Integrated Impact Assessment Report for Clinical Commissioning Policies

Policy Reference Number	E09X03		
Policy Title	Sodium oxybate for symptom control of narcolepsy with cataplexy (children)		
Accountable Commissioner	Penelope Gray	**Clinical Lead**	Paul Gringras
Finance Lead	Shekh Motin	**Analytical Lead**	Ceri Townley
Section K - Activity Impact			
Theme	**Questions**	**Comments** (Include source of information and details of assumptions made and any issues with the data)	
K1 Current Patient Population & Demography / Growth	K 1.1 What is the prevalence of the disease/condition?	K1. 1 This policy recommends to **routinely commission** sodium oxybate for narcolepsy with cataplexy in children. The **prevalence of paediatric narcolepsy** is likely to be underestimated due to misdiagnosis[i] and early studies reported a median delay between symptom onset and diagnosis of more than 10 years.[ii] It is thought that half the adults with narcolepsy-cataplexy will have had symptoms during childhood but not diagnosed until later[iii] although this pattern is improving with increased understanding of the condition. The overall prevalence of narcolepsy (paediatric and adult) in Western countries is estimated to be **20-50 per 100,000** population.[iv] Based on this, the prevalence of narcolepsy in England	

		(both children and adult) could be between 11,000 and 27,000 in 2014/15.[v] The estimated **incidence rate** is 1.37/100,000 per year for narcolepsy and 0.74/100,000 per year for narcolepsy with cataplexy.[vi] Among children, the incidence of narcolepsy in the UK is estimated to be 1.2 per million for children aged 0-4 and 12.2 per million for those aged 5-19.[vii] This represents c.100 new children every year, and c. 70 children per year who have narcolepsy with cataplexy[viii].
	K1.2 What is the number of patients currently eligible for the treatment under the proposed policy?	K1.2 The policy is intended for a subset of the patients suffering from narcolepsy with cataplexy identified in K1.1. Sodium oxybate will be routinely commissioned for post-pubescent children (weighing more than 40kg and less than18 years old) where attempts to control symptoms of narcolepsy with cataplexy have failed despite a trial of first and second line medications from each symptom group for at least three months.[ix] Clinical experience suggests c. 12 paediatric patients have severe and uncontrolled narcolepsy with cataplexy in England each year, of which 2 are pre-pubertal and/or weighing below 40kg.[x] As such, it is estimated that c. 10 paediatric patients per year are likely to be the cohort for this policy proposition. Further, there are around 10 – 12 patients who are already receiving sodium oxybate for this condition (who would continue to receive the treatment) and around 10 patients are currently waiting for the treatment (backlog).[xi]
	K1.3 What age group is the treatment indicated for?	K1.3 The policy is indicated for children (post puberty and under 18 years). However, the policy working group has noted the difference between pre and post-pubertal children under 18, with the latter more likely to resemble the adult cohort in terms of physiological development.

	K1.4 Describe the age distribution of the patient population taking up treatment?	K1.4 Most children who suffer from narcolepsy with cataplexy and do not respond to first and second line treatments are within the 5 to 17 age bracket, and the majority of patients are expected to be between 12 and 17.[xii]
	K1.5 What is the current activity associated with currently routinely commissioned care for this group?	K1.5 Sodium oxybate is not currently routinely commissioned for this cohort. However, as noted in K1.2, 10-12 children already receive sodium oxybate for narcolepsy with cataplexy. The remaining patients that would be eligible for this treatment are inadequately controlled by existing drugs such as stimulants, anti-depressants, histamine blockers and melatonin agonists[xiii].
	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 Given the issues in identifying paediatric prevalence stated in K1.1, no change to the future prevalence rate is assumed. The prevalent population identified in K1.1 (for children and adults) could grow in line with population growth and is expected to be:[xiv] • ~ 11,100 to 27,700 in 2016/17 (year 1) • ~ 11,200 to 27,900 in 2017/18 (year 2) • ~ 11,400 to 28,500in 2020/21 (year 5) As described in K1.2 the population eligible for treatment is, however, a subset of this patient group.
	K1.7 What is the associated projected growth in activity (prior to applying the new policy) in 2, 5 and 10 years?	K1.7 There are currently 10-12 children receiving Sodium oxybate[xv]. This is assumed to be the steady state under a do-nothing scenario (see K2.4 for scenario around the proposed policy).

	K1.8 How is the population currently distributed geographically?	K1.8 No evidence of differences in geographical distribution in England were 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 proposition establishes a **routinely commissioned position** for sodium oxybate for the target population identified in K1.2.
	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 None identified.
	K 2.3 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 None identified.
	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 As per the policy, the treatment will be routinely commissioned by NHSE for the target population (as defined in K1.2). The number of patients accessing the treatment in the first year will include: • **Existing activity in the system.** This equates to around 10 to 12 children who are already receiving the treatment, as

		identified in K1.5. • **Backlog.** Around 10 patients are waiting for the treatment, as identified in K1.2. • **New patients in the first year.** As noted in K1.2, around 10 new patients are expected to begin treatment each year. Further, patients will also **drop out of treatment** each year due to: • **Lack of continued treatment effectiveness.** This is estimated at around 10% of patients each year[xvi] • **Exceeding the age cut-off for the policy.** Once 18 years of age, the patients will move on to the treatment pathway for adults and will be out of scope of this policy pathway. It is assumed that patients are likely to be equally distributed across ages 12 to 17[xvii], then it could be assumed that c.17%[xviii] of the patients would drop out each year. In the subsequent years, the number of patients accessing the treatment will be determined by: • **Existing patients in the system.** This includes the patients who are already receiving the treatment, less those who drop out. • **New patients each year.** As noted above, around 10 patients will start the treatment each year. Based on the above, the **net increase** in the number of patients each year, i.e. those over and above the do-nothing activity in K1.7, is estimated to be in the region of: • ~ 18 in 2016/17 (year 1) • ~ 24 in 2017/18 (year 2) • ~ 33 in 2020/21 (year 5)

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.	K3.1 See K1.5
	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.	K3.2 Given the 'do-nothing' activity in K1.7 and the net increase in activity in K2.4, the number of patients receiving sodium oxybate under the policy is expected to be in the region of: • ~ 28 - 30 in 2016/17 (year 1) • ~ 34 - 36 in 2017/18 (year 2) • ~ 43 - 45 in 2020/21 (year 5)
	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.	K3.3 There are no direct comparator treatments for children who have not responded to first and second line treatments. Activity would be expected to remain equal to the do nothing identified in K1.7.
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 Sodium oxybate is currently not routinely commissioned for children. There is no defined pathway for the treatment of children, and those whose conditions are severe tend to go to specialist centres[xix].
	K4.2. What are the current treatment access criteria?	K4.2 Not applicable.

	K4.3 What are the current treatment stopping points?	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.	K5.1 There are no direct comparator treatments for Sodium oxybate, i.e. ones that address all symptoms of narcolepsy and cataplexy (including excessive day-time sleepiness and restless night-time sleep). First line treatment options include non-medical strategies such as scheduled daytime naps. Where symptoms prevail, the patient is referred to specialist sleep centres where the patient is prescribed one of the following first or second line medications. For treating the symptoms of narcolepsy, the following stimulants are prescribed (Modafinil, Methylphenidate and Dextroamphetamines), and anti-depressants (Velafaxine, Clomipramine and other SSRIs) for treatment of cataplexy. However, as noted by the policy working group, first and second line treatments are sub-optimal comparators to sodium oxybate. In the absence of sodium oxybate, increased dosages of these treatments might be required to manage the symptoms.
	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.	K5.2 See K5.1

K6 New Patient Pathway	K6.1 Describe or include a figure to outline associated activity with the patient pathway for the proposed new policy. K6.2 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.	K6.1 If the patient shows incomplete response within three months and/or has significant adverse effects after trial of medication options for narcolepsy and cataplexy, sodium oxybate would be considered. Initiated following an MDT discussion including a consultant paediatrician and psychologist, it is initially prescribed in two doses of 2.25g per day and adjusted at one-, to two-week intervals depending on response up to a maximum daily dose of 9g (in two equally divided doses). Prescribing consultant will regularly monitor patients' BMI. K6.2 If patient experiences serious adverse effects, including signs of respiratory depression, treatment will stop. If patient shows evidence of incomplete response at three months, as assessed by prescribing consultant according to the following examination criteria, treatment will stop. 1. For cataplexy: frequency and severity scores 2. For narcolepsy: the Epworth or Paediatric Sleepiness Scale. It is estimated that 1 patient per year is likely to stop treatment due to either incomplete response or serious adverse effects.
K7 Treatment Setting	K7.1 How is this treatment delivered to the patient? o Acute Trust: Inpatient/Daycase/ Outpatient o Mental Health Provider: Inpatient/Outpatient o Community setting o Homecare delivery	K7.1 The treatment can be administered at home. Due to risks relating to abuse of the drug, it is required that a parent/carer be with the child to administer the drug.

	K7.2 Is there likely to be a change in delivery setting or capacity requirements, if so what? *e.g. service capacity*	K7.2 No.
K8 Coding	K8.1 In which datasets (e.g. SUS/central data collections etc.) will activity related to the new patient pathway be recorded?	K8.1 As sodium oxybate is a high cost drug, activity may be recorded in the high cost drug data set.
	K8.2 How will this activity related to the new patient pathway be identified?(e.g. ICD10 codes/procedure codes)	K8.2 Not applicable.
K9 Monitoring	K9.1 Do any new or revised requirements need to be included in the NHS Standard Contract Information Schedule?	K9.1 No
	K9.2 If this treatment is a drug, what pharmacy monitoring is required?	K9.2 None required
	K9.3 What analytical information /monitoring/ reporting is required?	K9.3 Centres without an in-house database to be invited to participate in the European Narcolepsy Network (EU-NN) database.
	K9.4 What contract monitoring is	K9.4 None required

	required by supplier managers? What changes need to be in place?	
	K9.5 Is there inked information required to complete quality dashboards and if so is it being incorporated into routine performance monitoring?	K9.5 None required
	K9.6 Are there any directly applicable NICE quality standards that need to be monitored in association with the new policy?	K9.6 No
	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*	K9.7 Yes. Use of software systems to track audit and use of sodium oxybate by clinicians to be mandated.
Section L - Service Impact		
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)	L1.1 Hospital based services which review children on an outpatient basis with the following clinical specialties: Paediatric consultants, neurology, neurodisability, sleep and respiratory specialists, psychology and (sometimes) specialist nurse posts. There are ten clinics in England.

	L1.2 How will the proposed policy change the way the commissioned service is organised?	L1.2 No change
L2 Geography & Access	L2.1 Where do current referrals come from?	L2.1 Secondary care
	L2.2 Will the new policy change / restrict / expand the sources of referral?	L2.2 No
	L2.3 Is the new policy likely to improve equity of access?	L2.3 Yes, through a consistent commissioning position across the country.
	L2.4 Is the new policy likely to improve equality of access / outcomes?	L2.4 Yes, through a consistent commissioning position across the country.
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?	L3.1 Not expected.
	L3.2 Is there a change in provider physical infrastructure required?	L3.2 Not expected.

	L3.3 Is there a change in provider staffing required?	L3.3 Not expected.
	L3.4 Are there new clinical dependency / adjacency requirements that would need to be in place?	L3.4 Not expected.
	L3.5 Are there changes in the support services that need to be in place?	L3.5 Not expected.
	L3.6 Is there a change in provider / inter-provider governance required? (e.g. ODN arrangements / prime contractor)	L3.6 Not expected.
	L3.7 Is there likely to be either an increase or decrease in the number of commissioned providers?	L3.7 Yes, as new specialist sleep centres open (who meet the proposed governance arrangements as set out in Section 9 of the Policy Proposition).
	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 Through publication of the commissioning position and notification to providers.

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)
M1 Tariff	M1.1 Is this treatment paid under a national prices*, and if so which?	M1.1 No.
	M1.2 Is this treatment excluded from national prices?	M1.2 Sodium oxybate is a High Cost Drug excluded from the national tariff.[xx]
	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 The list price for sodium oxybate (Xyrem) is £360 for a 180ml bottle (500mg/ml).[xxi] Including VAT the cost would be £432[xxii].
	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 VAT could be recoverable in some cases for instance under shared-care arrangements with provision in primary care or under

		homecare delivery arrangements[xxiii].
	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 yearly cost of sodium oxybate currently lies between £5,840 and £13,140 (based on highest and lowest dosage).[xxiv, xxv] Including VAT[xxvi] this leads to a range of c. £7,008 and £15,768.
	M2.2 What is the revenue cost per patient in future years (including follow up)?	M2.2 Children who do not stop the treatment take sodium oxybate on a daily basis until they reach the age of 18 – the cost of the drug per patient would be the same as in year 1.[xxvii]
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 Based on the net change in the number of patients accessing sodium oxybate, as identified in K2.4, and the costs per patient identified in M2.1, this policy is expected to be a **cost pressure** to NHS England in the region of:[xxviii] • c. £125k to £285k in 2016/17 (year 1) • c. £170k to £380k in 2017/18 (year 2) • c. £230k to £520k in 2020/21 (year 5).
	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 the NHS as a whole	M4.1 Indicate whether this is cost saving, neutral, or cost pressure for other parts of the NHS (e.g. providers, CCGs).	M4.1 In the absence of sodium oxybate, the target population might incur additional costs around increased dosages of first/second line treatments and more frequent interactions with hospital services. As such, there may be some savings associated with routinely commissioning sodium oxybate, to the extent that these additional costs are avoided. However, there is not sufficient information available to quantify these savings.
	M4.2 Indicate whether this is cost saving, neutral, or cost pressure to the NHS as a whole.	M4.2 As described in M3.1 and M4.1.
	M4.3 Where this has not been identified, set out the reasons why this cannot be measured.	M4.3 Not applicable.
	M4.4 Are there likely to be any costs or savings for non NHS commissioners / public sector funders?	M4.4 In the do nothing scenario (in the absence of sodium oxybate), if symptoms are not adequately managed, there may be increased dependence on support services, including social care, input to schools for children who are unable to access the curriculum as a result of the condition.[xxix] These costs may be avoided if sodium oxybate were to be routinely commissioned. This may represent wider economic benefits to the public sector.
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 Risks Associated with Implementing this Policy	M6.1 What are the material financial risks to implementing this policy?	M6.1 No material risks have been identified.
	M6.2 Can these be mitigated, if so how?	M6.2 Not applicable.

	M6.3 What scenarios (differential assumptions) have been explicitly tested to generate best case, worst case and most likely total cost scenarios?	M6.3 All scenarios assume that:
		• There is a backlog of 10 patients who receive sodium oxybate in year 1;
		• Each year 10 new patients join the cohort year;
		• Patients drop-out of the cohort due to either:
		  • Sodium oxybate being ineffective (10% of patients); or
		  • Exceeding the treatment age (c. 17% of patients).
		
		In the low cost scenario it is assumed that:
		• 10 patients currently receive the drug; and
		• The annual cost of the drug is £7,008 (the lower estimate from M2.1).
		
		The high cost scenario assumes that:
		• 12 patients currently receive the drug; and
		• The annual cost of sodium oxybate per patient is £15,768 (the upper estimate from M2.1).

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*	M7.1 There were no studies assessing the cost effectiveness of the use of sodium oxybate in people under 18.

	M7.2 What issues or risks are associated with this assessment? *e.g. quality or availability of evidence*	M7.2 Not applicable.
M8 Cost Profile	M8.1 Are there non-recurrent capital or revenue costs associated with this policy? *e.g. Transitional costs, periodical costs*	M8.1 None identified.
	M8.2 If so, confirm the source of funds to meet these costs.	M8.2 Not applicable.

[i] Please refer to the policy proposition.

[ii] Morrish, E., King, M., Smith, I and Sheerson, J., "Factors associated with a delay in the diagnosis of narcolepsy", *in Sleep Med*, 2004; 5(1): 37-41.

[iii] Please refer to the policy proposition.

[iv] Longstreth, WT Jr et al., "The epidemiology of narcolepsy", in Sleep. 2007 Jan;30(1):13-26.

[v] Applying prevalence rates to the total population of England drawn from ONS – rounded to the nearest 1,000, given the uncertainty.

[vi]Silber, MH., Krahn, LE., Olson, EJ., Pankratz VS., "The Epidemiology of Narcolepsy in Olmsted County, Minnesota: A Population-Based Study", Sleep. 2002 Mar 15;25 (2):197-202.

[vii] Solutions for Public Health (SPH), Sodium Oxybate for Paediatric Narcolepsy, Evidence Summary Report, October 2015.

[viii] This uses the incidence rate mentioned above and ONS population data on the number of children in England.

[ix] Please refer to the policy proposition

[x] Based on discussions with the policy working group

[xi] Based on discussions with the policy working group

[xii] Based on discussions with the policy working group

[xiii] Based on discussions with the policy working group

[xiv] Demographic growth rates are sourced from ONS (2012) population projections

[xv] This excludes children receiving Sodium Oxybate through funding from the Department of Health (DH).

[xvi] Based on discussions with the policy working group

[xvii] Based on discussions with the policy working group

[xviii] Assuming an equal distribution across all age group between 12 and 17, i.e. 6 years.

[xix] Based on discussions with the policy working group

[xx] Annex 7B High cost drugs, devices and listed procedures, 2014/15 National Tariff Payment System.

[xxi] Dictionary of medicine: http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=10070911000001103&toc=nofloat, last accessed: 11/11/2015.

[xxii] Sodium Oxybate in the management of narcolepsy with cataplexy, NHS North East Treatment Advisory Group, (http://www.netag.nhs.uk/files/appraisal-reports/Xyrem-NETAG-Appraisal-Report-FINAL.pdf)

[xxiii] Sodium Oxybate in the management of narcolepsy with cataplexy, NHS North East Treatment Advisory Group, (http://www.netag.nhs.uk/files/appraisal-reports/Xyrem-NETAG-Appraisal-Report-FINAL.pdf)

[xxiv] The daily dosage of the drug lies between 4g and 9g. The cost for 90g of Xyrem (the drug which contains sodium oxybate) is £360. Hence the average cost per patient in the first year may be £5,840 to £13,140.

[xxv] The cost could fall in the future if further competition is introduced, in particular if any patents surrounding the medication are removed. Information regarding the patent expiration for Xyrem in Europe was not found; no UK/SPC patent was identified (NHS Pharmacy).

[xxvi] VAT of 20% is applied.

[xxvii] Their therapy then continues, but the incurred expenses would not be covered by this policy, which applies solely to children.

[xxviii] Please note that figures are rounded to the nearest £5k.

[xxix] Based on discussions with the policy working group