NHS England

Clinical Commissioning Policy: Intrathecal pumps for treatment of severe chronic pain

Reference: NHS England D08/P/a

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Description	NHS England has adopted a policy to not routinely commission this specialised treatment as described in this document.
Cross Reference	
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Document Status

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1 Executive Summary

Policy Statement

NHS England does not routinely commission Intrathecal Pumps for Severe Chronic Pain, in accordance with the criteria outlined in this document.

In creating this policy NHS England has reviewed this clinical condition and the options for its treatment. It has considered the place of this treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources.

Equality Statement

NHS England has a duty to have regard to the need to reduce health inequalities in access to health services and health outcomes achieved as enshrined in the Health and Social Care Act 2012. NHS England is committed to fulfilling this duty as to equality of access and to avoiding unlawful discrimination on the grounds of age, gender, disability (including learning disability), gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, gender or sexual orientation. In carrying out its functions, NHS England will have due regard to the different needs of protected equality groups, in line with the Equality Act 2010. This document is compliant with the NHS Constitution and the Human Rights Act 1998. This applies to all activities for which NHS England is responsible, including policy development, review and implementation.

Plain Language Summary

Intrathecal Drug Delivery plays an important role in the treatment of intractable pain in highly selected patients. Intrathecal Drug Delivery (ITDD) enables clinicians to formulate individualized treatment regimens that can provide effective analgesia (pain relief) with smaller doses, and with potentially fewer adverse effects than traditional opioid-based (morphine & morphine - like) therapies in highly selected patients.

2 Introduction

Intrathecal drug delivery (ITDD) offers a late resort alternative for a small cohort of patients with chronic non-cancer pain with a specific pain problem, who fail to obtain acceptable pain relief or suffer toxicity from systemic drug administration, interventional procedures, psychological and physical interventions. Examples include patients with, osteoporosis with multiple vertebral collapse, spinal stenosis not amenable to surgery, severe neuropathic pain such as post amputation pain refractory to neurostimulation. Some patients are offered intrathecal drug delivery to reduce the severe and sustained toxicity of their systemic opioids. The intrathecal route enables pain clinicians to use much smaller opioid doses and combine opioids with drugs that cannot be administered systemically such as local anaesthetics, clonidine.

3 Definitions

Intrathecal drug delivery system/PUMP for drug delivery (ITDD) – In this policy ITDD is the name of the treatment and device.

- Intrathecal catheter – Part of an ITDD device that is placed within the spinal cerebrospinal fluid (Subarachnoid space) to infuse pain medication stored in the pump reservoir. It is inserted via a needle, as a percutaneous technique or via a cut down open procedure.

- Implantable pump reservoir – Contains the drug, which is infused in to the cerebrospinal fluid and a power source that drives the pump. Programmable pumps allow variable flow to more easily titrate the daily dose to that which suits the individual patient. Programmable pumps are the gold standard for ITDD.

Trial of ITDD – A test period by which the patient can experience pain relief and improvement in function from a temporary application of drug to the cerebrospinal fluid. The result from the trial is useful towards the decision making process for permanent implantation.

Severe, Chronic Pain - Chronic pain which is continuous, long-term pain of either more than 12 weeks (6 months, 12 months according to other definitions or after the time that healing would have been thought to have occurred in pain after trauma or surgery.

Intractable pain – Pain, which despite expert management, is unresponsive or poorly responsive to conventional medical management or where the conventional pain relief causes unacceptable side effects.

Neuropathic pain - Pain initiated or caused by a primary lesion or dysfunction in the peripheral or central nervous system. For example pain following shingles, brachial plexus avulsion, amputation, or spinal cord trauma. Pain that occurs in diabetics or in patients with multiple sclerosis can also be neuropathic.

Nociceptive pain - Pain caused by damage to tissues.

CNMP: Chronic non-malignant pain or non-cancer pain.

Examples of chronic non cancer pain indications:

- Severe pain associated with multiple osteoporotic fractures of the spine not amenable to interventions and unresponsive to titration of systemic opioids.
- Neuropathic pain resulting from partial spinal cord injury/disease, brachial plexus avulsion and post amputation phantom pain. While some of the above are susceptible to neurostimulation, a subset of severe neuropathic pain are refractory to neurostimulation and responsive to ITDD.
- Complex regional pain syndrome with a poor response to neurostimulation and a dominant element of dystonia.
- Chronic severe postsurgical and posttraumatic pains refractory to spinal cord stimulation trial, appropriate opioid titration, interdisciplinary rehabilitation and non-pharmacological methods of pain relief.
- Failed back surgery syndrome was historically the largest cohort of patients managed on long term ITDD. With advances in neurostimulation technology and its application fewer of these patients require ITDD.

- Outcome measures – Measures of pain and pain relief, change of function, improvement in quality of life, reduction in oral pain medications and decrease in toxic side effects from systemic drugs.
- Outcome Indices will include BPI (Brief Pain Inventory), NRS (Numerical Rating Scale), BPI (Brief Pain Inventory), EQ5D-5L, and Patient's Global impression of change. Other measures such as: MPQ (McGill Pain Questionnaire) SF-36, BDI (Beck Depression Inventory), PDI (Pain Disability Index), oral and parenteral opioid use, are optional
- Outcomes should be formally assessed at 3 to 6 months and 9 to 12 months after initiation of ITDD and included in the National Neuromodulation Registry. It is good practice to measure outcomes annually thereafter.
- The National Neuromodulation Registry (NNR) will be available for the systematic collection of patient and device data on demography, disease severity and outcomes for all patients implanted with ITDD. The outcomes used are BPI, EQ5D-5L, Global impression of change, Intrathecal drug combinations and daily doses.
- The NNR is sponsored by the Neuromodulation Society of UK and Ireland (NSUKI) and has been created in partnership with the National Institute of Cardiovascular outcomes and Research (NICOR)

- Timing of assessment - (IASP recommendations as below)

a. Acute painful conditions should be treated immediately (e.g. painful sickle cell crises and pain related to trauma or surgery)
b. Most urgent (1 week): A painful severe condition with the risk of chronicity or deterioration, such as the acute phase of complex regional pain syndrome (CRPS), pain in children, or pain related to cancer or terminal or end-stage illness
c. Urgent or semi-urgent (1 month): Severe undiagnosed or progressive pain with the risk of increasing functional impairment, generally of 6 months' duration or less (back pain that is not resolving or persistent postsurgical or post-traumatic pain)
d. Routine or regular (8 weeks): Persistent long-term pain without significant progression.

4 Aims and Objectives

This aims and objectives of this policy are to set out the NHS England commissioning position for Intrathecal Pumps for Severe Chronic Pain.

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5 Epidemiology and Needs Assessment

The Health Survey for England (2011)11 published in December 2012 highlights that current service provision for pain management is inadequate and existing services are not evenly distributed across the country. The Chief Medical Officer's Annual Report (2008) also had a similar view on pain services provision in England. In order to look at the quality and provision of existing pain services, the National Pain Audit was commissioned. The report from phase one of the audits has highlighted that there are areas to be improved, particularly around the provision of multidisciplinary services for pain management.

Historical studies of the time trends in pain prevalence have highlighted the increase in prevalence of pain12. Harkness et al studied two cross sectional population surveys in the North of England undertaken 40 years apart which showed a significant rise in musculoskeletal pain. Similarly US researchers have found an increase in severe chronic impairing back pain in North Carolina from 4% to 10% in surveys conducted between 1992 and 2006 (Freburger et al 2009)13. For many patients, pain produces severe distress dominating and disrupting their quality of life. If the focus is narrowed to disabling chronic pain then estimates vary from 6 to 12% (Croft et al. 2010)12.

More women than men reported chronic pain. Overall, 31% of men and 37% of women reported this. The prevalence of chronic pain increased with age, with older people being more likely to report chronic pain than younger people. In those aged 16-34, 14% of men and 18% of women reported chronic pain. This rose to 53% of men and 59% of women aged 75 and over. The Royal College of General Practitioners made chronic pain a clinical priority area for 2011-2014, appointing a clinical champion to oversee the work.

European data reflects poor uptake of ITDD treatment generally in UK. This has to be considered in the context of the intractable nature of symptoms, disability and cost-effectiveness data now available for spasticity and chronic pain.

HES data and expert opinion suggests that 100 new patient ITDD pumps for Pain (about 50 for non-cancer pain) are implanted annually. Expert opinion suggests that there are currently 1000 patients who are using ITDD for non-cancer pain. These patients need to be maintained in addition to the new patients.

6 Evidence Base

NHS England concluded that there was not sufficient evidence to support the routine commissioning of this treatment for the indication. In the interests of transparency the evidence base that was described by the CRG is set out in Appendix A of this policy.

7 Rationale behind the Policy Statement

Intrathecal Pumps for the treatment of Severe Chronic Pain have been considered by NHS England who concluded that there was not sufficient evidence to support the routine commissioning of this procedure in this patient group.

8 Criteria for Commissioning

NHS England does not routinely commission Intrathecal Pumps for the treatment of Severe Chronic Pain.

9 Patient Pathway

Not applicable.

10 Governance Arrangements

Not applicable.

11 Mechanism for Funding

NHS England will not routinely fund Intrathecal Pumps for patients with Severe Chronic Pain.

12 Audit Requirements

Not applicable.

13 Documents which have informed this Policy

Not applicable.

14 Links to other Policies

This policy follows the principles set out in the ethical framework that govern the commissioning of NHS healthcare and those policies dealing with the approach to experimental treatments and processes for the management of individual funding requests (IFR).

15 Date of Review

This policy will be reviewed in April 2017 unless information is received which indicates that the proposed review date should be brought forward or delayed.

References

1 Pert CB, Synder SH. Opioid receptor: demonstration in nervous tissue. Science1973; 179: 1947-9.

2 Yaksh TL, Rudy TA. Narcotic analgesia produced by a direct action on the spinal cord. Science1976; 192: 1357-8.

3 Cousins MJ, Mather LE, Glynn CJ, Wilson PR, Graham JR. Selective spinal analgesia. Lancet1979; 1: 1141-2.

4 Behar M, Magora F, Olshwang D, Davidson JT. Epidural morphine in treatment of pain. Lancet 1979; 1: 527-9.

5 Wang J, Nauss LA, Thomas JE. Pain relief by intrathecally applied morphine in man. Anesthesiology 1979; 50: 149-51.

6 Gourlay GK, Cherry DA, Cousins MJ. Cephalad migration of morphine in CSF following lumbar epidural administration in patients with cancer pain. Pain1985; 23: 317-26.

7 Dickenson AH. Recent advances in the physiology and pharmacology of pain: plasticity and its implications for clinical analgesia. J Psychopharmacol1991; 5: 342-51

8 Collett B. et al: International Association for the Study of Pain Task Force on Wait-Times summary and recommendations. http://www.iasp-pain.org/AM/Template.cfm?Section=Wait_Times&Template=/CM/ContentDisplay.cfm&ContentID=13107

9 Health survey England 2011, published December 20, 2012, available at http://www.hscic.gov.uk/catalogue/PUB09300 Chronic Pain chapter available at https://catalogue.ic.nhs.uk/publications/public-health/surveys/heal-surv-eng-2011/HSE2011-Ch9-Chronic-Pain.pdf

10 Croft P, Blyth F, Van der Windt D. Chronic Pain Epidemiology. Oxford University press 2010

11 Freburger J.K. et al. The rising prevalence of low back pain. Arch. Intern. Med. 2009.199:251-258

12 Hayek SM, Deer TR, Pope JE et al. Intrathecal Therapy for Cancer and Non Cancer Pain. Pain Physician 201`;14:219-248.

13 Falco FJ, Patel VB, Hayek SM, Deer TR, Geffert S, Zhu J, Onyewu O, Coubarous S, Smith HS, Manchikanti L. Intrathecal infusion systems for long-term management of chronic non-cancer pain: an update of assessment of evidence. Pain Physician. 2013 Apr;16(2 Suppl):SE 185-216

14 Raphael JH, Duarte RV, Southall JL, et al. BMJ Open 2013:3:e003061.

15 van Rijn, MA. et al Intrathecal baclofen for dystonia of complex regional pain syndrome - Dose escalation study 2009 Pain 143(1-2): 41-47

16 Duarte R. et al Long-term Intrathecal Drug Administration for Chronic Nonmalignant Pain. J Neurosurg Anesthesiol 2012;24:63–70

17 Krishna K, Hunter G etal. Treatment of chronic pain by using intrathecal drug therapy compared with conventional pain therapies: a cost – effective analysis. J Neurosurg./Volume 97/ October, 2012

18 Bolash R, Belinda U et al. Longevity and Cost of Implantable Intrathecal Drug Delivery Systems for chronic pain management: A retrospective analysis of 365 patients. Neuromodulation 2014 ; DOI: 10.111/ner 12235

19 Gerhard MS, Hassenbusch SJ et al. Cost Effectiveness of Intrathecal Therapy for Pain. Neuromodulation, Volume 2, Number 2, 1999 77 -84

20 Prager J, Deer T., Levy R., Bruel B., Buchser E., Caraway D., Cousins M., Jacobs M., McGlothlen G., Rauck R., Staats P., Stearns L. Best Practices for Intrathecal Drug Deliver for Pain. Neuromodulation 2013

21 Medtronic urgent field safety notice on synchromed pump (FA553). Nov 2012. Accessed on line on 2nd June 2013 http://www.bfarm.de/SharedDocs/1_Downloads/EN/medDev/fca/01/2012/7002-12_Download_en.pdf?__blob=publicationFile

22 http://www.britishpainsociety.org/book_useof_meds_professional.pdf accessed on line on 17th June 2013

Appendix A

NHS England concluded that there was not sufficient evidence to support the routine commissioning of this treatment for the indication. In the interests of transparency the evidence base that was described by the CRG is set out below.

"*ITDD systems are a late stage intervention and are only indicated where other conservative pharmacologic, physical and psychological interventions have failed or are contraindicated and where the uncontrolled pain and therapy toxicity is causing a significant impact on physical and mental health. By positioning a catheter in the cerebrospinal fluid, ITDD allows smaller doses of drugs to be applied directly to the receptors of the central nervous system, achieving pain relief with much smaller doses and as a consequence fewer side effects, than with oral or parenteral routes. Intrathecal opioid delivery by an implantable pump improves pain relief, increases function and enhances patient quality of life. ITDDs achieve higher CSF drug concentrations with the delivery of smaller drug doses directly into the CSF, sparing the undesired secondary effects of these same medications when administered by other routes.*

History: Opioid receptors were identified in the spinal cord in 1973. Subsequent animal studies demonstrated that intrathecal opioids produce powerful and highly selective analgesia. Cousins in 1979 used the phrase 'selective spinal analgesia' to describe the phenomenon that spinally administered opioids could produce a specific analgesic effect with few motor, sensory or autonomic side effects. The first clinical use of epidural and intrathecal opioids followed, it was subsequently demonstrated that the analgesic effect was, in the main, due to the uptake of the opioid directly into the spinal cord and transported via the cerebrospinal fluid.

Intrathecal Drugs: Intrathecal baclofen are approved for this use by EMEA. Other drugs such as morphine, hydromorphone, bupivacaine and clonidine although routinely used in clinical practice have never been licensed for the purpose. Drug types and combinations are agreed by international panel of experts and are published in the polyanalgesic consensus conference 2012 as well as the British Pain Society Guidelines on intrathecal drug delivery.

Intrathecal opioids exert their analgesic effect pre and post synaptically by reducing neurotransmitter release and by hyperpolarising the membranes of neurones in the dorsal horn, thus inhibiting pain transmission.

Intrathecal local anaesthetics exert their effect by sodium channel blockade, which inhibits the action potential in neural tissue in the dorsal horn, producing a reversible analgesic effect. They also have an action on the intrathecal part of the nerve root.

Intrathecal clonidine, an α2 agonist, modulates pain transmission by suppression of the release of the C fibre neurotransmitters, Substance P and Calcitonin Gene Related Peptide (CGRP). It has been hypothesised that clonidine also suppresses preganglionic sympathetic outflow.

A literature search restricted to randomised control trials and systematic reviews was undertaken and a summary of the evidence is presented below.

Clinical effectiveness and safety

The evaluation of the data for intrathecal drug delivery has to be viewed with an awareness of a number of factors that limit the ability of researchers to conduct large scale clinical trials in this field:

- *The small numbers of ITDD procedures for non-cancer pain carried out in the UK 50-100/annum due to its position as a late resort intervention.*

- *There are barriers to conducting investigator led STIMPS (Clinical trials of investigational Medicinal Product), which are compounded by the need to use "special order" higher concentrations of preservative free preparations of drugs suitable for the intrathecal route and compatible with the pump.*

- *The lack of licensing for a number of drugs including opioids despite routine use in clinical practice.*

Two systematic reviews and one RCT were identified.

One systematic review was identified which evaluated the efficacy and safety of intrathecal infusions used in long-term management (> 6 months) of chronic refractory cancer pain and non- cancer pain Hayek et al. 2011). The search period covered 1966-2010. It identified 5 studies in total for cancer, which met its inclusion criteria - 1 randomised controlled trial (RCT) and 4 observational studies. For non-cancer pain, 15 observational studies were identified that met the inclusion criteria (8 prospective studies and 7 retrospective studies) for a minimum of follow up of 12 months. The authors concluded that the recommendation for intrathecal infusion systems for cancer-related pain is a moderate recommendation based on the high quality of evidence. For non-cancer pain the recommendation was limited to moderate.

The second systematic review evaluated the evidence (from 1966-2012) for intrathecal infusion systems for short (12 months) and long-term (>12 months) management of chronic non-cancer pain. A total of 7 non-randomised studies met the inclusion criteria. Overall, the 7 studies evaluating intrathecal infusion systems reported pain relief and improvement in function. There were 6 studies that showed positive results for long-term pain relief at ≥ 12 months. There were 3 studies that showed positive results for short-term relief at ≤ 12 months. Significant improvement in function was reported in 5 of the 7 studies both short-term ≤ 12 months and long-term at ≥ 12 months. The vast majority of complications reported in the 7 studies were minor, however some serious complications did occur. An increased mortality rate in patients with non-cancer pain receiving intrathecal opioid therapy (mortality rate of 0.088% at 3 days after implantation, 0.39% at one month and 3.89% at one year) was identified as likely related to the opioids as well as other factors that may be mitigated especially at the start of therapy. Other serious complications include granuloma formation that may be related to the amount and concentration of opiates, mostly morphine and hydromorphone. Other complications of ITDDS include catheter kinking, catheter fracture/leakage, catheter migration, cerebrospinal fluid (CSF) leak, seroma, hygroma, infection, pump erosion through the skin, and medication side effects. Based on the appraisal of the evidence, the authors concluded the evidence for intrathecal opioid infusion therapy is limited (based on observational studies) for

short-term and long-term pain relief and functional improvement in the treatment of chronic non-malignant pain.

In the RCT (Raphael et al 2013) aimed to investigate the efficacy of intrathecal morphine in the long term by hypothesising that a reduction of the intrathecal opioid dose following long-term administration would increase the level of pain intensity. 15 patients were randomised to control (n=5) or intervention (20% dose reduction) (n=10) and included in an intention-to-treat analysis. Owing to worsening of pain, seven patients (in the intervention arm) withdrew from the study prematurely, none withdrew from the control arm. The VAS change between baseline and the last observation was smaller in the control group (median, Mdn=11) than in the intervention group (Mdn=30.5), although not statistically significant, Z=−1.839, p=0.070; r=−0.47. Within groups, VAS was significantly lower at baseline (Mdn=49.5) than at the last observation (Mdn=77.5) for the reduction group, Z=−2.805, p=0.002; r=−0.627 but not for the control group (p=0.188). These findings are based on a small sample (n-=8) conducted at a single centre.

In Complex Regional Pain Syndrome (CRPS) van Rijn et al conducted a single-blind, placebo-run-in, dose-escalation study in 42 CRPS patients to evaluate whether dystonia responds to Intrathecal Baclofen (ITB). The dose-escalation study showed a dose-effect of baclofen on dystonia severity in 31 patients in doses up to 450 mcg/day. Thirty-six of the 38 patients, who met the responder criteria received a pump for continuous ITB administration, and were followed up for 12 months to assess long-term efficacy and safety (open-label study). Thirty-six patients entered the open-label study. Intention-to-treat analysis revealed a substantial improvement in patient and assessor-rated dystonia scores, pain, disability and quality-of-life (Qol) at 12 months.

Duarte et al followed up a cohort of 20 patients with chronic non-cancer pain treated with ITTD for an average 13 years. Statistically significant improvements were observed for the following sensory and psychosocial variables: pain intensity, pain relief coping, self-efficacy, depression, quality of life, housework, mobility, sleep, and social life between baseline and 4 year data. No statistically significant changes were detected between assessments at averages of 4 and 13.5 years.

Cost-effectiveness

Patients with pain of non-malignant origin often require treatment for several years. ITTD is often reserved as a late-resort therapy. Cost categories include pre-implant costs, implant procedure costs (OT, hospital stay, Equipment), post implant (maintenance, dose adjustment, drug refill, conventional pain medications) and complications. A Canadian study averaged the above costs annually over a 5 year period in two randomised groups - CPT and ITDD. Patients had failed back syndrome with a mean of 3.3 operations and one year continuous work absence. Both groups had 44 patients each. The number of patients who received a permanent ITDD implant following a successful trial response of ≥ 50% pain-relief was 23/44. The mean hospital stay for implantation was 6.24 days and the mean number of complications per implant was 0.77. Cumulative costs per year for a 5 year period totalled $29,410. This included pump replacement for battery depletion. There was no further surgery of the lumbar spine in this group. In the CPT group 5 year costs totalled $38,000 due to higher costs for pharmacotherapy, adjunctive therapies, break- through pain needing hospitalization and referrals to other allied health professionals.

ITDD was shown to be cost-effective both in the best and worst-case scenarios. In the best case scenario, the break-even point occurs at 26 months and in the worst-case scenario at 30 months. The mean 5 year VAS pain relief score was 61 ± 5.2% with an improvement in disability of 27%. (compared with 12% in the CPT group). Factors increasing cost-effectiveness were identified as patient selection, cost of pump, battery life and complications. The majority of the cost of ITDD is incurred at inception of the therapy. However the low costs of maintenance dramatically decrease the overall costs over long-term therapy.

Another US study showed the system cost of implanting and maintaining a pump to be $10 per day. The same study observed the median longevity of a pump to be 5.9 years. This was shortened with earlier replacement due to surgical or infectious complications. The latter will be reduced by proper patient selection and proper surgical technique. A simulated cohort of 1000 patients treated for 60 months showed that the cumulative cost of intrathecal morphine delivered with an ITDD

pump is less than the cost of medical management after 22 months and 11 months for base care (usual Medicare Fee) and best care scenarios, with a total 5 year cost of $82,893 and $53,468 respectively against $85,186 for medical management."