Integrated Impact Assessment Report for Clinical Commissioning Policies

Policy Reference Number	A03X01		
Policy Title	Pegvisomant for acromegaly as a third-line treatment (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 is a policy to **routinely commission** the use of pegvisomant for certain patients with acromegaly. Acromegaly is a rare condition with an estimated prevalence across the world of around 6 in every 100,000 persons,[i] which equates to a prevalence of c. 3,300 people in the England with the condition in 2014/15.[ii]	

	K1.2 What is the number of patients currently eligible for the treatment under the proposed policy?	K1.2 Patients with refractory, active uncontrolled acromegaly could be suitable for pegvisomant under the policy. The target population for pegvisomant comprises adults with uncontrolled acromegaly who have failed or were unsuitable for first line treatment (pituitary surgery), and second-line treatment options (medical therapy as monotherapy - somatostatin analogues (SSAs)) were not successful. Patients refractory to first and second line treatment will undergo radiotherapy (which has a gradual effect). Patients would undergo medical therapy with pegvisomant while waiting for radiotherapy to become effective.[iii] Pegvisomant is proposed as third line therapy where SSAs have not led to complete response (defined as IGF-1 ≥ 1.3x ULN - adjusted for age and sex); it would be used while waiting for radiotherapy to take effect, and would be discontinued once radiotherapy became effective.[iv] The number of patients that would have had uncontrolled acromegaly after first and second-line treatment in England is estimated to be approximately 350 (or about 10% of the prevalent population).[v] However, it is estimated that around 50% of these patients would have achieved biochemical control after a median of 10 years of radiotherapy.[vi] Therefore the remaining c. 175 patients would have active acromegaly, of which an estimated c. **150 patients could be suitable for pegvisomant** at any one time.[vii]

	K1.3 What age group is the treatment indicated for?	K1.3 This treatment is indicated for adults.
	K1.4 Describe the age distribution of the patient population taking up treatment?	K1.4 Acromegaly can affect people of any age, however, it is rare in children. The average age at which people are diagnosed is around 40-45. [viii]
	K1.5 What is the current activity associated with currently routinely commissioned care for this group?	K1.5 Pegvisomant is currently not routinely commissioned for acromegaly. Pegvisomant is a drug that is taken for a limited duration with an estimated average treatment duration of 5 to 10 years. This is while patients wait for radiotherapy to become effective.[ix] Current activity for the target population is difficult to estimate. Patients may receive **pegvisomant** through legacy arrangements or through individual funding requests. [x] [xi] Of the target population outlined in K1.2, it is estimated that c. 100 patients may be receiving pegvisomant.[xii] Based on a frequency of treatment at once per day[xiii], this results in c. 37k doses of pegvisomant in 2014/15. The remainder of target population set out in K1.2 (i.e. those who do not currently use pegvisomant) would receive radiotherapy and ongoing medical therapy with **SSAs**.[xiv] [xv] Of the target population outlined in K1.2, an estimated c. 50 patients are currently receiving SSAs such as octreotide. Octreotide is for administration by a health care professional[xvi] Based on injection once every four weeks, this corresponds to c. 650 daycases and doses in 2014/15 for the 50 patients.[xvii]

	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 There were no disease-specific growth rates identified (please also see K2.2). However, the prevalence would grow in line with demographic growth of the adult population,[xviii] and it is estimated that the future prevalence of acromegaly will be in the region of:[xix] • 3,300 persons in 2016/17 • 3,300 persons in 2017/18 • 3,400 persons in 2020/21
	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 case – which projects current activity forward as a 'steady state'—future activity for **pegvisomant** is estimated to stay constant at c. 100 patients per year. Activity in relation to **octreotide** is estimated to be in the region of c. 50 per year.[xx]
	K1.8 How is the population currently distributed geographically?	K1.8 Across England - no significant geographical differences 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 moves to a 'routine commissioning' position for pegvisomant in adult patients with acromegaly. Treatment for acromegaly currently falls under specialised commissioning.[xxi]

	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 Acromegaly typically occurs as the result of an adenoma. Most adenomas are not hereditary and usually develop spontaneously.[xxii] As such, no specific growth rate for the population has been quantified.
	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 There would be a **net increase** in the number of patients accessing the treatment each year under the policy. As the policy is to commission pegvisomant for the eligible population, the entire target population set out in K1.2 would be expected to access the treatment once the policy is fully implemented. As compared to the 'do nothing' scenario, the additional number of patients starting treatment is estimated in the region of:[xxiii] • c. 40 in 2016/17 (75% part year effect) • c. 50 in 2017/18 • c. 50 in 2020/21 These figures refer to the total number of patients as compared to the do nothing, rather than referring to a year-on-year increase.
K3 Activity	K3.1 What is the current annual activity for the target	K3.1 Current activity is described in K1.5; some patients would use pegvisomant,

	population covered under the new policy? Please provide details in accompanying excel sheet.	while others would continue on somatostatin analogues.
	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 If the policy is implemented, i.e. pegvisomant is routinely commissioned, it is assumed that the whole eligible target population (as described in K1.2) would receive pegvisomant. This results in an estimated future activity in the region of:[xxiv] • c. 140 patients (51k doses of pegvisomant) in 2016/17 • c. 150 patients (56k doses of pegvisomant) in 2017/18 • c. 150 patients (57k doses of pegvisomant) in 2020/21 There would be a decrease in the number of patients on SSAs such as octreotide, and there would be close to 0 patients of the target population (please refer to K1.2 for more information on the target population) on the drug in future years.
	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 If the policy were not implemented, activity figures would be as set out in K1.7; some patients would use pegvisomant, while others would continue on SSAs.
K4 Existing Patient Pathway	K4.1 If there is a relevant currently routinely commissioned treatment, what is the current patient pathway? Describe or include a figure to outline associated activity.	K4.1 There are three treatment options for patients diagnosed with acromegaly: surgery, radiation therapy and medical therapy. Multimodal approaches including all three are often required. Pituitary surgery is the first-line treatment of choice for most acromegaly patients and success rates of 75-95% can be achieved in the case of microadenomas; control rates are lower in patients with macroadenomas. For those patients who are not suitable for surgery and/or do not show optimal disease control after surgery, there are two second-line options: medical therapy

		with a somatostatin analogue (SSA), or medical therapy in combination with radiation therapy (fractionated or single fraction): 1. Medical therapy: SSAs are effective in lowering IGF-1 levels in most patients even though complete normalisation may be achieved in a minority (c. 45% of those treated or c. 350 patients in the UK, Howlett et al, 2013). 2. Medical in combination with radiation therapy: For those patients who do not respond adequately to SSA with significantly elevated IGF-1, and are not contraindicated to irradiation (teenage young adults and/or women desiring fertility), radiation therapy in combination with SSA is the principal treatment option. Radiation therapy is effective at controlling the tumour but the normalisation of IGF-1 is very delayed with a median of 10 years. In addition, there are significant adverse events including hypopituitarism, optic nerve damage and an increased risk of secondary malignancy. It is estimated that up to 22% of patients will require radiation therapy as part of their treatment (D05/PS/a)
	K4.2. What are the current treatment access criteria?	K4.2 (See K4.1)
	K4.3 What are the current treatment stopping points?	K4.3 Once patients have normalised IGF-1 levels (defined as <1.3xULN – adjusted for age and sex), treatment can be suspended and discontinued if IGF-1 levels remain normal 3 months after discontinuation.
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 See existing patient pathway (K4). By definition, for patients who have an incomplete response to SSA therapy, continued treatment with SSA is the next best treatment.

	K5.2 Where there are different stopping points on the pathway please indicate how many patients out of the number starting the pathway would be expected to finish at each point (e.g. expected number dropping out due to side effects of drug, or number who don't continue to treatment after having test to determine likely success). If possible please indicate likely outcome for patient at each stopping point.	K5.2 Once patients have normalised IGF-1 levels (defined as <1.3xULN – adjusted for age and sex), treatment can be suspended and discontinued if IGF-1 levels remain normal 3 months after discontinuation.
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 For patients who show incomplete response to second-line medical treatment (defined as IGF-1 ≥ 1.3x ULN - adjusted for age and sex) and/or have significant associated adverse effects to SSAs (e.g. development or worsening of Type 2 diabetes mellitus, severe gastrointestinal upset, or hypersensitivity reaction), medical therapy with pegvisomant is proposed as third-line treatment. In most patients radiation therapy (fractionated or single fraction) is proposed in addition to pegvisomant as it is effective in limiting the duration of medical treatment and preventing tumour progression. In patients in whom radiotherapy is contraindicated, pegvisomant will be considered as third-line monotherapy with ongoing monitoring of the tumour remnant
	K6.2 Where there are different stopping points on the pathway please indicate how many patients out of	K6.2 Pegvisomant stoping criteria: (i) Failure to normalise levels of IGF-1 AND failure to reduce IGF-1 by 50% despite maximum titration after 6 months; OR

	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.	(ii) Evidence of efficacy having been achieved with normalisation of IGF-1 levels three months after withdrawal of treatment. Once IGF-1 is normalised on pegvisomant, the dose will be titrated downward and pegvisomant discontinued if IGF-1 remains normal; OR (iii) Serious adverse effects OR (iv) Non-compliance indicated by elevated IGF-1, and clinical evaluation despite reasonable efforts to educate patients and/or secure regular drug administration; OR (v) Patient develops either related or unrelated severe life limiting condition(s) Of the c. 150 patients expected to be prescribed pegvisomant as either monotherapy or in combination with radiation therapy, it is estimated c. 91% are likely to complete treatment.
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 An initial loading dose of pegvisomant is administered subcutaneously under medical supervision in an outpatient setting.[xxv] Future treatment would then be delivered through homecare. There could be an outpatient attendance for training.[xxvi] K7.2 No anticipated change in delivery or 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 Pegvisomant is a high cost drug excluded from tariff, so it should be captured in the high cost drug dataset for routine commissioning.
	K8.2 How will this activity related to the new patient pathway be identified?(e.g. ICD10 codes/procedure codes)	K8.2 Activity should be identified through the high cost drug dataset, by drug name and indication. A standard naming convention is recommended.
K9 Monitoring	K9.1 Do any new or revised requirements need to be included in the NHS Standard Contract Information Schedule?	K9.1 No
	K9.2 If this treatment is a drug, what pharmacy monitoring is required?	K9.2 Trusts will be required to ensure that processes are in place to track both decision to treat and evidence of effectiveness, e.g. IGF-1 level monitoring. Use of software systems to track and audit use of pegvisomant by clinicians to be mandated, in order to ensure it is administered according to the Criteria for Commissioning.
	K9.3 What analytical information /monitoring/ reporting is required?	K9.3 Specific audit reports on the use of pegvisomant and specific outcomes in this patient group will be requested by the commissioner. Participation in research studies is encouraged. In addition, all eligible patients should be invited to participate in the national acromegaly database (see the UK Acromegaly register).

	K9.4 What contract monitoring is required by supplier managers? What changes need to be in place?	K9.4 None
	K9.5 Is there inked information required to complete quality dashboards and if so is it being incorporated into routine performance monitoring?	K9.5 No
	K9.6 Are there any directly applicable NICE quality standards that need to be monitored in association with the new policy?	K9.6 Yes. NICE CSG10 – Improving outcomes for people with brain and other central nervous system tumours.
	K9.7 Do you anticipate using Blueteq or other equivalent system to guide access to treatment? If so, please outline. *See also linked question in M1 below*	K9.7 A prior approval software platform should be used if available.
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 There are around 30 Adult Specialist Endocrinology Centres that provide services to patients; some deliver these services in more local hospitals through networking arrangements (Manual for prescribed specialised services, 2013/14, page 35)
	L1.2 How will the proposed policy change the way the commissioned service is organised?	L1.2 Management of refractory acromegaly and use of pegvisomant will be undertaken by tertiary centres where there is a fully constituted peer-reviewed pituitary MDT
L2 Geography & Access	L2.1 Where do current referrals come from?	L2.1 Patients present in various settings, often when seeking treatment for co-morbidities associated with acromegaly (incl. diabetes mellitus, hypertension, arthritis, sleep apnoea and cardiovascular disease). They are diagnosed after referral to Specialist Endocrinology Centres.
	L2.2 Will the new policy change / restrict / expand the sources of referral?	L2.2 No
	L2.3 Is the new policy likely to improve equity of access?	L2.3 Yes, by routinely commissioning appropriate interventions for which there is sufficient clinical evidence.
	L2.4 Is the new policy likely to improve equality of access / outcomes?	L2.4 Yes, through a consistent commissioning position across the country.

L3 Implementation	L3.1 Is there a lead in time required prior to implementation and if so when could implementation be achieved if the policy is agreed?	L3.1 No implementation requirements.
	L3.2 Is there a change in provider physical infrastructure required?	L3.2 No change in provider physical infrastructure.
	L3.3 Is there a change in provider staffing required?	L3.3 No change required.
	L3.4 Are there new clinical dependency / adjacency requirements that would need to be in place?	L3.4 No new requirements.
	L3.5 Are there changes in the support services that need to be in place?	L3.5 No change in support services.
	L3.6 Is there a change in provider / inter-provider governance required? (e.g. ODN arrangements / prime	L3.6 No change in governance required.

	contractor)	
	L3.7 Is there likely to be either an increase or decrease in the number of commissioned providers?	L3.7 No change in the number of providers anticipated.
	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 Publication of policy by NHS England, confirming whether it is routinely or not routinely commissioned.
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*,	M1.1 No, see M1.2.

	and if so which?	
	M1.2 Is this treatment excluded from national prices?	M1.2 Pegvisomant is a high cost drug excluded from tariff.[xxvii]
	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 As an excluded drug, the price is subject to local negotiations. The list price is £50 per vial for 1ml ampoules of 10mg, £75 per vial for 1ml ampoules of 15mg and £100 per vial for 1ml ampoules of 20mg (all excl. VAT).[xxviii] For reference, the maximum daily dosage is 30mg, although the population average is typically around 19.8mg.[xxix] For the yearly cost of the drug, see M2.1.[xxx]
	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 No new price is proposed.
	M1.5 is VAT payable (Y/N) and if so has it been included in the costings?	M1.5 If homecare delivery is used, VAT would be recoverable.[xxxi]
	M1.6 Do you envisage a	M1.6 No prior approval / funding authorisation is envisaged in order to implement

	prior approval / funding authorisation being required to support implementation of the new policy?	the policy.
M2 Average Cost per Patient	M2.1 What is the revenue cost per patient in year 1?	M2.1 Overall, there would be a **net revenue cost per patient** in year one of c. **£14,000** for new patients on pegvisomant.[xxxii] Assuming a daily dose of 19.8mg[xxxiii] of **pegvisomant**, at a cost of £100 per dose and an initial loading dose of 80mg (at a cost of £480)[xxxiv], the annual **cost** of the drug in year one is estimated in the region of **£37,000** per person. Moreover, additional training costs in the region of £100 per patient are estimated.[xxxv] For patients using pegvisomant, octreotide would not be used. **Octreotide** is a high-cost drug[xxxvi] and savings for octreotide are based on an average dose of 30mg administered once every four weeks.[xxxvii] Moreover, there are administration costs in addition to the cost of the drug.[xxxviii] This results in an estimated **savings** per patient in the region of c. **£23,000**.[xxxix]
	M2.2 What is the revenue cost per patient in future years (including follow up)?	M2.2 The revenue costs and savings per patient in future years could be similar (excluding the costs for the loading dose and training costs). These costs would continue until the patient no longer had active uncontrolled acromegaly, with an average use estimated at 5 to 10 years (as set out in K1.2).

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. As more patients access treatment, there could be an estimated cost pressure in the region of:[xl] • c. £530k in 2016/17 (75% part year effect) • c. £690k in 2017/18 • c. £710k in 2020/21
	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 following from the responses to M3.1 and M4.1.
	M4.3 Where this has not been identified, set out the reasons why this cannot be measured.	M4.3 Not applicable.

	M4.4 Are there likely to be any costs or savings for non NHS commissioners / public sector funders?	M4.4 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 the CPAG
M6 Financial Risks Associated with Implementing this Policy	M6.1 What are the material financial risks to implementing this policy?	M6.1 There is a risk that the number of patients that are intolerant of SSA might change if pegvisomant became available.[xli] No changes in incidence an prevalence are factored into the calculations above. The number of patients eligible for pegvisomant is based on estimates and not based on a national registry.
	M6.2 Can these be mitigated, if so how?	M6.2 As set out in the policy proposition, the use of pegvisomant would be monitored for each patient to ensure effectiveness of the treatment. This could mitigate the risk associated around the required dosage for each patient.
	M6.3 What scenarios (differential assumptions) have been explicitly tested to generate best case, worst case and most likely total cost scenarios?	M6.3 Scenarios have been tested around the average dosage of the comparator treatment as well as the size of the target population. The figures set out in M2 and M3 assume that octreotide has an average dose of 30 mg per month. In a low **cost pressure scenario**, the average dose of octreotide is estimated at 40mg per month per person.[xlii] Under this scenario, the

		cost pressure in 2017/18 is estimated in the region of £220k for the target population. The figures estimated in M3.1 assume that c.100 patients are currently on pegvisomant, and are therefore factored into the baseline. This implies an increase of 50 patients that could receive pegvisomant under the policy. However, if the increase in patients is higher, there could be a greater cost pressure on implementing the policy. If there were **100 new patients** accessing pegvisomant (instead of 50), the cost pressure could be in the region of c. £0.4m to £1.4m in 2017/18.
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 and M7.2 Cost effectiveness has not been widely reported, however the cost effectiveness of pegvisomant relative to standard care was assessed in one UK based un-peer reviewed analysis, using 2009 assumptions. The model was based on the pegvisomant drug manufacturer's model, and appeared to compare pegvisomant monotherapy for individuals who are inadequately controlled, compared with long-acting SSA treatment. The assumptions in this model included a total annual cost for PEG of £30,482 (£100 per 20 mg dose) and for standard care of £15,409.The model found that over a 20 year time horizon the cost effectiveness of PEG is very unlikely to fall below £80,000/QALY or £212,000/LYG. The study concluded that pegvisomant is unlikely to represent good value for money when considered against the current standards applied to interventions in the UK Health service. No other cost effectiveness comparisons were identified, e.g. for combination therapy. The quality of life coefficient based on all people with acromegaly, and those particularly effective of this would gain more. The model used did not include day case tariff for administration of SSA, and they did not build in the use of radiotherapy, which would limit the duration of therapy.
M8 Cost Profile	M8.1 Are there non-recurrent capital or revenue	M8.1 None.

	costs associated with this policy? *e.g. Transitional costs, periodical costs* M8.2 If so, confirm the source of funds to meet these costs.	 M8.2 Not applicable.

[i] Based on: Orphanet (2015). "Prevalence and incidence of rare diseases: Bibliographic data - Prevalence, incidence or number of published cases listed by diseases (in alphabetical order)". [Online] Available from http://www.orpha.net/orphacom/cahiers/docs/GB/Prevalence_of_rare_diseases_by_alphabetical_list.pdf [Accessed: 07/01/2016].

[ii] Based on the population of England in 2014/15 from: ONS (2015). Annual Mid-Year Population Estimates for the UK.

[iii] Based on discussions with clinicians and the policy working group in relation to the possible place of pegvisomant in the pathway.

[iv] Policy proposition.

[v] Based on discussions with the policy working group and Howlett et al. (2013). "Control of growth hormone and IGF1 in patients with acromegaly in the UK: responses to medical treatment with somatostatin analogues and dopamine agonists." The target population is estimated at c. 150 patients.

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

[vii] The remaining patients would be unable or unsuitable for the drug (estimate based on discussions with the policy working group).

[viii] A Banerjee et al. (2006). "Acromegaly –clinical manifestations and diagnosis." *Hospital Pharmacist*. Vol 13 p. 273ff.

[ix] Policy proposition.

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

[xi] 8 individual funding requests (IFRs) for the drug were submitted in 2014/15, whilst 21 IFRs were submitted in the first half of 2015/16. Based on data extracted from the national IFR database.

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

[xiii] Based on Freda PU et al. (2015). "Long-term treatment with pegvisomant as monotherapy in patients with acromegaly: experience from ACROSTUDY." *Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists.* 21(3):264-274; and discussions with the policy working group.

[xiv] The main alternative is octreotide (based on discussions with the policy working group).

[xv] Based on policy proposition (please refer to the policy proposition document), and discussions with the policy working group. Patients would use SSAs although complete control might not be achieved.

[xvi] Based on NHS Hertfordshire GGC (2011). *Use of Somatostatin Analogues in Adult Patients with Acromegaly*. [Online] Available from http://www.enhertsccg.nhs.uk/sites/default/files/Pharmacy/Local_Decisions/Herts%20Guidance%20and%20Shared%20Care%20for%20Somatostatin%20Analogues%20in%20Acromegaly%20%20201111(cost%20update%20201309).pdf [Accessed: 28/01/2016], and NHS North of Tyne Area Prescribing Committee (2014). *LANREOTIDE AND OCTREOTIDE – Information for Treatment of Adults with acromegaly or neuroendocrine tumours in Primary Care*. [Online] Available from http://www.northoftyneapc.nhs.uk/wp-content/uploads/sites/6/2014/03/Lanreotide-and-Octreotide-information-for-primary-care-January-2014v2-2.pdf [Accessed: 28/01/2016].

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

[xviii] This is because acromegaly is rare in children and predominantly affects adults [Source: NHS Choices (2014). *Acromegaly*. [Online] Available from http://www.nhs.uk/conditions/acromegaly/Pages/Introduction.aspx [Accessed: 07/01/2016]].

[xix] Applies demographic growth based on ONS (2012) population forecasts of the adult population to the prevalence figures set out in K1.1.

[xx] Applies demographic growth based on ONS (2012) population forecasts of the adult population to the prevalence figures set out in K1.5.

[xxi] More specifically, treatment falls under W [Based on NHS England (2014). Manual for Prescribed Specialised Services 2013/14].

[xxii] NHS Choices (2014). *Acromegaly*. [Online] Available from http://www.nhs.uk/conditions/acromegaly/Pages/Introduction.aspx [Accessed: 07/01/2016].

[xxiii] Based on the total eligible patient cohort identified in K1.2. The growth in the number of patients accessing services is estimated to grow in line with demographic factors as set out in K1.6. Moreover, it is assumed that 75% of full year effects are observed in 2016/17 increasing to 100% in the following years.

[xxiv] Based on the current activity as described in K1.5, which is grown by demographic growth of the adult population in England [Source: ONS (2012). Populations projections].The policy is assumed to have 75% effect in 2016/16 and full effect in following years. Moreover, it is assumed that pegvisomant is taken daily [Source: discussions with the policy working group].

[xxv] Based on: electronic Medicines Compendium (eMC).*SOMAVERT 10mg, 15mg, 20mg, 25mg and 30mg powder and solvent for solution for* injection. [Online] Available from http://www.medicines.org.uk/emc/medicine/14353 [Accessed: 14/01/2016].

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

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

[xxviii] Based on a total packet cost for 30 ampoules of 1ml vials of £1,500 for 10mg, £2,250 for 15mg and £3,000 for 20mg. [Sources: NHS indicative price. Dictionary of medicine. [Online] Available from http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=7543511000001108&toc=nofloat; http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=7543911000001101&toc=nofloat; and http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=7544311000001100&toc=nofloat [Accessed:07/01/2016]].

[xxix] Based on an average dose of 19.8mg for individuals with persistently elevated IGF-1 levels [reported in Freda PU et al. (2015). "Long-term treatment with pegvisomant as monotherapy in patients with acromegaly: experience from ACROSTUDY." *Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists.* 21(3):264-274

[xxx] Based on: electronic Medicines Compendium (eMC).*SOMAVERT 10mg, 15mg, 20mg, 25mg and 30mg powder and solvent for solution for* injection. [Online] Available from http://www.medicines.org.uk/emc/medicine/14353 [Accessed: 14/01/2016].

[xxxi] Based on correspondence with NHS England Pharmacists and HM Revenue & Customs (2014). Section 3.2, VAT Notice 701/57: health professionals and pharmaceutical products. [Online] Available from https://www.gov.uk/government/publications/vat-notice-70157-health-professionals-and-pharmaceutical-products/vat-notice-70157-health-professionals-and-pharmaceutical-products [Accessed: 14/01/2016].

[xxxii] All figures rounded in this section.

[xxxiii] Based on an average dose of 19.8mg for individuals with persistently elevated IGF-1 levels [reported in Freda PU et al. (2015). "Long-term treatment with pegvisomant as monotherapy in patients with acromegaly: experience from ACROSTUDY." *Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists.* 21(3):264-274].

[xxxiv] Based on (eMC).*SOMAVERT 10mg, 15mg, 20mg, 25mg and 30mg powder and solvent for solution for* injection. [Online] Available from http://www.medicines.org.uk/emc/medicine/14353 [Accessed: 14/01/2016] and the policy proposition document. Costs are based on the prices for 10mg, 15mg and 20mg vials reported in M1.3. Initial dose assumed to be outside of homecare arrangements and attract VAT.

[xxxv] Based on a reported cost of £93 for an outpatient attendance (for endocrinology –follow-up, single professional based on the 2014/15 Tariff). A 10% MFF has been applied. In addition, -1.6% (accounting for both inflation and the efficiency factor) has been applied to arrive at 2015/16 figures. The cost is therefore £101.

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

[xxxvii] Based on discussions with the policy working group. Patients in the target population would not show complete response to SSAs, and so would likely be at the highest dosage for the indication (30mg). A sensitivity in relation to the highest safe dose (40mg) is tested in M6.3 based on discussions with clinicians.

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

[xxxix] Based on NHS indicative prices of £998 for 30mg injection vials [Source: Dictionary of Medicines], plus a 20% uplift to include VAT. Moreover, administration costs are estimated at c. £550 per administration [based on the weighted average cost of a day case episode identified from a SUS data extract between 2011/12 and 2014/15 with the ICD10 code *E220 – Acromegaly* and OPCS code *X894 - Somatostatin analogues Band 1*, and a correction of-1.6% (accounting for both inflation and the efficiency factor)]. Prices based on the dictionary of medicines prices (e.g. for 10mg - http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=41506110000001104&toc=nofloat)

[xl] Based on the revenue costs per patient identified in M2.1 and M2.2 and the number of patients receiving pegvisomant and octreotide described in K1.7 and K3.2. Variation based on dosing rather than on variation in the underlying population. Figures rounded.

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

[xlii] Please refer to endnote xxxvii. Based on NHS indicative prices £799 for 20mg injection vials.