Integrated Impact Assessment Report for Clinical Commissioning Policies

Policy Reference Number	D08X03		
Policy Title	Ziconotide (intrathecal delivery) for chronic refractory cancer pain		
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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 a **non-routine commissioning** position for ziconotide (intrathecal delivery) for adults with chronic refractory cancer pain that is not responding to conventional management. **Chronic or persistent pain of** moderate to severe intensity is estimated to affect around 19% of adult Europeans.[i] In total there may therefore be around 8.1m adults in England with the condition.[ii]	
	K1.2 What is the number of patients	K1.2 The number of patients who may be eligible for treatment is only	

	currently eligible for the treatment under the proposed policy?	a subset of the prevalent population; those whose pain is related to cancer, who present for treatment and who do not respond to already commissioned pain management.[iii, iv]
		
		Currently, patients presenting with chronic pain are prescribed first line drug treatments, along with other treatment modalities as part of a multimodal approach e.g. physiotherapy, which include[v]:
		• analgesics (paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs) and opioids); or
		• for neuropathic pain: specific antidepressants and anticonvulsants.
		
		It is estimated that around 20% of patients fail to achieve adequate sustained pain relief when treated with these medications, and in these cases advanced interventional approaches may be necessary. [vi]These include:[vii]
		
		• nerve blocks;
		• surgery; and
		• intrathecal injections of drugs such as (given in combination in some cases):
		  • morphine
		  • hydromorphone
		  • fentanyl
		  • clonidine
		  • local anaesthetics
		
		It is estimated that only c. 100 cancer patients would be considered each year for Intrathecal Drug Delivery (ITDD) systems, and that those eligible for intrathecal ziconotide, would be no more than 10 new cases per year nationally.[viii]

	K1.3 What age group is the treatment indicated for?	K1.3 The treatment is indicated for adults (aged 18 years and over).
	K1.4 Describe the age distribution of the patient population taking up treatment?	K1.4 As the prevalence of chronic pain increases with age the number of patients with chronic pain is likely to increase along with this demographic.[ix]
	K1.5 What is the current activity associated with currently routinely commissioned care for this group?	K1.5 Currently, where the treatments outlined in K1.2 are ineffective, contraindicated or limited by adverse effects, a patient may be considered for ziconotide. It is estimated that there are approximately **three patients** on intrathecal ziconotide for cancer pain.[x] It is expected that the remaining c.7 patients would be eligible for ziconotide may currently be receiving either: • no treatment, or current standard treatment; or • one of the ITDD treatment options as listed in K1.5. It is expected, however, that these may not be fully effective and have an unacceptable side effects profile.[xi] As such it is likely that these patients have frequent interactions with the health service.
	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 future changes in the prevalence of chronic pain has been identified and therefore the prevalence rate outlined in K1.1 is expected to grow in line with demographics and be around:[xii] • ~8.2m in 2016/17 (year 1) • ~8.3m in 2017/18 (year 2) • ~8.4m 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 In the 'do nothing' the number of patients expected to receive ziconotide for chronic cancer pain is expected to remain at three patients per year, as identified in K1.5.
	K1.8 How is the population currently distributed geographically?	K1.8 No geographical distribution of patients with chronic pain has 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 proposes that ziconotide is **not routinely commissioned.**
	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 There are a number of different risk factors associated with chronic pain which include (amongst others):[xiii] • Socio-demographic; • Clinical; • Psychological; • Biological; and • Numbers surviving cancer and cancer treatment.
	K 2.3 Are there likely to be changes in	K2.3 No changes in demography or geography of the patient

	geography/demography of the patient population and would this impact on activity/outcomes? If yes, provide details.	population 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 The proposed policy establishes a 'not routinely commissioned' position 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. Other than any exceptional patients identified above, under the policy no new patients are expected to access the treatment. How current activity changes over time will depend on when the current patients stop receiving the drug. Depending on this there would therefore be a **net decrease** of between: • 0 and 3 patients in 2016/17 (year 1) • 0 and 3 patients in 2017/18 (year 2) • 0 and 3 patients in 2020/21 (year 5)
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 As identified in K2.4, the number of new patients receiving ziconotide is expected to be zero under the policy. The total number of patients receiving ziconotide each year will therefore depend on when the current 3 patients stop receiving the drug.

		The remaining c. 7 patients who could be considered for ziconotide are expected to receive the same treatment as in the 'do-nothing', as identified in K1.2. These patients are expected to continue to have frequent interactions with the health service if their pain is not appropriately managed.[xiv]
	K3.3 What will be the comparative activity for the 'Next Best Alternative' or 'Do Nothing' comparator if policy is not adopted? Please details in accompanying excel sheet.	K3.3 The 'do-nothing' activity is set out in K1.7.
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 a number of treatments for chronic pain that are routinely commissioned. Chronic pain is common and a number of patients will manage their own symptoms and not present to healthcare practitioners. Of those that do present, many will have their pain manged sufficiently in primary care using medications including paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs). Patients whose pain cannot be satisfactorily managed in primary care will be referred to specialist pain management services. If pain relief is inefficient, or side effects are intolerable, the patient will be referred on to a specialised pain centre where more invasive strategies can be used including nerve blocks, surgery and intrathecal injection of medications such as morphine, fentanyl or bupivacaine, alone or in combination.
	K4.2. What are the current treatment access criteria?	K4.2 Pain relief in primary care that is ineffective or limited by adverse effects. Referral and management in specialist pain centres with a broader biopsychosocial model of care that remains ineffective and where more specialised approaches are considered appropriate.

	K4.3 What are the current treatment stopping points?	K4.3 Patients whose pain is adequately managed where impact on quality of life is acceptable to patient will not progress further in the pathway. Patients may also stop medications when the side effects become intolerable.
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 As K4.1. Ziconotide would be an alternative to other ITDD medications when they are ineffective, contraindicated or limited by adverse effects.
	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 It is estimated that less than 10 patients per year would continue along the treatment pathway with cancer pain that is not managed by any other intervention.
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 – Ziconotide not routinely commissioned.
	K6.2 Where there are different stopping points on the pathway please indicate	K6.2 Not applicable – Ziconotide not routinely commissioned.

	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.	
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 Ongoing pump refills would be via a pump refill outpatient clinic in the specialised centre or by other means as organised and managed by the specialised centre.[xv] K7.2 Not applicable – Ziconotide not routinely commissioned.
K8 Coding	K8.1 In which datasets (e.g. SUS/central data collections etc.) will activity related to the new patient pathway be recorded? K8.2 How will this activity related to the	K8.1 Ziconotide is listed as a high cost drug[xvi] and therefore activity related to the treatment may be recorded in the high cost drug dataset. K8.2 Future activity in relation to the new patient pathway may be

	new patient pathway be identified?(e.g. ICD10 codes/procedure codes)	identified in the high cost drug database.
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 – Ziconotide not routinely commissioned.
	K9.2 If this treatment is a drug, what pharmacy monitoring is required?	K9.2 Not applicable – Ziconotide not routinely commissioned.
	K9.3 What analytical information /monitoring/ reporting is required?	K9.3 Not applicable – Ziconotide not routinely commissioned.
	K9.4 What contract monitoring is required by supplier managers? What changes need to be in place?	K9.4 Not applicable – Ziconotide not routinely commissioned.
	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 – Ziconotide not routinely commissioned.
	K9.6 Are there any directly applicable NICE quality standards that need to be monitored in association with the new	K9.6 Not applicable – Ziconotide not routinely commissioned.

	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 – Ziconotide not routinely commissioned.
Section L - Service Impact		
Theme	**Questions**	**Comments** (Include source of information and details of assumptions made and any issues with the data)
L1 Service Organisation	L1.1 How is this service currently organised? (i.e. tertiary centres, networked provision) L1.2 How will the proposed policy change the way the commissioned service is organised?	L1.1 Intrathecal ziconotide is currently only used within clinical trial settings or following approved individual funding requests. The implantation of the device is undertaken at a tertiary specialist pain centres. L1.2 Not applicable – Ziconotide not routinely commissioned.
L2 Geography & Access	L2.1 Where do current referrals come from? L2.2 Will the new policy change / restrict / expand the sources of referral?	L2.1 Referrals to the tertiary pain centre come from secondary care specialist pain services. L2.2 Not applicable – Ziconotide not routinely commissioned.

	L2.3 Is the new policy likely to improve equity of access?	L2.3 As ziconotide is not being routinely commissioned, equity of access will remain unchanged.
	L2.4 Is the new policy likely to improve equality of access / outcomes?	L2.4 As ziconotide is not being routinely commissioned, equality of access will remain unchanged.
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 Not applicable – Ziconotide not routinely commissioned.
	L3.2 Is there a change in provider physical infrastructure required?	L3.2 Not applicable – Ziconotide not routinely commissioned.
	L3.3 Is there a change in provider staffing required?	L3.3 Not applicable – Ziconotide not routinely commissioned.
	L3.4 Are there new clinical dependency / adjacency requirements that would need to be in place?	L3.4 Not applicable – Ziconotide not routinely commissioned.
	L3.5 Are there changes in the support services that need to be in place?	L3.5 Not applicable – Ziconotide not routinely commissioned.

	L3.6 Is there a change in provider / inter-provider governance required? (e.g. ODN arrangements / prime contractor)	L3.6 Not applicable – Ziconotide not routinely commissioned.
	L3.7 Is there likely to be either an increase or decrease in the number of commissioned providers?	L3.7 Not applicable – Ziconotide not routinely commissioned.
	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 – Ziconotide 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 Not applicable – Ziconotide not routinely commissioned.
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 Ziconotide is listed as a high cost drug and therefore is not paid under national prices.
	M1.2 Is this treatment excluded from	M1.2 The drug itself is excluded from national prices.

	national prices?	It is expected that these patients would already have an ITDD, which would be covered by the current commissioning policy on intrathecal pumps for treatment of severe chronic pain and as such is outside of the scope of this policy.[xvii, xviii]
	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 a high cost drug, ziconotide may be subject to local price negotiations. The list price of ziconotide, marketed under the trade name – Prialt®, is listed as : • £272, or £326 including VAT, for a 100 micrograms/1ml solution[xix] [xx]; or • £1,359, or £1,631, including VAT for a 500 micrograms/5ml solution.[xxi] The expiration date for the patent of ziconotide could not be confirmed.[xxii] As such there is uncertainty surrounding how the price of ziconotide may change in the future.
	M1.4 If a new price has been proposed how has this been derived / tested? How will we ensure that associated activity is not additionally / double charged through existing routes?	M1.4 Not applicable.
	M1.5 is VAT payable (Y/N) and if so has it been included in the costings?	M1.5 VAT would be recoverable under certain specific conditions[xxiii]. 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 policy?	M1.6 No.
M2 Average Cost per Patient	M2.1 What is the revenue cost per patient in year 1?	M2.1 The cost per patient in year one would depend on the dosage and treatment duration. It has been estimated that under the assumption of a starting dose of 2.4 µg/day and a dose regimen after titration of approximately 9.6 to 21.6 µg/day[xxiv], the cost of treatment for one year of ziconotide, including the cost of outpatient clinic appointments for pump refills, could be:[xxv] • ~ £3.1k for 2.4 µg/day; • ~ £12.2k for 9.6 µg/day; • ~ £27.3k for 21.6 µg/day.
	M2.2 What is the revenue cost per patient in future years (including follow up)?	M2.2 Where patients continue to receive ziconotide, the costs would be expected to be in the region of those identified 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 The policy is to **not routinely commission** this treatment. The 0-3 net decrease in patients accessing treatment each year identified in K2.4 would lead to a maximum likely annual cost saving to NHS England of £82k.[xxvi] It is therefore considered to be **cost neutral** overall.
	M3.2 Where this has not been identified, set out the reasons why this cannot be	M3.2 Not applicable.

	measured.	
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 This policy is likely to be **cost neutral** to other parts of the NHS.
	M4.2 Indicate whether this is cost saving, neutral, or cost pressure to the NHS as a whole.	M4.2 This policy is expected to be **cost neutral** to the NHS as a whole.
	M4.3 Where this has not been identified, set out the reasons why this cannot be measured.	M4.3 Not applicable.
	M4.4 Are there likely to be any costs or savings for non NHS commissioners / public sector funders?	M4.4 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 Not applicable.
M6 Financial Risks Associated with Implementing this Policy	M6.1 What are the material financial risks to implementing this policy?	M6.3 No material financial risks 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 Not applicable.
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 Dewilde et al, 2009, discuss a cost-effectiveness model for intrathecal ziconotide use in comparison to 'best supportive care' from a UK NHS perspective. The authors report a base case incremental cost-effectiveness ration (ICER) of £27,443 per QALY. The authors note a variability range from £15,500 - £44,700 due to dosing and discount rates.
	M7.2 What issues or risks are associated with this assessment? *e.g. quality or availability of evidence*	M7.2 The evidence uses 'best supportive care' as a comparator however it is focused on the cancer population. Sufferers of chronic pain from non-malignant sources are likely to continue trying alternative means of pain management. The evidence is also limited due to the use of expert opinion as the basis for some assumptions and therefore there exists a potential for bias.
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 identified.
	M8.2 If so, confirm the source of funds to	M8.2 Not applicable.

	meet these costs.	

[i] Breivik, H., Collett, B., Ventafridda, V., Cohen, R. and Gallacher, D. (2006). Survey of chronic pain in Europe: Prevalence, impact on daily life, and treatment. European Journal of Pain, 10(4), pp.287-287. [online] Available at: http://www.ncbi.nlm.nih.gov/pubmed/16095934/ [Accessed 14 Jan. 2016].

[ii] After applying the prevalence rate to the population of adults in England. Based on population projections for 2014. (ONS, 2012).

[iii] Please refer to the policy proposition.

[iv] Non-cancer pain is already covered by NHS England commissioning policy D08/P/a which sets a not routinely commissioned position for intrathecal drug delivery for non-cancer pain.

[v] Please refer to the policy proposition.

[vi] Please refer to the policy proposition.

[vii] Based on discussions with the policy working group

[viii] Based on discussions with the policy working group, updated to reflect that only approximately 50% of intrathecal drug delivery devices have historically been for cancer pain (See commissioning policy D08/P/a)

[ix] Based on discussion with the policy working group

[x] Based on discussions with the policy working group, adjusted to reflect cancer pain only (50%).

[xi] Please refer to the policy proposition.

[xii] After applying the p.a growth rate for the population of England between 2015 and 2025. ONS (2012). Population projections.

[xiii] Van Hecke, O., Torrance, N. and Smith, B. (2013). Chronic pain epidemiology and its clinical relevance. *British Journal of Anaesthesia*, 111(1), pp.13-18.

[xiv] Based on discussions with the policy working group

[xv] Based on discussions with the policy working group

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

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

[xviii] NHS England Clinical Commissioning Policy (D08/P/a): Intrathecal pumps for treatment of severe chronic pain.

[xix] Dmd.medicines.org.uk, (2016). Dictionary of Medicines and Devices Browser Portal. [online] Available at: http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=10605711000001107&toc=nofloat [Accessed 15 Jan. 2016].

[xx] Prialt 100micrograms/1ml solution for infusion vials (Eisai Ltd) 1 vial

[xxi] Dmd.medicines.org.uk, (2016). *Dictionary of Medicines and Devices Browser Portal*. [online] Available at: http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=10606011000001101&toc=nofloat [Accessed 15 Jan. 2016].

[xxii] The supplementary protection certificate is set to expire – although unconfirmed - in 2016 for the basic drug. There is a US patent also in place until 2024 for use as adjunct to opioids.

[xxiii] 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)

[xxiv] Scottish Medicines Consortium. (2007). Ziconotide, 100 micrograms/ml solution for intrathecal infusion (Prialt®) No. (405/07) [Online] available at: http://www.scottishmedicines.org.uk/files/405_07_ziconotide_Prialt_Sept07.pdf [Accessed 15. Jan 2016].

[xxv] This is based on a 500mg pack, as identified in M1.3, lasting for the number of days equal to 500mg divided by the dose per day, and a pack price of £1,631. When the pack runs out, an outpatient appointment is required for refill, as noted in K7.1. This is costed based on 2014/15 National Tariff - Outpatient Attendance (191 - Pain Management, £182 for first attendance and £96 for a follow-up) including 10% MFF.

[xxvi] This is based on 3 patients no longer receiving ziconotide at an annual cost of c. £27k as identified in M2.1.