Introduction

An artificial pancreas device system combines a glucose monitor and an insulin infusion pump. The goal is to try to match how a normal pancreas would work. The pancreas releases insulin based on changing levels of glucose in the blood. In this system, insulin is either withheld or released based on the blood glucose level shown on the monitor. For those with type 1 diabetes, these systems may help improve overall glycemic control. They can be especially helpful in controlling episodes of very low blood sugar at night. This policy discusses when an artificial pancreas device system may be considered medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

<table>
<thead>
<tr>
<th>Device</th>
<th>Medical Necessity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artificial pancreas device system</td>
<td>Using an artificial pancreas device system with a low-glucose suspend feature that has been approved by the U.S. Food and</td>
</tr>
</tbody>
</table>
Drug Administration (FDA) may be considered medically necessary in patients who meet all of the following criteria:

- Have a diagnosis of type 1 diabetes
- Age 16 years of age or older
- Glycated hemoglobin (hemoglobin A1c) value between 5.8% and 10.0%
- Used insulin pump therapy for more than 6 months
- At least two documented nocturnal hypoglycemic events in a two-week period (see definition below)

Use of an artificial pancreas device system is considered investigational when criteria above are not met.

<table>
<thead>
<tr>
<th>Device</th>
<th>Investigational</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hybrid closed loop insulin delivery system</td>
<td>Use of a hybrid closed loop insulin delivery system (age 14 and older) as an artificial pancreas device system is considered investigational.</td>
</tr>
</tbody>
</table>

**Coding**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCPCS</td>
<td></td>
</tr>
<tr>
<td>S1034</td>
<td>Artificial pancreas device system (eg, low glucose suspend [LGS] feature) including continuous glucose monitor, blood glucose device, insulin pump and computer algorithm that communicates with all of the devices</td>
</tr>
<tr>
<td>S1035</td>
<td>Sensor; invasive (eg, subcutaneous), disposable, for use with artificial pancreas device system, 1 unit = 1 day supply</td>
</tr>
<tr>
<td>S1036</td>
<td>Transmitter; external, for use with artificial pancreas device system</td>
</tr>
<tr>
<td>S1037</td>
<td>Receiver (monitor); external, for use with artificial pancreas device system</td>
</tr>
</tbody>
</table>
Related Information

Consideration of Age

The age stated in this policy for which the artificial pancreas system may be considered medically necessary is 16 and older which is based on the FDA approved indications for the device.

Evidence Review

Description

Artificial pancreas device systems link a glucose monitor to an insulin infusion pump. The device automatically adjusts the amount of insulin released (eg, suspends or increases) based on the glucose monitor reading. These devices are used to improve glycemic control in patients with insulin-dependent diabetes, in particular, control of nocturnal hypoglycemia.

Background

*Diabetes and Glycemic Control*

Tight glucose control in patients with diabetes has been associated with improved outcomes. The American Diabetes Association has recommended a glycated hemoglobin level below 7% for most patients. However, hypoglycemia, defined as plasma glucose below 70 mg/dL, can affect the ability to achieve tighter glycemic control. Hypoglycemic events in adults range from mild to severe based on a number of factors including the glucose nadir, presence of symptoms, and whether the episode can be self-treated or requires help for recovery.
**Hypoglycemia**

Hypoglycemia affects many aspects of cognitive function, including attention, memory, and psychomotor and spatial ability. Severe hypoglycemia can cause serious morbidity affecting the central nervous system (eg, coma, seizure, transient ischemic attack, stroke), heart (eg, cardiac arrhythmia, myocardial ischemia, infarction), eye (eg, vitreous hemorrhage, worsening of retinopathy), as well as cause hypothermia and accidents that may lead to injury. Fear of having hypoglycemia symptoms can also cause decreased motivation to adhere strictly to intensive insulin treatment regimens.

The definition of a hypoglycemic episode is not standardized. In the pivotal Automation to Simulate Pancreatic Insulin Response randomized controlled trial, a nocturnal hypoglycemic episode was defined as a sensor glucose value of 65 mg/dL or less between 10 PM and 8 AM for more than 20 consecutive minutes in the absence of a pump interaction within 20 minutes. In 2017, the American Diabetes Association defined serious, clinically significant hypoglycemia as glucose levels <54 mg/dL, and a glucose alert value as a glucose ≤70 mg/dL. These definitions were based on recommendations from the International Hypoglycaemia Study Group.¹

**Treatment**

According to the U.S. Food and Drug Administration (FDA), an artificial pancreas is a medical device that links a glucose monitor to an insulin infusion pump. By using a control algorithm, the pump automatically reduces or increases subcutaneous insulin delivery according to measured subcutaneous glucose levels. Because control algorithms can vary significantly, there are a variety of artificial pancreas device systems currently under development. These systems span a wide range of designs from a low glucose suspend (LGS) device system to the more complex bi-hormonal control-to-target system. FDA has described 3 main categories of artificial pancreas device systems: threshold suspend device systems, control-to-range systems, and control-to-target systems.²

**Threshold Suspend Device System**

With threshold suspend device systems, also called low glucose suspend (LGS) systems, the delivery of insulin is suspended for a set time when 2 glucose levels are below a specified low level, thus indicating hypoglycemia.
**Control-to-Range System**

With these systems, the patient sets his or her own insulin dosing within a specified range, but the artificial pancreas device system takes over if glucose levels go outside that range (higher or lower). Patients using this type of system still need to check blood glucose levels and administer insulin as needed.

**Control-to-Target System**

With this type of device, the system aims to maintain glucose levels near a target level, such as 100 mg/dL. Control-to-target systems are automated and do not require user participation except to calibrate the continuous glucose monitoring system. Several device subtypes are being developed; those that deliver insulin only, bi-hormonal systems and hybrid systems.

**Summary of Evidence**

**Low-Glucose Suspend Device**

For individuals who have type 1 diabetes who receive an artificial pancreas device system with a low-glucose suspend feature, the evidence includes 2 randomized controlled trials (RCTs) conducted in home settings. Relevant outcomes are symptoms, change in disease status, morbid events, resource utilization and treatment-related morbidity. Primary eligibility criteria of the key RCT, the Automation to Simulate Pancreatic Insulin Response (ASPIRE) trial, were ages 16- to 70 years old, type 1 diabetes, glycated hemoglobin levels between 5.8% and 10.0%, and at least 2 nocturnal hypoglycemic events (≤65 mg/dL) lasting more than 20 minutes during a 2-week run-in phase. Both trials required at least 6 months of insulin pump use. Both RCTs reported significantly less hypoglycemia in the treatment group than in the control group. In both trials, primary outcomes were favorable for the group using an artificial pancreas system; however, 1 trial was limited by its nonstandard reporting of hypoglycemic episodes, and the other trial was no longer statistically significant when 2 outliers were excluded from analysis. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.
**Hybrid Closed-Loop Insulin Delivery System**

For individuals who have type 1 diabetes who receive a hybrid closed-loop insulin delivery system, the evidence includes a single-arm study and a multicenter pivotal trial using a device cleared by the Food and Drug Administration and 3 crossover RCTs using a similar device approved outside the United States. Relevant outcomes are symptoms, change in disease status, morbid events, resource utilization and treatment-related morbidity. The single-arm study analysis is part of an ongoing study; it was not designed to evaluate the impact of the device on glycemic control and did not include a comparison intervention. The pivotal trial, submitted with other materials for device approval, evaluated the safety of the device and was not designed to address efficacy. Published data are needed on the efficacy of the semiautomatic insulin adjustment feature of the new device compared with current standard care. Of the 3 crossover RCTs assessing a related device conducted outside the United States, two found significantly better outcomes (ie, time spent in nocturnal hypoglycemia and time spent in preferred glycemic range) with the new device than with standard care and the other had mixed findings (significant difference in time spent in nocturnal hypoglycemia and no significant difference in time spent in preferred glycemic range). The evidence is insufficient to determine the effects of the technology on health outcomes.

**Ongoing and Unpublished Clinical Trials**

Some currently unpublished trials that might influence this review are listed in Table 1.

**Table 1. Summary of Key Trials**

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ongoing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02523131</td>
<td>Home Testing of Day and Night Closed Loop With Pump Suspend Feature (APCam11)</td>
<td>84</td>
<td>Oct 2017 (ongoing)</td>
</tr>
<tr>
<td>NCT02463097a</td>
<td>Hybrid Closed Loop Pivotal Trial in Type 1 Diabetes</td>
<td>127</td>
<td>May 2018</td>
</tr>
<tr>
<td>NCT02660827a</td>
<td>Safety Evaluation of the Hybrid Closed Loop (HCL) System in Pediatric Subjects With Type 1 Diabetes</td>
<td>200</td>
<td>Apr 2018</td>
</tr>
<tr>
<td>NCT02488616</td>
<td>Closed-loop Control of Glucose Levels (Artificial Pancreas) for 5 Days in Adults With Type 1 Diabetes</td>
<td>40</td>
<td>Nov 2018</td>
</tr>
</tbody>
</table>
Clinical Input from Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may provide appropriate reviewers who collaborate with and make recommendations during this process, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input on artificial pancreas device systems was received from 2 physician specialty societies and 4 academic medical centers when the policy was under review in 2015. Input was mixed on whether artificial pancreas systems, including closed-loop monitoring devices with a low-glucose suspend threshold feature, are considered medically necessary. Most reviewers thought there are sufficient supportive data on devices with a low-glucose suspend feature in patients at high risk of hypoglycemia, but some thought the data insufficient.

Practice Guidelines and Position Statements

American Diabetes Association

In 2017, the American Diabetes Association’s (ADA) confirmed its previous recommendation of sensor-augmented insulin pump therapy with a low-glucose suspend feature for patients with type 1 diabetes and nocturnal hypoglycemia. Additionally, the ADA referenced several trials of artificial pancreas devices, determining that “this technology may be particularly useful in insulin-treated patients with hypoglycemia unawareness and/or frequent hypoglycemic episodes.” The ADA’s 2017 standards in diabetes acknowledged that, while more long-term studies of continuous glucose monitoring are needed, the evidence indicates the safety of hybrid closed-loop systems.
Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

Regulatory Status

In 2013, the MiniMed® 530G System (Medtronic) was approved by the FDA through the premarket approval process. This system integrates an insulin pump and glucose sensor and includes a low-glucose suspend (LGS) feature. The threshold suspend tool temporarily stops insulin delivery when the sensor glucose level is at or below a preset threshold within the 60 to 90 mg/dL range. When the glucose value reaches this threshold, an alarm sounds. If patients respond to the alarm, they can choose to continue or cancel the insulin suspend feature. If patients fail to respond to the alarm, the pump automatically suspends action for 2 hours, and then insulin therapy resumes. The device is approved only for use in patients 16 years and older.

In 2016, the MiniMed® 630G System with SmartGuard™ (Medtronic) was approved through the premarket approval process (P150001). It is also for use in patients 16 years and older. The system is similar to the 530G but offers updates to the system components including waterproofing. The threshold suspend feature is the same as in the 530G. FDA product code: OZO.

In 2016, the MiniMed® 670G System (Medtronic) hybrid closed-loop insulin delivery system was approved by FDA through the premarket approval process (P160017). It consists of an insulin pump, a glucose meter, and a transmitter, linked by a proprietary algorithm, the SmartGuard Hybrid Closed Loop. The system includes an LGS feature that suspends insulin delivery either when the glucose level is low or before it becomes low, and it has an optional alarm. Additionally, the system involves semiautomatic insulin-level adjustment to preset targets. As a hybrid system basal insulin levels are automatically adjusted, but the patient needs to administer pre-meal insulin boluses. The system is approved for patients with type 1 diabetes who are at least 14 years old. It is contraindicated for children under age 7 and patients who require less than a total daily insulin dose of 8 units. The 670G system is expected to be available commercially in early 2017 through a priority access program, which will be offered to patients already using the Medtronic 630G system.

FDA product code: OZP.
References


<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>03/10/15</td>
<td>New Policy. Policy created with information on this topic previously addressed in Policy No. 1.01.522 and a literature review through December 20, 2014. FDA-approved artificial pancreas device system with low glucose suspend feature may be considered medically necessary for patients with type 1 diabetes who meet criteria; otherwise artificial pancreas device systems are considered investigational.</td>
</tr>
<tr>
<td>01/12/16</td>
<td>Annual Review. Added Related Policy 1.01.522 Continuous or Intermittent Monitoring of Glucose in Interstitial Fluid. Policy updated with literature review through October 1, 2015; references added. Policy statements unchanged.</td>
</tr>
<tr>
<td>04/12/16</td>
<td>Minor update. Removal of related policy 1.01.522, policy was archived on April 30, 2016.</td>
</tr>
<tr>
<td>11/08/16</td>
<td>Minor update. Language added to support that this policy applies only to those age 16 and older as indicated by FDA approval for the use of the device.</td>
</tr>
<tr>
<td>02/01/17</td>
<td>Annual Review, approved January 10, 2017. Policy updated with literature review through October 4, 2016; references added. Policy statements unchanged.</td>
</tr>
<tr>
<td>04/11/17</td>
<td>Policy moved into new format; no change to policy statements. Evidence Review section reformatted.</td>
</tr>
<tr>
<td>02/01/18</td>
<td>Annual Review, approved January 16, 2018. Policy updated with literature review through October 2017; references updated. Policy statement added that use of hybrid closed loop insulin delivery system as an artificial pancreas device system (age 14 and older) is considered investigational.</td>
</tr>
<tr>
<td>09/01/18</td>
<td>Minor update. Re-added language supporting that this policy applies to those age 16 and older; it was inadvertently removed in a previous update.</td>
</tr>
</tbody>
</table>

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U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)

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