Integrated Impact Assessment Report for Clinical Commissioning Policies			
Policy Reference Number	A13X05		
Policy Title	Rituximab for the treatment of dermatomyositis and polymyositis (adults)		
Accountable Commissioner	Jon Gulliver	**Clinical Lead**	Mike Ehrenstein / Peter Lanyon
Finance Lead	Craig Holmes	**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	K1.1 What is the prevalence of the disease/condition?	K1.1 This is a policy to **routinely commission** the use of rituximab for patients with active polymyositis or dermatomyositis who have autoantibodies relevant to myositis, and whose condition is inadequately controlled by conventional therapy. Both polymyositis and dermatomyositis are rare diseases and the prevalence is difficult to estimate. For **polymyositis,** prevalence is estimated at 1 in 14,000;[i] applied to the English population in 2014/15, this equates to an estimated 3,900 people that could be affected by the disease.[ii] The **prevalence of dermatomyositis** is estimated at 1 in 10,000;[iii] if applied to the English population in 2014/15, this

		equates to an estimated 5,400 people that could be affected by dermatomyositis.[iv] The total for both diseases is estimated at circa 9,300 in England in 2014/15. The **incidence** of both diseases is approximately 470 in England in 2014/15.[v]
	K1.2 What is the number of patients currently eligible for the treatment under the proposed policy?	K1.2 **Patients eligible** for treatment are those that have been diagnosed with active polymyositis or dermatomyositis with antibodies relevant to the disease (around 80%),[vi] and those that do not respond adequately to conventional therapies (around 15% of patients).[vii] The size of this target population is estimated at c. 60,[viii] or around 12% of the total incident population that would be eligible under the policy. The current second line treatment options for these patients include intravenous immunoglobulin (IVIg) or cyclophosphamide. Under the proposed pathway, rituximab could be offered as a second line therapy in place of cyclophosphamide and IVIg. Note that in acute situations, this would need to be considered in line with existing guidelines. The backlog of eligible patients is estimated to be circa 60 patients.[ix]
	K1.3 What age group is the treatment indicated for?	K1.3 The policy indicates rituximab for use in adults (18 years and over).
	K1.4 Describe the age distribution of the patient population taking up treatment?	K1.4 Polymyositis is a specific type of idiopathic inflammatory

		myopathy and most commonly affects adults aged 30-60.[x] Both polymyositis and dermatomyositis are more common in women, with a ratio of 2:1.[xi]
	K1.5 What is the current activity associated with currently routinely commissioned care for this group?	K1.5 The target population for rituximab under this policy refers to patients that are not adequately controlled on conventional treatment, which includes physiotherapy and steroids. The target population would be eligible for second line therapy, which currently includes the use of cyclophosphamide or intravenous immunoglobulin (see Appendix for details).[xii] Within the 2014/15 target population: • An estimated three quarters of patients may receive cyclophosphamide (circa 45 persons);[xiii] • An estimated one quarter of patients (circa 15 persons) may receive IVIg treatment;[xiv] A total of 7 individual funding requests (IFRs) were submitted for rituximab in 2014/15, and 4 in 2015/16.[xv]
	K1.6 What is the projected growth of the disease/condition prevalence (prior to applying the new policy) in 1, 2 and 5 years?	K1.6 Dermatomyositis and polymyositis can be associated with other diseases (see K2.2), but no disease-specific growth rate has been identified. The **prevalent** population is estimated to grow in line with demographic growth; as such the future prevalence of dermatomyositis and polymyositis is estimated as:[xvi] • ~9,400 persons in 2016/17 (year 1) • ~9,400 persons in 2017/18 (year 2) • ~9,600 persons in 2020/21 (year 5) The future **incidence** of both conditions is estimated to lie in the region of:[xvii] • circa 480 (of which ~60 are eligible under the policy) in 2016/17 (year 1)

<table>
<tr>
<td></td>
<td>K1.7 What is the associated projected growth in activity (prior to applying the new policy) in 1, 2 and 5 years?

K1.8 How is the population currently distributed geographically?</td>
<td>

circa 480 (of which ~60 are eligible under the policy) in 2017/18 (year 2)
circa 490 (of which ~60 are eligible under the policy) in 2020/21 (year 5)

K1.7 In the ‘do nothing’ case (i.e. assuming the policy is not implemented and activity grows with demographic growth), it is estimated that the target population – c. 60 per year – would grow at a low rate in line with the population as no other changes to the patient pathway were identified.[xviii]

In view of this, future activity is estimated at around:

<table>
<tr><th>Patients</th><th>Cyclophosphamide</th><th>IVIg</th></tr>
<tr><td>2016/17</td><td>c. 45</td><td>c. 15</td></tr>
<tr><td>2017/18</td><td>c. 45</td><td>c. 15</td></tr>
<tr><td>2020/21</td><td>c. 45</td><td>c. 15</td></tr>
</table>

It is estimated that 50% of patients who respond to rituximab therapy may only need one course of the drug,[xix] whilst 50% of patients would continue to take the drug when there is a relapse.[xx] For 17% of patients rituximab is not effective.[xxi]

K1.8 Across England – no significant geographical differences have been identified.
</td>
</tr>
<tr>
<td>K2 Future Patient Population & Demography</td>
<td>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?</td>
<td>K2.1 The new policy would routinely commission the use of rituximab as a second line treatment for patients with active polymyositis or dermatomyositis who have antibodies relevant to the disease, and whose condition is inadequately controlled by conventional therapy.</td>
</tr>
</table>

	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 As noted in K1.6, dermatomyositis and polymyositis may have associations with cancer and other autoimmune diseases, such as diabetes, thyroid disease and myasthenia gravis.[xxii] No disease-specific growth rate has been 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 1, 2 and 5?	K2.4 There would be a **net increase as compared to the 'do nothing' scenario** in the number of **new patients accessing** the treatment each year under the policy. Once the policy is fully phased in, the number of new patients starting treatment is estimated in the region of 60 each year, assuming rituximab would largely replace the use of cyclophosphamide and IVIg in patients with refractory dermatomyositis and polymyositis (as it would fall earlier in the treatment pathway).[xxiii] Note that in the policy proposition does not preclude the use of IVIG as second line therapy in line with existing guidelines, however 100% take up of the rituximab is modelled for the purpose of this impact assessment.[xxiv] In the first year, the number of new patients is estimated at 60 assuming a part year effect of 50% and some absorption of the backlog of patients waiting for treatment. In year one and two, the backlog of c. 60 patients is estimated to commence treatment (with c. 50% estimated to commence in 2016/17 (year one) and the remaining 50% in year two). After the policy is in effect the number of new patients each year is estimated to be **relatively constant over time** at c. 60 new patients each year. The **net increase as compared to the do nothing** in the

		number of **total patients accessing** the treatment is estimated at around: • c. 60 in 2016/17 (year 1) • c. 110 in 2017/18 (year 2) • c. 170 in 2020/21 (year 5) This is because activity in relation to the treatment is **cumulative for 41.5%** of patients in the target population (based on 83% of patients responding, and 50% relapsing).[xxv]
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 K3.2 What will be the new activity should the new / revised policy be implemented in the target population? Please provide details in accompanying excel sheet	K3.1 The current activity for the target population is set out in question K1.5; patients currently would receive treatment using IVIg or cyclophosphamide. (These treatments are understood not be used simultaneously.)[xxvi] K3.2 Under the policy, the number of **new patients** treated each year with **rituximab** is estimated to be in the region of: • circa 60 in 2016/17 (year 1 – includes backlog) • circa 85 in 2017/18 (year 2 – includes backlog) • circa 60 in 2020/21 (year 5) Of patients who try rituximab each year, it will not be successful for around 17%.[xxvii] Moreover, 41.5% will require retreatment (see Appendix for details).[xxviii] The total number of patients treated each year with **rituximab** is estimated to be in the region of:[xxix] • approximately 60 in 2016/17 (year 1) • approximately 110 in 2017/18 (year 2) • approximately 170 in 2020/21 (year 5) Each course is constituted of 2 day cases to administer a total of 2g of the drug intravenously.[xxx] It is estimated that the difference in diagnostics, steroids, and outpatient activity would vary little from the existing pathway.

	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 The 'do nothing' scenario refers to current activity, assumed to be the 'steady state' rolled forward in future years. The future activity levels are therefore set out in K1.7; patients would receive treatment with IVIg or cyclophosphamide.
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?	K4.1 Conventional treatment includes physical therapy to improve muscle strength and high dose steroid therapy. Immunosuppressants, intravenous immunoglobulin (IVIg) and topical therapies for the skin manifestations may also be used. K4.2 Access to treatment determined by diagnosis and severity of condition, treatment response and severity i.e. failure of adequate response or failure to reduce steroid dose would lead to consideration of the use of immunosuppresants. Access to IVIG is determined as per current DOH guidelines. K4.3 Stopping points involve lack of efficacy, resistance, and severe adverse effects. Around 5-20% of patients have conditions that are inadequately controlled by conventional therapy.
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	K5.1 See K4.1. K5.2 Stopping points are toxicity concerns and severe adverse effects.

	indicate likely outcome for patient at each 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 Rituximab should be used in patients who have failed with conventional treatment including corticosteroids and at least two immunosuppressive / immunomodulatory steroid-sparing drugs. Patients should also have positive autoantibodies. K6.2 Stopping points are as set out in the policy proposition.
K7 Treatment Setting	K7.1 How is this treatment delivered to the patient? ○ Acute Trust: Inpatient/Daycase/Outpatient ○ Mental Health Provider: Inpatient /Outpatient ○ Community setting ○ 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 It is proposed that the drug is delivered from an acute Trust in a day case setting. K7.2 Rituximab must only be used for treatment in specialised centres or in collaboration with specialised centres under the supervision of a multi-disciplinary team.
K8 Coding	K8.1 In which datasets (e.g. SUS/central data collections etc.) will activity related to the new patient pathway be recorded?	K.8.1 Rituximab is a high cost drug excluded from tariff, so it should be captured in the high cost drug dataset for routine commissioning.[xxxi] Delivery in a day case setting would be recorded in the SUS data set.

	K8.2 How will this activity related to the new patient pathway be identified?(e.g. ICD10 codes/procedure codes)	K.8.2 The activity could be identified using ICD-10 and OPCS codes.[xxxii]
K9 Monitoring	K9.1 Do any new or revised requirements need to be included in the NHS Standard 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 linked 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*	K9.1 No new or revised requirements identified. K9.2-9.6 Patient data to be mandatorily collected as part of the Myositis Disease Activity Assessment Visual Analogue Scales (MYOACT) Registry to monitor efficacy and safety according to agreed outcomes, subject to patient consent. An annual audit should report on the following outcomes, collected following the administration of a course of two injections: time to DOI(definition of improvement), time to clinical remission, duration of effect, timing of re-treatment, reduction/discontinuation in steroids/immunosuppressants, frequency of retreatment, and serious adverse effects. All patients receiving rituximab must be registered with the MYOACT Registry. For patients not consenting to MYOACT, information should be captured with a local audit. K9.7 Monitoring would be undertaken through a prior approval electronic platform.
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	L1.1 Specialist rheumatology centres L1.2 No change anticipated.

	way the commissioned service is organised?	
L2 Geography & Access	L2.1 Where do current referrals come from? L2.2 Will the new policy change / restrict / expand the sources of referral? L2.3 Is the new policy likely to improve equity of access? L2.4 Is the new policy likely to improve equality of access / outcomes?	L2.1 General rheumatologists. L2.2 No change anticipated. L2.3-2.4 New policy likely to improve equity and equality of access/outcomes for adult autoantibody positive patients with dermatomyositis or polymyositis due to a consistent national commissioning position in place, offering a wider range of effective treatments for this patient group.
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? L3.2 Is there a change in provider physical infrastructure required? L3.3 Is there a change in provider staffing required? 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?	L3.1 Usual lead in time after a policy is agreed (i.e. notification of pharmacists and other relevant parties of new policy). L3.2-3.7 No change anticipated. L3.8 Publication and notification of new policy.

	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)	
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 (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.[xxxiii] 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.[xxxiv]

	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 Overall this policy is estimated to be cost saving. A per-patient **cost of rituximab** of c. £5,400 is estimated to be incurred in year one based on one dose delivered over two day case visits.[xxxv] For patients that are successful on rituximab, there may be **IVIg savings** of c. £26,700 (3 courses per year).[xxxvi] Alternatively, patients that use rituximab successfully may be using it instead of treatment with **cyclophosphamide**, at a total **savings** per patient of c. £4,300.[xxxvii] These costs are similar to the 'do nothing' scenario.
	M2.2 What is the revenue cost per patient in future years (including follow up)?	M2.2 For an estimated **41.5% of patients** there are **no further costs** in year 2: one course of rituximab suffices.[xxxviii] For the estimated **41.5% of patients** where rituximab is successful but does not lead to long-term remission, patients would be administered **rituximab** when a relapse occurs, which may be every one to two years. At a rate of one relapse per year, the future yearly cost would be c. £5,400, whilst with one relapse every two years the average yearly cost would be c. £2,700.[xxxix] In the group of circa **17% of patients** that fail rituximab, those that take **IVIg** would incur yearly costs of c. £26,700. For patients treated with **cyclophosphamide**, they may have up to 3 courses of cyclophosphamide, at 3-year intervals,[xl] at a cost of £4,300 each.[xli]

<table>
<tr><td></td><td></td><td>Note that the cost of rituximab could fall by 30% in the next few years as the drug is out of patent and biosimilars may therefore enter the market.[xlii] This could lead to a cost of c. £4,100 (including administration) per year for yearly retreatment or c. £2,000 for treatment once every two years.[xliii]</td></tr>
<tr><td>M3 Overall Cost Impact of this Policy to NHS England</td><td>M3.1 Indicate whether this is cost saving, neutral, or cost pressure to NHS England?

M3.2 Where this has not been identified, set out the reasons why this cannot be measured?</td><td>M3.1 This policy is estimated to be cost saving. Savings may be in the region of:[xliv]

<table><tr><td>Year</td><td>2016/17 (Y1)</td><td>2017/18 (Y2)</td><td>2020/21 (Y5)</td></tr><tr><td>Savings</td><td>c. £150k</td><td>c. £400k</td><td>c. £1.1m</td></tr></table>
The cost savings mainly relate to where rituximab replaces the more costly IVIg therapy. The savings do not take into account the small number of patients that may be receiving rituximab outside of routine commissioning.

As outlined in the policy proposition, this assumes that patients that do not respond to rituximab would take either IVIg (c. 25%) or cyclophosphamide (c. 75%). (See M6.1 for an alternative scenario.)[xlv]

M3.2 Not applicable.</td></tr>
<tr><td>M4 Overall cost impact of this policy to the NHS as a whole</td><td>M4.1 Indicate whether this is cost saving, neutral, or cost saving for other parts of the NHS (e.g. providers, CCGs)

M4.2 Indicate whether this is cost saving,</td><td>M4.1 No cost pressures or benefits for other parts of the NHS were identified.

M4.2 Cost saving. (see M3.1).</td></tr>
</table>

	neutral, or cost pressure to the NHS as a whole?	
	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	M6.1 What are the material financial risks to implementing this policy?	M6.1 There is a risk that once the treatment is established, patients will begin using rituximab at an earlier stage in the pathway than they would have been considered for the current second line options IVIg or cyclophosphamide. This could increase the percentage of patients on rituximab, and could reduce the available savings because these additional patients would not be avoiding treatment with IVIg or cyclophosphamide. Also, fewer patients could switch to rituximab from IVIg in particular, which would reduce the savings. There is also uncertaintly around the number of relapses that require treatment.
	M6.2 Can these be mitigated, if so how?	M6.2 A prior approval software platform could be used to ensure rituximab is used at the correct point in the pathway, and trend analysis could be used to assess whether the correct questions are being asked to ensure proper use within the policy.

<table>
<tr>
<td></td>
<td>M6.3 What scenarios (differential assumptions) have been explicitly tested to generate best case, worst case and most likely total cost scenarios?</td>
<td>M6.3 The figures in M3.1 assume that, of those who do not respond to rituximab, c. 1/4 would take IVIg and c.3/4 would take cyclophosphamide.

If all patients that failed rituximab were subsequently on IVIg, then cost savings could be lower in the long term and be pressure in early years (estimates below):

<table>
<tr><td>Year</td><td>2016/17 (Y1)</td><td>2017/18 (Y2)</td><td>2020/21 (Y5)</td></tr>
<tr><td>Savings/(Pressure)</td><td>(c. £20k)</td><td>(c. £70k)</td><td>c. £100k</td></tr>
</table>

Equally, if a significant number of patients failed IVIg, then cost savings would be higher than stated in M3.1. Savings would also be higher if the current use of IVIg is relatively higher (for example, 50% IVIg and 50% cyclophosphamide), as indicated by some sources.

Note that the price for rituximab may fall by 30% in future when generics enter the market.[xlvi] Future cost savings could therefore be higher than those stated above.

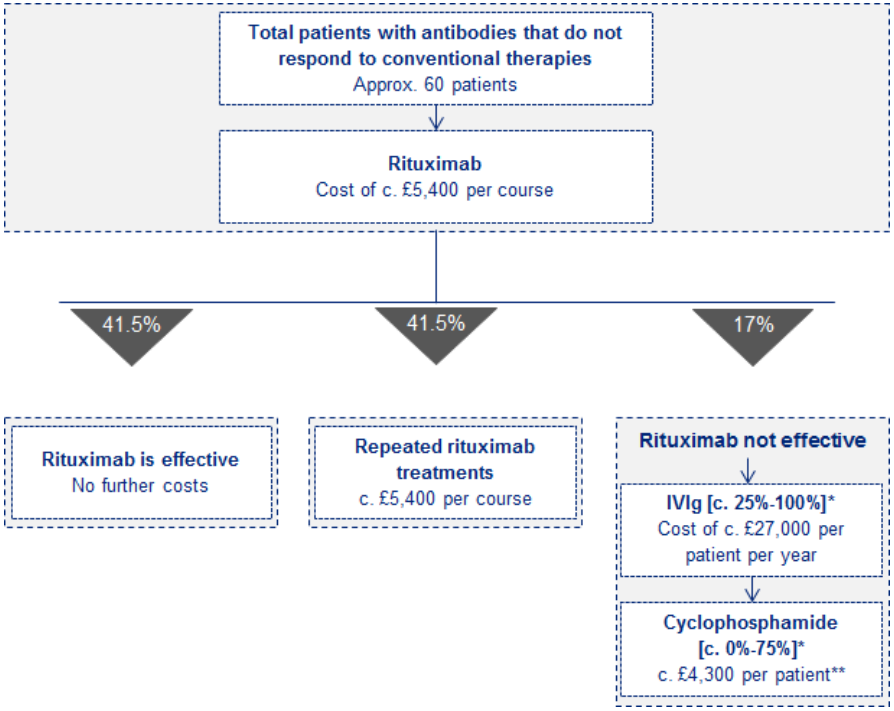
Estimations presented above assume that patients on rituximab under the policy avoid the use of either IVIg or cyclophosphamide as these are subsequent stages in the pathway. Furthermore, it assumes that most patients in the prevalent population that have already been diagnosed with PM or DM are already on an appropriate treatment and would not switch to rituximab.</td>
</tr>
<tr>
<td>M7 Value for Money</td>
<td>M7.1 What evidence is available that the treatment is cost effective? e.g. NICE</td>
<td>M7.1 No cost-effectiveness studies were found.</td>
</tr>
</table>

	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*	 M7.2 Not applicable as no cost effectiveness studies were found.
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. None identified. M8.2 Not applicable.

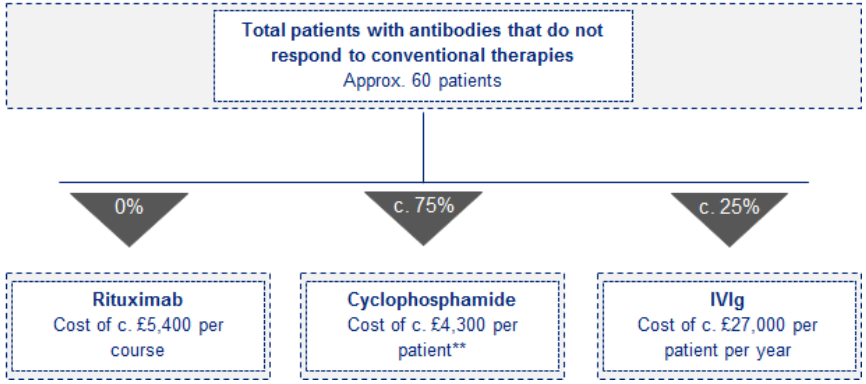
Appendix – Pathway for the target population

The graphs below illustrate the patient pathway for rituximab in relation to the 'current pathway' and the 'pathway under the policy' position. (For sources refer back to the answer to question M2.1 and the footnotes included therein for details about the cost calculations.)

Pathway under the policy



Current pathway (no national guidelines exist for treating PM and DM)*[xlvii]



*In the baseline scenario it is assumed c 25% take IVIg, whilst c. 75% receive cyclophosphamide.in line with the estimated existing treatment mix. In the alternative scenario discussed in the financial risk section M6.3, it is assumed that 100% of patients receive IVIg treatment.

**Cyclophosphimide could be repeated every 3 years.

[i] Orphanet. Polymyositis. http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Expert=732 last accessed: 11/12/2015.

[ii] Based on the stated prevalence rate multiplied by the 2014 England population based on the Office for National Statistics (ONS) data 2012.

[iii] Based on discussions with the policy working group. See also: Orphanet, "Dermatomyositis", accessed via: http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Expert=221, last accessed: 11/12/2015.

[iv] Based on the stated prevalence rate multiplied by the 2014 England population based on the Office for National Statistics (ONS) data 2012.

[v] Based on NHS England Specialised Commissioning Service Specification, 2013/14, cited in the Policy Proposition. The c. 470 figure for England is estimated based on the figure of 500 new cases per year for England and Wales and the ratio of populations in England and Wales, based on ONS data: http://www.ons.gov.uk/ons/rel/pop-estimate/population-estimates-for-uk--england-and-wales--scotland-and-northern-ireland/mid-2014/mid-year-population-estimates-for-the-uk-2014.html, last accessed: 07/12/2015.

[vi] Aggarwal, Rohit; Bandos, Andriy; Reed, Ann M.; Ascherman, Dana P.; Barohn, Richard J.; Feldman, Brian M.; Miller, Frederick W.; Rider, Lisa G.; Harris-Love, Michael O.; Levesque, Marc C.; RIM Study Group; Oddis, Chester V.. Predictors of clinical improvement in rituximab-treated refractory adult and juvenile dermatomyositis and adult polymyositis. 0 2014;66(3):740-749; Clinical consuensus in relation to 80% having auto antibodies (please refer to the policy proposition).

[vii] Allenbach, Y. et. al. (2015). Efficacy of Rituximab in Refractory Inflammatory Myopathies Associated with Anti- Synthetase Auto-Antibodies: An Open-Label, Phase II Trial. http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0133702, last accessed 07/01/2016. Confirmed with policy working groupPlease refer to the policy proposition.

[viii] This is calculated by applying the 15% and 80% rate cited in the policy proposition to the incidence of c. 470 patients in England (or 500 in England and Wales).

[ix] This corresponds to one year's incidence, as discussed with the policy working group.

[x] Policy Proposition.

[xi] Please refer to the sources set out in endnote i and iii.

[xii] See Policy Proposition.

[xiii] The c. 75%/25% split is based on the analysis of the SUS dataset, for line items where the first diagnosis coded refers to ICD-10 codes M330; M331; M332, and where OPCS codes X961 and X921 are taken to refer to IVIG and cyclophosphamide respectively. It assumes six infuses per course for cyclophosphamide up to three times. Assumes IVIg over 5 day cases three times per year. Other estimates indicate that IVIg use could be relatively higher (c. 50%).

[xiv] The c. 75%/25% split is based on the analysis of the SUS dataset, for line items where the first diagnosis coded refers to ICD-10 codes M330; M331; M332, and where OPCS codes X961 and X921 are taken to refer to IVIG and cyclophosphamide respectively. Assumes IVIg over 5 day cases three times per year. Other estimates indicate that IVIg use could be relatively higher (c. 50%).

[xv] IFR data request. Data for 2015/16 covers April to September 2015.

[xvi] The future figures were calculated based on the prevalence figures set out in K1.1 and assuming that growth is in line with population estimates, based on ONS population projections for the years 2014/15 to 2020/21. The growth rate that has been used accounts for a prevalence twice higher in women than in men: female population figures received a weight twice greater than that of men in calculating the growth rate. Figures are rounded.

[xvii] This uses the current incidence and growth of the population as set out in endnote xvi.

[xviii] Based on discussions with the policy working group there would be no other changes to the pathway.

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

[xx] The time to relapse is estimated at 1 to 2 years, based on discussions with the policy working group.

[xxi] Based on the 83% success rate as set out in the policy proposition, and estimated 17% would fail rituximab. For patients responding to rituxumab (c. 83%), around 50% might require long term treatment (or 41.5% of the target population), while the remaining 50% patients responding would require only a single dose. 83% based on Oddis CV et. al., (2013). Rituximab in the treatment of refractory adult and juvenile dermatomyositis and adult polymyositis: a randomized, placebo-phase trial. Arthritis and Rheumatism. 65(2). 314-24

[xxii] NHS Choices, http://www.nhs.uk/conditions/myositis/Pages/Introduction.aspx, last accessed: 11/12/2015.

[xxiii] Based on the c, 60 patients under the policy. See K1.5 for the current estimated breakdown of treatments. Note that there may be some patients using rituximab that have not been counted as the drug is not yet routinely commissioned for the specified indications.

[xxiv] Please see endnote xix.

[xxv] Please see endnote xxi.

[xxvi] See the policy proposition.

[xxvii] This is calculated using the 83% success rate of rituximab stated in the policy proposition.

[xxviii] This is calculated by using the 83% success rate and the estimate that 50% of patients for who rituximab is effective need only a single course, hence 41.5% of patients take it as a long-term therapy.

[xxix] Rituximab is a long-term treatment for 41.5% of new patients (for 41.5% one course of rituximab suffices, hence for 17% rituximab is ineffective).

[xxx] See EMC medicines website, http://www.medicines.org.uk/emc/medicine/2570, last accessed: 11/12/2015.

[xxxi] See K9.

[xxxii] In the SUS dataset, the following codes were used to identify activity related to rituximab (OPCS code X892) for dermatomyositis and polymyositis (ICD-10 codes: M330; M331; M332).

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

[xxxiv] Based on discussions with NHS England pharmacists and finance leads. Section 3.2, When can goods being provided on prescription be zero-rated for VAT purposes? https://www.gov.uk/government/publications/vat-notice-70157-health-professionals-and-pharmaceutical-products/vat-notice-70157-health-professionals-and-pharmaceutical-products. [Accessed 16/12/11].

[xxxv] Day case visit costing c. £600 based on analysis of SUS data costed at 2014/15 tariff where the first OPCS relates to delivery of monoclonal antibodies, and myositis appears as a diagnosis within the first three ICD-10 codes.

[xxxvi] As discussed with policy working group; see also: Department of Health, National IVIG Commissioning Guidelines, accessed via: http://www.ivig.nhs.uk/documents/dh_129666.pdf, last accessed: 08/12/2015. Based on three courses in a year and five day case visits (estimated cost c. £660 per visit based on 2014/15 costed SUS data for immunoglobulin administration for those with myositis diagnosed within the first 3 ICD-10s).

[xxxvii] The reason treatment with cyclophosphamide is generally not regarded as best-treatment is due to the high toxicity of the drug. The cost is based on a dosage of 19mg/kg, or c. 1,300mg for an assumed average patient weighing 70kg per patient. At a price of £9.66 per 500mg (DMD, http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=20970911000001105&toc=nofloat). and a 20% VAT rate, this is c. £30 per dose. In addition, administering the drug is estimated to cost £687 per day case (SUS dataset analysis, OPCS code X921, POD: DC). The drug is administered at six day cases over six months. This could be repeated once every three years.

[xxxviii] Please refer to section K2.4

[xxxix] This divides the yearly cost by two, based on discussions with the policy working group of relapse every 1 – 2 years.

[xl] Based on discussions with policy working group.

[xli] The reason treatment with cyclophosphamide is generally not regarded as best-treatment is due to the high toxicity of the drug. The cost is constituted of a dosage of 12.5-25mg/kg, an assumed average of 70kg per patient, a price of £9.66 per 500mg (DMD, http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=20970911000001105&toc=nofloat), and a 20% VAT rate. In addition, administering the drug is estimated to cost £687 (SUS dataset analysis, OPCS code X921, POD: DC). These costs are incurred 6 times in one year for a patient.

[xlii] Based on discussions with NHS Enlgand pharmacists

[xliii] Based on the costs set out in M2.1

[xliv] The cost is driven by the cost of IVIg: at a frequency of treatment of three courses per year.

[xlv] As set out in K1.5

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

[xlvii] Policy proposition.