Implantable Infusion Pump for Non-Musculoskeletal Conditions

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Overview
This Coverage Policy addresses implantable infusion pumps for non-musculoskeletal conditions.

Coverage Policy
A permanent implantable infusion pump and supplies are considered medically necessary when used to administer intrahepatic arterial infusion of chemotherapeutic drugs when the cancer is unresectable or the individual is not a surgical candidate for EITHER of the following indications:

- primary hepatocellular cancer
- metastatic cancer that is limited to the liver

The use of an implantable infusion pump for ANY other indication is considered experimental, investigational or unproven.
General Background

Infusion pumps are used to provide a method of drug delivery for a variety of medical conditions. Implantable infusion pumps are used to deliver therapeutic levels of drugs to a target organ or body compartment (site-specific) for a prolonged period of time (several weeks to years). The infusion pump may be either nonprogrammable fixed rate (i.e., delivers a predetermined constant rate of infusion) and generate flow by fluorocarbon propellant, or programmable (i.e., variable delivery rates) and generate flow by direct electromechanical action. Fixed rate infusion pumps allow the physician to change dose by changing the concentration of the drug in the reservoir; programmable infusion pumps allow the physician to alter the dose, give single doses, timed-specific doses, or change the continuous infusion rate by an external programmer. The pump is surgically implanted into a subcutaneous pocket and connects to a catheter that has been placed in the desired position. Implantable infusion pumps are able to provide a constant or a variable rate of infusion. Minimal intervention is required for refilling or reprogramming the pump. The drug reservoir can be refilled as needed through an external needle injection in the pump. Bacteriostatic water, saline and heparin are used during interruption of drug therapy to maintain catheter patency.

The objectives for using an implantable infusion pump are to allow long-term access to various compartments enabling site-specific drug delivery, to reduce infections associated with external devices, and to provide drug therapy that promotes patient mobility and independence. In addition to the infusion pump itself, components that may be a part of the device include: a reservoir, optional access port, connectors, catheters, filters, handheld programmer and other accessories.

Implantable infusion pumps may be considered medically necessary when the drug is medically necessary for the treatment of the patient’s condition; when it is medically necessary that the drug be administered by an implanted infusion pump; the drug is approved by the U.S. Food and Drug Administration (FDA) for the intended use; and when the infusion pump has been approved by the FDA to administer the drug prescribed. In addition, the prescribed drug must be stable and compatible with the implantable infusion device. Drugs that have been approved by the FDA for use with implantable infusion pumps include chemotherapeutic agents (e.g., floxuridine [FUDR], methotrexate) for intrahepatic arterial infusion.

U.S. Food and Drug Administration (FDA)

Devices such as programmable, implantable infusion pumps are regulated by the FDA as Class III devices. Class III is the most stringent regulatory category for devices. Implantable infusion pumps that have been granted FDA approval include, but are not limited to, SynchroMed II Programmable Infusion Pump (Medtronic, Neurological, Minneapolis, MN), Codman® Model 3000 Implantable Pump (Codman and Shurtleff, Inc. [a Johnson and Johnson company], Raynman, MA). In December 2017, the FDA approved an Implantable System for Remodulin® (ISR) for adult patients with Class I, II and III pulmonary arterial hypertension (PAH) receiving intravenous delivery of treprostinil (Remodulin) (P140032).

Hepatic Artery Chemotherapy

The hepatic artery is the main pathway in which a liver tumor receives its blood supply. Normal hepatocytes derive most of their blood supply from the portal vein and little from the hepatic artery. Hepatic arterial infusion by way of an implanted infusion pump provides delivery of chemotherapeutic agents directly to the liver through a catheter placed into the hepatic artery. This method of administration improves efficacy by increasing drug delivery directly to the site of the tumor. In addition, the primary function of the liver is metabolism and excretion. The ability of the liver to metabolize the infused agents increases the opportunity to increase dosages while limiting systemic effects (Fraker, Soulen, 2002). It has been suggested that intra-arterial infusion may increase survival time, delay tumor progression, and reduce side effects, thereby improving quality of life.

There is no single chemotherapy drug or combination that clearly demonstrates improved survival or improved quality of life administered through the hepatic artery. Combination chemotherapy generally produces better response rates than single drug therapies. The standard systemic therapy for metastatic colorectal cancer consists of various combinations of 5-flourouracil (5-Fu) based regimens (e.g., Saltz regimen, De Gramont regimen). Floxuridine (FUDR) is a 5-Fu analog and is commonly used for intrahepatic arterial infusion. It is often used in combination with other chemotherapeutic agents (e.g., cisplatin, doxorubicin). Pharmacologic studies
demonstrate that 97–99% of FUDR is cleared or metabolized during the first pass of infusion to the liver, while the clearance of 5-FU is lower.

Intrahepatic chemotherapy has been found to improve time to hepatic progression for unresectable disease in select individuals with primary hepatocellular cancer or metastatic cancer that is limited to the liver and unresectable. Some trials have demonstrated improved survival with this treatment. Current clinical practice guidelines recommend hepatic arterial infusion be considered selectively, as an option at institutions with extensive experience in both the surgical and medical oncologic aspects of the procedure. The National Comprehensive Cancer Network (NCCN) states that placement of a hepatic arterial port or implantable pump during surgical intervention for liver resection with subsequent infusion of chemotherapy directed to the liver metastases through the hepatic artery is an option (2B category) (National Comprehensive Cancer Network [NCCN], 2019a and 2019b).

Chan et al. (2015) conducted a meta-analysis including 11 retrospective and prospective studies (n=1514) to evaluate the potential role of hepatic arterial infusion chemotherapy (HAIC) as a neoadjuvant downstaging therapy, prior to hepatic resection with curative intent for initially unresectable colorectal liver metastases (CRLM). Chan et al. determined that for patients presenting with unresectable CRLM, HAIC in conjunction with current systemic chemotherapy may allow some patients to undergo resection and potentially provide long-term survival.

A Cochrane review concluded intrahepatic arterial chemotherapy using fluropyrimidines yielded higher tumor response rates compared to systemic therapy, although it did not translate into a significant survival advantage (Mocellin, et al., 2009). Additionally, there is some evidence in the form of randomized trials and meta-analyses which lend support to higher response rates (e.g., tumor response, tolerability of treatment, adverse effects) for hepatic artery infusion when compared to intravenous infusion (Harmantas, et al., 1996; Meta-Analysis Group in Cancer, 1996; Allen-Mersh, et al., 1994; Kemeny, et al., 1999). Treatment of unresectable colorectal liver metastasis with systemic chemotherapy results in response rates of 25–30% and with the use of more recent regimens is has been reported at 36–40%. Hepatic arterial infusion of chemotherapy in patients who were previously untreated yields response rates of approximately 50–70% (Kemeny, et al., 2002). Survival advantage has not been consistently reported in the medical literature and remains unclear.

Authors have evaluated the administration of adjuvant chemotherapy to patients after hepatic resection (Martin, et al., 2004; Onaitis, et al., 2003; Kemeny, et al., 2002). Reported outcomes are inconsistent, and the administration of hepatic artery chemotherapy as an adjuvant therapy to resection or ablation for colorectal metastasis is considered controversial. Most authors fail to report improved survival outcomes and have demonstrated significant toxicity (biliary sclerosis). A Cochrane review (Nelson, Freels, 2006) assessing the effect of posthepatic resection hepatic artery chemotherapy concluded that, although recurrence happened less in the remaining liver, overall survival was not improved and favored the control group. Currently, adjuvant posthepatic intra-arterial chemotherapy for colorectal metastasis is not considered a standard and recommended treatment (Elias, et al., 2004; Lorenz, Muller, 2000).

Diabetes
An implantable insulin pump is an emerging technology proposed as a method of delivering insulin either intraperitoneally or intravenously in a programmed and controlled manner to type I diabetic patients. These devices deliver insulin directly into the peritoneal cavity or superior vena cava and can be programmed for a continuous rate as well as a bolus of insulin. Proposed patient selection criteria generally include those with brittle type I diabetes; however, there is insufficient evidence to establish clear patient selection criteria. The goals of implantable insulin pump therapy are to achieve near normal blood glucose levels, control metabolic complications and to delay the onset of late-stage complications such as vascular disorders. Although there are no implantable insulin infusion pumps that are approved by the FDA, there are some devices have been granted Investigational Device status. There is a FDA-approved (September 2016) hybrid closed loop system that monitors glucose and automatically adjusts the delivery of long acting or basal insulin based on the user’s glucose reading. It is important to note that the pump is not implanted, only the glucose sensor (Medtronic MiniMed, Inc. 670G System).
The quantity of published medical literature evaluating implantable insulin pumps is limited. In some studies authors have reported improved glycemic control, fewer hypoglycemic events, and less glycemic variability.

Gin and associates (2003) reported on the safety and efficacy of implantable insulin pumps in type 1 diabetic patients. The author’s review of the available literature indicates the pump has been associated with a high incidence of malfunctioning (i.e., catheter obstruction); however, newer pump designs are expected to reduce the problem of obstruction. In a retrospective case series involving 63 patients Haveman et al. (2008) evaluated the surgical implications and complications of the implantable insulin pump device. Local infection and pain were the most common complications reported (19%), and in some cases required pump removal and reimplantation. The authors noted that with increased experience and technical improvements in the pump, operation-free periods for the subject group increased from 1.8 years to 6.5 years. In a randomized trial Logtenberg et al (2009) compared continuous intraperitoneal insulin infusion in type I diabetic subjects (n=12) with intensified insulin therapy in patients with inadequately controlled type I diabetes (n=12). There were no differences in the occurrence rate for severe hypoglycemic events or daily insulin use and no pump or catheter malfunction was observed during the study. The authors did note improved glycemic control with continuous infusion demonstrated by a 0.8% decrease in A1C and an 11% increase in the time spent in euglycemia compared with subcutaneous insulin administration.

A clinical trial (ClinicalTrials.gov Identifier: NCT00298740) evaluating the Medtronic MiniMed Implantable Insulin Pump has been completed as of August / September 2017. Results are not yet published.

**Osteomyelitis**

Osteomyelitis is an infection involving part or all of the bone. Most often, the bones that are affected are the legs, arms, spine, and pelvis. Treatment consists of antibiotic therapy and, in some cases, surgical debridement to remove areas that are slow healing or to drain abscesses. Prolonged intravenous therapy may be required in chronic cases. Outpatient parenteral antibiotic therapy has been proven to be effective for select patients. Implantable infusion pumps have been used to administer antibiotics (e.g., clindamycin) for the treatment of osteomyelitis in some cases. However, evidence in the published scientific literature is insufficient and does not support safety and efficacy regarding the use of implantable infusion pumps for the long-term administration of antibiotics. The evidence that is available dates back to the late 1980’s and early 1990’s and consists primarily of uncontrolled case series involving small patient populations.

**Thromboembolic Disease**

Implantable infusion pumps have been proposed for the administration of heparin for the treatment of recurrent thromboembolic disease, although few clinical trials have been conducted evaluating the effects of long-term intravenous heparin infusion (Buchwald, et al., 1980; Blackshear, et al., 1981). A review of the published scientific literature does not provide sufficient evidence to support safety and efficacy when used for these conditions.

**Pulmonary Hypertension (PH) Therapy**

Pulmonary arterial hypertension (PAH) is a progressive and fatal disease, characterized by increasing pulmonary vascular resistance (PVR), which may eventually lead to right ventricular failure and premature death. The primary mechanism of action of treprostinil is reduction in pulmonary artery pressure through direct vasodilation of the pulmonary and systemic arterial vascular beds, thereby improving systemic oxygen transport and increasing cardiac output with minimal alteration of the heart rate. Treprostinil is marketed under the trade names Remodulin for infusion, Orenitram for oral, and Tyvaso for inhalation. Currently, the standard method of parenteral treprostinil delivery involves an external delivery device.

The Implantable System for Remodulin® is indicated for adult patients with Class I, II and III pulmonary arterial hypertension (PAH) receiving intravenous delivery of Remodulin. The approval was based on results from the Delllvery for Pulmonary Arterial Hypertension (PAH) clinical study (NCT01321073), a prospective, single-arm, nonrandomized, open-label multicenter study (Waxman, et al., 2017). Waxman et al. (2017) reported of the 64 patients enrolled, four exited prior to implantation. All 60 implant procedures were successful. At baseline, all patients were receiving treprostinil via an external pump at a mean dose of 71.4 ± 27.8 ng/kg/min (range: 22-142 ng/kg/min). The implant averaged 102 ± 32 min (range: 47-184 min). Clinically significant implant procedure-related complications included one pneumothorax, two infections, and one episode of atrial fibrillation. There
were three postimplantation catheter dislocations in two patients. Common implant-related events that were not complications included implant site pain (83%) and bruising (17%). The authors concluded that PAH therapy, anticoagulation, and other comorbidities were safely managed during the surgical procedure and postoperatively. The implant procedure was successfully performed with a low complication rate by clinicians with a diverse range of specialty training. However, additional well-designed trials are needed comparing the long term health outcomes with the use of implantable pump infusion versus continuous IV or subcutaneous delivery.

A Hayes, Inc. Health Technology Brief on Continuous Subcutaneous Treprostinil for Treatment of Pulmonary Arterial Hypertension provides a C rating for use of continuous subcutaneous (SC) infusion of treprostinil (Remodulin) for World Health Organization Group 1 pulmonary arterial hypertension (PAH) in adults. Hayes does not specifically address an implantable pump (Published 2017; Annual review Feb 6, 2019).

The 2019 American College of Chest Physicians updated guideline on Therapy for Pulmonary Arterial Hypertension in Adults does not address the use of implantable pumps (Klinger, et al., 2019).

The American Board of Internal Medicine’s (ABIM) Foundation Choosing Wisely® Initiative
No implantable pump related statements.

Centers for Medicare & Medicaid Services (CMS)
• National Coverage Determinations (NCDs): None.
• Local Coverage Determinations (LCDs): None

Use Outside of the US
The availability and indications for use of implantable infusion pumps varies in countries outside the U.S. While there are no FDA-approved fully implantable insulin pumps available in the U.S, one is available for use in Europe.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

<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>96522</td>
<td>Refilling and maintenance of implantable pump or reservoir for drug delivery, systemic (eg, intravenous, intra-arterial)</td>
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<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>A4220</td>
<td>Refill kit for implantable infusion pump</td>
</tr>
<tr>
<td>C1772</td>
<td>Infusion pump, programmable (implantable)</td>
</tr>
<tr>
<td>C1891</td>
<td>Infusion pump, non-programmable, permanent (implantable)</td>
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<tr>
<td>E0782</td>
<td>Infusion pump, implantable, non-programmable (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>
</tr>
<tr>
<td>E0786</td>
<td>Implantable programmable infusion pump, replacement (excludes implantable intraspinal catheter)</td>
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References


