Clinical Policy Title: Implantable infusion pumps

Clinical Policy Number: 00.02.14

Effective Date: July 1, 2016
Initial Review Date: May 18, 2016
Most Recent Review Date: May 18, 2016
Next Review Date: May 2017

Related policies:
CP# 06.02.01 Insulin infusion therapy (insulin pumps)
CP# 03.03.01 Spinal cord stimulators for chronic pain

ABOUT THIS POLICY: Keystone First has developed clinical policies to assist with making coverage determinations. Keystone First’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by Keystone First when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Keystone First’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Keystone First’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First will update its clinical policies as necessary. Keystone First’s clinical policies are not guarantees of payment.

Coverage policy

Keystone First considers the use of implantable infusion pumps (IIPs) to be medically necessary durable medical equipment when all of the following criteria and indications are met:

- The infused drug is medically necessary for the treatment of the member.
- The IIP is medically necessary to administer the drug.
- Food and Drug Administration (FDA)-approved labeling for the pump specifies that the drug being administered and the purpose for which it is administered is an indicated use for the pump.
- The IIP is administered by providers who can fully accommodate all aspects of IIP drug delivery, including evaluation, trialing, implantation, long-term management and troubleshooting.

Indications for use:

- For intrathecal (IT) administration of preservation-free morphine sulfate or ziconotide monotherapy for severe, chronic intractable pain of malignant or nonmalignant origin and:
  - The member is age 18 or older.
The member has an inadequate response to noninvasive methods of pain control, such as systemic opioids (including attempts to eliminate physical and behavioral abnormalities that may cause an exaggerated reaction to pain).

A preliminary trial has been undertaken with a temporary IT catheter to substantiate adequately acceptable pain relief and degree of side effects (including effects on the activities of daily living) and patient acceptance.

- For the IT administration of baclofen to treat severe, generalized spasticity and dystonia of cerebral and spinal origins in members who meet all of the following criteria:
  - Age 4 and older.
  - Severity classified as Gross Motor Function Classification System (GMFCS) level III, IV or V.
  - Inadequate response to, or intolerant of, noninvasive anti-spasmotic drugs (e.g., oral baclofen) over a minimum six-week trial period.
    - A trial of oral baclofen is not a required prerequisite to IT baclofen therapy in children age 12 years or younger due to the increased risk of adverse effects from oral baclofen in this group.
  - Favorable response to a trial IT baclofen prior to permanent pump implantation. An IIP for continuous infusion is not medically necessary for members who do not respond to a 100 mcg IT bolus of baclofen.

- For administration of intrathecal chemotherapy (e.g., floxuridine [FUDR]) for members with Duke’s Class D colorectal cancer in whom metastases are limited to the liver and where the disease is unresectable or the member refuses surgical excision of the tumor and liver metastases.

For Medicare members only:

In addition to the above listed indications, Keystone First Medicare considers the use of IIPs to be clinically proven and, therefore, medically necessary durable medical equipment for members who meet the following criteria and indications:

- For administration of intrathecal FUDR-based chemotherapy for the treatment of primary hepatocellular carcinoma.
- For IT administration of morphine or ziconotide monotherapy for severe chronic intractable pain of malignant or nonmalignant origin in patients who have a life expectancy of at least three months and who have proven unresponsive to less invasive medical therapy.

Limitations:

- All other uses of IIPs are not medically necessary.
- Contraindications include:
  - Inability or unwillingness to have the pump refilled, including inadequate social support.
  - Presence of other implanted programmable devices, since crosstalk between devices may inadvertently change the prescription.
  - Significant coagulopathies.
  - Hemodynamic instability.
  - Spinal anomalies.
  - Intracranial hypertension.
  - Active infection.
  - Insufficient body size preventing device implantation.
  - Significant psychiatric comorbidities.
  - Allergy to drug being infused.
• Documentation in the medical record must include medical necessity for both the drug and IT or hepatic-artery-based infusion, successful trialing and continued drug administration using the IPP.
• Replacement or upgrade of an IIP or programmer is **not** medically necessary unless **either:**
  o The existing device malfunctions and cannot be repaired.
  o Replacement is required due to a change in the individual’s condition that makes the present device non-functional.
• Replacement of the entire IPP system (i.e., the catheter and programmer) is not generally required at the time of pump replacement due to the end of battery life.

Note: The following CPT/HCPCS codes are not listed in the Pennsylvania Medicaid fee schedule:

E0782 - Infusion pump, implantable, non-programmable (includes all components)
E0783 - Infusion pump, implantable, programmable (includes all components)

**Alternative covered services:**

• Noninvasive, nonpharmacologic interventions (e.g., physical therapy, occupational therapy or counseling).
• Oral medications (e.g., nonsteroidal anti-inflammatory drugs, antidepressants, anticonvulsants, serotonergic drugs, baclofen, opioids, benzodiazepines, dantrolene sodium or imidazolines).
• Systemic chemotherapy.
• Botulinum toxin (BTA) injections.
• Stimulation techniques.
• Regional anesthetic interventions.
• Surgery.

**Background**

IIPs are subcutaneously inserted devices that deliver drugs through central venous, intra-arterial, intraspinal (epidural or IT) or intraperitoneal (IP) catheters. An IIP is intended to provide long-term continuous or intermittent drug infusion directly to specific sites and can be programmed for continuous or variable rates of infusion. The IIP is surgically placed in a subcutaneous pocket under the infraclavicular fossa or in the abdominal wall, and a catheter is threaded into the desired position. IIPs are easily reversible, thus providing an important degree of therapeutic control for patients and physicians.

FDA regulates IPPs as combination products, which comprise two or more regulated components (e.g., drugs, devices and/or biological products) through the premarket approval process (FDA, 2011a; FDA product code: LKK). FDA has approved several IIPs for use with specific drugs for targeted neuromodulation and cancer treatment. The indications are:

• Chronic intraspinal (epidural and IT) infusion of preservative-free morphine sulfate sterile solution in the treatment of chronic intractable pain.
• Chronic IT infusion of preservative-free ziconotide sterile solution for the management of severe chronic pain.
• Chronic IT infusion of Lioresal® IT (baclofen injection) for the management of severe spasticity.
• Chronic intravascular infusion of FUDR or methotrexate for the treatment of primary or metastatic cancer.
**Searches**

Keystone First searched PubMed and the databases of:
- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).

We conducted searches on April 4 – 5, 2016. Search terms were: "infusions, parenteral" [Mesh], "infusion pumps, implantable" [Mesh], “intrathecal clonidine,” “intrathecal ziconotide,” and “intrathecal baclofen.”

We included:
- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews**.
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

We identified seven systematic review and meta-analyses, seven evidence-based guidelines and no economic analyses for this policy. Evidence of improved effectiveness using long-term targeted drug infusion in accordance with FDA requirements provides a rationale for using an IIP in carefully selected patients. The systematic reviews and meta-analyses in this policy comprised the following indications: chronic malignant and nonmalignant pain using IT morphine or ziconotide (Brookes, 2016; Falco, 2013; Hayek, 2011); chronic moderate to severe spasticity and dystonia using baclofen injection (Malaysian Health Technology Assessment Section [MHTAS], 2014); hepatic malignancy using hepatic artery-based infusion (HAI) of FUDR-based chemotherapy (Boehm, 2015; Mocellin, 2009); and primary epithelial ovarian cancer using IP delivery of chemotherapy (Jaaback, 2011).

Evidence from randomized controlled trials (RCTs) exists for all indications except chronic nonmalignant pain using IT opioid infusion. Complications are related to the surgical procedure, device and catheter, granuloma formation, and medications, and most are easily correctable.

**Chronic pain:**

The evidence is sufficient to support the use of IT morphine or ziconotide monotherapy in controlling refractory cancer and non-cancer-related pain in adult patients who have failed multiple other treatment modalities. FDA has approved only preservative-free morphine and ziconotide as monotherapy for the IT treatment of chronic pain in adults; the safety and effectiveness of IT administration of these drugs in combination with others (e.g., bupivacaine, clonidine and fentanyl) or in pediatric populations has not been established (FDA, 2004; FDA, 2005). There are no universally accepted guidelines or recommendations for patient selection, but in general, patients suffering from significant side effects of oral, transdermal or intravenous opioids that inhibit adequate titration of these medications or patients who cannot achieve adequate analgesia at high doses of opioids should be considered for IT therapy. Other factors include
surgical candidacy, anatomical features, psychological stability, social support system, disease prognosis and appropriate drug trialing (Saulino, 2014; Deer, 2011).

**Spasticity and dystonia:**

Low- to moderate-quality evidence suggests continuous IT baclofen infusion is effective in reducing spasticity, reducing pain and improving function and quality of life in patients ages 4 and older with generalized severe spasticity or dystonia (or both) who are unresponsive to or cannot tolerate oral baclofen. Studies included ambulant and non-ambulant individuals, spasticity and dystonia of cerebral and spinal origins and GMFCS level III, IV or V. FDA requires a trial of baclofen prior to implantation (FDA, 2011b).

Evidence-based recommendations vary in their support for continuous IT baclofen for treatment of spasticity. The Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society found insufficient evidence to support or refute the use of continuous IT baclofen for the treatment of spasticity in children with cerebral palsy (Delgado, 2010). The National Institute for Health and Care Excellence (NICE) recommends considering IT baclofen for children and young people with spasticity or dystonia that causes difficulty with pain or muscle spasms, posture or function, or self-care or ease of care by parents or caregivers (NICE, 2012).

**Chemotherapy:**

Locoregional chemotherapy infusion may be amenable to IIPs provided this approach confers a favorable outcome. Evidence from RCTs shows hepatic artery-based infusion (HAI) with FUDR, 5-fluorouracil (5-FU) alone produced a higher tumor response rate (42.9 percent) than systemic administration (18.4 percent) but not necessarily a survival advantage in persons with unresectable liver metastases from colorectal cancer. Modern systemic chemotherapy regimens that combine FU with oxaliplatin or irinotecan can obtain similar or even higher tumor response rates than those observed with fluoropyrimidine-based HAI (Mocellin, 2009). Still, current clinical practice guidelines recommend HAI with or without systemic 5-FU as an option at institutions with experience in both the surgical and medical oncologic aspects of the procedure (National Comprehensive Cancer Network [NCCN], 2016a and 2016b). The value of locoregional treatment with HAI for patients with unresectable intrahepatic cholangiocarcinoma is unclear (Boehm, 2015; NCCN, 2016c).

While the evidence suggests IP chemotherapy increases overall survival and progression-free survival from advanced primary epithelial ovarian cancer compared to intravenous (IV) therapy, the optimal dose, timing and mechanism of administration is still undetermined (Jaaback; 2011). Typically, infusion pumps are not recommended for IP infusions due to the incidence of needle dislocation from the high pressure of pump (Oregon Health and Science University, 2016).

**Summary of clinical evidence:**

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brookes (2016)</td>
<td>Ziconotide monotherapy for chronic neuropathic pain</td>
</tr>
<tr>
<td></td>
<td>Key points:</td>
</tr>
<tr>
<td>Citation</td>
<td>Content, Methods, Recommendations</td>
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<tr>
<td>Boehm (2015)</td>
<td>Results suggest ziconotide is beneficial for pain reduction in chronic neuropathic pain.</td>
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</table>

**Key points:**
- Meta-analysis of 20 studies (n = 657 patients) of HAI, transcatheter arterial chemoembolization (TACE), drug-eluting bead TACE (DEB-TACE), and Yttrium (90) radioembolization (Y-90).
- Median overall survival (months, 95 percent CI): HAI (22.8, 9.8 to 35.8); Y90 (13.9, 9.5 to 18.3); TACE (12.4, 10.9 to 13.9); DEB-TACE (12.3, 11.0 to 13.5).
- Complete and partial response to therapy (rate, 95 percent CI): HAI (56.9 percent, 41.0 to 72.8); Y90 (27.4 percent, 17.4 to 37.5); TACE (17.3 percent, 6.8 to 27.8).
- Grade III/IV toxicity (events per patient, 95 percent CI): HAI (0.35, 0.22 to 0.48); TACE (0.26, 0.21 to 0.32); DEB-TACE (0.32, 0.17 to 0.48).
- For patients with unresectable ICC treated with HAT, HAI offered the best outcomes in tumor response and survival, but may be limited by toxicity.

<table>
<thead>
<tr>
<th>Malaysian Health Technology Assessment Section (2014)</th>
<th>Key points:</th>
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</thead>
<tbody>
<tr>
<td>Continuous IT baclofen for severe spasticity and dystonia</td>
<td>Systematic review of six RCTs, two prospective follow-up studies of RCTs, 51 pre- and post-intervention studies, 13 observational studies (case-control, cohort and cross-sectional), and four cost-effectiveness analysis/cost-utility analysis.</td>
</tr>
</tbody>
</table>
- Overall quality: moderate.
- Continuous IT baclofen infusion was effective in reducing spasticity, reducing pain, improving function and quality of life in patients with severe spasticity or dystonia or both who were unresponsive or cannot tolerate oral baclofen.
- Device-related adverse events related to surgery (pocket seroma, pocket infection, cerebrospinal fluid CSF leak, surgical wound infection and programming errors) or catheter and pump (catheter breaking, kinking, dislodging, occluding, rupturing and migrating, site pain, and pump malfunction).

<table>
<thead>
<tr>
<th>Falco (2013)</th>
<th>Key points:</th>
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<tbody>
<tr>
<td>Long-term management of chronic non-cancer pain using IT opioids</td>
<td>Systematic review of seven non-randomized studies (n = 767).</td>
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</table>
- Quality assessment: low to moderate.

<table>
<thead>
<tr>
<th>Hayek (2011)</th>
<th>Key points:</th>
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<tbody>
<tr>
<td>IT infusions used in long-term management (&gt; six months) of chronic pain</td>
<td>Systematic review of 20 studies: 15 observational studies for non-cancer pain and five studies (four observational, one RCT) for cancer pain. Eleven studies assessed IT morphine alone or in combination with other analgesics; four studies assessed other analgesics, including ziconotide.</td>
</tr>
</tbody>
</table>
- Overall quality: moderate (high for the one RCT).
- IT therapy is moderately effective and safe in controlling refractory painful conditions that have failed multiple other treatment modalities, both in cancer and non-cancer related conditions.
- Complications: granuloma formation, catheter kinking, fracture/leakage and migration, CSF leak, seroma, hygroma, infection, pump erosion through the skin, and medication side effects.
<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jaaback (2011)</td>
<td><strong>Key points:</strong></td>
</tr>
<tr>
<td>Cochrane review</td>
<td> Systematic review and meta-analysis of nine RCTs (n = 2,119 women) comparing IP versus intravenous (IV) administration.</td>
</tr>
<tr>
<td>IP chemotherapy</td>
<td> Overall quality: high (for six RCTs).</td>
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<tr>
<td>for the initial</td>
<td> Overall survival (hazard ratio [HR], 95 percent CI): 0.81, 0.72 to 0.90 (eight RCTs, 2,026 women); disease-free interval (HR, 95 percent CI): 0.78, 0.70 to 0.86 (five RCTs, 1,311 women).</td>
</tr>
<tr>
<td>management of primary epithelial ovarian cancer</td>
<td> IP route was associated with greater serious toxicity (gastrointestinal effects, pain, fever and infection) but less ototoxicity than IV route.</td>
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<td></td>
<td> Clinical trials needed to address optimal dose, timing and mechanism of administration.</td>
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| Mocellin (2009)   | **Key points:**                    |
| Cochrane review   |  Systematic review and meta-analysis of 10 RCTs (n = 1,277 patients). |
| FUDR-based HAI    |  Overall quality: moderate to high. |
| versus systemic chemotherapy (SCT) for unresectable liver metastases from colorectal cancer (CRC) |  Tumor response rate: 42.9 percent and 18.4 percent for HAI and SCT, respectively (RR = 2.26; 95 percent CI, 1.80 to 2.84; P < 0.0001). |
|                   |  Mean weighted median overall survival (OS) times: 15.9 and 12.4 months for HAI and SCT, respectively: meta-risk of death was not statistically different between groups (HR = 0.90; 95 percent CI, 0.76 to 1.07; P = 0.24). |
|                   |  Evidence does not support the clinical or investigational use of FUDR-based HAI alone for the treatment of patients with unresectable CRC liver metastases: superior tumor response rate of HAI regimen does not translate into a survival advantage over SCT. |

**Glossary**

**Baclofen** — A muscle relaxer and an antispastic agent to treat muscle spasms.

**Dystonia** — A neurological movement disorder in which muscles contract involuntarily, causing an uncontrollable twisting of the affected body part.

**Spasticity** — A motor disorder usually caused by damage to the central nervous system that controls voluntary movement. Characterized by hypertonicity, hyperactive muscle stretch reflexes and abnormal spinal reflexes and, in some cases, clonus and muscle spasms (American Association of Neurological Surgeons, 2016).

**Ziconotide** — A neuronal-type calcium-channel blocker that must be administered IT via continuous infusion using a programmable implanted variable-rate microinfusion device or an external microinfusion device and catheter.

**References**

**Professional society guidelines/other:**


**Peer-reviewed references:**


Mocellin S, Pasquali S, Nitti D. Fluoropyrimidine-HAI (hepatic arterial infusion) versus systemic chemotherapy (SCT) for unresectable liver metastases from colorectal cancer. Cochrane Database Syst Rev. 2009; (3): Cd007823.


Clinical trials:

Searched clinicaltrials.gov on April 7, 2016, using terms implant AND infusion | Open Studies. 23 studies found, three relevant.


CMS National Coverage Determinations (NCDs):

Local Coverage Determinations (LCDs):


**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

<table>
<thead>
<tr>
<th>CPT Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>36260</td>
<td>Insertion of implantable intra-arterial infusion pump (eg, for chemotherapy of liver)</td>
</tr>
<tr>
<td>36261</td>
<td>Revision of implanted intra-arterial infusion pump</td>
</tr>
<tr>
<td>36563</td>
<td>Insertion of tunneled centrally inserted central venous access device with subcutaneous pump</td>
</tr>
<tr>
<td>36583</td>
<td>Replacement, complete, of a tunneled centrally inserted central venous access device, with subcutaneous pump, through same venous access</td>
</tr>
<tr>
<td>61215</td>
<td>Insertion of subcutaneous reservoir, pump or continuous infusion system for connection to ventricular catheter</td>
</tr>
<tr>
<td>62350</td>
<td>Implantation, revision or repositioning of tunneled intrathecal or epidural catheter, for long-term medication administration via an external pump or implantable</td>
</tr>
<tr>
<td>62351</td>
<td>Implantation, revision or repositioning of tunneled intrathecal or epidural catheter, for long-term medication administration via an external pump or implantable</td>
</tr>
<tr>
<td>62360</td>
<td>Implantation or replacement of device for intrathecal or epidural drug infusion; subcutaneous reservoir</td>
</tr>
<tr>
<td>62361</td>
<td>Implantation or replacement of device for intrathecal or epidural drug infusion; nonprogrammable pump</td>
</tr>
<tr>
<td>62362</td>
<td>Implantation or replacement of device for intrathecal or epidural drug infusion; programmable pump, including preparation of pump, with or without programming</td>
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<thead>
<tr>
<th>ICD-10 Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td></td>
<td>Broad range of ICD-10 codes.</td>
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<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>C1772</td>
<td>Infusion pump, programmable (implantable)</td>
</tr>
<tr>
<td>C1892</td>
<td>Infusion pump, nonprogrammable, permanent (implantable)</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
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<tr>
<td>C2626</td>
<td>Infusion pump, nonprogrammable, temporary (implantable)</td>
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<tr>
<td>E0782</td>
<td>Infusion pump, implantable, nonprogrammable (includes all components, e.g., pump, catheter, connectors, etc.)</td>
</tr>
<tr>
<td>E0783</td>
<td>Infusion pump system, implantable, programmable (includes all components, e.g., pump, catheter, connectors, etc.)</td>
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