



Health Technology Clinical Committee

Date: August 15, 2008

Time: 8:00 am – 5:00 pm

Location: Marriott Hotel – 3201 South 176th Street, Seattle, WA 98188

Teleconference Bridge: 1-309-946-5000 Access Code: 9461464

Final Adoption: October 17, 2008

HTCC MINUTES

Members Present: Brian Budenholzer; C. Craig Blackmore; Michael Myint; Carson Odegard; Daniel Abrahamson; Richard Phillips; Michelle Simon, Michael Souter, Louise Kaplan, and Jay Klarnet.

Members Absent: Lydia Bartholomew

HTCC FORMAL ACTION

1. **Call to Order:** Dr. Budenholzer, Chair, called the meeting to order at 8:00 a.m. Sufficient members were present to constitute a quorum.
2. **February 15, 2008 Minutes:** Dr. Budenholzer referred members to the draft minutes and called for further discussion or objection, and received none.
 - *Action:* The committee unanimously approved the February 15, 2008 minutes.
3. **CT Colonography Findings and Decision:** Dr. Budenholzer referred members to the draft findings and decision and called for further discussion or objection, and received none.
 - *Action:* The committee unanimously approved the CT Colonography findings and decision document.
4. **Discography Findings and Decision:** Dr. Budenholzer referred members to the draft findings and decision and called for further discussion or objection, and received none.
 - *Action:* The committee unanimously approved the Discography findings and decision document.
5. **Implantable Drug Delivery System Determination:** The HTCC reviewed and considered the Implantable Infusion Drug Delivery Systems (Infusion Pumps) for chronic non-cancer pain technology assessment report, information provided by the Administrator, state agencies, and public members; and heard comments from the evidence reviewer, HTA program, agency medical directors, a device manufacturer panel, and several public



members. The committee considered all the evidence and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

HTCC COMMITTEE COVERAGE DETERMINATION VOTE			
	Not covered	Covered Unconditionally	Covered Under Certain Conditions
Implantable Drug Delivery System	8	0	2

- *Action:* The committee chair directed HTA staff to prepare a Findings and Decision document on Implantable Drug Delivery Systems reflective of the majority vote for final approval at the next public meeting.

6. **Knee Arthroscopy for Osteoarthritis of the Knee Determination:** The HTCC reviewed and considered the Knee Arthroscopy technology assessment report, information provided by the Administrator, agency comments, the evidence reviewer’s presentation, and submitted comments. The committee considered all the evidence and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

HTCC COMMITTEE COVERAGE DETERMINATION VOTE			
	Not covered	Covered Unconditionally	Covered Under Certain Conditions
Knee Arthroscopy for Osteoarthritis	10	0	0

- *Action:* The committee chair directed HTA staff to prepare a Findings and Decision document on Knee Arthroscopy reflective of the majority vote for final approval at the next public meeting.

SUMMARY OF HTCC MEETING TOPICS, PRESENTATION, AND DISCUSSION

Agenda Item: Welcome & Introductions

The Health Technology Clinical Committee (HTCC) met on August 15, 2008. Leah Hole-Curry, HTA Program Director, opened the public meeting with an overview of the agenda, meeting guide and purpose, room logistics, and introductions. The primary technology topics to discuss were:

- ✓ *Intrathecal Drug Delivery Systems (Implantable Infusion Pumps)*: review of the evidence of the safety, efficacy and cost-effectiveness of Implantable Infusion Pumps for patients with chronic non-cancer pain.
- ✓ *Knee Arthroscopy*: review of the evidence of the safety, efficacy and cost-effectiveness of Knee Arthroscopy for patients with Osteoarthritis of the knee.

Agenda Item: Chair Remarks

Dr. Brian Budenholzer, Committee Chair, provided opening remarks. Dr. Budenholzer presented his thoughts on why the committee was created through the frame of a chronological history of a compelling treatment: high dose chemotherapy followed by bone marrow transplant for advanced breast cancer.

- 1988 - A 1988 Annals of Internal medicine article reported case series finding an 80% response rate; and an expert opined that the treatment could double survival.
- 1989- federal judge required a health insurer to cover on the following basis: *To require that patients wait until someone chooses to present statistical proof that satisfies all the experts would mean patients would be doomed to receive treatments that are not state of the art.*
- 1992 – JAMA article with case series and extrapolated data – indicated that using reasonable assumptions, autologous bone marrow transplant had benefit but at unknown cost
- 1993 – National Cancer Institute launched randomized control trial, but had trouble recruiting patients because many physicians and patients already concluded it was effective. Ultimately, trials were completed.
- 1994 – Federal Office of Personnel Management required all insurers providing insurance to federal employees to cover.
- 1995 – Journal of Clinical Oncology, South African randomized trial reported dramatic benefit; cited by over 300 papers, but ultimately found to be fraudulent
- 1999 – Eleven years after first case series reported: Four randomized trials reported at an American Society of Clinical Oncology showed no benefit.
- Dr. Eddy: *As a society, we have to accept that rigorous evaluation of a new treatment is essential. Skipping this step may seem like a compassionate act, but it can have devastating consequences.*

Dr. Gilbert Welch – who wrote a history of the treatment, presented some conclusions:

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- *Important to remember that preliminary evidence can be misleading; intermediate outcomes may not correlate to survival, historical controls may not be comparable; proponents can be persuasive but lesson is familiar – it is the case for randomization.*
- *It is premature to raise the issue of cost effectiveness when effectiveness is unknown.*
- *Public officials should not mandate coverage in the absence of clear data.*
- *Proponents of advances will always be more vociferous than detractors. They usually have stronger interests, both professional and financial, in arguing for a particular technology than detractors have in arguing against it. Given that the public is primed to believe in medical breakthroughs, we should focus on evidence of effectiveness before raising arguments about cost.*

Agenda Item: HTA Program Update and Chair Remarks

Leah Hole-Curry presented the draft minutes from the February 2008 meeting, explained that the minutes were drafted by HTA staff, posted to the web and circulated to committee members for comments. No comments were received. Dr. Brian Budenholzer, HTCC Chair, referred members to the February minutes, and called for further discussion, or a motion to approve.

- ✓ No further discussion, minutes were approved.

Leah Hole-Curry presented the draft findings and decision for CT Colonography, explained that the document was drafted by HTA staff, posted to the web and circulated to committee members for comments. No comments were received. Dr. Brian Budenholzer, HTCC Chair, referred members to the draft findings and decision, and called for further discussion, or a motion to approve.

- ✓ No further discussion, minutes were approved.

Leah Hole-Curry presented the draft findings and decision for discography, explained that the document was drafted by HTA staff, posted to the web and circulated to committee members for comments. An update was received and incorporated. Dr. Brian Budenholzer, HTCC Chair, referred members to the draft findings and decision, and called for further discussion, or a motion to approve.

- ✓ No further discussion, minutes were approved.

Agenda Item: Implantable Infusion Pumps Topic Review

Dr. Dave Flum, HTA Clinical Consultant, introduced the Implantable Infusion Pump topic overview.

Implantable Infusion Pump

- ✓ Implantable Drug Delivery Systems for chronic non-cancer pain (IDDS) is a device which is fully surgically implanted into the patient to provide round-the clock long-term drug therapy. In a surgical procedure, the pump itself is implanted, usually in the abdomen, and a catheter is tunneled to the site of drug delivery.
 - Because medications are delivered directly to the desired site, pain control is theoretically optimized while adverse events associated with systemic administration are theoretically minimized because the overall drug dose is reduced.



- ✓ IDDS treatment is invasive, prone to side-effects and complications, costly, and requires a large amount of technical support. IDDS for chronic non-cancer pain seeks to replace the route of opioid administration to achieve better pain control with fewer adverse effects.
- ✓ Centers for Medicare and Medicaid Services (CMS): a national coverage decision for all infusion pumps was issued in February 1994. Permanently implanted infusion pumps are covered, with certain conditions, for patients with chronic non-cancer pain. The latest version of the policy was adopted December 17, 2004. The initial determination included implantable infusion pumps for epidural or intrathecal administration of opioid drugs for chronic non-cancer pain was not updated since 2004.
 - This decision was based on a technology assessment completed in 1994 by the Office of Health Technology Assessment (OHTA) and used the only available literature which was from 1984 – 1992.
- ✓ Three entities published guidelines: American Society of Interventional Pain Physicians (2007); Siskin Hospital for Physical Rehabilitation (2005); and Internal Research Foundation for RSD / CRPS (2003).

Agenda Item: Implantable Infusion Pump Topic – Agency Data

Dr. Lee Glass, L&I Associate Medical Director, presented to the committee the agency utilization and outcomes for Implantable Infusion Pumps.

- ✓ All Washington agencies cover IDDS pumps without restrictions for cancer pain, chemotherapy, and spasticity.
- ✓ IDDS pumps for chronic non-cancer pain has historically been covered by DSHS and HCA, and it is recently covered at L&I with protocols, due to litigation.
 - Alternatives: agencies cover alternatives (coverage varies by agency) and include: cognitive behavior therapy, medication (anti-depressant, Acetaminophen, NSAID, Opioids), rehabilitation (psychological, exercise & education, interdisciplinary rehabilitation, spinal manipulation) and alternative and complimentary medicine (massage, acupuncture).
- ✓ L&I Summary of outcomes for workers with implantation since 2006:
 - 10 of 11 workers using drug(s) not FDA approved for intrathecal administration
 - 3 of 11 workers currently are receiving intrathecal dose(s) above the Polyanalgesic Consensus recommendation for maximum dose/day
 - 10 of 11 workers require on-going opioids (oral or transdermal) in addition to their intrathecal opioid dose
 - 5 workers taking same or higher oral/transdermal opioid dose than they were before pump implantation
 - 6 of 11 workers have reported side-effects, many serious
 - 9 of 11 workers have documented pre/post VAS scores
 - 4 workers have improved self-reported pain
 - 1 worker had a 29% reduction
 - 3 workers have between 13% - 18% reduction
 - 5 workers have same or higher pain levels
 - Function was reported in 3 of 11 workers
 - All 11 workers currently receiving time-loss (unable to work)

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- ✓ Safety Concerns: MAUDE data provided by the FDA in April 2007:
 - By event type (1996 – April 2007):
 - Death = 344
 - Serious Injury = 3,817
 - Malfunction = 2,692
 - Other = 2,174
 - Total = 9,026
 - MAUDE data is a voluntary reporting system and likely under-reports adverse events.
 - Medtronic Educational Brief, Patient Mortality after Implant - November 2006:
 - 9 patient deaths within 3 days of starting or re-starting IDDS opioid therapy. Approximately one person per 1,000 dies.
 - Five per 1,000 (0.49%) reported to develop inflammatory mass.
- By Outcome (1996 –April 2007):
 - Hospitalization = 4,358
 - Required Intervention = 2,665
 - Serious Medical Events = 2,091
 - Death = 344
 - Life Threatening = 93
- ✓ Efficacy Concerns: Consistent systematic reviews indicate weak evidence of pain reduction and insufficient evidence to address significant key health outcomes and safety issues.
- ✓ Utilization (2002 to 2008 all agency):

Service	Service Number	Total Cost
Implantations (all diagnosis)	324	\$ 5.2 Million
Implantations, Removals, Screenings	145	\$ 1.8 Million
Maintenance (analysis, refilling)	360	\$ 99,530
Pharmacy (oral medications)	32	\$ 16,301

IDDS Procedure	Patient Count – All Agencies	Average Cost Per Patient	Cost Range
Implantation (all diagnosis)	324	\$ 12, 769	\$ 10,268 - \$ 15,060
Implantation (CNCP Only)	93	\$ 12,664	\$ 10,268 - \$ 15,060
* Screening Trials	37	\$ 12,118	\$ 11,808 - \$ 15,472
Removal	15	\$ 11,898	\$ 10,972 - \$ 12,823

Agenda Item: Public Comments

- ✓ Scheduled Public Comments: A total of thirty-five minutes was provided for scheduled presentations from a manufacturer Panel (30 minutes) and an independent physician
- ✓ Medtronic has a panel present a thirty minute PowerPoint presentation. Presenters included: William Fehrenbach, Mike Baca, Mary Owens, David Caraway, Scott Guillemente. Dr. John Loeser was also scheduled to present (telephonically), he was invited to speak four times, but was not present at those times.
 - Context: Therapy is important for patients with no other options; Medtronic is committed to mitigating risks and ensuring patient safety and quality
 - Extensive pre-market approval process, the FDA determined that the benefits outweigh the risks.
 - Time limits ability of Medtronic to fully address all issues

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- HTCC decision shall be consistent with the federal Medicare program and expert treatment guidelines; there is a positive Medicare coverage decision and therapy has overwhelming support by societies and patient organizations.
- Advantages to intrathecal opioids, include: steady-state around the clock dosing; reduced side effects; may result in reduction in longitudinal costs; adjuvants; and compliance. Disadvantages included: more invasive; more difficult to discontinue therapy; acquisition costs; and if positioned as a salvage therapy for patients who have failed but remain on high dose systemic opioids outcomes are diminished.
 - L&I data shows 32 deaths between 1996 and 2002 from accidental overdose of prescription opioids or narcotics; statewide increase of 800 percent
- Medtronic is proactive in risk mitigation – the nine patient deaths investigated. Infusion pumps operated normally, but operational factors such as insufficient patient monitoring, concomitant medications, and co-morbid factors were at issue. Agree with AMDG opioid dosing – amount needs to be monitored and should be within guidelines
- Provided recommended approach was to perform and document history and psychological evaluation; document reasonable etiology; document failure of conservative therapy; psychological evaluation; create written goals of therapy; and consider discontinuation of systematic opioids prior to trial.
- Noted ongoing improvements to systems to drive higher quality, reliability, and manufacturability to enhance effective and safe use. Recent example can be seen in SynchroMed II with redesigned motor, elimination of gear shaft issue, and improved catheter design.
- ✓ Dr. Stuart DuPen, Pain Management Physician, provided five minute public comments.
 - Dr. DuPen provided testimony regarding his experience working with Implantable Infusion Pumps. His clinical opinion was that he saw Implantable Infusion Pumps assist many patients throughout his clinical career.
- ✓ Open Public Comments: Two individuals provided comments during the open portion (limited to three minute comments) –
 - Don Roller and Kathy Church. Implantable Infusion Pump patients whose travel was sponsored by Medtronic to attend.
 - Both individuals shared separately how Implantable Infusion pumps have significantly improved their pain and that they have a better quality of life and urged the committee to cover the devices.

Agenda Item: Evidence Review Presentation

ECRI Institute presented an overview of their evidence report.

- ✓ Key Questions for Implantable Infusion Pumps were on efficacy, safety, and cost:
 - What is the evidence for efficacy and effectiveness of implantable infusion pumps?
 - What is the safety profile of implantable infusion pumps?
 - Is there any evidence of differential efficacy or safety issues amongst special populations?
 - What are the cost implications and cost effectiveness for implantable infusion pumps?

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- ✓ Evidence Base: 549 abstracts identified; 88 retrieved; 16 included. 13 case series, 4 cost analysis, one study that was both case series and cost analysis
 - All case series – no control group means less certainty that effect is due to intervention; placebo response in pain patients is relatively small; history of pain pump candidates of stable unremitting pain despite exhaustive attempts at conservative therapy
 - 413 total patients (range of 11 to 30 per study); overall low internal validity ratings
- ✓ Effectiveness evidence
 - Pain relief:
 - Weak evidence indicating that implantable infusion pumps lead to clinically significant pain relief in patients with chronic non-cancer pain. No quantitative (numerical range) could be given.
 - 6 studies with 123 patients: 60% patients had at least 25% relief
 - 7 studies with 150 patients: 40% patients had at least 50% relief
 - Evidence sufficient for low stability quantitative conclusion on discontinuation of treatment due to insufficient pain relief: 8% discontinue.
 - 5 studies with 102 patients: 8% of patients discontinued due to insufficient pain relief
 - Use of IDDS and Medication changes: associated with decrease in use of other medication and treatment and increase in dosage of infused medication. No strength or stability of evidence rating because reasons not identifiable and differences in reporting.
 - 9 studies with 347 patients: all studies reported decrease in number of patients using other treatments and/or a decrease in the quantity of medications used.
 - No detail on studies showing increased dosage for infused
 - Quality of life improvement: Insufficient quantity of evidence to base conclusion.
 - Functional status: Insufficient quantity of evidence to base conclusion.
 - Change in employment: Inconsistent evidence.
- ✓ Adverse Events:
 - From Case Series: Discontinuation from study due to adverse events – low stability evidence that 8% of patients discontinued treatment due to adverse events and effects
 - Seven studies of 132 patients – 9 patients discontinued
 - From Case Series: Most common opioid-related adverse events included gastrointestinal (constipation, nausea, dyspepsia); headache; fatigue / lethargy / somnolence; and urinary (retention, hesitancy, “disturbance”), no life threatening adverse events.
 - From Case Series: device related adverse events included malfunctions; malpositioning; and surgical and post-surgical complications.
 - Patients who required re-operations ranged from 9% to 42%

- 3 studies reported 7 deaths
- FDA Manufacturer and User Facility Device Experience (MAUDE) Database – has limitations related to voluntary reporting (severity, duration, total number of pumps for denominator and rate information, ability to attribute definitively to pump)
 - Unfiltered search of implantable pump code: 9,082 reports.
 - 343 deaths, 3,817 serious injuries, 2,692 malfunctions, 2,174 other
 - ECRI Filtered search – 975 reports. 53 deaths; Serious infections – 128; Serious inflammatory masses – 83; serious respiratory difficulty 8; serious paralysis – 20 device related reoperation – 405; removal – 211; device related no requiring revision – 86; operator error – 35
- Other Data: - Early mortality report of 9 patient deaths between 12/2005 and 3/2006; endocrine effects (decreased libido, hypogonadism; amenorrhea; impotence); Granuloma – inflammatory mass estimated prevalence by manufacturer at .49%; catheter connection failure .015 to .22 incidence.
- ✓ Special Populations: Due to an absence of evidence, no conclusions can be drawn.
- ✓ Costs: Complex array of costs which include: screening; initial purchase; pump implantation; medication refills; consultations; complications; adjunctive medications; pump replacement or removal.
 - 4 cost analysis reviewed – inconclusive evidence - mixed results and all had limitations
 - deLissovoy(1997) - 5 year cost model: non-pump cost of \$83,000; and pump costs ranged from a best case of \$53,000, average of \$83,000, and worst case of \$125,000.
 - Kumar (2000) – Canadian empirical studies of costs of 67 patients. Five year pump costs \$44,000; five year non-pump cost \$56,000
 - Reden and Anders (2006) – insurance claims data from 1,647 patients. Hypothetical non-pump costs. Non-pump total 30 year costs: 2.0 Million; Pump total 30 year cost method 1: 2.18 million or Method 2: 1.54 million

Agenda Item: HTCC Implantable Infusion Pump Discussion

Brian Budenholzer, Committee Chair, led a discussion of the evidence related to the safety, efficacy, and cost effectiveness of Implantable Infusion Pumps beginning with identification of key factors and health outcomes, and then a discussion of what evidence existed on those factors.

Key Factors and Health Outcomes Considered

Efficacy: The committee identified multiple key health outcomes that were important for consideration in their overall decision on whether the technology was effective. Summary of committee consideration, discussion, comments

- Pain control - a primary studied outcome, important benefit to patient, substantial evidence that there is a pain control benefit for some patients, though evidence is weak due to low quality, patient population has few choices; pain is a subjective sensation so difficult to measure reliably, challenged assumption of little placebo affect in pain relief, unclear usefulness of VAS tool to measure pain where other tools may be more reliable and accurate, 143 patients in small case



series is a small evidence base, information doesn't identify how to select patients, benefits are spotty where some patients get stellar results and others get none, benefit durability.

- Functional Status - an important outcome to the committee, but only one study reported information and study low quality
- Employment Status – information from four case series low quality and results; local L&I data - no patient returned to work.
- Quality of life – while important outcome, studies did not report or very little data available
- Operator Use - discussion centered on several items related to the difference between the device itself and its “in practice” use. Primarily, discussion focused on who selects patients and performs the intervention, and whether restrictions, specialized training or other requirements were involved. Manufacturer does provide training; most are performed in hospital or facility and they have accreditation standards; only a small number of experienced practitioners used on L&I's patients, and the 3 removals were a patient and provider joint decision. Best available information from case series – presume highly trained and highly selected patients still had 8% removal; 8% discontinuation; and 9% to 42% reoperation rate. Ultimately committee did not use as key factor.
- Dosage / addiction issues - issues related to dose escalation of injected medication; adjuvant therapy; reduction of other pain medicine and treatments; patients receiving oral medication have addiction and overdose risks. Ultimately committee did not use as key factor

Safety: The committee discussed multiple outcomes related to safety, but ultimately addressed safety as a whole, rather than by individual outcomes.

- A primary theme discussed is that the data on safety indicates that there are definite risks on safety, though unclear how often events occur, so can't be sure that this is a safe procedure
- Agencies identified a 1 per 1000 death rate from a Medtronic document, but not validated
- 9 deaths in 2006 was concerning – whether operator error or device, the coverage is for both
- Case series represents somewhat of a best case scenario and adverse events reported included 8% discontinuation due to adverse events; 8% discontinuation due to no pain relief; 9 to 42% reoperation rate.
- Unclear whether discontinuation should be treated as an adverse or safety event, if not working, it is appropriate and positively viewed that it is removed (efficacy issue).
- Safety data represents a substantial risk to patients and procedure is performed where there is a serious, though not life threatening underlying condition
- No data presented on whether there are differences with other pump implantation uses (e.g. cancer)
- Maude Data voluntarily reported – since 1996 –total number of adverse events was over 9000 and ECRI filtered to about 900 based on their desire not to include other pump usage like insulin; categories of adverse events (deaths, serious injuries, malfunctions, other) not broken out
- Medical treatment has risks as well – personal experience with patients is addiction to drugs, overdose, depression common in these and so inconclusive about whether this infusion intervention will have more safety issue

Cost: The committee discussed cost and cost-effectiveness as a whole. This topic generated the least discussion because of the primary safety and effectiveness issues.

- General comments that costs appeared to be about equivalent or inconclusive cost-effectiveness (premature) because effectiveness not yet established



- There are a number of costs related to the pump including: screening; initial purchase; pump implantation; medication refills; consultations; complications; adjunctive medications; pump replacement or removal.
- 4 cost analysis were included and rated as inconclusive. Committee discussed briefly deLissovoy (1997) a five year cost model that showed: 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. For the Reden and Anders analysis, questions were raised about the appropriateness of the cost basis used for non-pump costs – (\$4k/month) may not be representative.

Medicare Decision and Expert guidelines

Committee reviewed and discussed the Medicare coverage decision and expert guidelines as identified and reported in the technology assessment report. Medicare has a National Coverage Decision that covers IDDS with conditions; one guideline suggests evidence is strong for short term pain relief and moderate for long term pain relief; a second guideline indicates IDDS did not meet criteria to recommend treatment; a third notes that morphine pumps have not been shown to be clinically superior.

Additional Item: HTCC Executive Session

Chair, Dr. Brian Budenholzer, after advice from the Assistant Attorney General called a break in the public meeting portion and requested the committee members remain present for an executive session. The Assistant Attorney General; all present committee members; the HTA Director and the HCA Assistant Administrator participated in an executive session for the Assistant Attorney General to advice on the statute and regulations governing committee decisions and the potential for litigation.

At the appointed time, the executive session was closed. The Chair called for a short break and then resumed the public meeting.

Agenda Item: HTCC Implantable Infusion Pump Vote

The clinical committee utilized their decision tool to first gauge committee judgment on the status of the evidence in the three primary areas of safety, efficacy, and cost.

Implantable Infusion Pump Evidence Votes:

Is there sufficient evidence under some or all situations that the technology is:

	Inconclusive (no)	Equivalent (yes)	Less (yes)	More (yes)
Effective	6	1	0	3
Safe	6	1	3	0
Cost-effective	4	6	0	0

Committee Discussion related to ad hoc group. Committee discussed whether an ad hoc group was needed to provide more information to the committee:



- Review of literature is well done; information is present to make decision; there is nothing out there that would likely change view
- Ad hoc committee would provide more opinion, but committee has good idea of what information is available and what the evidence is
- We have all the information before us, we just need to make a decision

HTCC Implantable Infusion Pump Coverage Decision

The HTCC reviewed and considered a comprehensive 2008 HTA Evidence Report on IDDS for chronic, non cancer pain that identified 549 potential articles and included and analyzed the relevant and highest quality studies: 13 case series, 4 cost analysis, and 1 combined case series and cost analysis. The committee also reviewed information provided by the Administrator, state agencies, and public members; and heard comments from the evidence reviewer, HTA program, agency medical director, a device manufacturer panel, and several public members.

Committee members focused on the question about whether this device, which presents a different (and maybe better) way of administering drugs, but is an invasive way of treating a non-life threatening condition that often involves multiple invasive procedures. There was a focus on an overall or net health benefit question weighing generally agreed weak evidence of pain improvement versus the lack of evidence on other key health outcomes, and the data showing significant safety events.

Representative summary comments included:

- Substantial amount of evidence on pain control, though weak, available to guide committee; patient population do not have a lot of options but it would not too hard to design a trial that would give us better than weak evidence;
- appears that there is a modest pain benefit from procedure
- Safety data represents a substantial risk to patients and procedure is performed where there is not a life threatening underlying condition
- Concerned about safety evidence raised unanswered questions that were not present previously; weak evidence of efficacy of patient pain relief in a proportion of patients
- Possible benefit but should be tightly controlled to best identify those who could benefit
- Quality of evidence is not robust, but there is a lot. Case series issues: eight of sixteen studies funded by industry, and even with that, evidence is not overwhelming that is extremely effective and there are safety concerns raised by what is a best case scenario, combined with safety issues raised by local data
- Risk is greater than benefit
- Evidence doesn't tell how to select patients, benefits are spotty where some patients get stellar results and others get none
- Medical treatment has risks as well – personal experience with these patients is addiction to drugs, overdose, depression common in these and so inconclusive about whether this intervention will have more safety issue
- Pain is a subjective sensation and sole focus of looking at pain relief, there is some evidence that it is useful; issue remains about global pain control
- Have most up to date evidence that exists, and safety data,
- All evidence equals methodologically flawed case series which is not sufficient to base decisions about care on and that do not have - there isn't trial data necessary to be confident
- Data on safety indicates that there are definite risks on safety, though unclear how often risks occur so can't be sure that this is a safe procedure
- Cost effectiveness not a large factor – appears to be fairly equal

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- Evidence is based on small case series of only a 143 patients related to pain relief, and is a small number; case series can be hypothesis raising; general rule that case series tends to overstate benefit and understate risks;
- Question about whether the device is a great device, but not used well (could be operator error); moved by patients that commented that had good results and mindful of patients no longer with us that couldn't make comments
- Need better information – this is a different way of administering drugs – case series may demonstrate that this may be a better way to administer drugs, but data does not show that

Based on the evidence provided and the information and comments presented, the committee moved to a vote on coverage.

HTCC COMMITTEE COVERAGE DETERMINATION			
	Not covered	Covered Unconditionally	Covered Under Certain Conditions
Implantable Infusion Pump	8	0	2

Committee Discussion related to Expert Treatment Guidelines and Medicare Decision

Decision is consistent with two of three expert guidelines, and not consistent with Medicare's decision to cover conditionally.

- Medicare coverage decision was in 1994, no overwhelming efficacy evidence developed since then, and the Maude (safety) data was not available at all
 - Approach of clinical decision making has changed substantially since 1994 and 2004 with focus need for strong clinical evidence is a new approach that these decisions did not account for
 - Majority of the committee did not feel that evidence presented shows that the technology is equivalent or more effective
 - Majority of committee did not feel evidence presented show the technology is safer;
 - Majority of committee did not feel evidence presented showed that the technology is cost-effective
 - Committee decision is based on all evidence, including the vendor, public, agency medical directors and report while it is unclear what information Medicare decision relied on.
- Outcome: The committee chair directed HTA staff to prepare a Findings and Decision document on Implantable Infusion Pumps reflective of the majority vote for final approval at the next public meeting.

Agenda Item: Knee Arthroscopy Topic Review

Dr. Dave Flum, HTA Clinical Consultant, introduced the Knee Arthroscopy topic overview.

Knee Arthroscopy

- ✓ Osteoarthritis (OA) is a non-inflammatory degenerative joint disease that is often characterized by pain and swelling that frequently requires medical and / or surgical intervention. Knee Osteoarthritis causes thinning and softening of the cartilage in the knee that absorbs shock and

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allows joint surfaces to glide over one another. Osteoarthritis affects more than 20 million people and is the most common joint disease in the United States. Medical treatment goal for Osteoarthritis is not curative; it is designed to alleviate symptoms, primarily pain and swelling.

- ✓ Lavage and debridement are arthroscopic surgical procedures intended to repair or restore cartilage in the knee.
 - Lavage aspirates intra-articular fluid and washes out the joint
 - Debridement involves removal of cartilage or meniscal fragments by variable methods including cartilage abrasion, excision of osteophytes and synovectomy.
 - Procedures often are performed together and intended as an attempt to delay total knee replacement.
- ✓ Benefits are thought to include the reduction of pain in patients with osteoarthritis. Although the harms are thought to be minimal, important clinical questions about the effectiveness of knee arthroscopy for osteoarthritis are present and nationally there is wide variation in its use for this and other conditions.
- ✓ National Medicare Coverage: The clinical effectiveness of arthroscopic lavage and arthroscopic debridement for the severe osteoarthritic knee has not been verified by scientifically controlled studies (2004). Following are not covered:
 - Arthroscopic lavage used alone for the osteoarthritic knee;
 - Arthroscopic debridement for osteoarthritic patients presenting with knee pain only; or,
 - Arthroscopic debridement and lavage with or without debridement for patients presenting with severe osteoarthritis.
- ✓ Specialty Organization Guidelines: Osteoarthritis Research Society International – OARSI (2008). *“the roles of joint lavage and arthroscopic debridement in knee OA are controversial. Although some studies demonstrated short term symptom relief, others suggest that improvement in symptoms could be attributable to a placebo affect.”*
- ✓ Safety concerns: Complications appear to be relatively low and non-fatal.
 - Compared with non-invasive medical management, surgical risks, infection, damage or injury based on improper portal placement; and
 - Failed surgery results into additional surgeries (occur more frequently).
- ✓ Effectiveness concerns: This is the primary issue of concern – whether the surgery (lavage or debridement) is effective at improving function or relieving pain.
 - Randomized trial showed no benefit for Osteoarthritis; yet, may be under reported due to coding issues;
 - Overall procedure utilization continues to rise and not accompanied by prior radiological findings of damage (e.g., Meniscus repair).
- ✓ Cost concerns: Knee Arthroscopy is in the top ten procedures, by cost, that are paid for by the Washington State agencies. For the Department of Social and Health Sciences, orthopedic surgeries are number four and include knee arthroscopy.
 - Surgical alternative are more expensive than medical management.



Agenda Item: Knee Arthroscopy Agency Data

Dr. Nancy Fisher, HCA Medical Director, presented to the committee the agency utilization and outcomes for Knee Arthroscopy.

- ✓ Coverage Policy: All Washington agencies cover knee arthroscopy for all diagnosis.
- ✓ Evidence Review Scope: The agencies are requesting a review for knee arthroscopy for the patients with osteoarthritis only.
- ✓ Participating Washington State agencies population for which diagnosis and management for knee related osteoarthritis is 18,305 clients / beneficiaries.
- ✓ Washington Agencies Population and OA Claims (SFY 2006):

State Agencies	Population	Patients with OA Claims
Uniform Medical Plan	173,000	8,245
Labor and Industries	150,000	212
Medicaid	450,000	11,337
Total	773,000 *	19,794

* Population figures fluctuate and agency direct purchasing totals are at least this level.

- ✓ Coverage Alternatives (coverage varies by agency) – includes:
 - Medications (Acetaminophen, NSAID, etc)
 - Rehabilitation
 - Physical Therapy
 - Psychological
 - Exercise & education
 - Interdisciplinary Rehabilitation
 - Alternative and complimentary medicine (massage, accumpuncture)
 - Surgical: Total knee replacement

- ✓ Agency Utilization for Osteoarthritis Services:

Agency	SFY 2005		SFY 2006	
	Patients	Cost	Patients	Cost
HCA	6,637	\$ 3,198,413	7,421	\$ 3,766,993
L&I	102	\$ 343,389	87	\$ 300,989
DSHS	10,258	\$ 2,461,920	10,797	\$ 2,591,280
Pharmacy (L&I/HCA)		\$ 18,201,852		\$ 19,139,000
Totals	16,997	\$24,205,574	18,305	\$25,798,262

- ✓ Knee Arthroscopy for Osteoarthritis of the Knee:

Year	Procedure	Diagnosis	Members	Paid
2005	Lavage	All	251	\$ 406,445
2005	Debridement	All	4,159	\$ 12,030,744
2005 Arthroscopy Total			4,410	\$ 12,437,189
2006	Lavage	All	252	\$ 446,440
2006	Debridement	All	4,472	\$ 13,727,466

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2006 Arthroscopy Total	4,724	\$ 14,173,906
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- ✓ State Agencies Summary View is consistent with systematic reviews, which indicate:
 - No evidence of benefit for treatment of Osteoarthritis;
 - Insufficient evidence to address significant issues:
 - Important and more objectively measured health outcomes; Additive treatment; Long term ramifications
 - Significant cost impact due to high utilization
 - Agencies can reduce utilization in sub-populations where evidence demonstrates no efficacy; Other utilization more targeted to population that will benefit
 - Patient selection doesn't currently require radiographic evidence to establish medical necessity.

Agenda Item: Technology Assessment Presentation

Dr. Dave Flum, HTA Clinical Consultant, presented for Oregon Health & Science University (OHSU) and the Delfini Group due to their absence a summary of the technology assessment report.

- ✓ Osteoarthritis is a common condition affecting approximately 27 million people. Osteoarthritis is commonly diagnosed in combination of symptoms, physical findings and radiographic findings.
- ✓ Medical management includes drug therapy, physical therapy or occupational therapy, heat and cold application, surgical intervention, and weight loss.
- ✓ Lavage and debridement are arthroscopic surgical procedures:
 - Lavage aspirates intra-articular fluid and washes out the joint;
 - Debridement involves removal of cartilage or meniscal fragments; may variably include cartilage abrasion, excision of osteophytes and synovectomy.
- ✓ Systematic Review Scope: 2007 AHRQ published systematic review of several treatments for Osteoarthritis of the knee, including Knee Arthroscopy.
 - Key Questions for patients with osteoarthritis:
 - What is the evidence that arthroscopic lavage reduces pain and improves function?
 - What is the evidence that arthroscopic debridement reduces pain and improves pain and improves function?
 - What is the evidence that either debridement or lavage reduces pain and improves function for any sub-population of patients with Osteoarthritis?
 - What is the evidence regarding adverse events from arthroscopic debridement and lavage?
 - HTA Program Key Question:

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- What is the evidence regarding cost or cost-effectiveness of arthroscopic lavage or debridement?
- ✓ Search Approach: Critical Appraisal of the systematic review published by AHRQ conducted by Blue Cross and Blue Shield Technology Evaluation Center (Samson, 2007).
 - Update: Literature search for additional systematic reviews and trials on safety and efficacy of arthroscopic debridement and lavage for knee osteoarthritis published after search date. Literature search for cost effectiveness analysis and review and summary of cost policies and treatment guidelines.
 - Search Results:
 - Efficacy: 31 articles retrieved for potential inclusion
 - Safety: 9 articles retrieved for potential inclusion
 - Cost analysis: 0 articles
 - Evidence Base included for Critical Appraisal:
 - AHRQ Publication (Samson 2007)
 - Cochrane Review (Laupattarakasem 2008)
 - Osteoarthritis Research Society International Recommendations (Zhang 2008)
- ✓ Efficacy: AHRQ Publication Findings – OHSU agrees with the authors of the AHRQ publication’s efficacy conclusions that the evidence is insufficient to conclude that arthroscopy and lavage or debridement for treatment of osteoarthritis of the knee results in pain reduction or improved function for patients. This includes any subgroups of patients.
 - *Review and Update Findings:* Neither arthroscopic lavage nor debridement have been found to be superior to sham arthroscopy in well-designed and conducted randomized controlled trials (RCTs).
 - Only one study (Moseley 2002) could be used as the foundation for our efficacy conclusion. The authors of this RCT evaluated the confidence intervals for the Knee-Specific-Pain Score (KSPS) at two years along with other measures of pain and function and determined that they did not include a clinically meaningful difference between either the debridement group and placebo or the lavage group and placebo group.
 - This study provides possibly useful evidence that neither arthroscopic lavage nor debridement is more effective than a placebo (sham) procedure for treatment of knee OA.
- ✓ Safety: AHRQ Publication Findings -- The AHRQ publication reported extensive safety data from observational studies (see below). As mentioned in the AHRQ publication, confidence in the accuracy of adverse events data is extremely low when it is derived from observational studies. Observational data; however, provide useful indicators that should raise end users’ awareness about safety concerns
 - *Review and Update Findings:* OHSU found only Grade U study (uncertain efficacy and usefulness) information on adverse effects from RCTs evaluating arthroscopy with lavage and debridement for knee OA primarily because the trials focused on efficacy and did not formally measure safety events. RCT and observational data of uncertain validity and usefulness (Grade U); however, provide some indications about safety that should raise



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- end users' awareness about potential harms. (Anesthesia risk information is not included in assessment below).
- ✓ Cost: AHRQ Publication Findings -- The AHRQ publication did not address the issue of cost or cost-effectiveness.
 - *Review and Update Findings:* OHSU found only Grade U study (uncertain efficacy and usefulness) information on cost and cost-effectiveness. As noted below, this is likely because effectiveness has not yet been demonstrated.
 - No useful economic modeling information was found in our MEDLINE searches.
 - An economic model was provided by The Medical Advisory Secretariat Ministry of Health and Long-Term Care, Toronto. The authors were unable to conduct a full economic analysis because effectiveness was not demonstrated in the literature. They state that based on the Moseley (2002) trial, cost effectiveness is likely to be unfavorable. However, they provide an outline of considerations (e.g., hospital costs, non-hospital costs, discounting, etc.) that may be useful in creating an economic model to inform cost estimates.
 - ✓ Patient Implications: When substantial benefits for patients have not been demonstrated through valid RCTs, it is imperative for patients and others to be appropriately informed of the uncertainty, potential harmful effects of an intervention along with the concomitant interventions that accompany it.
 - There is one case series, included in the AHRQ publication which reported 90% patient satisfaction with symptom and function with a mean follow-up of approximately 4 years.
 - OHSU found three case series reporting satisfaction. Overall, 63.2% (129 knees) were better, 21.1% (43 knees) were unchanged, and 15.7% (32 knees) were worse after surgery.
 - ✓ Systematic Review Conclusions: OHSU concurred with the implications stated in the AHRQ publication (Samson 2007) and the Cochrane review (Ramos 2007), namely that further high quality research is urgently needed in specific population groups. In addition, we would like to emphasize the following points:
 - To demonstrate that an intervention is likely to improve patients' health or quality of life requires valid evidence that meaningful patient benefits outweigh harms.
 - Low quality evidence or clinical experience is insufficient for demonstrating improved patient outcomes and may result in significant harms and costs.
 - There is an urgent need for additional double-blind RCTs of arthroscopic lavage and debridement in various patient groups with OA of the knee.

Agenda Item: Public Comments

- ✓ No public testimony for Knee Arthroscopy.

Agenda Item: HTCC Knee Arthroscopy Discussion and Vote

Brian Budenholzer, Committee Chair, led a discussion of the evidence related to the safety, efficacy, and cost effectiveness of Knee Arthroscopy.

Knee Arthroscopy:

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Effectiveness: Effectiveness was a key area of discussion for committee members. Factors that were important in the discussion included: does knee arthroscopy relieve pain and improve function for patients with osteoarthritis of the knee. The central study, a single placebo-controlled randomized clinical trial (RCT) was focused on:

- Regarding effectiveness – the key trial found no difference between in outcomes of patients treated with knee arthroscopy for osteoarthritis and placebo surgery. All other studies were not RCTs and were missing available were missing key factors such as, but not limited to: there was no outlined distinction between patients with primary or secondary osteoarthritis, the placebo effect was not investigated and no details of patient sampling were included.
- Regarding pain reduction – no statistically significant difference in knee pain between the placebo group and those who had surgery.
- Improved function – there was no evidence of improved function.

Safety: Key health outcomes important to the safety consideration for knee arthroscopy for osteoarthritis of the knee were discussed. The main safety concerns related to this being a surgical intervention that carries surgical risks, especially where efficacy is not demonstrated. Deep Vein Thrombosis risks were also discussed (.6 to 17%).

Cost: Knee arthroscopy for osteoarthritis of the knee is a high volume and high cost intervention and, as such, should be demonstrated to provide an acceptable benefit-risk ratio for patients through well-designed, conducted and evaluated RCTs. A review of the published literature showed cost studies that were uncertain in efficacy and usefulness. No full economic analysis is available; however, outlined costs for the surgery (e.g., hospital, physician services) may prove helpful in the future to do such an analysis. Committee members found that current evidence indicated that knee arthroscopy was not a cost-effective means of treating osteoarthritis of the knee in light of the lack of literature that it was effective and surgical intervention is costly.

Knee Arthroscopy for Osteoarthritis VOTES

Is there sufficient evidence under some or all situations that the technology is:

	Inconclusive (no)	Equivalent (yes)	Less (yes)	More (yes)
Effective	0	9	1	0
Safe	0	0	10	0
Cost-effective	0	0	10	0

HTCC Knee Arthroscopy Coverage Decision

The HTCC reviewed and considered the Knee Arthroscopy for Osteoarthritis of the Knee technology assessment report, information provided by the Administrator, and public and agency comments. A key overall benefit question committee members focused on: is knee arthroscopy (lavage and debridement) for osteoarthritis of the knee an effective measure for patient treatment. Factors considered related to the effectiveness of the surgery for pain treatment and improved function, as well as access to alternatives. Safety issues were related to the surgical intervention which, while less invasive than other surgeries, continues to carry surgical complication risks; and specific to

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arthroscopy, further damage to the joint and deep vein thrombosis. In many technologies reviewed, there has been a lack of evidence due to trial design to indicate whether a treatment may work. In this case a trial was well-designed and provided good evidence directly comparing the surgical treatment to a sham treatment, which resulted in equivalent outcomes and demonstrated no benefit. Information from this randomized controlled trial demonstrated that knee arthroscopy (lavage and debridement) for osteoarthritis of the knee had no more benefit than placebo (the sham surgery) and agencies do provide alternative methods of treatment (e.g., physical and occupational therapy). Further, surgical intervention carries significant risks over medical or less-invasive interventions. No useful economic analyses were found in the literature to help outline cost effectiveness. Based on the evidence presented on safety, efficacy and cost-effectiveness, committee voted as follows:

HTCC COMMITTEE COVERAGE DETERMINATION VOTE			
	Not covered	Covered Unconditionally	Covered Under Certain Conditions
Knee Arthroscopy	10	0	0

- *Outcome:* The committee chair directed HTA staff to prepare a Findings and Decision document on Knee Arthroscopy reflective of the majority vote for final approval at the next public meeting.

Medicare Decision and Expert Treatment Guidelines

- The decision is consistent with Medicare’s National Coverage Decision to not cover lavage for patients with knee pain only or debridement and lavage for patients with severe osteoarthritis.
- The coverage decision is consistent with the OARSI consensus statement that: the roles of joint lavage and arthroscopic debridement in knee OA are controversial. Although some studies demonstrated short term symptom relief, others suggest that improvement in symptoms could be attributable to a placebo affect.