New York Department of Health

Dossier Summary and Response – *Additional Evidence Submission*

Topic: Implantable Infusion Pumps for Non-cancer Pain **Date**: April 22, 2016

Dossier Submission

Medtronic, Inc. submitted additional references to the dossier submitted on implantable infusion pumps for chronic non-cancer pain on March 6, 2015. The original dossier was completed in accordance with the New York Department of Health's instructions and included 56 articles (52 summarized/reviewed) for review published between 1996 and 2014. The additional evidence submission included seven articles, and Medtronic did not assess the methodologic quality of these articles. The additional submitted articles provided information on the effects of intrathecal drug devices used for treating chronic non-malignant pain. Studies addressed both device- and medication-related harms of intrathecal drug therapy, and device-associated costs.

Dossier Review Process

In this document, the Center for Evidence-based Policy (Center) provides a review of the additional submitted evidence. Submitted articles were independently assessed for inclusion, methodological quality, and reported results. Given the recent dossier review and evidence search from the original dossier submission, the Center did not search for additional relevant evidence.

Review Results

<u>Evidence Evaluation – Included Studies</u>

In the original dossier review, Center staff performed a search to identify any additional articles relevant to the topic. Typically only comparative studies are included for evaluation of efficacy due to potential bias and uncontrolled confounding factors inherent in case series. However, because the body of evidence on this topic is overwhelmingly made up of non-comparative case series, case series were used to gather information about efficacy. Included studies were limited to English language, systematic reviews (SRs) with or without meta-analyses, randomized controlled trials (RCTs), or observational studies. In addition, only patient important outcomes have relevance for NY DOH. The rationale for study inclusion can be found in the New York Department of Health Dossier Methods Guidance (New York Department of Health, 2015). Exclusion criteria were selected prior to review of the studies, and study methods were assessed prior to review of outcomes to eliminate bias.

Exclusion criteria included:

- Original research with less than 10 participants
- Retrospective designs in which:
    - Study population was not drawn randomly or consecutively
    - Participants were required to recall their pre-intervention pain scores
- More than 15% of participants had cancer-related pain
- Less than six months of follow-up for efficacy outcomes (included for harms)
- Duplicate information from a research study published in more than one source (only the highest quality, most recent publication with outcome of interest was included)
- Intervention other than permanent implanted pump. Examples include:
    - Intrathecal drug trial period with a temporary catheter only. A successful trial period is often reported as greater than 50% pain improvement, and is often a clinical prerequisite to permanent implantation.
    - Comparative study of medications or device other than intrathecal infusion pump

The original dossier review included 12 systematic reviews (SRs), four randomized controlled trials (RCTs), 10 prospective cohort studies, seven retrospective cohort studies, four case series, and eight cost studies on the use of implantable infusion pumps for chronic non-cancer pain. This review of the additional evidence submission includes three case series (Caraway et al., 2015; Follett and Nauman, 2000; Grider et al., 2015) and one cost study (Hatheway et al., 2015).

Three of the seven additional references submitted for review were excluded. See Table 3 for a detailed list of exclusion rationale.

Evidence Review

This section provides an overview of included studies and a summary of the findings regarding effectiveness, harms, and costs related to intrathecal pumps for non-cancer pain. The quality ratings included in this section refer to the ratings by the CEbP unless otherwise specified. Table 1 provides a further detail of the studies with more information than included in the summary below.

Included Studies

This review includes three case series (one of fair methodologic quality and two of poor methodologic quality) of population sizes ranging from 58 to 209 participants, and one fair quality cost study. All studies were performed on participants receiving implanted intrathecal pumps for chronic pain. One study of device-related harms did not exclude participants in whom the pump was implanted for spasticity or cancer pain (Follett and Nauman, 2000),

however, it was included in this review because it addressed catheter-related complications and not harms due to medication.

Effectiveness

Pain outcomes

Average pain decreased after implantation of the intrathecal pump, and this was demonstrated in two of the case series submitted. In one case series, 73 patients had a temporary catheter placed with a trial of intrathecal morphine. Among those, 60 chose to have permanent implantation. Among the 58 who enrolled in the study, average pain on a 10-point visual analogue scale (VAS) decreased significantly from 7.8 points at pre-implantation to 5.7 points at implant, 4.4 points at 6 months, 4.8 points at 12 months, 5.1 points at 24 months, and 4.6 points at 36 months ($p<0.001$). A clinically significant reduction on this 10-point scale varies depending on condition, but is within a range of 1.1 to 1.4 points (Hawker et al., 2011). Among 13 patients who elected to continue oral pain medication and not proceed with pump implantation, the VAS score decreased from 8.1 points pretrial to 6.9 points at six months. However, the perceived need to take more pain medication was increased in these 13 patients at six months, suggesting dissatisfaction with treatment (Grider et al., 2015).

In a poor quality case series of 99 participants who were followed for one year or longer, average pain on Numeric Pain Rating Scale decreased approximately two points and remained stable at one year ($p<0.001$). A clinically meaningful reduction on this 11-point scale (0 to 10) is two points (Hawker et al., 2011). Average pain decreased by 2.9 points at five years ($p=0.05$), however, this estimate is not reliable due to incomplete follow-up (Caraway et al., 2015).

Quality of Life

The additional case series submitted did not address this outcome.

Disability

One study assessed pain interference using Multidimensional Pain Inventory score, a 60-item self-report inventory that assesses a patient's psychosocial and behavioral responses to pain. There was no significant difference in mean score before or after implantation of the intrathecal pump (pain interference pretrial; 51.9 ± 9.0 vs. 36 months; 50.6 ± 8.3; $p>0.05$) (Grider et al., 2015). A clinically important difference is considered greater than or equal to a 0.6 point decrease on interference (Dworkin et al., 2008). Authors also used the Global Pain Scale to assess the multidimensional aspects of pain including clinical outcomes and activities. While this tool has been validated, the clinically meaningful difference is not discussed (Gentile et al., 2011). Using the Global Pain Scale (100-point scale), average pain decreased significantly from 63.5 points at the time of the trial to 48.9 points six months post-implant, and remained

stable at 49.1 points at 36 months. A pre-trial global pain score was not collected (Grider et al., 2015).

*Oral Pain Medicatio*ns

Participants in the case series by Grider and colleagues (2015) were required to taper off oral opiate medications prior to implantation and enrollment. Thirteen of 73 participants chose to not proceed to implantation and continue oral pain medication. Of 58 participants who enrolled, two needed systemic oral therapy during the 36-month study period. One withdrew from intrathecal treatment due to a preference for oral therapy. One required supplemental oral opioids after a compression fracture.

In the case series by Caraway and colleagues (2015), the majority of participants tapered off systemic opioid medications (74% at six months, $p<0.001$). The percentage of patients who remained off oral opioids at later time periods is not reliable due to incomplete follow-up.

Table 1. *Evidence Review – Included References*

Citation, Study Details	Dossier QA	CEbP QA	Study Size (n)	Study Summary and Findings	Comments
Case Series					
Caraway et al. (2015) Study length 88/99 patients followed for 12 months or longer Indication Chronic pain Intrathecal Medication 1 or more of: morphine, hydromorphone, bupivacaine, ziconotide	n/a	Poor	n=99	Primary Outcome Percent of patients eliminating systemic opioids at specified time periods 1 month: 68% (67/98) 6 months: 74% (73/98) 1 year: 84% (74/88) 5 years: 92% (1/13) (p<0.001) Secondary Outcome Average decrease in NPRS pain scores from pre-implantation (11-point scale) 1 month: -2.1 (p<0.001) 6 months: -1.9 (p<0.001) 1 year: -1.8 (p<0.001) 5 years: -2.9 (p=0.05) Harms 10 (10%) patients underwent revision of their intrathecal device: 6 for battery replacement, and 4 for other reasons	8% of patients had cancer-related pain Retrospective, incomplete follow-up Unclear how population selected Single center Non-comparative Small sample size
Follett and Nauman (2000)	n/a	Poor	n=209	Harms	Catheter inserted for cancer pain or spasticity in 22.5% of

Citation, Study Details	Dossier QA	CEbP QA	Study Size (n)	Study Summary and Findings	Comments
Study length Median 8.4 months Indication Pain (cancer or non-cancer pain) and spasticity Intrathecal Medication NR				Percent of patients experiencing catheter- or procedure-related complication over an average of 8 months: 18% Percent of patients experiencing ≥ 2 complications: 4.3% Number of catheter-related complications: 7 Number of procedure-related complications: 42	cases, however, included because harms are catheter-specific Criteria for drawing population not discussed Concern for selection bias
Grider et al. (2015) Study length 36 months Indication Chronic pain Intrathecal Medication Opioids (mean morphine equivalent dose < 350 µg/day)	n/a	Fair	Temporary Catheter n=73 Implanted n=60 Enrolled n=58	Benefits Pain: Reduction in mean VAS and GPS scores Pre-implant: 7.8 ± 1.6 (SE) Implant: 5.7 ± 2.5, p<0.001 6 months: 4.4 ± 2.3, p<0.001 12 months: 4.8 ± 2.4, p<0.001 24 months: 5.1 ± 2.4, p< 0.001 36 months: 4.6 ± 2.5, p<0.001 Harms Worse neuropathic pain: 14% Catheter malfunction requiring revision: 7% Seroma requiring pocket revision: 3%	Patients tapered off systemic opioids prior to IPP implantation Urinary retention and lack of analgesic benefit were most common reasons for patients not proceeding to implantation Patients not proceeding to implantation were followed Non-comparative Small sample size

Abbreviations: GPS = global pain scale; n/a = not applicable; IPP = implantable pain pump; NPRS= Numeric Pain Rating Scale; NR = not reported; SE = standard error; VAS = visual analog scale

Harms

A poor quality case series of 209 patients drawn from 22 centers in the U.S., Europe, and Australia evaluated a one-piece catheter system (Model 8709, Medtronic, Inc.) inserted for pain or spasticity (Follett and Naumann, 2000). The mean duration of follow-up was 8.4 months. One hundred patients were followed for nine months or greater. The primary indication for catheter insertion was nonmalignant pain (73%). The remaining patients had the catheter inserted for cancer pain (5%) or spasticity (23%). Because this case series addressed catheter, and not drug-specific harms, it was included in this review. Thirty-seven patients (18%) had procedure- or catheter-related complications over the course of the study. There were a total of 49 complications, with four percent of patients having two or more complications. Procedure-related complications (42 events) were more common that catheter-related complications (7 events), and infection (15 patients) and catheter dislodgement or migration (10 patients) were the most common procedure-related complications (Follett and Naumann, 2000).

In a poor quality case series including 58 participants who underwent permanent implantation of an IPP for chronic pain and followed for 36 months, 14% experienced worse neuropathic pain (Grider et al., 2015). Magnetic resonance imaging revealed no granuloma in any of those patients. Catheter malfunction requiring revision occurred in seven percent and seroma requiring revision of the pump pouch occurred in three percent of patients (Grider et al., 2015).

In a poor quality case series including 99 patients with chronic pain who were followed for 12 months or longer, 10 patients underwent revision of their pump. Six of the revisions were for battery replacement and four revisions were for other reasons (Caraway et al., 2015). Additional complications are listed in Table 2.

Table 2. *Frequency of Device-Related Adverse Events from Observational Studies*

Adverse event	Frequency	Citations and Study Size (n)
Case series		
Procedure-related complications		Follett and Naumann (2000), n=209
Infection	7 %	Grider et al. (2015), n=58
Catheter migration	5%	
Occlusion	2%	
CSF leak/hygroma or spinal HA	2%	
Leakage	1.0%	
Catheter disconnection	0.5%	
Other Complications		
Worse radicular pain	14%	

Adverse event	Frequency	Citations and Study Size (n)
Granuloma	0	
Pruritis	5%	
Peripheral edema	5%	
Urinary retention	3%	
Seroma	3%	
Catheter-related complications	3 to 7%	

Evidence Evaluation – Excluded Studies

Table 3 provides exclusion criteria for submitted articles that were not included in this evaluation.

Table 3. *Submitted References – Reason for Exclusion*

Citation	Exclusion Criteria
Bohnert et al. (2011)	Intervention: Does not evaluate effectiveness or safety of implantable infusion pumps
Gomes et al. (2011)	Intervention: Does not evaluate effectiveness or safety of implantable infusion pumps
Ooi et al. (2011)	Included in Falco et al. (2013) systematic review which was reviewed in original dossier

Evidence Evaluation – Overall Strength of Body of Evidence by Outcome

Table 4 presents the submitter's assessment of the strength of evidence for the submitted outcomes, as well as the assessment of CEbP and rationale for this assessment.

Table 4. *Outcomes – Strength of Evidence*

	Strength of Evidence Assessment		
Outcome	Submitter	CEbP	Rationale
Level of pain (e.g., Global McGill, VASPI, Oswestry or Global pain indices)	High	Low	Assessment has not changed from original dossier review. There are two additional case series which demonstrate a reduction in pain pre/post, but the overall strength of evidence has not improved.
Quality of Life (e.g., CGI patient satisfaction scale, SF-36 quality of well-	Moderate to High	Very low	Assessment has not changed from original dossier review. The additional case series did not specifically address quality of life.

Outcome	Strength of Evidence Assessment		Rationale
	Submitter	CEbP	
being, mood, activity level)			
Level of disability (e.g., Oswestry disability, chronic illness problem inventory)	Moderate	Very low	Assessment has not changed from original dossier review. One case series did not detected a difference in pain interference.
Pain-killer use (concomitant opioid or concurrent other painkillers)	Moderate	Very low	Assessment has not changed from original dossier review. In one case series elimination of systemic opioids was a prerequisite.
Economic outcomes (e.g., cost-effectiveness/quality of life years, cumulative total cost, cost/period of time)	Moderate	Very low	Assessment not changed from original dossier review. One cost-benefit analysis reports savings among those with intrathecal pump who tapered off opioids compared to those who did not.
Harms			
Mortality	Low	Very low	Assessment not changed from original dossier review. No additional evidence presented.
Intrathecal granuloma	Low to Moderate	Very low	Assessment not changed from original dossier review.
Infection	Moderate	Low	Assessment not changed from original dossier review.
Neurologic impairment due to inflammatory mass	Low	*None*	Assessment not changed from original dossier review. No additional evidence presented.
Cerebrospinal/dural fluid leak due to puncture, post dural puncture headache	Moderate to High	Low	Assessment not changed from original dossier review.
Drug overdose/ toxicity due to component or system failure	Very low	Very low	Assessment not changed from original dossier review. No additional evidence presented.
Bleeding, wound dehiscence	Very low	Very low	Assessment not changed from original dossier review. No additional evidence presented.

Outcome	Strength of Evidence Assessment		Rationale
	Submitter	CEbP	
Tissue damage due to catheter migration	Moderate	Low	Assessment not changed from original dossier review.
Pocket seroma, hematoma, or migration	Moderate	Low	Assessment not changed from original dossier review.
Reoperation or pump replacement due to pump or catheter failure	Moderate to High	Low	Assessment not changed from original dossier review.

Section 6: "The service must be cost-effective or cost neutral outside the investigational setting"

One additional fair quality cost-benefit analysis was submitted for review (Hatheway et al., 2015). This cost study performed a review of a large claims database to select a population of 389 individuals who had received an intrathecal infusion pump for pain. Those with a current diagnosis of cancer or spasticity were excluded. Patients were followed for a year, and 12% of the 389 participants had tapered off opioids (based on pharmaceutical claims) within a 30-day washout period. Fifty-one percent of participants had tapered off opioids at the end of the year. Total health care expenditures for one year (beginning 30 days after implantation) for patients with an implanted device ranged from $30,700 to $32,168. Costs were lower for those who stopped taking systemic opioids, and decreased by 14 to 17% of total expenditures, depending on the point in time when a patient tapered off of systemic opioids. The study is limited in that it used claims data which may inaccurately define the population. In addition, costs alone are considered without knowledge of pain relief or other device benefit. Also of importance is the potential for confounding. Those who tapered off medications had lower costs pre-implantation as well, and this group may be a lower cost group for reasons other than the elimination of systemic opioids. These potential confounders were not explored or adequately controlled for in the analysis.

Table 5. Evidence Review- Economic Studies

Study Citation	Dossier QA	CEbP QA	Study Size (n)	Findings	Limitations / Comments
Hatheway et al. (2015)	n/a	Fair	389	51% percent of patients had tapered off systemic opioids one year after IPP implantation; 12% tapered within a 30-day wash-out period	Claims data used to define populations There is potential for unmeasured

Study Citation	Dossier QA	CEbP QA	Study Size (n)	Findings	Limitations / Comments
				Eliminating systemic opioids within 120 to 210 days post implantation was associated with a $3,388 to $4,465 reduction in inpatient and outpatient expenditures (10 to 14% of expenditures) and a $4,689 to $5,571 (14 to 17%) reduction in inpatient, outpatient, and pharmacy expenditures.	confounding factors, baseline expenditures were lower for those who tapered off opioids

Section 7: Other payer coverage of the service

Center staff did not conduct an additional search of payer coverage of implantable infusion pumps for non-cancer pain.

Summary

The additional submitted case series and cost-benefit analysis are consistent with the overall body of evidence on intrathecal pumps for chronic non-cancer pain reviewed as part of the original dossier submission and do not change the original assessment. There is a fairly consistent body of poor quality evidence drawn mostly from fair to poor quality mostly non-comparative observational studies demonstrating both short- and long-term clinically significant (greater than or equal to 30%) reduction in pain among patients with chronic non-cancer pain treated with intrathecal drug therapy. Some studies report improvement in quality of life and functional capabilities, but this is done inconsistently and magnitude of benefit cannot be determined. Common device-related complications include pump failure, reoperation due to pump or catheter failure, and headache. Infection, seroma, granuloma, and catheter migration are reported less frequently. There are no long-term randomized controlled trials comparing intrathecal drug therapy to conventional pain therapy. The population of patients studied is limited to those with chronic pain who have failed multiple other therapies. Studies are variable in population, intrathecal medications, and length of follow-up, and due to this heterogeneity, the overall strength and consistency of either benefits or harms cannot be estimated.

Appendix A. Quality Assessment Forms

Table 5. *Case Series Study Quality Appraisal*

Risk of Bias Assessment Criteria	Caraway et al. (2015)		Follett and Nauman (2000)		Grinder et al. (2015)	
	Submitter	CEbP	Submitter	CEbP	Submitter	CEbP
1.1 The study addresses an appropriate and clearly focused question.	*Study not quality assessed by submitter*	Yes	*Study not quality assessed by submitter*	Yes	*Study not quality assessed by submitter*	Yes
1.2 Were eligibility criteria (inclusion/exclusion) criteria clearly described?		No		Yes		Yes
1.3 Were patients recruited or included from more than one center (i.e. multi-center)?		No		Yes		No
1.4 Was the likelihood that some eligible subjects might have the outcome at the time of enrollment assessed and taken into account in the analysis (pertinent for screening and Yes diagnostic topics)?		n/a		n/a		n/a
1.5 Was the study based on a consecutive sample or other clearly defined relevant population?		No		No Not stated. Cannot exclude selection bias.		Yes
1.6 Were patients recruited prospectively?		No		Yes		Yes
1.7 Did all of the individuals enter the study at a similar point in their disease progression? If not, were the results reported separately?		Yes		Yes		Yes
1.8 Were patients in the sample representative of those seen in practice?		Yes		Unclear Demographics not provided		Yes
1.9 Were outcomes assessed using objective criteria (i.e. medical records) or was blinding used?		Yes		Unclear		Yes Objective outcome measures used without blinding
1.10 Was follow-up long enough for important events to occur?		Yes		Yes		Yes
1.11 Was there a low dropout or withdrawal rate (<10%)?		No		No 16% discontinued the study, none for catheter-related reasons		Yes
1.12 Were the main potential confounders identified and taken into account in the design and/or analysis?		No		No		Yes

Risk of Bias Assessment Criteria	Caraway et al. (2015)		Follett and Nauman (2000)		Grinder et al. (2015)	
	Submitter	CEbP	Submitter	CEbP	Submitter	CEbP
1.13 Competing interests of members have been recorded and addressed.		Yes Multiple authors have affiliations with Medtronic		No		Yes Multiple authors are consultants for Medtronic but reportedly did not receive money for this project
1.14 Views of funding body have not influenced the content of the study.		Yes Funded by Medtronic, Inc.		Unclear		No "Funding not provided by any government or commercial source"
2.1 How well was the study done to minimize the risk of bias or confounding, and to establish a causal relationship between exposure and effect?		**Poor**		**Poor**		**Fair**
2.2 Are the results of this study directly applicable to the patient group targeted by this topic?		Yes		Yes		Yes
2.3 Comments		---		Prospective study without mention of characteristics of population or those who were not enrolled, cannot judge if there is selection bias		---

Table 6a. *Economic Study Quality Appraisal*

Risk of Bias Assessment Criteria	Hatheway et al. (2015)	
	Submitter	CEbP
1.1 The results of this study are directly applicable to the patient group targeted by this key question.	*Study not quality assessed by submitter*	Yes
1.2 The healthcare system in which the study was conducted is sufficiently similar to the system of interest in the topic key question(s).		Yes
2.1 The research question is well described.		Yes
2.2 The economic importance of the research question is stated.		Yes
2.3 The perspective(s) of the analysis are clearly stated and justified (e.g. healthcare system, society, provider institution, professional organization, patient group).		Yes Healthcare system
2.4 The form of economic evaluation is stated and justified in relation to the questions addressed.		Yes
2.5 Details of the methods of synthesis or meta-analysis of estimates are given (if based on a synthesis of a number of effectiveness studies). *OR* Details of the design and results of effectiveness study are given (if based on a single study).		Yes Based on claims data
2.6 Estimates of effectiveness are used appropriately.		Yes
2.7 Methods to value health states and other benefits are stated.		Yes
2.8 Outcomes are used appropriately.		Yes
2.9 The primary outcome measure for the economic evaluation is clearly stated.		Yes
2.10 Details of the subjects from whom valuations were obtained are given.		Yes
2.11 Competing alternatives are clearly described.		n/a
2.12 All important and relevant costs for each alternative are identified.		n/a
2.13 Methods for the estimation of quantities and unit costs are described.		n/a
2.14 Quantities of resource use are reported separately from their unit costs.		No
2.15 Productivity changes (if included) are reported separately.		No
2.16 The choice of model used and the key parameters on which it is based are justified.		n/a
2.17 All costs are measured appropriately in physical units.		Yes
2.18 Costs are valued appropriately.		Yes
2.19 Outcomes are valued appropriately.		n/a
2.20 The time horizon is sufficiently long enough to reflect all important differences in costs and outcomes.		No Followed participants for one year and average pump failure occurs around years
2.21 The discount rate(s) is stated.		n/a
2.22 An explanation is given if costs and benefits are not discounted.		n/a

Risk of Bias Assessment Criteria	Hatheway et al. (2015)	
	Submitter	CEbP
2.23 The choice of discount rate(s) is justified.		n/a
2.24 All future costs and outcomes are discounted appropriately.		n/a
2.25 Details of currency of price adjustments for inflation or currency conversion are given.		Yes
2.26 Incremental analysis is reported or it can be calculated from the data.		No
2.27 Details of the statistical tests and confidence intervals are given for stochastic data.		Yes
2.28 Major outcomes are presented in a disaggregated as well as aggregated form.		No
2.29 Conclusions follow from the data reported.		Yes
2.30 Conclusions are accompanied by the appropriate caveats.		Yes
3.1 The approach to sensitivity analysis is given.		n/a
3.2 All important and relevant costs for each alternative are identified.		n/a
3.3 An incremental analysis of costs and outcomes of alternatives is performed.		n/a
3.4 The choice of variables for sensitivity analysis is justified.		n/a
3.5 All important variables, whose values are uncertain, are appropriately subjected to sensitivity analysis.		n/a
3.6 The ranges over which the variables are varied are justified.		n/a
4.1 Competing interests of members have been recorded and addressed.		Yes Multiple authors have an affiliation with Medtronic but reportedly did not receive funding for this project
4.2 Views of funding body have not influenced the content of the study.		No Funded by Medtronic
5.1 How well was the study done to minimize bias?		**Fair**
5.2 If coded as fair or poor, what is the likely direction in which bias might affect the study results?		The major limitation of this study is that a claims database was used – may not be appropriately categorizing the population by using claims data. Also, total inpatient, outpatient, and pharmacy expenditures were the outcomes, and patients who taper their systemic opiates may also be likely to decrease their opiates due to a confounding factor.
5.3 Other reviewer comments:		---

References

Caraway D., Walker V., Becker L., & Hinnenthal J. (2015). Successful discontinuation of systemic opioids after implantation of an intrathecal drug delivery system. *Neuromodulation*, e-pub ahead of print. DOI: 10.1111/ner.12318.

Dworkin, R. H., Turk, D. C., Wyrwich, K. W., Beeton, D., Cleeland, C. S., Faarar, J.T… Zavisic, S. (2008). Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *The Journal of Pain*, *9*(2), 105-121.

Follett, K. A., & Naumann, A. P. (2000). A prospective study of catheter-related complications of intrathecal drug delivery systems. *Journal of Pain and Symptom Management, 19*(3), 209-215.

Gentile, D. A., Woodhouse, J., Lynch, P., Maier, J., &McJunkin, T. (2011). Reliability and validity of the global pain scale with chronic pain sufferers. *Pain Physician, 14*, 61-70

Grider, J. S., Etscheidt, M. A., Harned, M. E., Lee, J., Smith, B., Lamar, C, & Bux, A. (2015). Trialing and maintenance dosing using a low-dose intrathecal opioid method for chronic nonmalignant pain: A prospective 36-month study. *Neuromodulation*, e-pub ahead of print. DOI: 10.1111/ner.12352.

Hatheway, J. A., Caraway, D., David, G., Gunnarsson, C., Hinnenthal, J., Ernst, A. R., & Saulino, M. (2015). Systemic opioid elimination after implantation of an intrathecal drug delivery system significantly reduced health-care expenditures. *Neuromodulation, 18*, 207–213. DOI: 10.1111/ner.12278.

Hawker G. A., Mian S., & Kendzerska T., French M. (2011). Measures of adult pain. *Arthritis Care & Research, 63*(S11), S240-S252. DOI 10.1002/acr.20543

New York Department of Health (NY DOH). (2015). *Dossier methods guidance*. Albany, NH: NY DOH. Retrieved from http://www.health.ny.gov/health_care/medicaid/redesign/docs/dossier_methods_guidance.pdf

Ooi, Y. C., Saulion, M., Williams, K. A., & Sharan, A. (2011). Observational analysis of successful reimplantation of explanted intrathecal drug delivery systems: A case series. *Pain Medicine and Rehabilitation, 3*(), 175-178. DOI: 10.1016/j.pmrj.2010.08.004.

About the Center for Evidence-based Policy

The Center for Evidence-based Policy (Center) is recognized as a national leader in evidence-based decision making and policy design. The Center understands the needs of policymakers and supports public organizations by providing reliable information to guide decisions, maximize existing resources, improve health outcomes, and reduce unnecessary costs. The Center specializes in ensuring diverse and relevant perspectives are considered, and appropriate resources are leveraged to strategically address complex policy issues with high-quality evidence and collaboration. The Center is based at Oregon Health & Science University in Portland, Oregon. Further information about the Center is available at www.ohsu.edu/policycenter.

Suggested citation: Pensa, M., Thielke, A., & King, V. (2016). *Implantable infusion pumps for chronic non-cancer pain (additional references submitted) – dossier review.* Portland, OR: Center for Evidence-based Policy, Oregon Health & Science University.

Conflict of Interest Disclosures: No authors have conflicts of interest to disclose. All authors have completed and submitted the Oregon Health & Science University form for Disclosure of Potential Conflicts of Interest, and none were reported.

Funding/Support: This research was funded by the Center for Evidence-based Policy's Medicaid Evidence-based Decisions project at Oregon Health & Science University.

This document was prepared by the Center for Evidence-based Policy at Oregon Health & Science University (Center). This document is intended to support participant organizations and their constituent decision-making bodies to make informed decisions about the provision of health care services. The document is intended as a reference and is provided with the understanding that the Center is not engaged in rendering any clinical, legal, business, or other professional advice. The statements in this document do not represent official policy positions of the Center, projects conducted through the Center, or participating organizations. Researchers and authors involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.