

LMMG New Medicine Assessment

Eslicarbazepine acetate (Zebinix[®])

For adjunctive therapy in adults with partial-onset seizures with or without secondary generalisation

Recommendation: Amber 0

Eslicarbazepine acetate is recommended for adjunctive therapy in adults with focal (partial onset) seizures with or without secondary generalisation, only for highly refractory patients in whom standard adjunctive treatment is ineffective or not tolerated.

Treatment should only be considered following referral to or discussion with a tertiary care specialist.

This recommendation covers adults and children, as per NICE CG 137. However, it should be noted that at the time of publication eslicarbazepine acetate did not have UK marketing authorisation for children. Informed consent should be obtained and documented.

Summary of supporting evidence:

- Three pivotal phase III RCTs demonstrate the effectiveness of eslicarbazepine acetate against placebo when administered as adjunctive therapy for adults with partial onset seizures with or without secondary generalisation.
- 3%, 3.8%, 8% and 2% were seizure free during the maintenance dose period for the eslicarbazepine acetate 400 mg, 800 mg, 1200 mg and placebo groups respectively.
- The achievement of a response rate of at least 50% reduction in seizure frequency is considered to be clinically relevant; an integrated analysis showed response rates of 23%, 36% (NNT 8), 44% (NNT 5) and 22% for the doses 400 mg, 800 mg, 1200 mg and placebo respectively.
- The 400 mg dose of eslicarbazepine acetate was not significantly more effective against placebo in any of the trials.
- The trials were of short duration (12 weeks maintenance dose) and the one year extension studies did not measure effectiveness as the primary outcome.
- NICE Clinical Guideline 137 on the management of epilepsy recommends eslicarbazepine acetate for adjunctive therapy in adults with partial onset seizures with or without secondary generalisation.
- The AWMSG and SMC recommend eslicarbazepine acetate for highly refractory partial onset seizures for adults who remain uncontrolled with existing AEDs.
- There are no head to head trials comparing eslicarbazepine acetate to other AEDs used in the management of focal seizures to able to recommend it ahead of other therapies as adjunctive treatment for highly resistant focal seizures.
- In a pooled analysis it was found in the double blind phases of the phase III studies that the incidence of treatment emergent adverse events (AEs) increased with increasing doses of eslicarbazepine acetate 400 mg, 800 mg and 1200 mg; 60.7%, 62.7% and 67.5% respectively, with 46.4% in the placebo group.
- It is anticipated that eslicarbazepine acetate will be an alternative option to other AEDs already being prescribed across the locality and so should not exert an additional a cost pressure. Using the NICE costing template and numbers suggested by the requesting clinician it is expected that the approximate spend on eslicarbazepine acetate would be £397,000 per annum.

Details of Review

Name of medicine (generic & brand name): Eslicarbazepine acetate (Zebinix®)
Strength(s) and form(s): 800 mg tablets
Dose and administration: Added to existing anticonvulsant therapy. The recommended starting dose is 400 mg once daily which should be increased to 800 mg once daily after one or two weeks. Based on individual response, the dose may be increased to 1200 mg once daily. ¹
BNF therapeutic class / mode of action 4.8.1 Control of the epilepsies ²
Licensed indication(s): As adjunctive therapy in adults with partial-onset seizures with or without secondary generalisation ¹
Proposed use (if different from, or in addition to, licensed indication above): As per licence
Course and cost: Long term; 30 x 800 mg tablets; £136.00* *Cost based on MIMS list price – Accessed 30/10/14
Current standard of care/comparator therapies: As per NICE clinical guideline 137: <ol style="list-style-type: none">1) Adjunctive treatment in children, young people and adults with refractory focal seizures as per below and;2) Adjunctive treatment in children and young people with benign epilepsy with centrotemporal spikes, Panayiotopoulos syndrome or late-onset childhood occipital epilepsy (Gastaut type) as per below; If adjunctive treatment is ineffective or not tolerated, discuss with, or refer to, a tertiary epilepsy specialist. Other AEDs that may be considered by the tertiary epilepsy specialist are eslicarbazepine acetate, lacosamide, phenobarbital, phenytoin, pregabalin, tiagabine, vigabatrin and zonisamide. Carefully consider the risk–benefit ratio when using vigabatrin because of the risk of an irreversible effect on visual fields. ³
Relevant NICE guidance: NICE Clinical Guideline 137; The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care (as above). ³

Background and context

Epilepsy is a common neurological condition characterised by recurring seizures. It is estimated to have an incidence of 50 per 100,000 per year in the UK, with a prevalence of active epilepsy of 5 -10 per 1000. Approximately two thirds of people with active epilepsy are satisfactorily controlled with anti-epileptic drugs (AEDs).³

The National Institute for Health and Care Excellence (NICE) has published guidelines “The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care” in January 2012, which were modified in December 2013. These guidelines recommend that AEDs should be initiated in adults on the recommendation of a specialist and in children and young people should be initiated by the specialist. The AEDs should only be started once the diagnosis of epilepsy has been confirmed and generally after the second epileptic seizure. The AED drug should be chosen based on the epilepsy syndrome. The seizure type(s) and epilepsy syndrome, aetiology and co-morbidity should be determined, because failure to classify the epilepsy syndrome correctly can lead to ineffective treatment and persistence of seizures.³

Focal seizures are defined as a seizure that originates within networks limited to one hemisphere, discretely localised or more widely distributed. The term focal seizure has replaced the terms partial seizure and localisation-related seizure.³

It is recommended that **focal seizures** are managed first line with carbamazepine or lamotrigine. If these are unsuitable or not tolerated then levetiracetam, oxcarbazepine or sodium valproate can be considered. If the first AED is not effective an alternative from these five should be chosen. Consider adjunctive treatment with carbamazepine, clobazam, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, sodium valproate or topiramate if a second well-tolerated AED is ineffective. If the adjunctive treatment is ineffective or not tolerated it is recommended that there is a discussion with or referral to a tertiary epilepsy specialist. The additional AEDs which may be considered by the tertiary specialists are **eslicarbazepine acetate**, lacosamide, phenobarbital, phenytoin, pregabalin, tiagabine, vigabatrin and zonisamide.³

Eslicarbazepine acetate is rapidly and extensively metabolised to eslicarbazepine, it is a dibenzazepine AED in the same pharmacological class as carbamazepine and oxcarbazepine. Eslicarbazepine is the active metabolite of oxcarbazepine. Eslicarbazepine acetate works by blocking voltage gated sodium channels, subsequently leading to a decrease in repetitive neuronal firing.⁵

Across the Lancashire Health Economy eslicarbazepine acetate has differing RAG ratings. The purpose of this review is to assess the evidence for eslicarbazepine acetate in the requested indication (adjunctive therapy in adults with partial-onset seizures with or without secondary generalisation) and to recommend a RAG status for adoption across the Lancashire Health Economy.

NICE recommends eslicarbazepine acetate for other epilepsy syndromes, however, the new medicine application has only requested use in partial seizures with or without secondary generalisation, which is within its licensed indication, and therefore other uses have not been discussed further in this review.

The Scottish Medicines Consortium [8th October 2010] has also reviewed the use of eslicarbazepine acetate as adjunctive therapy in adults with partial onset seizures with or without secondary generalisation. Its use was recommended for this indication but was restricted to those patients with highly refractory epilepsy who have been heavily pre-treated and remain uncontrolled with existing AEDs.⁴

The All Wales Medicines Strategy Group [October 2012] recommends eslicarbazepine acetate is restricted to the treatment of highly refractory patients who remain uncontrolled with, or are intolerant to, other antiepileptic medicine combinations, within its licensed indication as adjunctive therapy in adults with partial-onset seizures, with or without secondary generalisation.⁵

The Cochrane Collaboration reviewed eslicarbazepine acetate as add-on for drug-resistant partial epilepsy in December 2011 and summarised that both the 800 mg and 1200 mg strengths of eslicarbazepine acetate taken once daily can significantly reduce seizure frequency in adults with treatment-resistant partial epilepsy, in the short term. For the patients entered into the trials, approximately 7 patients needed to be treated with eslicarbazepine for every additional patient with a 50% or greater reduction in seizure frequency when compared to placebo. Dizziness, nausea and diplopia were significant adverse effects. [see appendix 1 for the summary produced by the Cochrane review]⁶

Summary of evidence

Summary of efficacy data in proposed use:

There are three pivotal phase III RCTs which recruited adults experiencing simple or complex partial seizures with or without secondary generalisation for at least 12 months who had at least four seizures per four week period, despite treatment with one or two AEDs. One of the studies allowed treatment with up to three AEDs. The 8 week baseline period was single-blind placebo-controlled in the first study and observational in the other two studies and subject to them having at least 4 seizures per four week period with no seizure-free interval of more than 21 days patients were then randomised equally in a double blind fashion to eslicarbazepine acetate or placebo. Following a two week dose titration phase the patients received 12 weeks of eslicarbazepine acetate 400 mg, 800 mg or 1200 mg daily (one of the studies did not include the 400 mg daily dose). Following 12 weeks of maintenance treatment patients could enter a one year open-label extension study.

The primary outcome was four-week seizure frequency during the 12 week maintenance period in the intention to treat (ITT) population compared to placebo for each treatment arm by analysis of covariance (ANCOVA) that modelled seizure frequency as a function of baseline seizure frequency and treatment. The ITT population were all patients who received at least one dose of the study drug and at least one post baseline seizure frequency assessment.⁴

ANCOVA derived LS (least square) means (95% confidence intervals) seizure frequency per 28 days during 12 week maintenance within ITT population^{4,7,8,9}

Study	Placebo	ESL 400 mg	ESL 800 mg	ESL 1200 mg
A	N=102	N=99	N=98	N=98
(Elger 2009)	7.6 (6.8-8.6)	6.7 (6.0-7.7)	5.7 (5.0- 6.5)*	5.4 (4.6-6.1)*
B	N=100	N=96	N=100	N=97
(Ben-Menachem 2010)	9.8 (8.7-11.1)	8.7 (7.7-9.9)	7.1 (6.2-8.2)*	7.0 (6.0-8.1)*
C	N=84	-	N=84	N=77
(Gil Nagel 2009)	7.3 (6.3-8.5)	-	5.7 (4.9-6.7)**	5.5 (4.6-6.5)*

ESL = eslicarbazepine acetate, *significant difference versus placebo, **p=0.048 versus placebo

Secondary Outcomes

The achievement of seizure freedom or at least 50% reduction in seizure frequency are considered to be the most clinically relevant outcomes.³

Secondary efficacy results for eslicarbazepine acetate over the 12 week maintenance period:^{5,7,8,9}

Treatment regimen	Eslicarbazepine acetate			
	Placebo	400 mg	800 mg	1,200 mg
Study A				
Major secondary endpoints				
Median relative reduction in standardised seizure frequency (%)	-16.4	-25.8	-36.1 p < 0.01	-45.3 p < 0.001
Patients with a ≥ 50% decrease in seizure frequency (%)	19.6	23.2	33.7 p < 0.05	42.9 p < 0.001
Patients with seizure freedom (%)	2.0	2.0	4.1	8.2
Study B				
Major secondary endpoints				
Median relative reduction in standardised seizure frequency (%)	-5.0	-20.9	-32.6 p < 0.01	-32.9 p < 0.001
Patients with a ≥ 50% decrease in seizure frequency (%)	18.0	19.8	32.0 p < 0.01	35.1 p < 0.001
Patients with seizure freedom (%)	2.0	1.0	3.0	5.2
Study C				
Major secondary endpoints				
Median relative reduction in standardised seizure frequency ()	-17.0	-	-37.9 p < 0.05	-41.9 p < 0.05
Patients with a ≥ 50% decrease in seizure frequency (%)	22.6	-	34.5	37.7 P < 0.05
Patients with seizure freedom (%)	1.2	-	4.8	3.9

Compared to placebo the proportion of patients experiencing a response (reduction of at least 50% in seizure frequency during the 12 week maintenance period compared with baseline) was significantly greater with eslicarbazepine acetate 1200 mg in all three studies and for 800 mg only in studies A and B. For the 400 mg dose there was no significant difference in any of the studies compared to placebo. An integrated analysis showed 50% responder rates of 23%, 36%, 44% and 22% for the doses 400 mg, 800 mg, 1200 mg and placebo respectively. 3%, 3.8%, 8% and 2% were seizure free during the maintenance dose period for the 400 mg, 800 mg, 1200 mg and placebo groups respectively.^{4,7,8,9,10}

857 patients completed the phase III studies and 97% of these entered an open label extension. 73% of these completed one year of treatment with eslicarbazepine acetate (median dose of 800 mg). In the ITT, mean relative reductions from baseline in seizure frequency during weeks 41 to 52 were; 41%, 39% and 58% for studies A, B and C respectively.^{4,11,12,13}

NICE recommended eslicarbazepine acetate based on the trial data above, they summarised that significantly more participants on eslicarbazepine acetate adjunctive therapy than placebo experienced at least 50% reduction in seizure frequency and that significantly more participants on eslicarbazepine acetate adjunctive therapy than placebo experienced seizure freedom, but stated the quality of the evidence was low. It should be noted that for all drugs recommended at this stage in the management of epilepsy treatment pathway that the overall quality of evidence was low and that most studies had unclear or no details of randomisation, allocation, concealment or blinding and higher drop out in the treatment arms.³

NICE considered that eslicarbazepine acetate showed efficacy but did not include it (and other newer drugs) in their first line adjunctive recommendations as there was less long term evidence for its efficacy and cost effectiveness for adjunctive treatment.³

The SMC summarised that eslicarbazepine acetate reduced seizure frequency compared to placebo over a 12 week maintenance period. Direct comparative data versus other AEDs are unavailable, particularly comparisons with other cheaper agents with a very similar mode of action.⁴

Summary of safety data:

In a pooled analysis of the double blind phases of the phase III studies, the incidence of treatment emergent adverse events (AEs) increased with increasing doses of eslicarbazepine acetate 400 mg, 800 mg and 1200 mg; 60.7%, 62.7% and 67.5% respectively, with 46.4% in the placebo group. This increasing incidence with increasing dose was also found for the discontinuation of the study drug due to AEs; 8.7%, 11.6%, 19.3% for the 400 mg, 800 mg and 1200 mg doses, and 4.5% for placebo. The percentage of patients discontinuing treatment increasing noticeably with an increasing dose of eslicarbazepine acetate, most discontinuations were due to unacceptable AEs.^{4,7}

The most common treatment emergent AEs were dizziness, headache, nausea and somnolence. There were 3.7% serious AEs in the eslicarbazepine acetate group (all doses) compared to 1.4% for placebo.^{5,8,9,10}

The EMA commented that although there were no direct comparative data the general profile of at least possibly related treatment emergent AEs appears similar to oxcarbazepine and some

appear to occur less frequently compared to the known frequencies with oxcarbazepine e.g. headache, diplopia, nausea and vomiting. However, active comparator studies would be needed for results to be conclusive.^{4,7}

Strengths and limitations of the evidence:

There are no head to head trials comparing eslicarbazepine acetate to other AEDs used in the management of focal seizures to able to recommend it ahead of other therapies.

In the integrated analysis and the three phase III trials those patients who discontinued treatment prematurely during one of the treatment periods were still categorised as treatment responders for that period if their seizure frequency was reduced by 50% or more before discontinuation. Supplementary analysis in which patients who discontinued were regarded as non-responders were consistent with the original analyses.⁴

The EMA noted that the frequency and character of the major protocol violations of study C raised doubts about the reliability of the study results. However, when it was excluded from the integrated analysis the outcomes were not significantly different from the overall integrated analysis.^{4,7}

Although the request wishes to position eslicarbazepine acetate for use in patients who have failed to respond to numerous AEDs it should be noted that the available efficacy data are derived from studies in which some patients may have only received one previous AED. The information on patients' lifetime previous AED use was not recorded in these studies, therefore it is not possible to estimate efficacy within the subgroup of patients who have failed to respond to numerous AEDs.⁴

In the phase III studies of those who were randomised to treatment with eslicarbazepine acetate, 58% of them were already taking carbamazepine (which is within the same pharmacological class). A post hoc analysis of the pooled data revealed that similar efficacy results were observed for those who were on both carbamazepine and eslicarbazepine acetate compared to the overall study population.⁴

In the open label one year extension studies efficacy was only a secondary endpoint. The main primary and secondary efficacy results were collected over a 12 week duration.⁵

Summary of evidence on cost effectiveness:

NICE stated in the economic analysis undertaken for the epilepsy guidelines that eslicarbazepine acetate, lacosamide, pregabalin, tiagabine and zonisamide were all more costly and less effective than the other cost effective treatment alternatives. They concluded that these preparations should not be recommended among initial adjunctive therapy options. Rather these drugs should only be considered for cases where previously recommended drugs are contraindicated or have been tried and were either ineffective or not tolerated.

The results of the cost effectiveness analysis undertaken for the guidelines showed that the addition of eslicarbazepine acetate was associated with increased costs and better health outcomes (higher QALYs) than continuation of existing therapy alone (placebo), but with an

expected incremental cost effectiveness ratio (ICER) of £53,585 per QALY which exceeds the NICE willingness to pay threshold. Note when all relevant comparators were evaluated together with the NCGC analysis, adjunctive eslicarbazepine acetate was dominated by adjunctive levetiracetam, oxcarbazepine, pregabalin and topiramate. The conclusion was consistent across a range of sensitivity analyses (directly applicable and minor limitations). The ICER per QALY gained for lacosamide and zonisamide were £66,256 and £68,397 respectively.³

Prescribing and risk management issues:

A MHRA safety alert was issued in December 2012 for: Carbamazepine, oxcarbazepine and eslicarbazepine: The risk of serious skin-related adverse drug reactions, including Stevens-Johnson syndrome, occurring with carbamazepine may be increased in the presence of the HLA-A*3101 allele in patients of European descent or Japanese origin. However, there are currently insufficient data to support screening for this allele before starting carbamazepine treatment. Patients of European descent or Japanese origin who are known to be positive for this allele should only receive carbamazepine, oxcarbazepine or eslicarbazepine after careful consideration of the benefits and risks. See link <http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON214944>

Commissioning considerations:

Comparative unit costs: Based on NICE recommended place in therapy comparators.

Drug	Example regimen Usual maintenance dose for adjunctive therapy	Pack cost	Cost per patient per course/ per year (ex VAT)
Eslicarbazepine acetate	800 mg daily	800 mg x £136.00/30	£1,655*
Lacosamide	100 mg twice daily	100 mg x £86.50/56	£1,128^
Phenobarbital	60 -180 mg daily	60 mg x £7.44/28	£97 - £290^
Phenytoin	200 – 500 mg	100 mg x £54.00/84	£469 -£1,173^
Tiagabine	15 – 45 mg daily	15 mg x £156.13/100	£570 - £1,710*
Zonisamide	300 – 500 mg daily	100 mg x £62.72/56	£1,226 - £2,044^
Retigabine	600 – 1200 mg daily	400 mg x £127.68/84	£832 - £1,664*

*Costs based on MIMS online accessed 30th October 2014

^Costs based on Drug Tariff October 2014

This table does not imply therapeutic equivalence of drugs or doses.

Associated additional costs or available discounts:

None

Productivity, service delivery, implementation:

Patients would have to be referred to a tertiary specialist for initiation/recommendation. This service should already be in place as per NICE CG 137. It is anticipated that there would be no impact on service delivery.

Anticipated patient numbers and net budget impact:

NICE stated that there are 40,235,268 people in England and that 321,882 (0.8%) of these suffer from epilepsy. The number of people with a diagnosis of partial onset epilepsy with or without secondary generalisation is 167,379 (52%). 50,214 (30%) will have epilepsy considered to be refractory to treatment with anti-epileptic drug monotherapy and who are using adjunctive or combination therapy. Of the 50,214 people in England whose epilepsy is considered refractory to treatment with AED monotherapy and who are using adjunctive or combination therapy, a proportion may switch treatment from existing second-line therapies to eslicarbazepine acetate because they have not provided an adequate response or have not been tolerated. The proportion of people who may switch treatment is unknown. Eslicarbazepine acetate is recommended as an alternative treatment option to other AEDs, lacosamide, pregabalin, tiagabine and zonisamide and more recently retigabine.¹⁴

Applying NICE's estimates to the Lancashire Health Economy of the 1,500,000 people, 12,000 will suffer from epilepsy, 6,240 will have a diagnosis of partial onset epilepsy with or without secondary generalisation and 1,872 of these will have epilepsy considered to be refractory to treatment with antiepileptic drug monotherapy and who are using adjunctive and combination therapy. The submitting clinicians have stated that not all patients would be seen by them and estimate that 2% of all cases of epilepsy would be considered for eslicarbazepine. This would equate to 240 people, at an annual cost of £397,000.

The expenditure in primary care on eslicarbazepine acetate over the last 12 months across the Lancashire Health Economy was £33,929.

Innovation, need, equity:

There is currently inequity of access across the Health Economy, some areas have approved the use of eslicarbazepine acetate and others have not.

References

1. Summary Product Characteristics. Zebinix 800 mg tablets. Updated 28 May 2014. Available at: <http://www.medicines.org.uk/emc/medicine/22376>. Accessed 13th October 2014.
2. Joint Formulary Committee. British National Formulary. 68th ed. London: British Medical Association and Royal Pharmaceutical Society of Great Britain; September 2014.
3. National Institute for Health and Care Excellence. Clinical Guideline 137. The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care. Jan 2012 (modified Dec 2013). Available at: <http://guidance.nice.org.uk/CG137>. Accessed October 2014.
4. Scottish Medicines Consortium. Eslicarbazepine acetate 800 mg tablet (Zebinix). SMC No. 592/09. 8 October 2010 (resubmission) https://www.scottishmedicines.org.uk/files/advice/eslicarbazepine_Zebinix_RESUBMISSION_FINAL_October_2010.doc_for_website.pdf. Accessed October 2014.
5. All Wales Medicines Strategy Group. Final Appraisal Recommendation: Eslicarbazepine acetate (Zebinix[®]) 800 mg tablets. Advice number: 3512. October 2012. Available at: <http://www.awmsg.org/awmsgonline/app/sitesearch.jsessionid=ce37081deefb83f4ca948dfef769?execution=e1s1>. Accessed October 2014.
6. Chang XC, Yuan H, Wang Y, Xu HQ, Zheng RY on behalf of the Cochrane Collaboration. Eslicarbazepine acetate add-on for drug-resistant partial epilepsy (Review). The Cochrane Library; 7 Dec 2011. Available at: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008907.pub2/pdf>. Accessed October 2014.
7. European Medicines Agency. Assessment Report for eslicarbazepine acetate. Procedure No.: EMEA/H/C/000988. Feb 2009. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/000988/WC500047229.pdf. Accessed October 2014.
8. Gil-Nagel A, Lopes-Lima J, Almeida L et al. Efficacy and safety of 800 and 1200 mg eslicarbazepine acetate as adjunctive treatment in adults with refractory partial-onset seizures. *Acta Neurol Scand* 2009; 120 (5): 281-7.
9. Ben-Menachem E, Gabbai AA, Hufnagel A et al. Eslicarbazepine acetate as adjunctive therapy in adult patients with partial epilepsy. *Epilepsy Res* 2010; 89 (2-3): 278-85.
10. Elger C, Halasz P, Maia J. et al. Efficacy and safety of eslicarbazepine acetate as adjunctive treatment in adults with refractory partial-onset seizures: a randomized, double-blind, placebo-controlled, parallel-group phase III study. *Epilepsia* 2009; 50 (3): 454-63.
11. Lopes-Lima J, Gil-Nagel A, Maia J et al. Long-term treatment of partial epilepsy with eslicarbazepine acetate (ESL): results of a one-year open-label extension of study BIA-2093-303. 2010.
12. Gabbai AA, Ben-Menachem E, Maia J et al. Long-term treatment of partial epilepsy with eslicarbazepine acetate (ESL): results of a one-year open-label extension of study BIA-2093-302. 2010.

13. Halasz P, Cramer JA, Hodoba D et al. Long-term efficacy and safety of eslicarbazepine acetate: results of a 1-year open-label extension study in partial-onset seizures in adults with epilepsy. *Epilepsia* 2010; 51 (10): 1963-9.
14. National Institute of Health and Care Excellence. Costing statement: Retigabine for the adjunctive treatment of partial onset seizures in epilepsy (TA232). Available at: <http://www.nice.org.uk/guidance/ta232/resources/ta232-epilepsy-partial-retigabine-adjutant-costing-statement2>. Accessed October 2014.

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