Integrated Impact Assessment Report for Clinical Commissioning Policies

Policy Reference Number	A03X02		
Policy Title	Tolvaptan for hyponatraemia secondary to the Syndrome of Inappropriate Antidiuretic Hormone (SIADH) in patients requiring cancer chemotherapy		
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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 **routinely commission** the use of tolvaptan for patients with mild to moderate hyponatraemia secondary to the Syndrome of Inappropriate Antidiuretic Hormone (**SIADH**), in whom initiation of chemotherapy is delayed as a result of the hyponatraemia. The prevalence of hyponatraemia has been estimated at c. 1.7% in the general population[i] and may therefore affect around 935,000 people in England in 2014/15.[ii]	

	K1.2 What is the number of patients currently eligible for the treatment under the proposed policy?	Whilst it is difficult to quantify how many patients will have chemotherapy delayed due to hyponatraemia, one centre[iii] estimates that[iv]: • There are c. 500 new cases of lung cancer diagnosed each year; • Of which, 10 – 15% (50 to 75 patients) are small cell lung cancer; and • An estimated 5% (3 to 4 patients) each year will have SIADH preventing chemotherapy from commencing and thus requiring tolvaptan. There is uncertainty around how this would translate into a national estimate. Based on the number of patients in the scenario and centre, clinical opinion is that a national level estimate could be in the region of 30 to 40 patients each year.[v]
	K1.3 What age group is the treatment indicated for?	K1.3 For both paediatric patients and adults (all ages).
	K1.4 Describe the age distribution of the patient population taking up treatment?	K1.4 The age distribution of the patients taking up the treatment is likely to be varied given this is a specific group of patients whose chemotherapy treatment is being delayed.[vi]
	K1.5 What is the current activity associated with currently routinely commissioned care for this group?	K1.5 The number of patients in this group currently receiving tolvaptan is unknown. Data from the national IFR database shows that 12 IFRs were considered by NHS England in 2014/15 and 21 in 2013/14. It is unclear; however, how many of these were approved or whether they relate to the specific patient group covered by this policy. It is expected that current annual activity could be in the region of **10**

		to 20 patients.[vii] In the absence of tolvaptan, patients may be treated simply with fluid restriction but this is generally a slow process and adherence to this treatment varies by patient.[viii] For this patient group, however, it is expected that fluid restriction would be unsuitable, as patients often require intravenous hydration, rather than restriction, prior to chemotherapy.[ix] Demeclocycline may also be used; however this drug is linked with adverse effects and unpredictable pharmacology which limit its use.[x]
	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 It assumed that activity would grow in line with demographic growth (see K2.2). As such, the prevalence of the condition could be: • ~ 950,000 in 2016/17 (year 1) • ~ 955,000 in 2017/18 (year 2) • ~ 975,000 in 2020/21 (year 5)
	K1.7 What is the associated projected growth in activity (prior to applying the new policy) in 2,5 and 10 years?	K1.7 Prior to applying the new policy, it assumed that activity would grow in line with demographic growth and therefore be broadly 10 to 20 in each of years 1, 2 and 5.[xi,'xii]
	K1.8 How is the population currently distributed geographically?	K1.8 Across England, no significant geographical differences have been identified in this review.
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	K2.1 The new policy would add a treatment option for patients where hyponatraemia secondary to SIADH is preventing chemotherapy from proceeding.

	restrict an existing treatment threshold / add an additional line / stage of treatment / other?	
	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 Hyponatraemia is common in cancer patients, particularly in patients with lung cancer, and more specifically small cell lung cancer.[xiii] A key cause of lung cancer is smoking.[xiv] Increasing smoking rates for women and decreasing smoking rates for men drive the trend of respectively increasing and decreasing lung cancer rates.[xv]
	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 No changes have been 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 Given the target population of c. 30 to 40 patients, as identified in K1.2, and current annual activity estimated at 10 to 20 patients, as identified in K1.5, the net increase in patients could therefore be in the region of **10 to 30 patients**, with a mid-estimate of **20 patients** per year in each of years 1, 2 and 5.[xvi]
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 As set out in question K1.5, it is unclear what the current activity is for the target population and it is estimated that 10 to 20 patients currently receive tolvaptan for this indication.

	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 number of patients receiving tolvaptan under the policy would comprise those currently receiving it, identified in K1.5, and the net increase in those receiving as a result of the policy, as identified in K2.4. Therefore an estimated 30 to 40 patients, equal to the size of the target population group from K1.2, would receive tolvaptan in year 1 (2016/17) should the policy be implemented.[xvii]
	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 this policy is not adopted, then current activity, assumed to be the 'steady state' would be expected to roll forward in future years. The future activity levels are therefore estimated to be equal to those set out in K1.5.
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 Inpatient hyponatraemia is common and first line therapy is fluid restriction, managed by the inpatient clinicians. Second line therapy is demeclocycline although this is rarely used as it causes gastrointestinal disturbance, renal toxicity and gives an unpredictable response with a slow onset of action. Whilst hyponatraemia does affect many inpatients the result of this is normally limited, however there is a group of patients where the slow correction of hyponatremia is delaying chemotherapy. There is currently no pathway for access to tolvaptan therapy, with some patients receiving therapy via individual funding requests (IFRs).
	K4.2. What are the current treatment access criteria?	K4.2 Current treatment for these patients is fluid restriction and/or demeclocycline. There are no specific criteria to undergo fluid restriction although patients awaiting chemotherapy have to be well pre-hydrated and thus fluid restriction may not be a suitable treatment for hyponatraemia in this subset of patients. Please refer to the British National Formulary for the contraindications.

	K4.3 What are the current treatment stopping points?	K4.3 Fluid restriction will be stopped after clinical and biochemical improvement for symptoms and serum sodium.
K5 Comparator (next best alternative treatment) Patient Pathway	K5.1 If there is a 'next best' alternative routinely commissioned treatment what is the current patient pathway? Describe or include a figure to outline associated activity. K5.2 Where there are different stopping points on the pathway please indicate how many patients out of the number starting the pathway would be expected to finish at each point (e.g. expected number dropping out due to side effects of drug, or number who don't continue to treatment after having test to determine likely success). If possible please indicate likely outcome for patient at each stopping point.	K5.1 As K4.1-K4.3 K5.2 As K4.1-K4.3
K6 New Patient Pathway	K6.1 Describe or include a figure to outline associated activity with the patient pathway for the proposed new policy. K6.2 Where there are different stopping	K6.1 For cancer patients in whom chemotherapy is being delayed, tolvaptan will be routinely commissioned for mild-moderate hyponatraemia according to the patient pathway diagram in the appendix. The treating oncologist will need to discuss the patient with the locally designated endocrinologist to confirm appropriate use of tolvaptan. K6.2 Tolvaptan will be stopped after a maximum of 10 days even if it

	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.	has been ineffective. Tolvaptan will also be stopped if serum sodium has increased enough to allow chemotherapy to be commenced.
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 This would be delivered to the patient in an inpatient setting.[xviii]
	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 anticipated change. Tolvaptan will be used for inpatients only, similar to fluid restriction.
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 Tolvaptan is a high cost drug excluded from tariff, so it should be captured in the high cost drug dataset for routine commissioning. An annual audit for this indication should be undertaken for monitoring and assurance purposes.[xix]

	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 Whilst using tolvaptan, daily serum sodium and renal function tests will need to be performed, as well as fluid balance monitoring.
	K9.3 What analytical information /monitoring/ reporting is required?	K9.3 Please refer to K8.1.
	K9.4 What contract monitoring is required by supplier managers? What changes need to be in place?	K9.4 None as no changes to the NHS Shared Contract Information Schedule are expected.
	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	K9.6 No.

	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 A prior approval software platform would be used if available.[xx]
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 Hyponatraemia is common and occurs in approximately 30% of inpatient admissions (Upadhyay et al, 2006). All hospital clinicians are responsible for the day to day management of a patient's fluid balance. Oncologists intending to treat patients with chemotherapy are responsible for ensuring adequate hydration and general health of the patient prior to commencing this intervention. There is no specific service specification in relation to the management of hyponatraemia.
	L1.2 How will the proposed policy change the way the commissioned service is organised?	L1.2 Treating oncologists will be required to liaise with the locally designated endocrinologist (or other specialist) who is responsible for confirming the appropriate use of tolvaptan.
L2 Geography & Access	L2.1 Where do current referrals come from?	L2.1 Individual funding requests from the treating clinician.

	L2.2 Will the new policy change / restrict / expand the sources of referral?	L2.2 Oncologists are expected to seek approval from locally designated endocrinologists (or other specialists) for the appropriate use of tolvaptan. The patient will not be referred to the endocrinology services and will remain under the care of the treating oncologist.
	L2.3 Is the new policy likely to improve equity of access?	L2.3 The new policy is anticipated to improve the equity of access to tolvaptan.
	L2.4 Is the new policy likely to improve equality of access / outcomes?	L2.4 The new policy is anticipated to improve the equality of access to tolvaptan and the outcomes of hyponatraemic cancer patients.
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 lead in time.
	L3.2 Is there a change in provider physical infrastructure required?	L3.2 No change anticipated
	L3.3 Is there a change in provider staffing required?	L3.3 As mentioned in K9.7, where a prior approval software platform would be used, there would need to be the appropriate staffing requirements in Trusts.
	L3.4 Are there new clinical dependency / adjacency requirements that would need to be in place?	L3.4 None required.

	L3.5 Are there changes in the support services that need to be in place?	L3.5 No change required.
	L3.6 Is there a change in provider / inter-provider governance required? (e.g. ODN arrangements / prime contractor)	L3.6 No change required.
	L3.7 Is there likely to be either an increase or decrease in the number of commissioned providers?	L3.7 All hospitals will be able to prescribe tolvaptan via the locally designated endocrinologist (or other specialist) for the specific cohort defined in the policy.
	L3.8 How will the revised provision be secured by NHS England as the responsible commissioner? (e.g. publication and notification of new policy, competitive selection process to secure revised provider configuration)	L3.8 New policy publication.
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, please refer to M1.2.

	national prices*, and if so which?	
	M1.2 Is this treatment excluded from national prices?	M1.2 Tolvaptan is a high cost drug excluded from tariff. *Please note that at the request of the Finance Lead and Accountable Commissioner, it has been put to the Tariff Pricing Group to consider whether tolvaptan should be included within the tariff for its use under this policy.*
	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 tolvaptan is listed as a high cost drug, the price is subject to local negotiations. The list price is for 10 tablets of 15mg or 30mg is c. £747, or c. £895 including VAT. This is the same cost for either a 15mg or 30mg tablet.[xxi] Note that in the 5-year horizon considered, no change to the price of tolvaptan is expected.
	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 – though as noted in M1.2, the pricing of this is subject to consideration by the Tariff Pricing Group.
	M1.5 is VAT payable (Y/N) and if so has it been included in the costings?	M1.5 VAT would be recoverable under certain specific conditions[xxii]. It is assumed here that VAT would not be recoverable.
	M1.6 Do you envisage a prior approval / funding authorisation being required to support implementation of the new	M1.6 No.

	policy?	
M2 Average Cost per Patient	M2.1 What is the revenue cost per patient in year 1?	M2.1 Depending on dosage and treatment duration, the cost of tolvaptan per patient may be between c. £360 and £1,705. Patients would initiate treatment at a dose of 15mg once daily, to be raised up to a maximum of 60mg daily.[xxiii] The treatment duration could last between 4 and 10 days.[xxiv] With treatment duration of 4 days and a daily dose of 15-30mg, the cost of tolvaptan per patient would be c. £360. For treatment duration of 10 days, with the starting dose of 15mg on the first day followed by a daily dose of 45-60mg for another 9 days, the cost of tolvaptan would be c. £1,705. Tolvaptan is administered orally and as such no costs of administration have been assumed. Where it is successful in raising sodium levels, the patient would then go on to receive chemotherapy. These costs, however, would be incurred in the 'do nothing' case and the impact of tolvaptan is to allow the patient to begin their treatment sooner.[xxv] As such chemotherapy costs remain unchanged. The cost per patient is therefore expected to range between **£360 and £1,705.**
	M2.2 What is the revenue cost per patient in future years (including follow up)?	M2.2 Tolvaptan would be used for a maximum of 4 to 10 days and is not proposed to be used as a long-term treatment. As such, the cost per patient in future years for tolvaptan would be zero.
M3 Overall Cost Impact of this Policy to NHS England	M3.1 Indicate whether this is cost saving, neutral, or cost pressure to NHS	M3.1 Please refer to M4.2.

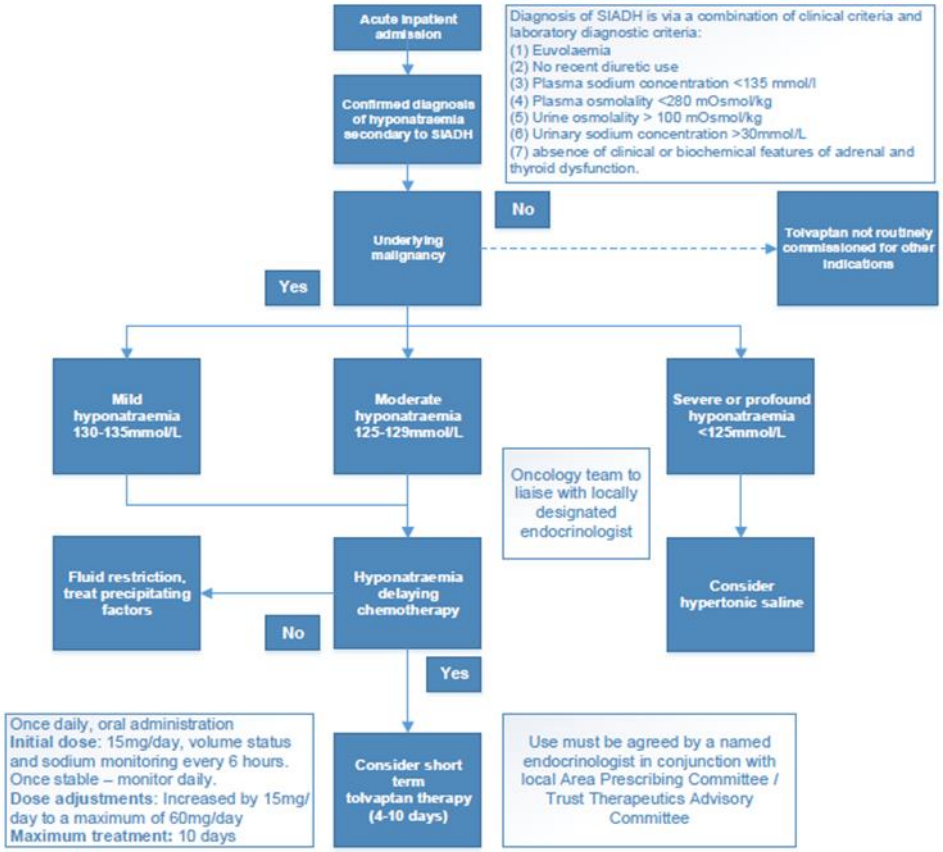
	England. M3.2 Where this has not been identified, set out the reasons why this cannot be measured.	 M3.2 Not applicable.
M4 Overall cost impact of this policy to the NHS as a whole	M4.1 Indicate whether this is cost saving, neutral, or cost pressure for other parts of the NHS (e.g. providers, CCGs). M4.2 Indicate whether this is cost saving, neutral, or cost pressure to the NHS as a whole.	M4.1 Please refer to M4.2. M4.2 There could be a slight cost pressure to the NHS as a whole from the increased use of tolvaptan; however, as discussed in M1.2, it has been put to the Tariff Pricing Group to consider whether or not the use of tolvaptan for this policy should be included within tariff. Based on a mid-net increase of 20 patients, identified in K2.4, and the cost per patient in M2.1, it is estimated that there would be a cost pressure in the region of c. **£7,000 to £35,000** each year.[xxvi] A range of estimates are considered in M6.1. If tolvaptan remains a high cost drug excluded drug from tariff, then this cost pressure would be borne by NHS England. If tolvaptan would be included within the tariff, then this would instead be borne by providers. Whilst there is no conclusive evidence around impacts on length of stay (see M7.1), any potential impacts could lead to some savings for commissioners or providers.[xxvii]

	M4.3 Where this has not been identified, set out the reasons why this cannot be measured.	M4.3 Not applicable.
	M4.4 Are there likely to be any costs or savings for non NHS commissioners / public sector funders?	M4.4 No.
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 discussed at CPAG.
M6 Financial Risks Associated with Implementing this Policy	M6.1 What are the material financial risks to implementing this policy?	M6.1 No material financial risks have been identified.
	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 most likely total cost scenarios?	M6.3 The scenarios considered are based on different doses of the drug, treatment duration and the number of additional patients. [xxviii] The range of £7,000 to £35,000[xxix] identified in M3.1 is based on: **The low figure of £7,000** is estimated using 20 additional patients receiving: • 15mg of tolvaptan once a day for 4 days. **The high figure of £35,000** is estimated using 20 additional patients

		receiving: • 15mg of tolvaptan on day 1; and • 45-60mg of tolvaptan for a further 9 days. The lowest cost pressure is estimated at c. **£4,000**.[xxx] This uses a net increase of 10 patients (see K2.4), all using the low dosage of tolvaptan: • 15mg of tolvaptan once a day for 4 days. The highest cost pressure is estimated at c. **£52,000**.[xxxi] This uses a net increase of 30 patients (see K2.4), all using • 15mg of tolvaptan on day 1; and • 45-60mg of tolvaptan for a further 9 days.
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 There is no evidence on cost effectiveness of using tolvaptan to improve hyponatraemia in order to allow chemotherapy to commence. Whilst there is one study looking into the impact on length of stay (19.5% reduction as in Dasta et al, 2012) this result was not statistically significant. M7.2 This study is limited as performed on data from US hospitals and patients with severe hyponatraemia, not just mild and moderate as covered in this policy.
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 None expected.

	M8.2 If so, confirm the source of funds to meet these costs.	M8.2 Not applicable.

Appendix: Patient Pathway



[i] Mohan, S. et al., "Prevalence of hyponatremia and association with mortality: results from NHANES", American Journal of Medicine, 2013 Dec;126(12):1127-37.e1. doi: 10.1016/j.amjmed.2013.07.021, accessed via: http://www.ncbi.nlm.nih.gov/pubmed/24262726, last accessed: 28/01/2016.

[ii] This uses the prevalence rate and ONS (2012) population projections.

[iii] Leicester University Hospital NHS Trust (Source: policy proposition).

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

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

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

[vii] Based on discussions with the policy working group. As noted, based on the IFR data there is uncertainty around this estimate.

[viii] Policy Proposition.

[ix] Policy Proposition.

[x] Policy Proposition.

[xi] As noted in K1.5, there is uncertainty around the current activity estimates.

[xii] Demographic growth is applied to these figures, however given the low values they remain broadly constant.

[xiii] Policy Proposition.

[xiv] Cancer Research UK, http://www.cancerresearchuk.org/about-cancer/type/lung-cancer/about/lung-cancer-risks-and-causes, last accessed: 28/01/2016.

[xv] See Cancer Research UK: http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/lung-cancer/incidence#heading-Two, last accessed: 28/01/2016.

[xvi] As noted in K1.2 and K1.5, there is uncertainty around the size of the target population and current activity, and as such in the net increase in activity under the policy.

[xvii] As noted in K1.2, there is uncertainty around the size of the target population.

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

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

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

[xxi] Dictionary of medicine, http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=15934611000001100&toc=nofloat, last accessed: 25/11/2015.

[xxii] Please refer to Section 3.2 of VAT Notice 701/557 (https://www.gov.uk/government/publications/vat-notice-70157-health-professionals-and-pharmaceutical-products/vat-notice-70157-health-professionals-and-pharmaceutical-products)

[xxiii] EMC website: http://www.medicines.org.uk/emc/medicine/22210, last accessed: 28/01/2016.

[xxiv] Policy Proposition.

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

[xxvi] Please note that figures are rounded to the nearest thousand.

[xxvii] This could lead to a slight cost saving for providers, where the spell is within the trimpoint, or to the commissioner, where the spell had exceeded the trim point as this would reduce excess bed day charges. As a point of reference, and proxy for potential savings, the excess bed day tariff ranges between c. £190 and £410 per day (Source: NHS national tariff 2014/15 range in per day long stay payments).

[xxviii] As noted in K1.2 and K1.5, there is uncertainty around the size of the target population and current activity, and as such in the net increase in activity under the policy.

[xxix] Please note that figures are rounded to the nearest thousand.

[xxx] Please note that figures are rounded to the nearest thousand.

[xxxi] Please note that figures are rounded to the nearest thousand.