Integrated Impact Assessment Report for Clinical Commissioning Policies

Policy Reference Number	F06X05		
Policy Title	Intravenous immonuglobulin for acute disseminated encephalomyelitis and autoimmune encephalitis		
Accountable Commissioner	Jane Pearson-Moore	**Clinical Lead**	Philip Wood
Finance Lead	Justine Stalker-Booth	**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 The policy proposes **to not routinely commission** the use of intravenous immunoglobulins (IVIg) in treating patients with acute	

		disseminated encephalomyelitis (ADEM); acute transverse myelitis (TM) or autoimmune encephalitis (AIE) who do not respond to first line treatments such as steroid therapy.[i] The incidence of **ADEM** is estimated at up to around 4 per million population (pmp),[ii] or an estimated 220 people in England in 2014/15.[iii] The incidence of TM is estimated at 250 new cases per year in England.[iv] **Acute TM** is a subset of TM; its incidence is unclear. The incidence of encephalitis is estimated at 52 per million population (pmp), with a range of 43 to 87pmp.[v] Of these approximately 7% may be autoimmune encephalitis.[vi] Thus **AIE** is estimated to affect circa 200 (160 to 330) persons in England in 2014/15.[vii] The overall incidence for the three conditions may therefore be estimated at 630 to 800 in England in 2014/15. (Note: the above figures use the incidence of TM as opposed to acute TM, whose incidence is unclear. It may therefore be an overestimate.)
	K1.2 What is the number of patients currently eligible for the treatment under the proposed policy?	K1.2 The proposed policy establishes a 'not routinely commissioned' proposal for patients with ADEM, Acute TM or AIE. It is unclear what share of the overall incidence of patients would be suitable to receive IVIg treatment. However, the policy proposition does state that IVIg could be a second line treatment if treatment using steroids had failed.
	K1.3 What age group is the treatment indicated for?	K1.3 The policy relates to patients of all ages.

	K1.4 Describe the age distribution of the patient population taking up treatment?	K1.4 The three conditions affect different age groups. **ADEM** predominantly affects children under the age of 10.[viii] **Acute TM** can affect persons of any age; incidence is highest for the 10 to 19 and 30 to 39 age groups.[ix] **AIE** can affect any age group; however young women are most likely to be affected.[x]
	K1.5 What is the current activity associated with currently routinely commissioned care for this group?	K1.5 For patients who do not respond to steroids alone, **plasma exchange** (PLEX) may be used.[xi] SUS data indicates that in 2014/15 there were c. 30 spells related to plasma exchange for ADEM or TM.[xii] In 2014/15, it is estimated that 160 patients within the target population received **IVIg** based on the national IVIg database; c. 130 patients may currently use IVIg for AIE, and c. 30 for ADEM, and under five with TM.[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 As set out in K2.2, no specific factors affecting the target population over time were identified, however the number of new patients per year affected by the three conditions may grow over time in line with demographic growth.[xiv] As such, the new number of patients with **ADEM** could be: • c. 220 in 2016/17 • c. 220 in 2017/18 • c. 225 in 2020/21[xv] The new number of patients with **acute TM** could be:

		• c. 255 in 2016/17 • c. 255 in 2017/18 • c. 265 in 2020/21[xvi] The new number of patients with **AIE** could be: • c. 165 to 335 in 2016/17 • c. 165 to 335 in 2017/18 • c. 170 to 345 in 2020/21[xvii]
	K1.7 What is the associated projected growth in activity (prior to applying the new policy) in 2,5 and 10 years?	K1.7 Activity under the do nothing scenario, current activity is assumed to be 'steady state' in future years (as set out in K1.5). The activity in a 'do nothing' scenario in future years for **IVIg** is estimated to grow in line with demographic growth, and is estimated to be: [xviii] • c. 160 patients in in 2016/17 • c. 165 patients in in 2017/18 • c. 165 patients in in 2020/21[xix] Use of plasma exchange would also be expected to grow in line with demographic growth. As such, activity could be estimated in the region of: [xx] • c. 30 patients in 2016/17 • c. 30 patients in 2017/18 • c. 30 patients in 2020/21
	K1.8 How is the population currently distributed geographically?	K1.8 Across England – no significant geographical differences in the disease have been identified.
K2 Future Patient Population &	K2.1 Does the new policy: move to a non-routine commissioning position /	K2.1 The policy is to not routinely commission the use of IVIg for the conditions outlined in K1.1.

Demography	substitute a currently routinely commissioned treatment / expand or restrict an existing treatment threshold / add an additional line / stage of treatment / other?	
	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 There are no known factors that may affect the growth of the patient population.[xxi]
	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 The proposed policy establishes a 'not routinely commissioned' proposal for the relevant population (the specific cohort set out in K1.2). As such there may be close to no activity for IVIg in future years. The net decrease in the number of patients who receive IVIg as compared to the do nothing case is therefore estimated to be c. 160 patients (with close to no patients on IVIg in future years).[xxii]
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 The current activity has been set out in 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 As the recommendation for IVIg is to not routinely commission for the conditions listed in the policy, there is estimated to be a reduction in the level of activity for IVIg. Under the policy, the number of patients using **IVIg** would be close to nil in future years. There is estimated to be an increase in **plasma exchange** under the policy proposition in future years.[xxiii] If patients using IVIg were treated with plasma exchange instead, there could be c. 190 patients having plasma exchange each year.[xxiv] However, provision of PLEX is variable across the country, meaning some patients may not be able to access PLEX and the number may be lower. In year one it is estimated that there would be a part year effect of 75% (2016/17). As such, the number of patients on IVIg may be c. 40, with c. 150 patients having plasma exchanges. There may also be longer hospital stays as a result of using PLEX rather than IVIg.
	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 Under the do nothing scenario, the current level of activity is taken to represent the 'steady state', which is rolled forward in future years (as set out 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 – K4.3 Once a diagnosis is made ADEM, TM, or AIE, high dose steroids are usually recommended as first line treatment. If the condition does not respond to steroids, or steroids are contraindicated, IVIg or PLEX may be recommended as second line treatment.

	K4.2. What are the current treatment access criteria? K4.3 What are the current treatment stopping points?	IVIg is currently commissioned according to the DoH Clinical Guidelines for Immunoglobulin Use (July 2011). In some cases, a combination of steroids and PLEX may be recommended. If the condition does not respond to IVIg, the treatment should be stopped. Likewise, if the condition does not respond to PLEX, the treatment should be stopped
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. K5.2 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-K5.2 The next best alternative routinely commissioned treatment is the same as the new patient pathway, as this policy proposes to decommission the use of IVIG. See K6.1-K6.2
K6 New Patient Pathway	K6.1 Describe or include a figure to outline associated activity with the patient pathway for the proposed new	K6.1-K6.2 Once a diagnosis is made ADEM, TM, or AIE, high dose steroids are usually recommended as first line treatment.

	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.	If the condition does not respond to steroids, or steroids are contraindicated, in future only PLEX may be recommended as second line treatment (i.e. IVIg will no longer be a routine treatment option). In some cases, a combination of steroids and PLEX may be recommended. If the condition does not respond to PLEX, the treatment should be stopped.
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 IVIg is administered in an inpatient setting.[xxv]

	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 Data would be recorded in the National Immunoglobulin Database and administration recorded via the SUS data set.
	K8.2 How will this activity related to the new patient pathway be identified?(e.g. ICD10 codes/procedure codes)	K8.2 The data within SUS could be identified using OPCS and ICD-10 codes.[xxvi] On the IVIg databse, the indications listed could be used to identify usage.
K9 Monitoring	K9.1 Do any new or revised requirements need to be included in the NHS Standard Contract Information Schedule?	K9.1 – 9.5 Not applicable, as decision is to not routinely commission.
	K9.2 If this treatment is a drug, what pharmacy monitoring is required?	
	K9.3 What analytical information /monitoring/ reporting is required?	
	K9.4 What contract monitoring is 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?	
	K9.6 Are there any directly applicable NICE quality standards that need to be monitored in association with the new policy?	K9.6 Not applicable.
	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 Not applicable, as proposal is to not routinely commission.
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 Specialist neurology centres, often in collaboration with specialist immunological, rheumatology and respiratory centres.
	L1.2 How will the proposed policy change the way the commissioned service is organised?	L1.2 No change required.

L2 Geography & Access	L2.1 Where do current referrals come from?	L2.1 Specialist neurology centres
	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 – L2.4 There is a risk that this policy will reduce equity of access and have a negative impact on equality of outcomes, as the accepted alternative treatment, plasma exchange (PLEX) is not widely available across the country. Therefore some patients will no longer be able to access second line treatment.[xxvii]
	L2.4 Is the new policy likely to improve equality of access / outcomes?	
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 There may be a requirement to invest in plasma exchange facilities, as demand is expected to increase
	L3.2 Is there a change in provider physical infrastructure required?	L3.2 No
	L3.3 Is there a change in provider staffing required?	L3.3 No

	L3.4 Are there new clinical dependency / adjacency requirements that would need to be in place?	L3.4 No
	L3.5 Are there changes in the support services that need to be in place?	L3.5 No
	L3.6 Is there a change in provider / inter-provider governance required? (e.g. ODN arrangements / prime contractor)	L3.6 No
	L3.7 Is there likely to be either an increase or decrease in the number of commissioned providers?	L3.7 No
	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 N/A
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 There are no plans to review whether this service should be commissioned by CCGs.

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 (see M1.2).
	M1.2 Is this treatment excluded from national prices?	M1.2 This drug is excluded from national prices as a high cost drug.
	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 IVIg would be negotiated under local arrangements. The list price for IVIg is £42.50 per gram (excl. VAT).[xxviii] The estimated annual cost per patient 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 As immunoglobulin is a blood derived product VAT would not be added.[xxix]
	M1.6 Do you envisage a prior approval / funding authorisation being required to	M1.6 Not applicable.

	support implementation of the new policy?	
M2 Average Cost per Patient	M2.1 What is the revenue cost per patient in year 1?	M2.1 The policy is estimated to be cost neutral as patients could undergo plasma exchange instead of IVIg treatment at a broadly similar cost. The average **cost** per patient of **plasma exchanges** is estimated at c. **£7,000** for the target population.[xxx] This compares with an estimated cost of c. **£6,000** per patient per dose of **IVIg**.[xxxi] (based on a dosage of 2g per kg,[xxxii] and an estimated average patient weight of 70kg, at a cost of IVIg of £42.50 per g).[xxxiii] Patients may have a second dose as part of their treatment. If the average number of doses was 1.5, this would be **c. £9,000**. Note that ADEM affects mainly children; as such, the cost per patient for patients with ADEM could be lower[xxxiv] – depending on the weight of the child treated with IVIg. Depending on the number of plasma exchanges or IVIg doses needed to treat a patient, as well as the patient's weight and age, there could be a net cost or saving.
	M2.2 What is the revenue cost per patient in future years (including follow up)?	M2.2 For the indications covered in this policy, IVIg is not used as a long-term treatment.[xxxv] These conditions are acute, and so costs would likely be borne in the first year of treatment.
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 This policy is estimated to be cost neutral as the costs of the alternative plasma exchange may be similar to IVIg. Scenarios around this are set out in M6.3.

	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 No cost pressures or benefits for other parts of the NHS were identified.
	M4.2 Indicate whether this is cost saving, neutral, or cost pressure to the NHS as a whole.	M4.2 Cost neutral (see M3.1).
	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 No evidence of costs or savings beyond the NHS has been 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 Risks Associated with	M6.1 What are the material financial	M6.1 Not applicable.

Implementing this Policy	risks to implementing this policy? M6.2 Can these be mitigated, if so how? M6.3 What scenarios (differential assumptions) have been explicitly tested to generate best case, worst case and most likely total cost scenarios?	 M6.2 Not applicable. M6.3 The activity-weighted cost of PLEX listed above is relatively high as a number of patients underwent multiple exchanges. If a greater number of patients had a single exchange (which has a lower tariff), this would lead to savings. Similarly, if the average weight of patients or the number of doses of IVIg needed is low, this could lead to a cost pressure. In one scenario (assuming £7,000 on average per patient for PLEX, a patient weight of 70 kg and an average of 1.5 doses if on IVIG, the cost saving would be c. £250k in 16/17). In a scenario assuming £7,000 on average per patient for PLEX, a patient weight of 50 kg and an average of 1 dose if on IVIG, the cost pressure would be c. £350k in 16/17. In a scenario assuming £600 on average per patient for PLEX (in relation to a single exchange in a non elective setting),[xxxvi] a patient weight of 50 kg and an average dose of 1 if on IVIG, the cost savings would be c. £450k in 16/17.
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 and M7.2 There are no published studies evaluating cost effectiveness of IVIg in ADEM, TM or AIE.

	M7.2 What issues or risks are associated with this assessment? *e.g. quality or availability of evidence*	
M8 Cost Profile	M8.1 Are there non-recurrent capital or revenue costs associated with this policy? *e.g. Transitional costs, periodical costs* M8.2 If so, confirm the source of funds to meet these costs.	M8.1 There may be a need to invest in plasma exchange facilities to increase access across the country and meet potential growth in demand. The financial implication of this will need to be considered once the service specification for the revised pathway is defined. M8.2 Not applicable.

[i] Or where first line treatments are contra-indicated, see Policy Proposition.

[ii] See Banwell et al, 2009; Leake et al, 2004; Pohl et al., 2007 (as cited in Policy Proposition); and Orphanet, Acute disseminated encephalomyelitis. http://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=EN&Expert=83597, last accessed: 14/01/2016.

[iii] This applies the incidence rate and the percentage of autoimmune cases to the population estimates, based on ONS

[iv] This uses the incidence figure for the UK of 300 (Brain and Spine Foundation, 2013, Transverse Myelitis: A guide for patients and carers. accessed via: http://www.brainandspine.org.uk/sites/default/files/documents/transverse_myelitis.pdf, last accessed: 14/01/2016) stated in the Policy Proposition and applies the ratio of the English to UK population to estimate the incidence for England.

[v] Granerod et al, 2013, New Estimates of Incidence of Encephalitis in England. Emerg Infect Dis. 19(9). accessed via: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3810913/, last accessed: 14/01/2016.

[vi] Relates to anti-NMDA-receptor encephalitis and VGKC-complex antibody positive encephalitis. Granerod et al, 2010, Causes of encephalitis and differences in their clinical presentations in England: a multicentre, population-based prospective study . The Lancet . Vol 10. accessed via: http://www.encephalitis.info/files/6513/9394/6343/Causes_of_encephalitis_and_diff_erences_in_their_clinical_presentations_in_England.pdf, last accessed: 25/01/2016.

[vii] This applies the incidence rate and the percentage of autoimmune cases to the population estimates, based on ONS.

[viii] Orphanet, Acute disseminated encephalomyelitis. http://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=EN&Expert=83597, last accessed: 14/01/2016.

[ix] Transverse Myelitis Association, 2015, Transverse Myelitis Fact Sheet. http://www.ninds.nih.gov/disorders/transversemyelitis/detail_transversemyelitis.htm, last accessed: 25/01/2016.

[x] Autoimmune Encephalitis Alliance, FAQ. accessed via: https://aealliance.org/faq/, last accessed: 14/01/2016.

[xi] Policy Proposition.

[xii] This refers to OPCS code X322 to X325 (exchange of plasma) within the spell. For spells where acute transverse myelitis in demyelinating disease or acute disseminated encephalitis was coded within the first three ICD-10 positions. It was not possible to identify activity relating specifically to AIE in the data.

[xiii] Based on an extract received from the National Immunoglobulin Database.

[xiv] The growth rate of the general adult population is used to approximate the growth of the patient population based on ONS projections for the population. This is estimated at a growth rate of approx. 0.7% per annum over the next ten years.

[xv] Figures are rounded to the nearest five.

[xvi] Figures are rounded to the nearest five.

[xvii] Figures are rounded to the nearest five.

[xviii] The growth rate of the general adult population is used to approximate the growth of the patient population based on ONS projections for the population. This is estimated at a growth rate of approx. 0.7% per annum.

[xix] Figures rounded.

[xx] The growth rate of the general adult population is used to approximate the growth of the patient population based on ONS projections for the population. This is estimated at a growth rate of approx. 0.7% per annum.

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

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

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

[xxiv] Based on the existing estimate of c. 30 patients per year based on identifiable SUS data and the c. 160 patients that would be using IVIg

[xxv] For the indications under the policy, administration is typically in an acute setting. Based on discussions with the policy working group.

[xxvi] ICD-10 codes relating to ADEM (G040) or Acute TM (G373) and other related diagnoses; OPCS code X961 (Immunoglobulins Band 1)

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

[xxviii] Dictionary of Medicine, one possible price could be http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=19805211000001108&toc=nofloat, last accessed: 01/02/2016.

[xxix] Based on correspondence with NHS England Pharmacists and HM Revenue & Customs (2014). Section 5.1, VAT Notice 701/31: health institutions. available via: https://www.gov.uk/government/publications/vat-notice-70131-health-institutions/vat-notice-70131-health-institutions. las accessed: 12/01/2016.

[xxx] The cost of plasma exchange has been calculated using 2015/16 tariff (with an average MFF of 10% applied) codes SA13 and SA14 (elective and non-elective). These have been weighted by activity (activity from a SUS data extract for those with ADEM or TM coded in the first three ICD-10 fields, based on a combination of OPCS and POD). This data accounts for relative frequency of single treatments and more than one treatment.

[xxxi] The cost of administration is not included because patients would already be in hospital when requiring the drug, as discussed with policy working group.

[xxxii] Policy Proposition.

[xxxiii] Dictionary of Medicine, price of Gamunex was used: http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=19805211000001108&toc=nofloat, last accessed: 01/02/2016.

[xxxiv] Please see K1.4.

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

[xxxvi] 2014/15 Tariff.