Cigna Medical Coverage Policy

Subject: Implantable Infusion Pump for Non-Musculoskeletal Conditions

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Table of Contents
Coverage Policy .................................................. 1
General Background ........................................... 1
Coding/Billing Information ................................... 4
References .......................................................... 5

Related Coverage Resources
Botulinum Therapy
Deep Brain and Motor Cortex Stimulation
Minimally Invasive Intradiscal/Annular Procedures and Trigger Point Injections
Transarterial Chemoembolization

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Coverage Policy
Cigna covers a permanent implantable infusion pump and supplies 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

Cigna does not cover the use of an implantable infusion pump for ANY other indication, including the following, because it is considered experimental, investigational or unproven (this list may not be all-inclusive):

- cancer conditions that do not meet the above criteria
- administration of insulin for diabetes
- administration of antibiotics for osteomyelitis
- administration of heparin for thromboembolic disease

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., floxouridine [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) and Codman® Model 3000 Implantable Pump (Codman and Shurtleff, Inc. [a Johnson and Johnson company], Raynman, MA).

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.

Literature Review: 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 (National Comprehensive Cancer Network [NCCN], 2016a and 2016b). A Cochrane review concluded intrahepatic arterial chemotherapy using fluoropyrimidines 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., 1987). 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, 2004) 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. 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. Currently, there are no implantable insulin infusion pumps that are approved by the FDA however some devices have been granted Investigational Device status. In addition, there is insufficient evidence to establish clear patient selection criteria.

Literature Review: 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.

Hayes published a Medical Technology Directory report (2011, reviewed 2015) and concluded the evidence reviewed, which consisted of uncontrolled prospective studies, crossover design studies, three randomized controlled trials and data from the French registry, “Evaluation dans le Diabète du Traitement par Implants Actifs (EVADIAC)”, supports use of implantable insulin pump therapy for selected adult patients with type 1 or insulin-dependent type 2 Diabetes Mellitus, who have not achieved adequate glycemic control despite intensive insulin therapy with multiple daily injections or an external insulin pump, and who are fully compliant with diabetes self-care.
Professional Societies/Organizations: The American Diabetes Association (ADA) 2016 Clinical Practice Recommendations do not include the use of an implantable insulin infusion pump for the treatment of diabetes.

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.

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.

Summary
There is sufficient evidence of improved clinical outcomes to support the use of implantable infusion pumps for the administration of intra-arterial chemotherapy for the treatment of unresectable liver cancer. The use of an implantable infusion device for the treatment of diabetes is currently available only through clinical trials. The published, scientific literature does not provide sufficient evidence to support the use of these devices for the treatment of thromboembolic disease or osteomyelitis.

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.

Covered when medically necessary:

<table>
<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
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<tr>
<td>36260</td>
<td>Insertion of implantable intra-arterial infusion pump (eg, for chemotherapy of liver)</td>
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<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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<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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</thead>
<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>
</tr>
<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>
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Implantable programmable infusion pump, replacement (excludes implantable intraspinal catheter)


References


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