# Integrated Impact Assessment Report for Clinical Commissioning Policies

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| **Policy Reference Number** | D04X01 | | |
| **Policy Title** | Amifampridine phosphate for Lambert Eaton Myasthenic Syndrome | | |
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## Section K - Activity Impact

| **Theme** | **Questions** | **Comments** (Include source of information and details of assumptions made and any issues with the data) |
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| K1 Current Patient Population & Demography / Growth | K 1.1 What is the prevalence of the disease/condition? | K1.1 This policy recommends **not routinely commissioning** amifampridine phosphate for patients with Lambert-Eaton myasthenic syndrome.<br><br>Lambert-Eaton myasthenic syndrome (LEMS) is a rare condition with an estimated prevalence of between 2.3[i] and 3.4[ii] per million of the population.[iii] There are therefore estimated to be between 125 and 185 people in England with LEMS in 2014/15.[iv] |
| | K.1.2 What is the number of patients currently eligible for the | K1.2 Amifampridine phosphate aims to improve neuromuscular |

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| | treatment under the proposed policy? | transmission in patients with LEMS by stimulating greater release of acetylcholine. This is a first line treatment that aims to manage the symptoms of LEMS and therefore the entire prevalent population (c. 125 to 185 patients in 2014/15) could be eligible for the treatment.[v] |
| | K1.3 What age group is the treatment indicated for? | K1.3 The treatment is indicated for adults aged 16 years and older.[vi] |
| | K1.4 Describe the age distribution of the patient population taking up treatment? | K1.4 Most patients present with LEMS after the age of 40. It can, however, present at any age, although patients usually present in adulthood. [vii]<br>The mean age of onset was found to be 60 years, with an initial peak in onset at age 35 years and the second peak at 60 years.[viii] |
| | K1.5 What is the current activity associated with currently routinely commissioned care for this group? | K1.5 In 2014/15 around five patients requested **amifampridine phosphate** through an individual funding request (IFR);[ix] however the number of those receiving amifampridine phosphate could not be confirmed and are estimated to be low.[x]<br><br>Patients could be treated with **alternatives**:[xi]<br>• Pyridostigmine<br>• Intravenous immunoglobulin therapy<br>• Immunosuppressive therapy<br>  − azathioprine<br>  − cyclophosphamide<br>  − mycophenolate mofetil<br>  − cyclosporine<br>  − prednisone<br>  − methylprednisolone<br><br>Some of the remaining patients in the target population may receive the generic version of the drug, **3, 4-Diaminopryidine** (DAP), which is not routinely commissioned.[xii] |

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| | K1.6 What is the projected growth of the disease/condition prevalence (prior to applying the new policy) in 2, 5, and 10 years | K1.6 No change to the future prevalence rate has been identified. However, the prevalent population identified in K1.1 could grow in line with population growth. Over the next five years, it is estimated to remain in the region of around 125 to 185 patients (as the growth rate of the population is low).[xiii] |
| | K1.7 What is the associated projected growth in activity (prior to applying the new policy) in 2,5 and 10 years | K1.7 In the do nothing scenario, activity would remain similar to the current activity noted in K1.5 as there would be relatively low growth in the target population. |
| | K1.8 How is the population currently distributed geographically? | K1.8 Across England -- based on the evidence reviewed, no significant geographical differences in the disease have been identified. |
| K2 Future Patient Population & Demography | K2.1 Does the new policy: move to a non-routine commissioning position / substitute a currently routinely commissioned treatment / expand or restrict an existing treatment threshold / add an additional line / stage of treatment / other? | K2.1 This policy proposes a **non-routine commissioning position**. |
| | K2.2 Please describe any factors likely to affect growth in the patient population for this intervention (e.g. increased disease prevalence, increased survival) | K2.2 In about a half of patients, the disease is associated with underlying lung cancer, in particular, small cell lung cancer (SCLC), and in the other half, there are no obvious associations.[xiv] A factor that may affect the prevalence of the SCLC form may be smoking rates in the population.[xv] [xvi] There is limited evidence to suggest that any factors affect the prevalence of the non-SCLC form.[xvii] |
| | K2.3 Are there likely to be changes in geography/demography of the patient population and would this impact on activity/outcomes? If yes, provide details | K2.3 No evidence of changes. |

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| | K2.4 What is the resulting expected net increase or decrease in the number of patients who will access the treatment per year in year 2, 5 and 10? | K2.4 The proposed policy establishes a 'not routinely commissioned' position for the relevant population (the specific cohort set out in K1.2). The number of patients who fall outside of the cohort covered by the proposed policy, or for whom exceptionality might be demonstrated is likely to be very small.<br><br>As the number of patients currently estimated to be on the treatment is minimal, there is expected to be no net change in the number of patients accessing the treatment under the policy as compared to the 'do nothing' scenario. |
| K3 Activity | K3.1 What is the current annual activity for the target population covered under the new policy? Please provide details in accompanying excel sheet<br><br>K3.2 What will be the new activity should the new / revised policy be implemented in the target population? Please provide details in accompanying excel sheet<br><br>K3.3 What will be the comparative activity for the 'Next Best Alternative' or 'Do Nothing' comparator if policy is not adopted? Please details in accompanying excel sheet | K3.1 Current annual activity is identified in K1.5; few patients will use the licenced version of amifampridine, and 3,4-DAP and other drugs may be used.<br><br>K3.2 As the policy is to not routinely commission, the activity under the policy would be similar to the 'do nothing' scenario is as described in K1.7; few patients will use amifampridine phosphate, and 3,4-DAP and other drugs may be used.<br><br>K3.3 The activity in the 'do nothing' scenario is as described in K1.7; few patients will use amifampridine phosphate, and 3,4-DAP and other drugs may be used. |
| K4 Existing Patient Pathway | K4.1 If there is a relevant currently routinely commissioned treatment, what is the current patient pathway? Describe or include a figure to outline associated activity. | K4.1 Anyone who has been diagnosed with LEMS must first be investigated for possible underlying cancer. If cancer is present, this needs to be treated. Removal of the cancer can significantly improve symptoms. |

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| | K4.2. What are the current treatment access criteria?<br><br>K4.3 What are the current treatment stopping points? | K4.2 Access is based on diagnosis of LEMS through a series of physical, blood and nerve conduction tests.<br><br>K4.3 Not applicable. |
| K5 Comparator (next best alternative treatment) Patient Pathway | K5.1 If there is a 'next best' alternative routinely commissioned treatment what is the current patient pathway? Describe or include a figure to outline associated activity.<br><br>K5.2 Where there are different stopping points on the pathway please indicate how many patients out of the number starting the pathway would be expected to finish at each point (e.g. expected number dropping out due to side effects of drug, or number who don't continue to treatment after having test to determine likely success). If possible please indicate likely outcome for patient at each stopping point. | K5.1 LEMS cannot be cured but symptoms can be managed by a variety of other approaches.<br><br>K5.2 Not applicable. |
| K6 New Patient Pathway | K6.1 Describe or include a figure to outline associated activity with the patient pathway for the proposed new policy<br><br>K6.2 Where there are different stopping points on the pathway please indicate how many patients out of the number starting the | K6.1 – 6.2 Not applicable as position is to not routinely commission. |

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| | pathway would be expected to finish at each point (e.g. expected number dropping out due to side effects of drug, or number who don't continue to treatment after having test to determine likely success). If possible please indicate likely outcome for patient at each stopping point. | |
| K7 Treatment Setting | K7.1How is this treatment delivered to the patient?<br>o Acute Trust: Inpatient/Daycase/Outpatient<br>o Mental Health Provider: Inpatient /Outpatient<br>o Community setting<br>o Homecare delivery<br><br>K7.2 Is there likely to be a change in delivery setting or capacity requirements, if so what?<br>e.g. service capacity | K7.1 The treatment is prescribed in an outpatient setting.<br><br>K7.2 Not applicable as position is to not routinely commission. |
| K8 Coding | K.8.1 In which datasets (e.g. SUS/central data collections etc.) will activity related to the new patient pathway be recorded?<br><br>K8.2 How will this activity related to the new patient pathway be | K8.1 Use of amifampridine phosphate would be recorded in the registry for high cost drugs.<br><br>K8.2 The drug is used almost exclusively for LEMS, and so most instances of the drug's use would relate to the pathway. |

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| | identified?(e.g. ICD10 codes/procedure codes) | |
| K9 Monitoring | K9.1 Do any new or revised requirements need to be included in the NHS Standard Contract Information Schedule?<br><br>K9.2 If this treatment is a drug, what pharmacy monitoring is required?<br><br>K9.3 What analytical information /monitoring/ reporting is required?<br><br>K9.4 What contract monitoring is required by supplier managers? What changes need to be in place?<br><br>K9.5 Is there inked information required to complete quality dashboards and if so is it being incorporated into routine performance monitoring?<br><br>K9.6 Are there any directly applicable NICE quality standards that need to be monitored in association with the new policy?<br><br>K9.7 Do you anticipate using Blueteq or other equivalent system to guide access to treatment? If so, please outline. *See also linked question in M1 below* | K9.1- 9.7 Not applicable as position is to not routinely commission. |

| Section L - Service Impact | | |
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| **Theme** | **Questions** | **Comments** (Include source of information and details of assumptions made and any issues with the data) |
| L1 Service Organisation | L1.1 How is this service currently organised (i.e. tertiary centres, networked provision)<br><br>L1.2 How will the proposed policy change the way the commissioned service is organised? | L1.1 Neurology centres.<br><br>L1.2 Not applicable as position is to not routinely commission. |
| L2 Geography & Access | L2.1 Where do current referrals come from?<br><br>L2.2 Will the new policy change / restrict / expand the sources of referral?<br><br>L2.3 Is the new policy likely to improve equity of access?<br><br>L2.4 Is the new policy likely to improve equality of access / outcomes? | L2.1 Neurologists and oncologists<br><br>L2.2 Not applicable as position is to not routinely commission.<br><br>L2.3 – 2.4 New policy not likely to impact equity and equality of access given interim policy position was to not routinely commission as well. |
| L3 Implementation | L3.1 Is there a lead in time required prior to implementation and if so when could implementation be achieved if the policy is agreed?<br><br>L3.2 Is there a change in provider physical infrastructure required?<br><br>L3.3 Is there a change in provider staffing required? | L3.1-3.6 Not applicable as position is to not routinely commission. |

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| | L3.4 Are there new clinical dependency / adjacency requirements that would need to be in place? | |
| | L3.5 Are there changes in the support services that need to be in place? | |
| | L3.6 Is there a change in provider / inter-provider governance required? (e.g. ODN arrangements / prime contractor) | |
| | L3.7 Is there likely to be either an increase or decrease in the number of commissioned providers? | L3.7 No change anticipated. |
| | L3.8 How will the revised provision be secured by NHS England as the responsible commissioner (e.g. publication and notification of new policy, competitive selection process to secure revised provider configuration) | L3.8 Publication and notification of new policy. |
| L4 Collaborative Commissioning | L4.1 Is this service currently subject to or planned for collaborative commissioning arrangements? (e.g. future CCG lead, devolved commissioning arrangements)? | L4.1 No |
| **Section M - Finance Impact** | | |

| **Theme** | **Questions** | **Comments** (Include source of information and details of assumptions made and any issues with the data) |
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| M1 Tariff | M1.1 Is this treatment paid under a national prices*, and if so which? | M1.1 Amifampridine phosphate would be excluded from national prices as a high cost drug. |
| | M1.2 Is this treatment excluded from national prices? | M1.2 The drug is excluded from national prices. |
| | M1.3 Is this covered under a local price arrangements (if so state range), and if so are you confident that the costs are not also attributable to other clinical services? | M1.3 As a high cost drug, amifampridine phosphate may be subject to local price negotiations.<br><br>Based on the dictionary of medicines (DMD), the price for amifampridine phosphate is listed at £1,815 for a pack of 100 x 10mg tablets (excl. VAT).[xviii] [xix] The estimated cost per patient per year is set out in M2.1. |
| | M1.4 If a new price has been proposed how has this been derived / tested? How will we ensure that associated activity is not additionally / double charged through existing routes? | M1.4 Not applicable. |
| | M1.5 is VAT payable (Y/N) and if so has it been included in the costings? | M1.5 Not applicable as the policy is to not routinely commission. |

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| | M1.6 Do you envisage a prior approval / funding authorisation being required to support implementation of the new policy? | M1.6 No |
| M2 Average Cost per Patient | M2.1 What is the revenue cost per patient in year 1? | M2.1 The revenue cost per patient per year would be nil as the decision is to not routinely commission.<br><br>As a point of reference, the revenue cost per patient per year for the **licensed version of amifampridine** is estimated to range between £9,800 and £39,200 (the lower bound assumes a dose of 15mg a day, whereas the upper bound assumes a dose of 60mg a day).[xx]<br><br>This is significantly higher than the price of **3,4-DAP**, which is estimated to cost £1,200 per patient per year.[xxi] |
| | M2.2 What is the revenue cost per patient in future years (including follow up)? | M2.2 The revenue cost per patient is not anticipated to change with a non-routinely commissioned policy.<br><br>The cost per patient in future years for amifampridine phosphate may be flat until 2022/23 at least. The patent for amifampridine phosphate is set to expire in 2022.[xxii] Following the expiration of the patent, the price for amifampridine (phosphate form) may decrease. |
| M3 Overall Cost Impact of this Policy to NHS England | M3.1 Indicate whether this is cost saving, neutral, or cost pressure to NHS England? | M3.1 Cost neutral. Amifampridine phosphate is currently not routinely commissioned, and the policy will not change this position. |
| | M3.2 Where this has not been identified, set out the reasons why this cannot be measured? | M3.2 Not applicable. |
| M4 Overall cost impact of this policy to | M4.1 Indicate whether this is cost pressure, neutral, or cost saving for | M4.1 Cost neutral. |

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| the NHS as a whole | other parts of the NHS (e.g. providers, CCGs)<br><br>M4.2 Indicate whether this is cost saving, neutral, or cost pressure to the NHS as a whole?<br><br>M4.3 Where this has not been identified, set out the reasons why this cannot be measured?<br><br>M4.4 Are there likely to be any costs or savings for non NHS commissioners / public sector funders? | <br><br>M4.2 Cost neutral.<br><br>M4.3 Not applicable.<br><br>M4.4 None identified. |
| M5 Funding | M5.1 Where a cost pressure is indicated, state known source of funds for investment, where identified e.g. decommissioning less clinically or cost-effective services | M5.1 Not applicable. |
| M6 Financial | M6.1 What are the material financial risks to implementing this policy<br><br>M6.2 Can these be mitigated, if so how?<br><br>M6.3 What scenarios (differential | M6.1 Not applicable.<br><br>M6.2 Not applicable.<br><br>M6.3 Not applicable. |

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| | assumptions) have been explicitly tested to generate best case, worst case and most likely total cost scenarios | |
| M7 Value for Money | M7.1 What evidence is available that the treatment is cost effective? *e.g. NICE appraisal, clinical trials or peer reviewed literature*<br><br>M7.2 What issues or risks are associated with this assessment? *e.g. quality or availability of evidence* | M7.1 No stu dies reporting on the cost-effectiveness of amifampridine phosphate were identified.<br><br>M7.2 Not applicable as no studies were identified. |
| M8 Cost Profile | M8.1 Are there non-recurrent capital or revenue costs associated with this policy? *e.g. Transitional costs, periodical costs*<br><br>M8.2 If so, confirm the source of funds to meet these costs. | M8.1 None identified.<br><br>M8.2 Not applicable. |

[i] Wirtz, P., Nijnuis, M., Sotodeh, M., Willems, L., Brahim, J., Putter, H., Wintzen, A. and Verschuuren, J. (2003). The epidemiology of myasthenia gravis, Lambert-Eaton myasthenic syndrome and their associated tumours in the northern part of the province of South Holland. Journal of Neurology, 250(6), pp.698-701.

[ii] Titulaer, M., Lang, B. and Verschuuren, J. (2011). Lambert–Eaton myasthenic syndrome: from clinical characteristics to therapeutic strategies. The Lancet Neurology, 10(12), pp.1098-1107.

[iii] Clinical Commissioning Policy Statement: Amifampridine (Firdapse) for Lambert Easton Myasthenic Syndrome (LEMS). Published date: April 2013. Reference : NHSCB/D04/PS/a notes 5 per 2 million, falling within the range in the prevalence studies in the Netherlands.

[iv] This applies the prevalence rate to the ONS (2012) population projections for the population of England in 2014.

[v] The LEMS specificity in patients with distinct muscle weakness is nearly 100%. Gilhus, N. (2011). Lambert-Eaton Myasthenic Syndrome; Pathogenesis, Diagnosis, and Therapy. Autoimmune Diseases, 2011, pp.1-5. Accessed online via http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3182560/; Lindquist S. and Martin Stangel. (2011). Update on treatment options for Lambert–Eaton myasthenic syndrome: focus on use of amifampridine. Neuropsychiatric Disease and Treatment. Vol 7. Accessed online via: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3148925/

[vi] Based on discussions with the policy working group.

[vii] Mareska, M. and Gutmann, L. (2004). Lambert-Eaton Myasthenic Syndrome. Seminars in Neurology, 24(2), pp.149-153.
[viii] Titulaer, M., et. al. (2011).
[ix] The IFR data for 2014/15 lists 5 IFRs for amifampridine for LEMS.
[x] Based on discussions with the policy working group.
[xi] Mantegazza, R., Meisel, A., Sieb, J., Le Masson, G., Desnuelle, C. and Essing, M. (2015). The European LEMS Registry: Baseline Demographics and Treatment Approaches. Neurology and Therapy.
[xii] The drug is only available to patients who submit a declaration that they are aware of the risks of drug and that it is not lisenced. Based on discussions with the clinical and policy working group.
[xiii] Demographic growth rates are sourced from ONS (2012), Population projections. The demographic growth rate for the over 16s is applied.
[xiv] Gilhus, N. (2011). Lambert-Eaton Myasthenic Syndrome; Pathogenesis, Diagnosis, and Therapy. Autoimmune Diseases, 2011, pp.1-5.
[xv] Mareska, M. and Gutmann, L. (2004). Lambert-Eaton Myasthenic Syndrome. Seminars in Neurology, 24(2), pp.149-153.
[xvi] 'All patients with SCLC had a positive smoking history and 86% were still smoking at diagnosis' Titulaer, M., Wirtz, P., Willems, L., van Kralingen, K., Smitt, P. and Verschuuren, J. (2008). Screening for Small-Cell Lung Cancer: A Follow-Up Study of Patients With Lambert-Eaton Myasthenic Syndrome. Journal of Clinical Oncology, 26(26), pp.4276-4281.
[xvii] Wirtz, P., Smallegange, T., Wintzen, A. and Verschuuren, J. (2002). Differences in clinical features between the Lambert-Eaton myasthenic syndrome with and without cancer: an analysis of 227 published cases. Clinical Neurology and Neurosurgery, 104(4), pp.359-363.
[xviii] Firdapse may only be sold in this quantity and dose size. Patients may have to take tablets in fractional doses.
[xix] The price is listed on the DMC. Accessed online via: http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=18036311000001102&toc=nofloat
[xx] This range in dose was based on discussions with the clinical and policy working group. Price excludes VAT.
[xxi] East Midlands Specialised Commissioning Group (2010). Commissioning Policy (EMSCGP038V1). Accessed online via http://www.emscg.nhs.uk/Library/EMSCGP038V1PolicyFirdapse050711.pdf.
[xxii] The supplementary protection certificate is not set to expire until 2022 (UKMi data).