
Health Technology Clinical Committee Findings and Coverage Decision

Topic: Implantable Drug Delivery System
Meeting Date: August 15, 2008
Final Adoption: November 14, 2008

Number and Coverage Topic

20080815A – Implantable Drug Delivery System for Chronic non-cancer pain.

HTCC Coverage Determination

Implantable drug delivery systems (Infusion Pump or IDDS) for treatment of chronic non-cancer pain is **not a covered benefit**. This decision does not apply to the use of IDDS for other purposes.

HTCC Reimbursement Determination

❖ **Limitations of Coverage**

Not Applicable

❖ **Non-Covered Indications**

Chronic Non-cancer pain

❖ **Agency Contact Information**

Agency	Contact Phone Number
Labor and Industries	1-800-547-8367
Public Employees Health Plans	1-800-762-6004
Health and Recovery Services Administration	1-800-562-3022

Health Technology Background

The infusion pump topic was selected by the HCA Administrator and published in August 2007 to undergo an evidence review process per RCW 70.14.100(1)(a). Infusion pumps are surgically implanted devices used to deliver drugs to a specific site in the body, rather than relying on systemic levels of medication(s) that are administered orally or by other routes. The Infusion pump topic was reviewed for the indication of chronic non-cancer pain (CNCP) where an infusion pump is permanently implanted for opioid administration.

The HCA Administrator contracted with an independent technology assessment center for a systematic evidence based technology assessment report of the technology's safety, efficacy, and cost-effectiveness consistent with RCW 70.14.100(4). On June 27, 2008, the HTA posted a draft report, invited public comment, and posted a final report on July 18, 2008. The contractor reviewed publicly submitted information, and searched, summarized, and evaluated trials, articles, and other evidence about the topic. This

comprehensive, public and peer reviewed, report is approximately 190 pages, identified 549 potentially relevant articles, a Medicare coverage decision and 3 expert treatment guidelines. Based on pre-established criteria and clinical research methodology, the technology assessment center included the most relevant and best available evidence on the safety, effectiveness, and cost effectiveness of the infusion pump for treatment of CNCP. The result is a critical appraisal of 13 case series and 4 cost analyses. Using a formal, objective method of evaluating evidence, the evidence based technology assessment report concluded that the case series rated as low overall internal validity for all key questions.

On August 15th, 2008, the HTCC, an independent group of eleven clinicians, met at an open public meeting to decide on whether state agencies should pay for the infusion pump for treatment of CNCP. The HTCC reviewed the TA report, including peer and public review comments; and invited and heard public comments at the meeting. Meeting minutes detailing the discussion are available through the HTA program or online at <http://www.hta.hca.wa.gov> in the committee section.

Committee Findings

Having considered the evidence based technology assessment report and the written and oral comments, the committee identified the following key factors and health outcomes, and evidence related to those health outcomes and key factors:

1. Evidence availability and technology features

The committee finds the following key factors relevant to the coverage decision:

- 1.1. The evidence based technology assessment report indicates that chronic pain is burdensome and costly; an important and common medical concern. There are many conservative treatments for chronic pain and medical treatment also includes treatment of the underlying disorder, when possible. The permanent implantation of infusion pumps is an invasive alternative for medication delivery and requires ongoing maintenance and successive surgeries to replace the infusion pump approximately every five years.
- 1.2. The evidence based technology assessment report searched peer reviewed medical literature, submitted comments and other sources and did not identify any relevant randomized controlled trials or other controlled trials.
- 1.3. The thirteen case series identified in the evidence based technology assessment report included 413 patients overall (11 to 30 patients per study) averaging in age from mid-forties to mid-fifties. Internal validity rating of the case series for all outcomes was low; with factors limiting validity including high attrition, failure to compare characteristics of completers and non-completers, use of ancillary treatments, and funding from a source with a financial interest in the outcome.
- 1.4. The evidence based technology assessment report identified three expert treatment guidelines and included the Medicare national coverage decision.
- 1.5. Medicare national coverage decision covers implantable pumps for epidural or intrathecal administration of opioid drugs for chronic non-cancer pain. Decision rendered in 1994 and updated in 2004. However, the update addressed coverage of insulin pumps and no update to the infusion pump for CNCP was completed.

- 1.6. Two expert treatment guidelines identified through the National Guidelines clearinghouse search did not support use of infusion pumps for chronic pain or morphine use.
- 1.7. One expert treatment guideline supported use of implantable intrathecal infusion systems for long term management of chronic pain.

2. Is the technology safe?

The committee found that adverse events were the most significant safety outcome measure. The report identified the following evidence:

- 2.1. Case series reported 8% discontinuation rate due to adverse events.
- 2.2. Case series reported 9% to 42% re-operation rate for major and minor complications.
- 2.3. Case series reported 8% rate of discontinuation of device due to inadequate pain control.
- 2.4. FDA reports of 9 deaths reported in 2006 within 3 days of pump implantation.
- 2.5. FDA database of adverse events. Of over 9,000 filed for infusion pumps, the evidence based technology assessment report identified 975 directly relevant events, including 53 deaths.
- 2.6. FDA's database highest number of serious reports included infection (128), inflammatory masses (83), and paralysis (20).

3. Is the technology effective?

The committee found that there were four key health outcomes that were most significant in assessing the technology's effectiveness. The report identified the following evidence:

3.1. Pain Control

- 3.1.1. Pain is a subjective sensation and was measured in the studies by the visual analogue scale (VAS).
- 3.1.2. The committee focused on the evidence based technology assessment report's analysis of seven case series that measured at least 50% pain reduction which included 150 patients. The studies were assessed as low quality internal validity, limited by high attrition, failure to compare characteristics of completers and non-completers, use of ancillary treatments, and funding from a source with financial interest in outcome.
- 3.1.3. Evidence based technology assessment report meta-analyzed results of the seven case series and concluded that there was weak evidence that 41% of patients treated indicated that they experienced more than 50% pain relief, and 59% of patients indicated that they had not. The percentage varied widely among studies, from 11% to 100% attaining relief, and due to unexplained differences and inconsistency among studies, the statistic is unstable.
- 3.1.4. The Evidence based technology assessment report concluded overall that there is weak evidence of clinically significant pain relief, but the percent of patients that would experience relief and the amount of pain relief could not be calculated due to the low evidence quality.

3.2. Functional Status

- 3.2.1. The evidence based technology assessment report indicated only one low quality study addressed functional status, and thus there was insufficient quantity of evidence to form an evidence based conclusion.

3.3. Return to Work

- 3.3.1. Four low quality studies identified in the evidence based technology assessment report, which included 115 patients, found that the results were too imprecise to permit an evidence based conclusion (the variation supported two inconsistent conclusions- either employment reduces slightly after pump implantation or increases greatly).
- 3.3.2. Washington State's small worker's compensation experience which was not peer reviewed and was similar to the case series data (11 claimants) shows no claimant receiving the pump has returned to work.

3.4. Quality of Life:

- 3.4.1. The evidence based technology assessment report indicated that two studies, ranked low quality of internal validity, had inconsistent findings (one low quality study found no observed change while another low quality study observed a dramatic improvement).

4. Is the technology cost-effective?

The committee found that there was key information about cost and value:

- 4.1. The evidence based technology assessment report identified a number of costs related to the infusion pump including: screening; initial purchase; pump implantation; medication refills; consultations; complications; adjunctive medications; pump replacement or removal.
- 4.2. The evidence based technology assessment report identified four peer-reviewed articles addressing cost analysis that indicated mixed results, several with equivalent costs with wide confidence intervals.
- 4.3. The higher up front and maintenance of the pump costs may be offset by longer term medication and other medical services reduction.
- 4.4. One analysis in the report was a five year cost model that concluded: non-pump cost of \$83,000; and pump costs ranging from a best case of \$53,000 (average of \$83,000, and worst case of \$125,000).

Committee Conclusions

Having made findings as to the most significant and relevant evidence regarding health outcomes, key factors and identified evidence related to those factors, primarily based on the evidence based technology assessment report, the committee concludes:

5. Evidence availability and technology features

The committee concludes that the best available evidence on infusion pumps has been collected and summarized, however the overall quality of this evidence is low, methodologically challenged and not robust as follows:

- 5.1. Efficacy is best proven via randomized or well designed controlled trials, with adequate participants, assessment of all patient centered health outcomes, and for sufficient duration. Despite growing use for several decades, the

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- entire body of literature on infusion pumps for CNCP (all studied outcomes) includes only 13 case-review articles on 413 patients. As a result, the quality of evidence for outcomes was at best rated as weak. On the other hand, complications and adverse events can be identified by case-review studies and other sources such as the FDA database.
- 5.2. Chronic pain is burdensome and significantly impacts patients, but is not life threatening. Many non-invasive alternatives are available and currently covered by the agencies.

6. Is it safe?

The committee concludes that the comprehensive evidence reviewed does not show that the technology has been proven safe, indicating that the infusion pumps were either less safe or unproven to be as safe or safer. Key factors to the committee's conclusion included:

- 6.1. Safety data identifies a substantial risk to patients. This procedure is performed where there is a serious, though not life threatening underlying condition.
- 6.2. FDA reporting is a voluntary database, which most likely under reports the total number of actual adverse events.
- 6.3. The 9 reported deaths in 2006 within 3 days of implantation confirmed that this invasive treatment, especially when use in real practice settings carries significant risk. The overall rate remains unknown due to the fact that reporting is voluntary and the denominator or total number of implantations is not required to be released. Until such information is made available, the significant adverse events cannot be ignored.
- 6.4. Even in the case series trial setting which presents a best case scenario for selection, experience, and monitoring; significant adverse events occurred and the variation among trials was large: reoperation rate due to complications ranged from 9% to 42%; and overall discontinuation for adverse events was high at 8%.

7. Is it effective?

The committee concludes that the comprehensive evidence reviewed does not show that the technology has been proven effective:

- 7.1. Of the four identified key health outcomes impacting effectiveness, only one outcome had a sufficient quality of evidence to draw even weak proof of effect from use of implanted infusion pumps in the treatment of CNCP.
- 7.2. Pain control was a primary studied outcome and is an important benefit to patients. The totality of the low quality evidence showed that there is a pain control benefit for some patients, though the proportion of those benefiting to those who did not was not capable of being determined. This was a weak evidence conclusion based on combining, or meta-analyzing the case series. Committee members placed low confidence in the individual studies and in combining the low internal validity studies to produce a combined effect because, methodologically it is problematic to meta-analyze poor quality case series data, as also noted by the methodology peer reviewer. In this case, the following factors weighed heavily: pain is a subjective sensation so

- difficult to measure reliably, the report and the case series did not provide sufficient information to confirm that all other alternatives had been exhausted; the assumption of little placebo effect from this intervention in pain relief was challenged; a primary measurement tool, the VAS, has unclear usefulness to measure pain and other available tools may be more reliable and accurate; 150 patients in small case series is a very small evidence base and represented only a subset of the 413 total patients included in the analyzed studies; the benefit over time is not well measured even though this is proposed as a permanent treatment; most patients continued oral pain medications; and the pain control benefit is highly inconsistent.
- 7.3. Even with low quality evidence of some pain relief, it is not possible to identify which patients might benefit and which do not.
 - 7.4. Functional status, employment status, and quality of life are important health outcomes that combined would demonstrate overall effect of the treatment, but no reliable data demonstrates improvement in these outcomes.

8. Is it cost-effective?

The Committee concludes that the comprehensive evidence review does not show that the technology is more cost effective. Although cost-effectiveness was not a major decision factor, the committee concluded that it is likely of equivalent cost:

- 8.1. Four peer-reviewed articles addressing cost analysis indicated mixed results and indicated equivalent costs with wide confidence intervals.
- 8.2. Because the committee could not find high quality evidence demonstrating effectiveness, a determination of cost-effectiveness, which requires a positive benefit, cannot yet be established.

9. Medicare Decision and Expert Treatment Guidelines

The committee deliberations included a discussion of National Medicare Decisions and expert treatment guidelines, and an understanding that the committee must find substantial evidence to support a decision that is contrary. RCW 70.14.110. Based on the following, the Committee concludes that a decision consistent with two expert treatment guidelines and contrary to the National Medicare Coverage Decision and one treatment guideline is justified:

- 9.1. The independent evidence vendor identified four relevant policies, two supporting the infusion pump and two that did not support use. The committee decision is consistent with two expert treatment guidelines and inconsistent with an expert treatment guideline and Medicare national coverage decision. For those policies that are inconsistent, the committee was persuaded by the evidence cited above from the evidence based technology assessment report, and less persuaded by the older policies that, while citing some evidence, were not supported by an independent assessment and grading of the evidence. In particular:
 - 9.1.1. Committee found that it had the most complete and current evidence available.

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- 9.1.2. Committee found that this substantial evidence reviewed does not currently demonstrate that the technology is equally safe or safer, equally or more effective, or more cost effective.
 - 9.1.3. Medicare Coverage Decision on infusion pumps for CNCP was from 1994 and did not include a review of the many recent studies noted in the evidence report, and most importantly any safety data.
 - 9.1.4. The critical safety data from the FDA, including the 9 deaths occurring in 2006 was neither available nor reviewed by Medicare or identified in the treatment guideline.

Committee Decision

Based on the deliberations of key health outcomes, the committee decided that evidence on infusion pumps did not demonstrate net health benefit because weak or unproven evidence of some effectiveness for certain patients was undermined by significant evidence of serious harms and adverse events associated with the implantation of infusion pumps. The committee found that infusion pumps were not proven to be equally or more safe or effective, and the cost, while not a significant factor for this decision was likely equivalent. Based on these evidentiary findings, the committee voted 8 to 2 for non-coverage.

The committee has received public comments through October 10th 2008 and at the October 17th and November 14th, 2008 public meetings and has incorporated those comments into finalizing this decision.

Health Technology Clinical Committee Authority

Washington State's legislature believes it is important to use a scientific based, clinician centered approach for difficult and important health care benefit decisions. Pursuant to chapter 70.14 RCW, the legislature has directed the Washington State Health Care Authority, through its Health Technology Assessment program to engage in a process for evaluation process that gathers and assesses the quality of the latest medical evidence using a scientific research company and takes public input at all stages. Pursuant to RCW 70.14.110 a Health Technology Clinical Committee (HTCC) composed of eleven independent health care professionals reviews all the information and renders a decision at an open public meeting. The Washington State [Health Technology Clinical Committee \(HTCC\)](#), determines how selected health technologies are covered by several state agencies. RCW 70.14.080-140. These technologies may include medical or surgical devices and procedures, medical equipment, and diagnostic tests. HTCC bases their decisions on evidence of the technology's safety, efficacy, and cost effectiveness. Participating state agencies are required to comply with the decisions of the HTCC. HTCC decisions may be re-reviewed at the determination of the HCA Administrator.