Integrated Impact Assessment Report for Clinical Commissioning Policies

Policy Reference Numbers	A13X06 + A13X12		
Policy Titles	(A13X06) Tocilizumab for large Takayasu arteritis (adults) (A13X12) Tocilizumab for Giant cell arteritis (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 This policy considers the population with large vessel vasculitis (LVV), specifically, those with **giant cell arteritis (GCA)** and **Takayasu arteritis (TAK)**. This policy presents a position to **routinely commission** tocilizumab for those with TAK and to **not routinely commission** for those with GCA**.** **GCA** is the most common systemic vasculitis in western countries and has an estimated minimum **prevalence** for those aged over 55 years in the UK of c.17 in 10,000.[i] There are therefore at least c.33,000 people in England with GCA if this rate is applied to those	

		aged over 50.[ii] The **incidence** of GCA has been estimated at 220 (150-250) cases per million in the population a year.[iii] There are therefore estimated to be around 8,100 to 13,600 new cases of GCA a year in England in 2014/15.[iv] **TAK** is less common with a **prevalence** of c.1 in 200,000 in the population and an estimated **incidence** of c. 1-2 cases per million. [v vi] There are therefore estimated to be around 270 people in England with TAK and 50 to 110 new cases of TAK a year in England in 2014/15.[vii]
	K1.2 What is the number of patients currently eligible for the treatment under the proposed policy?	K1.2 The population suitable for treatment with tocilizumab is a subset of the incident population for whom the standard therapies are not suitable or effective, and who require a biologic agent.[viii] The policy proposes not to routinely commission the use of tocilizumab for **GCA**. For reference, for GCA, tocilizumab would be a third line treatment for use after first and second line treatments of steroids, plus a non-biologic immunosuppressant and possibly cyclophosphamide. Of those with GCA, it is estimated that 8-9.6% of new patients would reach this stage in the pathway.[ix] There are therefore between c. 650 and 1,300 GCA patients that would be suitable for tocilizumab each year. The policy proposes to routinely commission tocilizumab for **TAK**. In **TAK**, tocilizumab would be a third line treatment for use after first and second line treatments of steroids plus a non-biologic immunosuppressant and possibly cyclophosphamide. Of those with TAK, it is estimated that 50% of patients may require tocilizumab or another biologic agent as they have failed earlier lines of treatment or those lines are not suitable.[x] There are therefore estimated to be between c. 30 and 55 patients that may require tocilizumab each year.[xi] If patients are retreated on tocilizumab, there could be c. 135

		patients on the drug in a year.
	K1.3 What age group is the treatment indicated for?	K1.3 The treatment is indicated for adults (age 18 and above).
	K1.4 Describe the age distribution of the patient population taking up treatment?	K1.4 The age at onset differs between the GCA and TAK. TAK typically occurs in patients below the age of 50, while GCA usually begins in patients over the age of 50.[xii] The average age of presentation for GCA is between 70 and 80 and in international studies was estimated at 72.5 years for women and 70.3 for men.[xiii] In an international study, the median age of diagnosis for TAK has been reported as 23 years.[xiv]
	K1.5 What is the current activity associated with currently routinely commissioned care for this group?	K1.5 **Typical treatment of patients with LVV** (including both TAK and GCA) follows a stepwise approach: [xv] [xvi] 1. Patients start with standard steroid therapy, such as prednisolone, co-prescribed with osteoporosis prophylaxis (weekly bisphosphonate and calcium or vitamin D supplementation) [xvii] (*For GCA*) 2. If patients have ischaemic features associated with their condition, they may also be considered for methotrexate, azathioprine or leflunomide (or other disease modifying anti-rheumatic drugs, DMARDs), in addition to steroid treatment (with potential lowering of steroids) (*for all TAK + GCA with ischemic features*). 3. The patients that do not achieve remission from these treatments may then be considered for further treatments such as cyclophosphamide and DMARDs not yet trialled, e.g. mycophenolate mofetil.

		For those with TAK in the **target population** (those that do not achieve remission from first or second line treatments), tocilizumab would be considered as a third line treatment. In 2014/15 around seven patients requested **tocilizumab** through an individual funding request (IFR) for LVV. [xviii] In the absence of biologic therapies, an estimated c. 50% or patients may undergo **re-vascularising surgery**. Some patients would require repeated revascularisation.[xix]
	K1.6 What is the projected growth of the disease/condition prevalence (prior to applying the new policy) in 2, 5, and 10 years?	K1.6 No change to the future incidence rate is anticipated; however, the **incident population with GCA** identified in K1.1 could grow in line with population growth and is estimated to be in the region of: [xx] • ~8,400 to 14,100 in 2016/17 (year 1) • ~8,600 to 14,400 in 2017/18 (year 2) • ~9,200 to 15,300 in 2020/21 (year 5) The **incident population of those with TAK** is estimated in the region of around 50 to 115 in the next five years .A subset of those with TAK would be eligible for treatment with tocilizumab as set out in K1.2 (c. 30 – 60 patients per year).[xxi]
	K1.7 What is the associated projected growth in activity (prior to applying the new policy) in 2,5 and 10 years?	K1.7 In the 'do nothing' (prior to applying the new policy), it is estimated that the current activity profile would remain the steady stage. As such, the activity identified in K1.5 would increase in line with growth in the target population (as described in K1.6).[xxii]

	K1.8 How is the population currently distributed geographically?	K1. Across England - GCA, has been found to be more common in the south than in the north of England; with rates in the south and south east of England double that in Scotland.[xxiii]
K2 Future Patient Population & Demography	K2.1 Does the new policy: move to a non-routine commissioning position / substitute a currently routinely commissioned treatment / expand or restrict an existing treatment threshold / add an additional line / stage of treatment / other?	K2.1 This policy deals considers the population with large vessel vasculitis (LVV), specifically, those with giant cell arteritis (GCA) and Takayasu arteritis (TAK). This policy presents a position to routinely commission tocilizumab for those with TAK and to not routinely commission for those with GCA**.**
	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 prevalence of GCA, in particular, may be affected by the growth in the population over 50. This is because the incidence of GCA increases with age.[xxiv] Other factors that may affect the incidence of GCA in the future include smoking and obesity rates.[xxv] Due to the rarity of TAK in the population, diagnosis rates tend to be low.[xxvi] With increased awareness for the condition, the growth in the patient population may increase.
	K 2.3 Are there likely to be changes in geography/demography of the patient	K2.3 No evidence of changes.

	population and would this impact on activity/outcomes? If yes, provide details.	
	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 Under the policy, there is expected to be an increase in the number of TAK patients taking up the treatment (tocilizumab), whilst there is expected to be no net change in the number of GCA patients accessing the treatment as it is not routinely commissioned for GCA. Under the policy, almost all patients are expected to begin treatment.[xxvii] After the first year of the policy, the **total number of patients** accessing the treatment each year may vary depending on retreatment rates. The level of retreatment is uncertain, and so the range (from 0% requiring retreatment following the initial course to all requiring retreatment on a recurrent basis) is estimated to be, as set out in K1.6:[xxviii] • ~c. 27 to c. 135 patients in 2016/17 (year 1) • ~28 - 140 patients in 2017/18 (year 2) • ~28 - 140 patients in 2020/21 (year 5) This is not a year on year increase, but rather an increase in comparison to the 'do nothing' scenario in which tocilizumab is not commissioned for TAK. In 2016/17, it is assumed that patients that succeed on treatment would only receive 9 months of the drug (as this would be implemented only 3 months into the year).
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 Current annual activity is identified 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 Under the policy it is estimated that the eligible population with **TAK**, as defined in K1.2, would receive treatment. It is assumed that the target population receives a dose of 8mg/kg via infusion as an initial loading dose, and then continues treatment for six months with weekly subcutaneous doses (of 162mg). Following six months, those who have not shown response discontinue (10%) whilst those who respond (90%) continue for an additional six months.[xxix] It is possible that patients who achieve remission may require retreatment with tocilizumab after the initial course if they experience a relapse. Under the policy, the number of patients with TAK using tocilizumab is estimated as:[xxx] • c. 27 - 135 patients in 2016/17 • c. 28 - 140 patients in 2017/18 • c. 28 - 140 patients in 2020/21 Under the policy, the number of patients undergoing vascularisation procedures is estimated to be low:[xxxi] Activity for those with **GCA** would be as in the 'do nothing' case described in K1.5 and K1.7.
	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 activity would be as set out in K1.7.

K4 Existing Patient Pathway		Treatment pathway for TAK and GCA follows a stepwise approach.
	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 Yes. See K1.5
	K4.2. What are the current treatment access criteria?	K4.2 Patient presents with symptoms of active TAK or GCA according to at least one Birmingham Vasculitis Activity Score (BVAS) or Indian Takayasu Arteritis Activity (ITAS) or on MR/CT imaging.
	K4.3 What are the current treatment stopping points?	K4.3 Toxicity complications and limited efficacy.
K5 Comparator (next best alternative treatment) Patient Pathway	K5.1 If there is a 'next best' alternative routinely commissioned treatment what is the current patient pathway? Describe or include a figure to outline associated activity.	K5.1 Surgical intervention. In addition, around 40% may require further surgical intervention despite good initial outcomes because of ongoing vascular inflammation.
	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	K5.2 Not applicable.

	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 New Patient Pathway	K6.1 Describe or include a figure to outline associated activity with the patient pathway for the proposed new policy.	K6.1 A small minority of patients with TAK will not respond to steroids with or without non-biological immunosuppressive agents, and will continue to have active or progressive disease that is refractory to conventional treatment. These patients will, in the absence of toxicity, be administered tocilizumab (initially 8mg/kg intravenously) followed by treatment for six months with weekly subcutaneous doses of 162mg. For non-responders, treatment will be stopped at 6 months. For non-responders who have active or progressive disease, surgical intervention to perform vascular re-constructive surgery is considered. For responders, treatment will continue for another 6 months before the patient is gradually stepped down to DMARD therapy. If the patient is deteriorating during step-down, as assessed by BVAS/ITAS scores, tocilizumab to be indicated for 12 months to maintain remission. For patient with GCA, no new patient pathway is proposed.
	K6.2 Where there are different stopping	For patients with TAK who do not respond to tocilizumab, the

	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.	treatment will stop at 6 months if: 1. There is a development of >1 new stenosis of ≥50% lumen diameter in a large vessel, or limited dilation ≤50% limen dimeter (without definite aneurysm formation) on MR or CT angiography studies; OR 2. No increase, or up to 50% reduction in arterial wall PET enhancement of the arterial tree. For responders, defined as improvement or stability of imaging findings, treatment will continue for another 6 months (before patient is stepped down) if patient: 1. Fails to develop further increases in arterial wall thickness, stenosis or dilation/aneurysm, based on MR or CT angiography studies; OR 2. Achieves resolution of PET enhancement without anatomical progression of arterial disease. For patients with GCA, no new patient pathway is proposed.
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,	K7.1 Tocilizumab may be delivered to patients by a homecare arrangement after the initial loading dose delivered in hospital setting.[xxxii] K7.2 No change anticipated.

	if so what? *e.g. service capacity*	
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 Patients that receive tocilizumab may be recorded on the UKIVAS registry.[xxxiii] The cost of excluded drugs would be recorded by Trusts and submitted to the local area teams as part of standard reporting.
	K8.2 How will this activity related to the new patient pathway be identified?(e.g. ICD10 codes/procedure codes)	K8.2 Not applicable.
K9 Monitoring	K9.1 Do any new or revised requirements need to be included in the NHS Standard Contract Information Schedule?	K9.1 None required.
	K9.2 If this treatment is a drug, what pharmacy monitoring is required?	K9.2 None required.
	K9.3 What analytical information /monitoring/ reporting is required?	K.9.3 Patients receiving tocilizumab for TAK will be invited to join the UKIVAS registry. Where patients choose not to join, patient data will be reported to local network of specialist centres and presented at regional level.
	K9.4 What contract monitoring is	K9.4 None required.

	required by supplier managers? What changes need to be in place?	
	K9.5 Is there inked information required to complete quality dashboards and if so is it being incorporated into routine performance monitoring?	K9.5 None required.
	K9.6 Are there any directly applicable NICE quality standards that need to be monitored in association with the new policy?	K9.6 No.
	K9.7 Do you anticipate using Blueteq or other equivalent system to guide access to treatment? If so, please outline. *See also linked question in M1 below*	K.9.7 Yes. Treatment centres will be required to use Blueteq to track and audit the use of tocilizumab in the treatment of TAK. No system usage required for GCA.
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 Service currently delivered in tertiary centres or secondary centres associated with them.
	L1.2 How will the proposed policy	L1.2 Networked care arrangements between local and specialist

	change the way the commissioned service is organised?	centres to be put in place to provide clinical support in cases where lead clinician manages a low case load of patients.
L2 Geography & Access	L2.1 Where do current referrals come from?	L2.1 Majority of referrals come from secondary care and, in rare instances, from primary care.
	L2.2 Will the new policy change / restrict / expand the sources of referral?	L2.2 For TAK: Yes, as secondary care providers treat patients with TAK under collaboration with regional networks. For GCA: None required.
	L2.3 Is the new policy likely to improve equity of access?	L2.3 – L2.4 Policy likely to improve equity of access by creating a uniform commissioning position across England.
	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 None required.
	L3.2 Is there a change in provider	L3.2 None required.

	physical infrastructure required?	
	L3.3 Is there a change in provider staffing required?	L3.3 None required.
	L3.4 Are there new clinical dependency / adjacency requirements that would need to be in place?	L3.4 For TAK: Yes, out of (principle treatment) hospital imaging services need to be set up where absent to provide the diagnostics specified in the policy. For GCA: None required.
	L3.5 Are there changes in the support services that need to be in place?	L3.5 For TAK: Yes, services underpinning the network need to, where absent, be put in place to support the provision of care via regional networks. This includes: patient data sharing, physical transport and administrative support. For GCA: None required.
	L3.6 Is there a change in provider / inter-provider governance required? (e.g. ODN arrangements / prime contractor)	L3.6 Yes, to support the regional network. This includes clinical governance and imaging services, where absent.
	L3.7 Is there likely to be either an increase or decrease in the number of commissioned providers?	L3.7 For TAK: There is likely to be an increase. Though not expected, potentially each secondary care hospital in England will be, if collaboration with a regional network, be able to provide this service. For GCA: 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 Through publication of policy, to be incorporated into relevant provider contracts.
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 Tocilizumab is a high cost drug and therefore would be excluded from national tariff.
	M1.2 Is this treatment excluded from national prices?	M1.2 Tocilizumab is a high cost drug excluded from national tariff.
	M1.3 Is this covered under a local price arrangements (if so state range), and if so are you confident that the costs are not also attributable to other clinical services?	M1.3 The list price for tocilizumab for infusion is £102.40 for eighty mg before VAT.[xxxiv] The list price for Tocilizumab (subcutaneous injection) is £913.12 for four weeks supply (excl. VAT).[xxxv]

	M1.4 If a new price has been proposed how has this been derived / tested? How will we ensure that associated activity is not additionally / double charged through existing routes?	M1.4 Not applicable.
	M1.5 is VAT payable (Y/N) and if so has it been included in the costings?	M1.5 VAT could be recoverable if homecare delivery arrangements are used. VAT has not been included in the cost estimates in this document for subcutaneous dose, but it has been included for the loading dose.[xxxvi]
	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 The first year of treatment is estimated to cost c. £12,500 for those who receive treatment for a year and c. £6,500 for those treated for six months. The cost is based on: • a loading dose of 8mg/kg via infusion (incl VAT) at c. £750, administered in a day case setting (c. £750) [xxxvii] • subcutaneous injection delivery of tocilizumab after the initial loading dose at c. £913 per month.[xxxviii] [xxxix] [xl] The other costs associated with blood tests would be similar for those treated with tocilizumab as compared to those treated with existing treatments.,[xli]

		In addition, there could be a reduction in the costs of treating the consequences of high steroid use (e.g. fractures) if the dose of steroids can be lowered, however this could not be quantified. Patients may avoid revascularisation following treatment (with an estimated cost of c. £2,800). Patients undergoing revascularisation frequently require retreatment.[xlii]
	M2.2 What is the revenue cost per patient in future years (including follow up)?	M2.2 After year one, for those patients that are successful and require only 12 months of treatment, there would be no cost. However, for those patients requiring retreatment (see the high scenario described in M3.1 and M6.3), patients might receive an average of 11 months of treatment with subcutaneous tocilizumab in future years. The cost per patient for tocilizumab is likely to be flat up to 2020/21. The patent for tocilizumab is due to expire in June 2020.[xliii] In the years after, biosimilars may enter the market and the price of tocilizumab may fall.
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 pressure. The cost pressure estimated in the region of c. £200k to £1.2m in 2016/17 and c. £300k to c. £1.4m in 2017/18. This range is based on two scenarios 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 Cost neutral.
	M4.2 Indicate whether this is cost saving, neutral, or cost pressure to the NHS as a whole.	M4.2 Cost pressure as set out in M3.
	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 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 To be determined at CPAG.
M6 Financial Risks Associated with Implementing this Policy	M6.1 What are the material financial risks to implementing this policy?	M6.1 The number of patients in the cohort is estimated and not based on data from a disease specific registry. There may be need for retreatment with tocilizumab.[xliv]

	M6.2 Can these be mitigated, if so how?	M6.2 None identified.
	M6.3 What scenarios (differential assumptions) have been explicitly tested to generate best case, worst case and most likely total cost scenarios?	M6.3 There is uncertainty as to whether tocilizumab would be used once, or whether retreatment would be required. In a low scenario set out in M3.1, tocilizumab is only used for a period of 12 months per patient. There are therefore c. 27 patients per year using the treatment. In a high scenario, around 50% of the prevalent population requires treatment, and patients require retreatment soon after they finish their initial course over 12 months. As a result, c. 50% of the prevalent population takes tocilizumab for around 11 months per year. Around 27 of these patients are new to the cohort each year (and c. 27 leave the cohort).[xlv] In both scenarios, it is assumed that new patients with Takayasu that are not controlled on earlier lines of treatment might avoid a revascularisation surgery. It is possible that they may also avoid further revascularisations (which occur in c. 70% of patients within 6.5 years).[xlvi]
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 No studies identified.

	M7.2 What issues or risks are associated with this assessment? *e.g. quality or availability of evidence*	M7.2 Not applicable.
M8 Cost Profile	M8.1 Are there non-recurrent capital or revenue costs associated with this policy? *e.g. Transitional costs, periodical costs*	M8.1 No.
	M8.2 If so, confirm the source of funds to meet these costs.	M8.2 Not applicable.

[i] Yates, Max, Graham, Karly, Watts, Richard and Macgregor, Alexander (2015) The Prevalence of Giant Cell Arteritis and Polymyalgia Rheumatic in a UK Primary Care Population..

[ii] This applies the prevalence rates to ONS (2012) population projections for 2014/15.

[iii] Policy proposition; Ponte et al (2015), Giant cell arteritis: Current treatment and management. World J Clin Cases 2015 June 16; 3(6): 484-494.

[iv] This applies the incidence rates to ONS (2012) population projections for 2014/15.

[v] Watts, R., Al-Taiar, A., Mooney, J., Scott, D. and MacGregor, A. (2009). The epidemiology of Takayasu arteritis in the UK. Rheumatology, 48(8), pp.1008-1011. Accessed online via: http://rheumatology.oxfordjournals.org/content/48/8/1008.full.pdf

[vi] Policy proposition; O'Neill, L., Ponte, C., Sznajd, J., Rodrigues, A., Seeliger, B. and Luqmani, R. (2015). Giant Cell Arteritis and Takayasu Arteritis: Are they a different spectrum of the same disease?. Indian Journal of Rheumatology.

[vii] This applies the incidence rates to ONS (2012) population projections for 2014/15. Figures rounded.

[viii] The incident population, rather than the prevalent population, was deemed the most appropriate measure for the target population as patients receive tocilizumab for a maximum of 12 months through discussions with the policy working group. The use of prevalent population, as a measure, would overstate the eligible population as those that have used the drug for one year would no longer be eligible for treatment.

[ix] Based on discussions with the clinical and policy working group. For GCA: first line - steroids with or without MTX/AZA (52-60% success rate), second line - steroids with MTX/AZA and consider cyclophosphamide or MMF (assume 80% success rate), third line - tocilizumab (assume 70% success rate), fourth line - anti-TNF or rituximab. For

TAK: first line - steroids with MTX/AZA (16-54% success rate), second line steroids with cyclophosphamide or MMF (80% success rate), third line - TCZ (70% success rate), fourth line - anti-TNF or rituximab.

[x] Based on discussions with the clinical and policy working group. An example of unsuitable treatment is use of cyclophosphamide in women who have not yet completed their families.

[xi] Figures rounded.

[xii] Luqmani, R. (2012). Large vessel vasculitides. Current Opinion in Cardiology, 27(6), pp.578-584.

[xiii] Policy proposition; Baldursson O, Steinsson, K, Bjornsson, J, et al. Giant cell arteritis in Iceland. An epidemiologic and histopathologic analysis. Arthritis Rheum 1994;37:1007-1012.fckLR

[xiv] Mohammad, A. and Mandl, T. (2015). Takayasu Arteritis in Southern Sweden. The Journal of Rheumatology, 42(5), pp.853-858.

[xv] Horizon Scanning Centre for the National Institute for Health Research (2014). Tocilizumab (RoACTEMRA) for giant cell arteritis – first and second line. NIHR HSC ID: 9049

[xvi] Based on discussions with the clinical and policy working group.

[xvii] Once patients are confirmed to have GCA or TA (by either an ultrasound scan or biopsy),

[xviii] The IFR database lists 7 IFR requests for tocilizumab in the treatment of large vessel vasculitis in the financial year 2014/15. It is not known, however, how many of these IFRs were approved nor the split between the two indications of TA and GCA.

Surgery has been estimated as required in 12% to 70% of cases [Source; Perera et. al. (2012). Takayasu Arteritis: Criteria for Surgical Intervention Should Not Be Ignored. International Journal of Vascular Medicine. Accessed online via: http://www.hindawi.com/journals/ijvm/2013/618910/ [Last accessed: 17 February 2016]]. For the target population that would have failed earlier lines of treatment, it is estimated that 50% might require surgery, with c. 70% requiring repeat surgery. Based on discussions with the working group; Saadoun et al (2012). Retrospective analysis of surgery versus endovascular intervention in Takayasu arteritis: a multicenter experience.. Circulation, Accessible via: http://www.ncbi.nlm.nih.gov/pubmed/22230484 [Last accessed: 24 February 2016].

[xx] The demographic specific growth rate is estimated using the cohorts from the ONS (2012) population projections. These are then adjusted to account for the age group of 20 years and older for TA and for 55 years and older for GCA.

[xxi] This is based on the prevalence figures set out in K1.1 and demographic growth rates in endnote xx. 50% might be eligible as set out in K1.2.

[xxii] Based on discussions with the policy working group. It was discus This applies the incidence rates to ONS (2012) population projections for 2014/15.sed that in the 'do nothing' activity could increase due to more demand for tocilizumab following greater awareness of the tocilizumab.

[xxiii] Smeeth, L. (2006). Incidence of diagnosed polymyalgia rheumatica and temporal arteritis in the United Kingdom, 1990-2001. Annals of the Rheumatic Diseases, 65(8), pp.1093-1098.

[xxiv] Please refer to K1.4

[xxv] Larsson K, et.al. (2006). Early menopause, low body mass index, and smoking are independent risk factors for developing giant cell arteritis. Annals of Rheumatic Diseases. 65(4), pp. 529-532.

[xxvi] Policy working group discussions

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

[xxviii] Figures at the high end of the range are rounded.

[xxix] Discussions with the policy working group.

[xxx] Figures may be rounded.

[xxxi] Based on the evidence review in which tocilizumab is effective treatment. Assumes that only patients with new refractory TAK who did not respond to tocilizumab would require revascularisation.

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

[xxxiii] The UKIVAS registry is a component of The Vasculitis Rare Disease Working Group of the UK and Ireland.

[xxxiv] The list price (Tocilimuzab – RoActemra - 80mg/4ml concentrate for solution for infusion vials) is £102.40 http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=16099511000001101&toc=nofloat

[xxxv] The list price (Tocilimuzab – RoActemra - CF pack - 4 pre-filled syringes, 162mg) is £913.12 http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=24780911000001107&toc=nofloat

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

[xxxvii] Based on discussions with the policy working group; policy proposition and the price set out in relation to M1.3. Daycase cost based on the delivery of monoclonal antibodies to those with Takayasyu as the first spell diagnosis, costed at 2014/15 prices. Based on a weight of c. 70 kg.

[xxxviii] 'In clinical practice, the SC formulation could be used in patients already stable on IV tocilizumab therapy and in new patients.' London Medicines Evaluation Network Review (2014).

[xxxix] The costs associated with the IFRs for tocilizumab indicated that in all cases a subcutaneous injection was used. These costs were based on estimates submitted by the requesting clinicians.

[xl] London Medicines Evaluation Network Review (2014), Tocilizumab subcutaneous injection for rheumatoid arthritis.

[xli] 'The frequency for patient follow-up should be guided by their clinical manifestations and adverse advents. The BSR recommends follow-up during the first year at weeks 0, 1, 3, 6, then months 3, 6, 9, 12 and if new symptoms or adverse effects occur. At each visit bloods tests for ESR, CRP, full blood count, glucose as well as monitoring relevant to any DMARD use should be performed.' Ponte et al (2015), Giant Cell Arteritis: Current treatment and management. World Journal of Clinical cases.

[xlii] Surgery has been estimated as required in 12% to 70% of cases [Source; Perera et. al. (2012). Takayasu Arteritis: Criteria for Surgical Intervention Should Not Be Ignored. International Journal of Vascular Medicine. Accessed online via: http://www.hindawi.com/journals/ijvm/2013/618910/ [Last accessed: 17 February 2016]]. For the target population that would have failed earlier lines of treatment, it is estimated that 50% might require surgery, with c. 70% requiring repeat surgery. Based on discussions with the working group; Saadoun et al (2012). Retrospective analysis of surgery versus endovascular intervention in Takayasu arteritis: a multicenter experience.. Circulation,

Accessible via: http://www.ncbi.nlm.nih.gov/pubmed/22230484 [Last accessed: 24 February 2016]. Cost of revascularisation based on an extract of the SUS dataset for TAK in 1st diagnosis code - OPCS relating to heart and artery/vein procedures and 2014/15 tariff.

[xliii] The supplementary protection certificate is set to expire in June 2020.

[xliv] As discussed with the policy working group.

[xlv] Based on high estimate of incident population and the assumption that the prevalent population is growing at a relatively low rate (see K2.2, K1.1).

[xlvi] Based on discussions with the working group; Saadoun et al (2012). Retrospective analysis of surgery versus endovascular intervention in Takayasu arteritis: a multicenter experience.. Circulation, Accessible via: http://www.ncbi.nlm.nih.gov/pubmed/22230484 [Last accessed: 24 February 2016].