Integrated Impact Assessment Report for Clinical Commissioning Policies

Policy Reference Number	A03X11		
Policy Title	Pasireotide for acromegaly as 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 policy proposes to **not routinely commission** the use of pasireotide in adult patients with acromegaly. Acromegaly is a rare condition with an estimated prevalence across the world of around 6 in every 100,000 people[i], which equates to a prevalence of 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 This policy proposes to not routinely commission the use of pasireotide in adult patients with acromegaly. The cohort covered by the policy is those patients with refractory, active uncontrolled acromegaly that could be suitable for pasireotide as third line treatment. The target population for paseriotide comprises adults with uncontrolled acromegaly who have failed or are unsuitable for first line treatment (pituitary surgery), and second-line treatment options (medical therapy as monotherapy - somatostatin analogues (SSAs). Patients with refractory to first and second line treatment will undergo radiotherapy (which has a gradual effect). Medical therapy with pasireotide while waiting for radiotherapy to become effective.[iii] Pasireotide is proposed as third line therapy where SSAs have not led to complete response; it would be used while waiting for radiotherapy to take effect.[iv] The number of adult 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.

	K1.3 What age group is the treatment indicated for?	K1.3 This treatment is indicated for adults (ages 18 and above).
	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.[vii]
	K1.5 What is the current activity associated with currently routinely commissioned care for this group?	K1.5 Pasireotide is currently not routinely commissioned for acromegaly. Pasireotide is a drug that is taken for a limited duration with an estimated average treatment duration of 5 to 10 years.[viii] This is while patients wait for radiotherapy to become effective.[ix] Current activity for **pasireotide** is difficult to estimate and only very few patients might have access to it. One individual funding request (IFR) for the drug was submitted in 2014/15, whilst 2 IFRs were submitted in the first half of 2015/16.[x] Pasireotide can be considered in conjunction with ongoing radiotherapy treatment for some patients. It is estimated that without pasireotide, all the patients in the eligible population would receive other third line therapy (which includes radiotherapy and ongoing medical therapy with **SSAs** (such as octreotide))[xi] until acromegaly is controlled.[xii]
	K1.6 What is the projected growth of the disease/condition prevalence (prior to applying the new policy) in 2, 5, and 10	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, and it is estimated that the future prevalence of

	years?	acromegaly will be in the region of:[xiii] • 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 Without routine commissioning, in future years, new patients would not receive pasireotide as a third line treatment option in future. These patients are likely to use comparator treatments such as medicinal therapy with SSAs.[xiv]
	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 'non-routine commissioning' position for pasireotide in adult patients with acromegaly.
	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 usually occurs as the result of an adenoma. Most adenomas are not inherited and usually develop spontaneously.[xv] Therefore, no specific factors affecting growth of the patient population other than demographic factors were 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 2, 5 and 10?	K2.4 The proposed policy establishes a 'not routinely commissioned' proposal for the relevant population (the specific cohort set out in K1.2). The number of patients who fall outside of the cohort covered by the proposed policy, or for whom exceptionality might be demonstrated is likely to be very small.
K3 Activity	K3.1 What is the current annual activity for the target population covered under the new policy? Please provide details in accompanying excel sheet.	K3.1 Current activity is described 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 The proposed policy establishes a 'not routinely commissioned' proposal for the relevant population (the specific cohort set out in K1.2). The number of patients who fall outside of the cohort covered by the proposed policy, or for whom exceptionality might be demonstrated is likely to be very small. As such, the target population is expected to undergo comparator treatments in future. The number of new patients undergoing treatment with comparators is therefore estimated in the region of 180 in future years.[xvi]
	K3.3 What will be the comparative	K3.3 If the policy were not implemented, 'do nothing' activity figures

	activity for the 'Next Best Alternative' or 'Do Nothing' comparator if policy is not adopted? Please details in accompanying excel sheet.	would be as set out in K1.7; patients would use 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 – K4.3 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. Patients diagnosed with acromegaly.
	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 Yes (see K4.1).
	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 Not applicable.
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 Not applicable – no new pathway proposed.

	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.	K6.2 Not applicable – no new pathway 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	K7.1 Pasireotide is administered in an outpatient setting by intramuscular injection.[xvii]
	K7.2 Is there likely to be a change in delivery setting or capacity requirements, if so what? *e.g. service capacity*	K7.2 No
K8 Coding	K8.1 In which datasets (e.g. SUS/central data collections etc.) will activity related to the new patient pathway be recorded?	K8.1 Pasireotide is a high cost drug excluded from tariff, so it would 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 Not applicable as position is to not routinely commission.
K9 Monitoring	K9.1 Do any new or revised requirements need to be included in the NHS Standard Contract Information Schedule?	K9.1 Not applicable.
	K9.2 If this treatment is a drug, what pharmacy monitoring is required?	K9.2 Not applicable.
	K9.3 What analytical information /monitoring/ reporting is required?	K9.3 Not applicable.
	K9.4 What contract monitoring is required by supplier managers? What changes need to be in place?	K9.4 Not applicable.
	K9.5 Is there inked information required to complete quality dashboards and if so is it being incorporated into routine performance monitoring?	K9.5 Not applicable.
	K9.6 Are there any directly applicable	K9.6 Not 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*	K9.7 Not applicable.
Section L - Service Impact		
Theme	**Questions**	**Comments** (Include source of information and details of assumptions made and any issues with the data)
L1 Service Organisation	L1.1 How is this service currently organised? (i.e. tertiary centres, networked provision)	L1.1 Endocrinology Service has 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 No changes proposed.
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 – no changes proposed.
	L2.3 Is the new policy likely to improve equity of access?	L2.3 - 4 Yes, 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 No – no lead in time required.
	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 – no changes required.
	L3.4 Are there new clinical dependency / adjacency requirements that would need to be in place?	L3.4 No – no changes required.

	L3.5 Are there changes in the support services that need to be in place?	L3.5 No – no changes needed.
	L3.6 Is there a change in provider / inter-provider governance required? (e.g. ODN arrangements / prime contractor)	L3.6 No – no changes required.
	L3.7 Is there likely to be either an increase or decrease in the number of commissioned providers?	L3.7 No – no new policy proposed.
	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 Not applicable.
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	M1.1 No, see M1.2.

	national prices*, and if so which?	
	M1.2 Is this treatment excluded from national prices?	M1.2 Pasireotide is a high cost drug excluded from 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 As an excluded drug, the price is subject to local negotiations. The list price is £2,300 for 20mg, 40mg, and 60mg solvent for suspension for injection vials (excl. VAT)[xviii]. For the yearly cost of the drug, see 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 No new price is proposed.
	M1.5 is VAT payable (Y/N) and if so has it been included in the costings?	M1.5 Yes. The drug is administered in an outpatient setting[xix] and as such, VAT would be recoverable.[xx] VAT is therefore included in the calculations sections M2 and M3.
	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 As the policy proposes not to routinely commission pasireotide, for acromegaly, there would be no revenue impact. For reference, the revenue cost per patient for **pasireotide** in year 1 is estimated in the region of £37,000.[xxi] The cost for the **SSA** comparator, **octreotide** is based on an average dose of 30mg to 40mg administered once every four weeks.[xxii] This results in an estimated revenue cost per patient in the region of £22,600 to £32,000.[xxiii]
	M2.2 What is the revenue cost per patient in future years (including follow up)?	M2.2 For reference, the costs per patient in future years are not likely to change and are assumed to be as set out in M2.1.
M3 Overall Cost Impact of this Policy to NHS England	M3.1 Indicate whether this is cost saving, neutral, or cost pressure to NHS England.	M3.1 Cost neutral, as the policy is to not routinely commission pasireotide, and there is little identified activity for pasireotide in the 'do-nothing' scenario (see K1.5).
	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 for the reasons given in M3.1.

	M4.2 Indicate whether this is cost saving, neutral, or cost pressure to the NHS as a whole.	M4.2 Cost neutral for the reasons given in M3.1.
	M4.3 Where this has not been identified, set out the reasons why this cannot be measured.	M4.3 Not applicable.
	M4.4 Are there likely to be any costs or savings for non NHS commissioners / public sector funders?	M4.4 Not applicable.
M5 Funding	M5.1 Where a cost pressure is indicated, state known source of funds for investment, where identified. *e.g. decommissioning less clinically or cost-effective services*	M5.1 Not applicable.
M6 Financial Risks Associated with Implementing this Policy	M6.1 What are the material financial risks to implementing this policy?	M6.1 Not applicable.
	M6.2 Can these be mitigated, if so how?	M6.2 Not applicable.
	M6.3 What scenarios (differential assumptions) have been explicitly tested to generate best case, worst case and	M6.3 Not applicable.

	most likely total cost scenarios?	
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 No published and peer reviewed studies have evaluated cost effectiveness of pasireotide treatment when compared to other therapies.
M8 Cost Profile	M8.1 Are there non-recurrent capital or revenue costs associated with this policy? *e.g. Transitional costs, periodical costs* M8.2 If so, confirm the source of funds to meet these costs.	M8.1 None identified. M8.2 Not applicable.

[i] Based on: Orphanet Report (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 pasireotide 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."

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

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

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

[ix] Policy proposition.

[x] Based on data extracted from the national IFR database.

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

[xii] Based on policy proposition (please refer to the policy proposition document), and discussions with the policy working group.

[xiii] Based on ONS (2012). Population projections and the prevalence described in K1.1.

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

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

[xvi] Based on the target population identified in K1.2 and demographic growth rates of the adult population [Source: ONS (2012). Population projections].

[xvii] Based on discussions with the policy working group and Novartis (2015). *SIGNIFOR LAR (pasireotide) –Dosing & Administration*. [Online] Available from http://hcp.novartis.com/products/signifor-lar/acromegaly/dosing-administration/#administration [Accessed: 12/01/2016]

[xviii] NHS indicative price. Dictionary of Medicines. [Online] Available from http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=29897411000001102&toc=nofloat [Accessed: 12/01/2016] for 20mg solvent.

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

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

[xxi] Based on injections every four weeks with a dose of 20mg to 60mg. [Source: The electronic Medicines Compendium (eMC). *Signifor powder and solvent for injection.* [Online] Available from http://www.medicines.org.uk/emc/medicine/30342 [Accessed: 12/01/2016]], and costs of administering the drug of £101 (based on a reported tariff for an 'Endocrinology' outpatient attendance of £93 [Source: 2014/15 National tariff] and including a 10%uplift for MFF and a correction for inflation and efficiency of -1.6% to arrive at figures for 2015/16 [Source: NHS England finance lead]). 20% VAT was added to the costs reported in M1.3.

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

[xxiii] Based on NHS indicative prices of £799 for 20mg injection vials and £998 for 30mg injection vials [Source: Dictionary of Medicines], plus a 20% uplift to include VAT. Administration costs are estimated at £542 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=4150611000001104&toc=nofloat)