Integrated Impact Assessment Report for Clinical Commissioning Policies

Policy Reference Number	D04X10		
Policy Title	Rituximab for chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), multifocal motor neuropathy (MMN), vasculitis of the peripheral nervous system and IgM paraprotein-associated demyelinating neuropathy (Adults)		
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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)
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 rituximab in treating patients with four selected immune-mediated peripheral neuropathies who do not respond to first line treatments. The selected neuropathies are: • Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP); • Multifocal motor neuropathy (MMN); • Vasculitis of the peripheral nervous system; and • Immunoglobulin M (IgM) paraprotein-associated demyelinating neuropathy. Estimates of the prevalence of **CIDP** range from c. 20 to 89 per million, or an estimated 1,090 to 4,860 people with the disease in England in 2014/15.[i] The incidence of CIDP is around c. 4 to16 per million population[ii] or c. 220 to 870 persons in England in 2014/15.[iii] The prevalence of **MMN** is estimated at around 10 to 20 people

		per million,[iv] which is around to 550 to 1,090 patients England-wide in 2014/15.[v] The incidence is estimated at around 2 to under 3 per million or around 110 to 140 nationally in 2014/15.[vi] **Vasculitis** of the peripheral nervous system is very rare, and the prevalence of vasculitis of the peripheral nervous system in England is unknown.[vii] Its incidence is estimated at around 1 per million or less, or around 55 patients across England in 2014/15.[viii] **IgM paraprotein-associated demyelinating neuropathy** has an estimated prevalence of around 12 to 20 per million or 650 to 1,090 England-wide in 2014/15, with an incidence of around 2 to 5 per million or around 110 to 270 in 2014/15.[ix]
	K.1.2 What is the number of patients currently eligible for the treatment under the proposed policy?	K1.2 Only a subset of the population set out in K1.1 could be eligible for rituximab. Eligibility for rituximab would vary by condition: For **CIDP**, patients who show an inadequate response (modified Rankin score of 2+) following treatment with intravenous immunoglobulin (IVIg).[x] Overall, around 60% of the population with **CIDP** is estimated to require immunotherapy treatment,[xi,] and IVIg is not effective in 30% to 50% of CIDP patients.[xii] The relevant population is therefore estimated at around 15% to 30% of the prevalent population, or around 260 to 1,170 patients in 2014/15.[xiii] For **MMN,** patients who have an inadequate response (modified Rankin score of 2+) following treatment with IVIg.[xiv] IVIg is recognised as a first line treatment of MMN,[xv] but may be ineffective in around ~30% of cases.[xvi,xvii] Based on this, the relevant population is estimated at 160 to 330.[xviii] For **vasculitis**, patients with inadequate response to conventional treatment or with concerns surrounding side

		effects.[xix] The relevant population is estimated at up to around 55 patients per year.[xx] For patients with **IgM paraprotein-associated demyelinating neuropathy,** there are very limited treatment options available.[xxi] [xxii] For the relevant population in this group (defined by progressive disability) there are an estimated c. 55 to 110 patients with IgM requiring the treatment.[xxiii] The **overall** range (for all four conditions) of relevant patients is estimated to be 500 to 1,700 in 2014/15.
	K1.3 What age group is the treatment indicated for?	K1.3 The policy indicates this treatment for use in adults (over 18 years).
	K1.4 Describe the age distribution of the patient population taking up treatment	K1.4 The four conditions affect different **age groups**. **CIDP** can begin at any age and is more common in men. [xxiv] **MMN** is contracted more by those aged 35 to 70. It is twice as common in men as in women.[xxv] **Vasculitis** can affect people of all ages.[xxvi] **IgM paraprotein-associated demyelinating neuropathy** is most common in men, and is often diagnosed in those 60 to 65 years old.[xxvii]
	K1.5 What is the current annual activity for the target population covered under the new policy?	K1.5 Currently, it is estimated that some patients within the target population may be receiving **rituximab** through individual funding requests (IFRs) or legacy arrangements. [xxviii] Rituximab is added to a patient's treatment only when existing treatments are ineffective or not appropriate. In the absence of access to rituximab, patients may be using **IVIg** in an attempt to prevent worsening disability. Activity in relation to IVIg in 2014/15

		is set out below: • In 2014/15, based on data from the IVIg database it is estimated that around 210 to 350 patients in the eligible **CIDP** population could be receiving IVIg treatment.[xxix] • In 2014/15, based on data from the IVIg database it is estimated that around 100 patients in the eligible **MMN** population received IVIg treatment.[xxx] • In 2014/15, based on data from the IVIg database it is estimated that fewer than five patients received IVIg treatment.[xxxi] • For **IgM**, in 2014/15, based on data from the IVIg database it is estimated that 17 patients received IVIg treatment.[xxxii]
	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 prevalence rate over time were identified, however the number of people living with the immune mediated peripheral neuropathy may grow over time in line with demographic growth.[xxxiii] The number of patients with **CIDP** is estimated to be in the range of : • 1,110 to 4,930 in 2016/17 • 1,120 to 4,970 in 2017/18 • 1,140 to 5,070 in 2020/21 The number of patients with **MMN** is estimated to be in the range of: • 550 to 1,110 in 2016/17 • 560 to 1,120 in 2017/18 • 570 to 1,140 in 2020/21 The number of patients diagnosed each year with **vasculitis** is estimated to be in the range of:

	K1.7 What is the associated projected growth in activity (prior to applying the new policy) in 2, 5 and 10 years?	• circa 55 in 2016/17 • circa 56 in 2017/18 • circa 57 in 2020/21. The number of patients with **IgM** is estimated to be in the range of: [xxxiv] • 680 to 1,130 in 2016/17 • 700 to 1,160 in 2017/18 • 740 to 1,230 in 2020/21 K1.7 Activity under the do nothing scenario refers to current activity, assumed to be 'steady state' in future years (as set out in K1.5). The activity in future years for **IVIg** is estimated to grow in line with demographic growth, and is estimated to be in the range of:[xxxv] **CIDP** • 215 to 358 patients in 2016/17 • 216 to 361 patients in 2017/18 • 221 to 368 patients in 2020/21. **MMN** • Circa 103 in 2016/17 • Circa 104 in 2017/18 • Circa 106 in 2020/21. **Vasculitis** • Under 5 in 2016/17 • Under 5 in 2017/18 • Under 5 in 2020/21. **IgM** • Circa 18 in 2016/17 • Circa 18 in 2017/18 • Circa 19 in 2020/21.

	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 The policy is to not routinely commission the use of rituximab for the conditions outlined in K1.1.
	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 The causes of these diseases are not well understood – although they may be triggered by events such as illness – no specific factors affecting prevalence have been identified.[xxxvi]
	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). 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.
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 K3.3 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	K3.2 As the recommendation for rituximab is to **not routinely commission** for the conditions listed in the policy, activity is estimated to be as set out in K1.7.[xxxvii] 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 K4.2. What are the current treatment access criteria? K4.3 What are the current treatment stopping points?	K 4.1 Conventional treatment is steroids, intravenous immunoglobulin treatment (IVIG) or plasma exchange. Individuals who do not respond to these treatments can be referred to a specialist neurology centre. First line treatment for vasculitis of the peripheral nervous system is corticosteroids with tapering over months. In rapid progressive neuropathy cyclophosphamide for short term, bridging with long-term methotrexate or azathioprine has been recommended. K4.2 Treatment for these patients will vary significantly depending on their individual circumstances. There are no standardised treatment pathways. K4.3 Conventional treatments are stopped based on partial or complete lack of response.
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	K5.1 See K4.1. K5.2 See K4.2.

	stopping point	
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-K6.2 Not applicable as position is to not routinely commission.
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 K7.2 Is there likely to be a change in delivery setting or capacity requirements, if so what? e.g. service capacity	K7.1 Rituximab is delivered in a day case setting.[xxxviii] K7.2 No change in delivery expected.
K8 Coding	K8.1 In which datasets (e.g. SUS/central data collections etc.) will activity related to the new patient pathway be recorded? K8.2 How will this activity related to the new patient pathway be identified?(e.g. ICD10 codes/procedure codes)	K8.1 Not applicable. K8.2 Not applicable.
K9 Monitoring	K9.1 Do any new or revised requirements need to be included in the NHS Standard	K9.1-9.5 Not applicable as position is to not routinely commission.

	Contract Information Schedule? 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? K9.7 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*	K9.6 None identified. K9.7 Not applicable.
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) L1.2 How will the proposed policy change the way the commissioned service is organised?	L1.1 Patients are referred to specialist centres for treatment. L1.2 No change expected.
L2 Geography & Access	L2.1 Where do current referrals come from?	L2.1 Referrals come from secondary centres and GPs.

	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 Equity will be improved by having a consistent commissioning position across England.
	L2.4 Is the new policy likely to improve equality of access / outcomes?	L2.4 No
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 No
	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	L3.8 Not applicable.

	selection process to secure revised provider configuration)	
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)	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 (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 Rituximab would be negotiated under local arrangements. The list price for MabThera is £873.15 for 500mg/50ml (excl. VAT).[xxxix] The annual cost per patient (including VAT) 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 VAT would be payable as it is envisaged the drug would be administered in a day case setting.[xl]
	M1.6 Do you envisage a prior approval / funding authorisation being required to support implementation of the new policy?	M1.6 Not applicable.
M2 Average Cost per Patient	M2.1 What is the revenue cost per patient in year 1?	M2.1 There would be no revenue cost in year one as the policy is to not routinely commission.

		For reference, the unit cost of the treatment per patient per year is estimated at c. £11,580 in the first year. This is calculated as follows: • An initial dose of 2g of the drug (at c. £4,192 incl. VAT) delivered over two day case visits (at c. £800 each) • A second dose after 9 months (at again 2g of Rituximab delivered over two day case visits.[xli] Hence the cost of the drug is c. £8,380 (incl. of VAT)[xlii] in the first year and c. £3,200 for the day case administrations.[xliii]
	M2.2 What is the revenue cost per patient in future years (including follow up)?	M2.2 For patients that successfully trial rituximab and continue to take rituximab on an ongoing basis, the estimated frequency of dosage is once every nine months.[xliv] On an annualised basis, the treatment cost is c. £7,720.[xlv] As the patent for rituximab expired in 2013, biosimilars may enter the market in the next few years, at which point the price for the drug may fall by c. 30%.[xlvi] This would imply an annualised treatment cost of c. £6,050.[xlvii]
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, as the position is to not routinely commission.
	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 saving for other parts of the NHS (e.g. providers, CCGs)	M4.1 Cost neutral, as the position is to not routinely commission.
	M4.2 Indicate whether this is cost saving, neutral, or cost pressure to the NHS as a whole?	M4.2 Cost neutral, as the position is to not routinely commission.

	M4.3 Where this has not been identified, set out the reasons why this cannot be measured? M4.4 Are there likely to be any costs or savings for non-NHS commissioners/ public sector funders?	M4.3 Not applicable. 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? 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?	M6.1 Not applicable. M6.2 Not applicable. M6.3 Not applicable.
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* M7.2 What issues or risks are associated with this assessment? *e.g. quality or availability of evidence*	M7.1 – M7.2 To date there have been no studies evaluating cost effectiveness of rituximab as a treatment for adult patients with immune mediated peripheral neuropathy (CIDP, MMN, vasculitis of the peripheral nervous, IgM paraprotein-associated demyelinating neuropathy with our without anti –MAG antibodies.
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 Not applicable. M8.2 Not applicable.

[i] The low end of the range estimate is based on discussions with the policy working group and Yusuf A. Rajabally et. al. (2009). Epidemiologic variability of chronic inflammatory demyelinating polyneuropathy with different diagnostic criteria: Study of a UK population. Muscle & Nerve, 39(4) 432-438 [Online] accessible at: http://onlinelibrary.wiley.com/doi/10.1002/mus.21206 [Accessed: 10/11/2015]. The high estimate is calculated by multiplying the population in England in 2014/15 based on ONS projections by the 89 per million population prevalence rate. The latter is taken from: Laughlin, R. S., Dyck, P. J., Melton, L. J., Leibson, C., Ransom, J., & Dyck, P. J. B. (2009). Incidence and prevalence of CIDP and the association of diabetes mellitus. Neurology, 73(1), 39–45, [Online] accessible at http://doi.org/10.1212/WNL.0b013e3181aaea47, [Accessed: 10/11/2015].

[ii] Rajabally et. al. (2009); Laughlin et. al. (2009).

[iii] This estimate uses the stated incidence rates for CIDP multiplied by the 2014/15 ONS data on population estimates.

[iv] This is based on an estimate of around 3-4 patients for a population of 200,000 to 250,000 as discussed with the policy working group and the prevalence range cited by Orphanet, the portal for rare diseases and orphan drugs, accessible at: http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=641, [Accessed: 21/10/2015].

[v] The stated prevalence rates for MMN are multiplied by the ONS population estimates for the year 2014/15 to estimate the prevalent population in 2014/15.

[vi] This is based on an estimate of one patient for every 400,000 to 500,000 of the population from clinician experience (as discussed with the policy working group).

[vii] No sources of prevalence were identified, including no mention of rates in overview documents such as Lehmann, H. C., et al. (2009). Pathogenesis and Treatment of Immune-Mediated Neuropathies. Therapeutic Advances in Neurological Disorders, 2(4). [Online] accessible at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3002632/ [Accessed: 17/11/11]. The policy working group was not aware of any additional sources to consult on the prevalence of the disease. The prevalent population may be less clinically relevant for vasculitis given the acute presentation of the disease.

[viii] Based on discussions with the policy working group, the incidence is estimated at approximately 1 in every million or fewer patients in England currently.

[ix] Based on discussions with the policy working group, the incidence is estimated at around 1 in 200,000 to 250,000 population every year to two years. Prevalence of around 3-4 in 200,000 to 250,000 is estimated. The population figures are estimated by multiplying the stated rates for prevalence and incidence by the ONS population projections estimated for 2014/15.

[x] Discussions with the policy working group.

[xi] Rajabally et. al. (2009); correspondence with the policy working group.

[xii] Gorson KC. (2012). An update on the management of chronic inflammatory demyelinating polyneuropathy. Therapeutic Advances in Neurological Disorders. 5(6):359-373.[Online] accessible at: doi:10.1177/1756285612457215[Accessed: 13/11/2015].

[xiii] Based on the 60% requiring treatment and assuming 30% to 50% would not be successful on IVIg: use 24% multiplied by the prevalence estimates in K1.1.

[xiv] Discussions with the policy working group.

[xv] As noted in studies such as Stieglbauer, K (2009). Beneficial effect of rituximab monotherapy in multifocal motor neuropathy. Neuromuscul Disord. 19(7):473-5. doi: 10.1016/j.nmd.2009.04.013. [Accessed: 11/11/15]; Chaudhry V (2010). An open-label trial of rituximab (Rituxan®) in multifocal motor neuropathy. J Peripher Nerv Syst. 15(3):196-201. http://www.ncbi.nlm.nih.gov/pubmed/21040141. [Accessed: 11/11/15].

[xvi] Different levels of efficacy are reported depending on the outcome studied. Source: van Schaik, I N. (2005). Intravenous immunoglobulin for multifocal motor neuropathy. Cochrane Database Syst Rev. 18 (2). [Online] http://www.ncbi.nlm.nih.gov/pubmed/15846714 [Accessed: 11/11/15].

[xvii] Around 70% of naïve patients significantly improved (14 of 20) - Leger, J M.et al (2008) . Intravenous immunoglobulin as short- and long-term therapy of multifocal motor neuropathy: a retrospective study of response to IVIg and of its predictive criteria in 40 patients. J Neurol Neurosurg Psychiatry. 79(1):93-6. [Online] http://www.ncbi.nlm.nih.gov/pubmed/18079302 [Accessed: 11/11/15]; High effectiveness suggested in van Schaik I N. (2011). "Chapter 21: Multifocal motor neuropathy" in *European Handbook of Neurological Management*: Volume 1, (2nd Edition) eds. by N. E. Gilhus, M. P. Barnes and M. Brainin [Online] http://www.eaneurology.org/fileadmin/user_upload/guidline_papers/EFNS_guideline_2011_Multifocal_motor_neuropathy.pdf [Accessed: 11/11/15]

[xviii] It was noted in discussions with the policy working group that few individuals in the UK have been trialled on rituximab to date. The 30% estimate of ineffective use of IVIg has been multiplied by the prevalence estimates for MMN as set out in K1.1 to give an approximation of possibly eligible patients.

[xix] Discussions with the policy working group; policy proposition.

[xx] The number of patients for whom the side effects of cyclophosphamide would be prohibitive is not known, and therefore the upper limit of 55 people per year is used.

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

[xxii] In one study 82% do not respond to IVIg. Source: Joint Task Force of the EFNS and the PNS, "European Federation of Neurological Societies/Peripheral Nerve Society Guideline* on management of paraproteinemic demyelinating neuropathies. Report of a Joint Task Force of the European Federation of Neurological Societies and the Peripheral Nerve Society – first revision" in *Journal of the Peripheral Nervous System* 15:185–195 (2010),[Online] accessible at http://static1.squarespace.com/static/53e0d272e4b0ea4fa48a8d40/t/53f1d938e4b0b354426b6eca/1408358712211/GuidelinesPN.pdf [Accessed: 10/11/2015].

[xxiii] Based on discussions with the policy working group, it would take several years for newly diagnosed patients to reach disability levels where rituximab might be appropriate. Given the older demographic affected by IgM, some might never require treatment. Clinicians estimated that around 1 to 2 per million in a year might be using the drug for IgM if use were to be routinely commissioned.

[xxiv] GBS CIDP Foundation International. All About CIDP. [Online] accessible at https://www.gbs-cidp.org/cidp/all-about-cidp/ [Accessed: 11/11/15]

[xxv] GBS CIDP Foundation International. Multifocal Motor Neuropathy (MMN) Progress and Challenges. [Online] accessible at: https://www.gbs-cidp.org/variants/mmn-overview/multifocal-motor-neuropathy-mmn-progress-challenges/ [Accessed: 11/11/15].

[xxvi] American College of Rheumatology, http://www.rheumatology.org/I-Am-A/Patient-Caregiver/Diseases-Conditions/Vasculitis, [Accessed: 17/12/2015]

[xxvii] Based on discussions with the policy group.

[xxviii] The number of IFRs considered by NHS England for individuals with the conditions listed within this policy was 20 in 2014/15 and 14 in the first half of 2015/16, based on IFR registry data.

[xxix] This is based on data supplied to the National Immunoglobulin Database for the year 2014/15. The average quantity of IVIg used per patient per year was calculated assuming an average weight per patient of 70kg and a 2g/kg dosage per course, with courses repeated every 6 weeks, based on the total units of IVIg recorded for use for CIDP. Of the estimated 700 number of patients using IVIg for CIDP, an estimated 30% to 50% (as set out in K1.2) might require further treatment as IVIg would not be sufficient.

[xxx] This is based on data supplied to the National Immunoglobulin Database for the year 2014/15. The average quantity of IVIg used per patient per year was calculated assuming an average weight per patient of 70kg and a 2g/kg dosage per course, with courses repeated every 6 weeks, based on the total units of IVIg recorded for use for MMN. Of the estimated 340 number of patients using IVIg for MMN, an estimated 30% (as set out in K1.2) might require further treatment as IVIg would not be sufficient.

[xxxi] This is based on data supplied to the National Immunoglobulin Database for the year 2014/15. The average quantity of IVIg used per patient per year was calculated assuming an average weight per patient of 70kg and a 2g/kg dosage per course, with courses repeated every 6 weeks, based on the total units of IVIg recorded for use for vasculitis.

[xxxii] This is based on data supplied to the National Immunoglobulin Database for the year 2014/15. The average quantity of IVIg used per patient per year was calculated assuming an average weight per patient of 70kg and a 2g/kg dosage per course, with courses repeated every 6 weeks based on the total units of IVIg recorded for use for IgM.

[xxxiii] For conditions apart from IgM, 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 in 2014/15 and 2024/25. This is estimated at a growth rate of approx. 0.7% per annum.

[xxxiv] As the average age at diagnosis of patients with IgM is circa 60, the population growth rate of the population of age 55+ was used to approximate the growth rate of the prevalence of IgM. The compounded annualised rate calculated based on ONS population projections for this age group from 2014/15 to 2024/25 is estimated at ~1.9%.

[xxxv] Demographic growth has been used as IVIg is a rationed product, with tight guidelines around its use. The increase in usage would thus be estimated to follow the increase in the numbers needing treatment. The growth rates used are as set out in K1.6.

[xxxvi] National Organisation of Rare Diseases. (2015) Chronic Inflammatory Demyelinating Polyneuropathy. [Online] https://rarediseases.org/rare-diseases/chronic-inflammatory-demyelinating-polyneuropathy/. [Accessed: 17/11/15].; Lehmann, H. C., et al. (2009). Pathogenesis and Treatment of Immune-Mediated Neuropathies. Theraputic Advances in Neurological Disorders, 2(4). [Online] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3002632/ [Accessed: 17/11/11].

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

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

[xxxix] Dictionary of medicine, entry for MabThera is £873.15 for 500mg/50ml [Online] http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=7697211000001103&toc=nofloat [Accessed: 13/11/2015]

[xl] Based on discussions with NHS England pharmacists and finance leads.

[xli] Discussions with the policy working group; policy proposition.

[xlii] Please refer to M2.1 for the underlying price of the drug.

[xliii] This is an approximate cost estimated based on SUS data extracted for the period 2011/12 to September 2015 and costed based on 2014/15 tariff rates (accounting for relevant market forces factor and specialised top ups). The cost relates to the approximate average cost of day cases with OPCS code X892 (Monoclonal antibodies Band 2).

[xliv] Discussions with the policy working group; policy proposition.

[xlv] This is based on the cost of one course of treatment (c. £800 per day case administration and c. £4,190 for the cost of rituximab), multiplied by 12 months over 9 months.

[xlvi] Discussion with NHS England Pharmacy Lead.

[xlvii] This is based on the cost of one course of treatment (c. £800 per day case administration and 70% of c. £2,930 for the cost of rituximab incl VAT), multiplied by 12 months over 9 months.