Preauthorization is required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient’s contract at the time the services are rendered.

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals:</td>
<td>Interventions of interest are:</td>
<td>Comparators of interest are:</td>
<td>Relevant outcomes include:</td>
</tr>
<tr>
<td>• With type 1 diabetes</td>
<td>• Artificial pancreas device system with a low-glucose suspend feature</td>
<td>• Nonintegrated continuous glucose monitoring plus insulin pump</td>
<td>• Symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Self-monitoring blood glucose and multiple dose insulin injection therapy</td>
<td>• Change in disease status</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Morbid events</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Resource utilization</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Treatment-related morbidity</td>
</tr>
</tbody>
</table>

DESCRIPTION

Automated insulin delivery systems, also known as artificial pancreas device systems link a glucose monitor to an insulin infusion pump that automatically takes action (e.g., suspend or adjusts insulin infusion) based on the glucose monitor reading. These devices are proposed to improve glycemic control in patients with insulin-dependent diabetes, in particular, control of nocturnal hypoglycemia.

SUMMARY OF EVIDENCE

For individuals who have type 1 diabetes who receive an artificial pancreas device system with a low glucose suspend feature, the evidence includes two 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 two nocturnal hypoglycemic events (≤65 mg/dL) lasting more than 20 minutes during a two-week run-in phase. Both trials required at least six 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, one trial was limited by its nonstandard reporting of hypoglycemic episodes, and the other trial was no longer statistically significant when two outliers were excluded from analysis. The evidence is insufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have type 1 diabetes who receive an artificial pancreas device system with a hybrid closed-loop insulin delivery system, the evidence includes multicenter pivotal trials using devices cleared by the Food and Drug Administration, supplemental data and analysis for expanded indications and more recent studies focused on children and adolescents. Three crossover RCTs using a similar first-generation device approved outside the United States have been reported. Relevant outcomes are symptoms, change in disease status, morbid events, resource utilization, and treatment-related morbidity. Of the three crossover RCTs assessing a related device conducted outside the United States, two found significantly better outcomes (i.e., time spent in nocturnal hypoglycemia and time spent in preferred glycemic range). For the U.S. regulatory registration pivotal trial, the primary outcomes were safety and not efficacy. Additional evidence from device performance studies and clinical studies all demonstrate reductions in time spent in various levels of hypoglycemia, improved time in range (70-180 mg/dL), rare diabetic ketoacidosis and few device-related adverse events. The evidence is sufficient that the magnitude of reduction for hypoglycemic events in the T1D population is likely to be clinically significant. The variations in the definition of primary and secondary outcomes in the study design and conduct of the published evidence are limitations that preclude determining the effects of the technology on net health outcomes. Evidence reported through clinical input supports that the use of hybrid closed loop APDS systems provides a clinically meaningful improvement in net health outcome and is consistent with generally accepted medical practice. Reduction in the experience of hypoglycemia and inappropriate awareness of hypoglycemia and glycemic excursions were identified as important acute clinical outcomes in children, adolescents, and adults and are related to the future risk for end-organ complications. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcomes.

**POLICY**

Use of a U.S. Food and Drug Administration-approved automated insulin delivery system (artificial pancreas device system) with a low glucose suspend feature may be considered **medically necessary** in patients with type 1 diabetes who meet all the following criteria:

- Age 14 and older
- Glycated hemoglobin level between 5.8% and 10.0%
- At least two documented nocturnal hypoglycemic events in a two-week period;

Use of a Food and Drug Administration–approved automated insulin delivery system (artificial pancreas device system) designated as hybrid closed-loop insulin delivery system (with low glucose suspend and suspend before low features) may be considered **medically necessary** in patients with type 1 diabetes who meet all of the following criteria:

- Age 7 and older
- Glycated hemoglobin level between 5.8% and 10.0%
- At least two documented nocturnal hypoglycemic events in a two-week period.
Use of an automated insulin delivery system (artificial pancreas device system) is **investigational** for individuals who do not meet the above criteria.

Use of an automated insulin delivery system (artificial pancreas device system) not approved by the Food and Drug Administration is **investigational**.

**BACKGROUND**

**DIABETES AND GLYCEMIC CONTROL**

Tight glucose control in patients with diabetes has been associated with improved health 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, may place a limit on 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.

Table 1 is a summary of selected clinical outcomes in T1D clinical management and research.

**Table 1. Outcome Measures for Type 1 Diabetes**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Definition</th>
<th>Guideline type</th>
<th>Organization</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemia</td>
<td>Same as Type 1 Diabetes Outcome Programa</td>
<td>Professional Practice Committee with systematic literature review</td>
<td>ADA</td>
<td>2019</td>
</tr>
<tr>
<td>Level 1</td>
<td>Glucose &lt;70 mg/dl but ≥ 54 mg/dl</td>
<td>Stakeholder survey, expert opinion with evidence review</td>
<td>Type 1 Diabetes Outcome Programa</td>
<td>2017</td>
</tr>
<tr>
<td>Level 2</td>
<td>Glucose &lt;54 mg/dl</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level 3</td>
<td>Event characterized by altered mental/physical status requiring assistance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>Clinical alert for evaluation and/or treatment</td>
<td>Clinical Practice Consensus</td>
<td>ISPAD</td>
<td>2018</td>
</tr>
<tr>
<td>Clinical alert for evaluation and/or treatment</td>
<td>Glucose &lt;70 mg/dl</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinically important or serious</td>
<td>Glucose &lt;54 mg/dl</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe hypoglycemia</td>
<td>Severe cognitive impairment requiring external assistance by another person to take corrective action</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>Glucose &gt;180 mg/dL and ≤250 mg/dL</td>
<td>Type 1 Diabetes Outcome Programa</td>
<td>2017</td>
<td></td>
</tr>
<tr>
<td>Level 1</td>
<td>Glucose &gt;250 mg/dL</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Measure | Definition | Guideline type | Organization | Date
---|---|---|---|---
Level 2 | Time in Range \(^b\) | Percentage of glucose readings in the range of 70–180 mg/dL per unit of time | Type 1 Diabetes Outcome Program\(^3\) | 2017
Diabetic ketoacidosis (DKA) | Elevated serum or urine ketones > ULN | Type 1 Diabetes Outcome Program\(^3\) | 2017
Serum bicarbonate <15 mEq/L
Blood pH <7.3

ADA: American Diabetes Association, ISPAD: International Society for Pediatric and Adolescent Diabetes; ULN: upper limit of normal.

\(^a\)Steering Committee: representatives from American Association of Clinical Endocrinologists (AACE), American Association Diabetes Educators, the American Diabetes Association (ADA), the Endocrine Society, JDRF International, The Leona M. and Harry B. Helmsley Charitable Trust, the Pediatric Endocrine Society, T1D Exchange.

\(^b\)Time in range: has also been adopted by researchers evaluating the precision and effectiveness of emerging glucose monitoring and automated insulin delivery technologies.

Treatment

Type 1 diabetes is caused by the destruction of the pancreatic beta cells which produce insulin, and the necessary mainstay of treatment is insulin injections. Multiple studies have shown that intensive insulin treatment, aimed at tightly controlling blood glucose, reduces the risk of long-term complications of diabetes, such as retinopathy and renal disease. Optimal glycemic control, as assessed by glycated hemoglobin, and avoidance of hyper- and hypoglycemic excursions have been shown to prevent diabetes-related complications. Currently, insulin treatment strategies include either multiple daily insulin injections or continuous subcutaneous insulin infusion with an insulin pump.

The use of the continuous glucose monitoring (CGM) component of diabetes self-management is specifically addressed in the Protocol Continuous or Intermittent Monitoring of Glucose in Interstitial Fluid.

Restoration of pancreatic function is potentially available through islet cell or allogeneic pancreas transplantation. These interventions are in the Islet Transplantation and Allogeneic Pancreas Transplant Protocols, respectively.

REGULATORY STATUS

In 2013, the MiniMed\(^\circledR\) 530G System (Medtronic) was approved by FDA through the premarket approval process (P120010). This system integrates an insulin pump and glucose meter and includes an LGS feature. The threshold suspend tool temporarily suspends 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, the pump automatically suspends action for two hours, and then insulin therapy resumes. The device is approved only for use in patients 16 years and older.

In 2016, the MiniMed\(^\circledR\) 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), a 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 and, the SmartGuard Hybrid Closed Loop. The system includes an LGS feature that suspends insulin delivery; either suspend on low or suspend before low and have 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 seven and patients who require less than a total daily insulin dose of eight units. The 670G system is expected to be available commercially in 2017 through a priority access program, which will be offered to patients already using the Medtronic 630G system.

FDA product code: OZP.

RELATED PROTOCOL
Continuous or Intermittent Monitoring of Glucose in Interstitial Fluid

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.

REFERENCES
We are not responsible for the continuing viability of web site addresses that may be listed in any references below.


