based on a daily dose of 12.5 mg for a child and 25 mg for an adult (The British National Formulary 62). The cost of clobazam has been taken from the Electronic Drugs Tariff (December 2011).
3.4 **Levetiracetam**

**Recommendation**

3.3.4 Levetiracetam is not cost effective at June 2011 unit costs\(^9\). Offer levetiracetam\(^10\), oxcarbazepine\(^10\) or sodium valproate (provided the acquisition cost of levetiracetam falls to at least 50% of June 2011 value documented in the National Health Service Drug Tariff for England and Wales) if carbamazepine and lamotrigine are unsuitable or not tolerated. If the first AED tried is ineffective, offer an alternative from these five AEDs... [Recommendations 1.9.3.2 and 1.9.11.3]

**Potential cost impact**

3.3.5 NICE clinical guideline 20 recommended levetiracetam as an option for treating epilepsy if older AEDs were not suitable. The updated guideline states that levetiracetam is not cost effective at June 2011 unit costs for first-line treatment in the patient groups specified. It states that levetiracetam should only be offered if its acquisition cost falls to at least 50% of June 2011 value. The manufacturer of levetiracetam made us aware that the drug has been made available to pharmacies at a discounted cost. Commissioners should check current prices locally. There are potential savings if the drug is used as part of current practice at a price that is not cost effective.

4 **Conclusion**

4.1.1 Because there is uncertainty around current practice and how clinicians will respond to the recommendations it has not been possible to predict whether the partial update of NICE clinical guideline 20 will have a significant national resource impact.

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\(^9\) Estimated cost of a typical average daily dose of 1500 mg was £2.74 at June 2011. Cost taken from the National Health Service Drug Tariff for England and Wales, available at [http://www.ppa.org.uk/ppa/edt_intro.htm](http://www.ppa.org.uk/ppa/edt_intro.htm)

\(^10\) At the time of publication (January 2012), levetiracetam and, oxcarbazepine did not have UK marketing authorisation for first-line treatment in children and young people with benign epilepsy with centromental spikes, Panayiotopoulos syndrome or late-onset childhood occipital epilepsy (Gastaut type). See appendix E of the NICE guideline for details. Informed consent should be obtained and documented in line with normal standards in emergency care.
4.1.2 The report ‘Wasted money wasted lives’ published in 2007 by the All Party Parliamentary Group on Epilepsy states that there is evidence of non-implementation of NICE clinical guideline 20. The report states that there are potential savings through reducing misdiagnosis, making surgery available to all people with epilepsy for whom it is indicated and increasing the number of people who are seizure-free with optimal treatment. Feedback received during development suggests that the original NICE clinical guideline has still not been fully implemented.

4.1.3 Organisations should estimate the resource impact locally. Local commissioners are encouraged to talk to providers to establish current practice and how this might change after publication of the guideline. Revisiting the original NICE recommendations and improving the diagnosis of people with epilepsy may release some resources that can be invested in prescribing in line with the latest recommendations.