External Insulin Infusion Pumps

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Introduction

External insulin infusion pumps are addressed by this guideline.

Criteria

An **insulin pump and related supplies** (HCPCS E0784, A4224, A4225, A4230, A4231, A4232, A4238, A4239) are considered medically necessary when an individual meets **all** of the following initial coverage criteria:

- The individual has type 1 ot type 2 diabetes mellitus.
- The individual uses insulin to manage their diabetes with either multiple daily injections or continuous infusion.
- The individual checks their blood glucose at least four times a day or uses a continuous glucose monitor (CGM).
- There is documentation of **any** of the following:
  - The individual has a glycated hemoglobin (HbA1c) greater than 7%.
  - The individual has fasting blood sugars in the morning that are over 200mg/dl (dawn phenomenon).
  - The individual has a history of frequent low blood sugar readings of less than 70 mg/dl.
  - The individual has a history of problems with high or low blood sugar levels.
  - The individual has blood sugar levels that are difficult to control.
- The individual has ongoing participation in a diabetes management program.

Note:

Refer to the Medical Background FDA approval manufacturer age specifications.

Supplies

When an external insulin infusion pump is considered medically necessary, all associated supplies required for its effective use are also considered medically necessary.

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Not Covered

- The following devices are not covered as they do not meet the definition of durable medical equipment (DME):
  - An implanted infusion pump (HCPCS E0782, E0785, E0786) for the infusion of insulin to treat diabetes.
  - A disposable external insulin infusion pump (e.g., OmniPod® Insulin Management System, V-Go® disposable insulin delivery device) (HCPCS A9274) and related supplies.

Definitions

Hypoglycemia in individuals with diabetes mellitus is defined as abnormally low plasma glucose concentration <70 mg/dL (3.9 mmol/L).

Diabetes mellitus (DM) describes diseases of abnormal carbohydrate metabolism that are characterized by hyperglycemia. DM is associated with a relative or absolute impairment in insulin secretion, along with varying degrees of peripheral resistance to the action of insulin.

According to the Centers for Disease Control and Prevention (CDC) National Diabetes Statistics Report of 2024, the estimated prevalence of DM for 2021 in the United States (US) was 38.4 million people or approximately 11.6% of the population. The percentage of adults with DM increases with age, estimated to be close to 30% in those aged 65 years or older.

Type 1 diabetes mellitus (T1DM) is a condition of insulin deficiency resulting from autoimmune destruction of the insulin-producing beta cells in the islets of Langerhans. T1DM is one of the most common chronic diseases in childhood. In addition to the clinical presentation and history, laboratory tests such as pancreatic beta-cell (β-cell) autoantibodies or insulin and C-peptide levels may assist in the diagnosis of T1DM. Management involves measuring blood glucose and urine ketone concentrations, administering insulin, and recognizing and treating hypoglycemia.

Type 2 diabetes mellitus (T2DM) is a heterogeneous disease characterized by hyperglycemia, insulin resistance, and relative impairment in insulin secretion. Management of individuals with T2DM includes education, evaluation for microvascular and macrovascular complications, achievement of target glycemia, treatment of cardiovascular risk factors, and avoidance of drugs that can aggravate abnormalities of glucose or lipid metabolism. Weight reduction, diet modification, oral medication, or insulin administration may be needed to maintain glycemic targets.

Gestational diabetes mellitus (GDM) develops in pregnant individuals whose pancreatic function is insufficient to overcome the insulin resistance associated with the

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pregnant state. The American Diabetes Association (ADA) notes that GDM is diagnosed in the second or third trimester, and is not present prior to conception.

Time in range (TIR) is the time in the target glucose range of 70 to 180 mg/dL (3.9 to 10 mmol/L) over a 14-day period. TIR is used as a measure of diabetes control, and low TIR is correlated with long-term microvascular complications.

Glycated hemoglobin (HbA1c) is a blood test that reflects average glycemia over the lifespan of the red blood cell (100 to 120 days), however 50% of HbA1c is determined by glycemia during the month preceding measurement. HbA1c monitors long-term glycemic control and provides an indication of the average of blood glucose levels over the preceding three months. Increased HbA1c is associated with an increased risk of long-term complications.

The primary mechanisms for **insulin delivery** include:

- **Injection**: Injecting insulin with a syringe or pen is the delivery method used by most people with insulin dependent diabetes mellitus.
- **Inhalation**: Inhaled insulin is available only as rapid-acting insulin, and is typically used for mealtime dosing. It is used in conjunction with an insulin injection regimen for individuals with T1DM and T2DM on intensive therapy, or as an alternative to injected mealtime bolus injections for individuals with T2DM with no other insulin requirement.
- **Infusion**: An insulin pump, also known as a continuous subcutaneous insulin infusion (CSII) pump, is an external ambulatory infusion device used for managing insulin dependent diabetes mellitus. It works by continuous administration of short-acting insulin at preselected rates.

Blood glucose monitoring (BGM) devices measure the glucose level of a small amount of blood (usually from the fingertip), typically three to four times per day. BGM readings look at specific glucose values at specific points in time, generating a pattern of variability.

Continuous glucose monitoring (CGM) devices measure the glucose content of interstitial fluid every five to 15 minutes, depending on the device. CGM systems provide visualization of the current glucose value as well as trend arrow analysis, which indicates the direction of changing glucose. This technology can help individuals fine-tune diabetic treatment.

A **sensor-augmented pump (SAP)** is an insulin pump that is integrated with a CGM using software. The SAP and CGM devices function independently, and insulin delivery must be adjusted by the user.

Predictive low glucose threshold suspend (PLGS) insulin pump systems reduce or temporarily stop insulin infusion when the trend in CGM results predicts that hypoglycemia will occur.

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Automated insulin delivery (AID) systems are advanced integrated systems wherein CGM sensor data is used by the insulin pump to directly adjust insulin dosing, as well as suspend insulin infusion when necessary.

A **bihormonal, fully automated insulin pump system (bionic pancreas)** is a closed-loop system in which insulin and glucagon are infused based upon continuous glucose sensing.

Evidence Discussion

Purpose of technology/description of device

An insulin pump, also known as a continuous subcutaneous insulin infusion (CSII) pump, is an external ambulatory infusion device used for managing insulin dependent diabetes mellitus. It works by administering continuous subcutaneous short-acting insulin at preselected rates. Basal insulin requirements are supplied in the form of mini-boluses delivered every five minutes. This infusion generally constitutes 40% to 50% percent of the total daily insulin dose. In addition to basal insulin delivery, mealtime insulin bolus doses are given to minimize postprandial glucose excursions.

Traditional pumps deliver insulin via plastic tubing ending with a subcutaneously placed cannula that needs to be replaced every 1-3 days. Other insulin pumps are designed with the insulin reservoir located with the cannula at the cannula site; these devices do not require tubing for infusion. With a patch pump, the insulin reservoir, batteries, and cannula are aggregated into a wearable disposable device ("pod"), which delivers insulin subcutaneously. The pod is changed every two to three days.

Sensor-augmented pumps are insulin pumps can be integrated with a continuous glucose monitor (CGM). SAP therapy incorporates the use of a real-time continuous glucose monitor (rtCGM) or intermittently scanned CGM (isCGM), which communicates data to the compatible insulin pump. The user must access the CGM data to manually adjust the insulin dosing with SAP. When the monitor transmits information to the pump software to suspend insulin dosing, the SAP is referred to as a low glucose suspend system.

Automated insulin delivery (AID) systems are more advanced integrated systems, where CGM sensor data is used by the pump to directly adjust insulin infusion, as well as suspend it. AID systems may be referred to as hybrid closed-loop systems, integrated CGMs (iCGMs), or artificial pancreas systems. These devices use advanced algorithms which allow insulin infusion as needed to keep glucose control at a preset value without external input. The AID system includes the continuous glucose monitor, insulin pump, sensor, receiver, algorithm for automated insulin delivery, and a blood glucose monitoring device.

Medical background

Continuous subcutaneous insulin infusion (CSII) has been used for T1DM since the 1970s. MiniMed® introduced their first insulin pump, the MiniMed® 502, in 1983, and subsequent external pumps have gotten progressively smaller, more user-friendly, and more integrated with glucose monitoring systems (Kesavadev et al., 2020).

In 2003, MiniMed® and BD® introduced the first "intelligent" insulin pump, in which data from the BD® blood glucose monitor was wirelessly transmitted to the insulin pump, and insulin doses were then suggested to the user via a Bolus Wizard® calculator.

Tubeless patch pumps were introduced via the Insulet OmniPod® in 2011. MiniMed® introduced the first integrated insulin pump and CGM system in 2006 with the Paradigm™ REAL-Time sensor-augmented pump (SAP).

Sensor-augmented pump (SAP) systems are insulin pumps that are integrated with a CGM using software. In 2009, Medtronic® began marketing the MiniMed® Veo™, the first SAP with a low glucose suspend feature.

Some insulin pumps can suspend insulin delivery when glucose readings reach a prespecified low glucose threshold or are predicted to reach that threshold. The threshold suspend feature reduces the frequency and duration of nocturnal hypoglycemia. The United States Food and Drug Administration (FDA) approved the Medtronic MiniMed® 530G with an Elite® sensor in 2013. It was considered to be a first-generation artificial pancreas device, and included threshold suspend automation.

The first hybrid closed-loop system, or automated insulin delivery (AID) system, was approved by the FDA in 2016, and introduced in 2017 with the Medtronic MiniMed® 670G insulin pump and the Guardian® Sensor 3 CGM. The 670G had an auto mode which adjusted basal insulin delivery every 5 minutes based on the CGM data in order to keep blood glucose levels within a specific target range.

The Insulet Omnipod Dash® system with Bluetooth® wireless technology was approved by the FDA in 2018, and was the first insulin pump certified for cyber and information security (Kesavadev et al., 2020).

Some insulin pumps have offered a predictive low glucose suspend (PLGS) feature. In contrast to low glucose threshold suspend, in which insulin delivery was suspended when the glucose reading reaches the threshold value, predictive low glucose threshold suspend reduced or suspended insulin infusion when the trend in CGM results predicted that hypoglycemia would occur. In 2019, the FDA approved the Tandem Diabetes Care T:Slim® X2 as the first alternate controller enabled (ACE) interoperable insulin pump, which also featured PLGS (FDA, 2019). The t:Slim® X2 could work with an AID system, CGM, BGM, or other electronic devices used for diabetes management.

The first bihormonal bionic pancreas was developed in 2015. The Beta Bionics iLet® was a closed-loop system consisting of two pumps - one for insulin and one for

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glucagon. These pumps were integrated with a CGM and connected to a smartphone application. This device was granted the breakthrough device designation by the FDA in 2019 (Kesavadev et al., 2020), and was subsequently approved through the 510(k) process in 2023 (FDA, 2023).

The insulin pump has increasingly been the standard of care for the pediatric population in resource-abundant settings, based on accumulating evidence for benefits in the areas of glycemic control, safety, and overall satisfaction compared with MDI for most children. An automated insulin delivery (AID) system, also known as a hybrid closed-loop (HCL) insulin pump, has been recommended for most children and adolescents. These systems were associated with greater time in range and a reduction in time below range compared with standard insulin pumps.

The prescribing clinician should verify approved ages for use for specific devices prior to ordering the devices. The Dana Diabecare® IIS (Sooil Development) insulin pump is approved for individuals seven years of age and older. The T:Slim® X2 insulin pump with Basal IQ® technology (Tandem Diabetes Care®) can be used alone or in combination with CGM and is approved for individuals age six and older. The MiniMed® 630G system (Medtronic®) pump can be used alone or as an integrated system and is approved for individuals age 14 and older when used with Guardian® Sensor 3, or for individuals 16 years old and older when used with the Enlite® sensor. The Insulet Omnipod® products are the only insulin pumps approved for individuals of any age. The Beta Bionics iLet® ACE Pump and software was FDA approved for individuals six years and older with diabetes.

Literature review

- Forlenza et al. (2018) performed a randomized cross-over study to evaluate the effectiveness and safety of a predictive low-glucose suspend (PLGS) system to reduce hypoglycemia compared with sensor-augmented pump (SAP) therapy. Predictive low-glucose suspend (PLGS) technology used sensor glucose concentration trends to predict glucose values into the future (e.g., 30 minutes) and then suspended insulin delivery when hypoglycemia was predicted, ideally before hypoglycemia occurred. The study randomized 103 individuals with type 1 diabetes mellitus (T1DM) (age 6–72 years, mean HbA1c 7.3%) to use the PLGS for a three-week period and the SAP for another three-week period. The primary outcome was CGM-measured time <70 mg/dL in each three-week period. Median time <70 mg/dL was reduced from 3.6% at baseline to 2.6% during the 3-week period in the PLGS arm compared with 3.2% in the SAP arm (P<0.001). There was one severe hypoglycemic event in the SAP arm and none in the PLGS arm. The authors concluded that the PLGS system significantly reduced hypoglycemia without rebound hyperglycemia, indicating that the system can improve glycemic control in adults and youth with T1DM.

- A randomized controlled trial reported by Abraham et al. (2018) examined the long-term effectiveness and safety of a predictive low-glucose suspend (PLGS) system compared with sensor-augmented pump (SAP) therapy alone in children and adolescents with type 1 diabetes mellitus (T1DM). The study included 154 participants (age 8 to 20 years) who had T1DM for at least one year duration, HbA1c of <10%, and had used insulin pump therapy for greater than six months. The primary objective of the study was the comparison of the average percentage of time spent in hypoglycemia. The participants were followed up at three and six months after randomization. Over the six-month study duration, PLGS was associated with a reduction in hypoglycemia compared with SAP (P<0.0001). The use of SAP did not significantly reduce the time spent in hypoglycemia during the day but showed a mild reduction at night. In contrast, PLGS was associated with reduced day and nighttime hypoglycemia, with greater reduction at night. Moreover, the PLGS group spent approximately half the time in hypoglycemia with fewer hypoglycemic events as compared with SAP alone. There were no PLGS-related serious adverse events. Hence, the authors concluded that PLGS was an effective method to reduce hypoglycemia in children and adolescents with T1DM without compromising glycemic control or quality of life.
- Bergenstal et al. (2013) conducted a randomized controlled trial to evaluate sensor-augmented insulin pump (SAP) therapy with and without the threshold-suspend feature in individuals with nocturnal hypoglycemia. The threshold-suspend feature of SAP was designed to minimize the risk of hypoglycemia by interrupting insulin delivery at a preset sensor glucose value. The study randomized 247 individuals with type 1 diabetes mellitus (T1DM) and nocturnal hypoglycemia to SAP therapy with or without a threshold suspend feature. The primary safety outcome was the change in the glycated hemoglobin (HbA1c) level. The primary efficacy outcome was the area under the curve (AUC) for nocturnal hypoglycemic events. After three months, change in HbA1c was similar in the two groups. The mean AUC for nocturnal hypoglycemic events was 37.5% lower in the threshold-suspend group than in the control group (P<0.001). In addition, nocturnal hypoglycemic events were significantly lower in the group with the threshold suspend feature (1.5 versus 2.2 events per person per week) (P<0.001). Four individuals in the control group had a severe hypoglycemic event. Thus, the investigators concluded that over a three-month period, the use of SAP with the threshold-suspend feature reduced nocturnal hypoglycemia without increasing HbA1c values.
- Alotaibi et al. (2020) performed a systematic review and meta-analysis to evaluate the effectiveness and safety of predictive low-glucose suspend (PLGS) in children and adolescents with type 1 diabetes mellitus (T1DM). The analysis included five randomized controlled trials with a total sample size of 493 children aged 6 to 18 years that compared PLGS versus sensor-augmented pumps (SAP). The authors reported high quality evidence that PLGS is superior to SAP in decreasing time spent in hypoglycemia, without increasing percentage of time spent in hyperglycemia or

episodes of diabetic ketoacidosis (DKA). In summary, the authors concluded that PLGS was superior to SAP in decreasing daytime and nocturnal hypoglycemia without increasing the risk of DKA or hyperglycemia.

Automated insulin delivery (AID) systems:

- In a multicenter randomized controlled trial, Brown et al. (2019) evaluated the effectiveness of closed-loop systems that automate insulin delivery to improve glycemic outcomes in individuals with type 1 diabetes mellitus (T1DM). The study randomized 168 individuals (ages 14 to 71) with T1DM to receive treatment with a closed-loop system (closed-loop group) or a sensor-augmented pump (SAP) (control group). The primary outcome was the percentage of time that the blood glucose level was within the target range of 70 to 180 mg per deciliter as measured by continuous glucose monitoring (CGM). The mean percentage of time that the glucose level was within the target range increased in the closed-loop group from 61±17% at baseline to 71±12% during the six months and remained unchanged at 59±14% in the control group (P<0.001). No serious hypoglycemic events occurred in either group; one episode of diabetic ketoacidosis occurred in the closed-loop group. Thus, the authors concluded that compared to the use of SAP, a closed-loop system was associated with a greater percentage of time spent in a target glycemic range.
- In 2020, Breton and colleagues reported on a multicenter randomized controlled trial that evaluated the effectiveness of a closed-loop system of insulin delivery (artificial pancreas) on glycemic outcomes in children with type 1 diabetes mellitus (T1DM). The study randomized 101 children aged six to 13 years old with T1DM to receive treatment with a closed-loop system of insulin delivery (closed-loop group) or a sensor-augmented insulin pump (SAP) (control group). The primary outcome was the percentage of time that the glucose level was in the target range of 70 to 180 mg per deciliter, as measured by continuous glucose monitoring (CGM). At 16 weeks, the mean percentage of time that the glucose level was in the target range of 70 to 180 mg per deciliter increased from 53±17% at baseline to 67±10% the closed-loop group and from 51±16% to 55±13% in the control group (P<0.001). In both groups, the median percentage of time that the glucose level was below 70 mg per deciliter was low (1.6% in the closed-loop group and 1.8% in the control group). In the closed-loop group, the median percentage of time that the system was in the closed-loop mode was 93%. No episodes of diabetic ketoacidosis or severe hypoglycemia occurred in either group. The authors found that glucose levels were in the target range for a greater percentage of time in individuals who used a closed-loop system of insulin delivery system compared with those who used an SAP. Moreover, there were no significant differences in HbA1c changes between the groups.
- Weisman et al. (2017) conducted a systematic review and meta-analysis of randomized controlled trials comparing artificial pancreas systems (insulin only or insulin plus glucagon) with conventional pump therapy (continuous subcutaneous insulin infusion [CSII] with blinded continuous glucose monitoring [CGM] or unblinded

sensor-augmented pump [SAP] therapy) in adults and children with type 1 diabetes mellitus (T1DM). The analysis included 27 comparisons from 24 studies (23 crossover and one parallel design) including a total of 585 participants (219 in adult studies, 265 in pediatric studies, and 101 in combined studies). The primary outcome was the difference in percentage of time that blood glucose was within target range compared to conventional pump therapy. Time in target range was 12.59% higher with artificial pancreas systems (P<0.001). The authors concluded that the use of artificial pancreas systems uniformly improved glycemic control in outpatient settings.

- A 2020 randomized controlled trial (McAuley et al.) investigated glycemic and psychosocial outcomes with hybrid closed-loop (HCL) versus user-determined insulin dosing with multiple daily injections (MDI) or insulin pump. One hundred-twenty adults with type 1 diabetes mellitus (T1DM) using MDI or an insulin pump without continuous glucose monitoring (CGM) were randomized to 26 weeks of HCL or continuation of current therapy. The primary outcome was CGM time in range (TIR; 70–180 mg/dL) during the final three weeks. HCL TIR increased from 55% (SD 13%) at baseline to 70% (SD 10%) at 26 weeks. The control group was unchanged from baseline (55%, SD 12%) to 26 weeks (55%, SD 13%) (P < 0.0001). In addition, the HCL group had a lower HbA1c level. Seventeen (nine device-related) versus 13 serious adverse events occurred in the HCL and control groups, respectively. In summary, at six-month follow-up, hybrid closed-loop insulin delivery was associated with an increased percentage of time in range, decrease in HbA1c level, and improved diabetes-specific quality of life compared with manual insulin dosing.
- In 2021, a multicenter single-arm prospective study by Brown and colleagues evaluated the efficacy and safety of a tubeless on-body automated insulin delivery system in 235 children and adults with type 1 diabetes mellitus (T1DM). A 2-week standard therapy phase (usual insulin regimen) was followed by three months of automated insulin delivery. Primary safety outcomes were incidence of severe hypoglycemia and diabetic ketoacidosis. Primary effectiveness outcomes were change in HbA1c and percent time in range (70–180 mg/dL). At three-month follow-up, HbA1c was significantly reduced in children by 0.71% (7.8 mmol/mol) (P < 0.0001) and in adults by 0.38% (4.2 mmol/mol) (P < 0.0001). Time in range was improved from standard therapy by 15.6 ± 11.5% in children and 9.3 ± 11.8% in adults (P < 0.0001). Thus, at three-month follow-up, the use of the tubeless automated insulin delivery system was associated with a reduction in HbA1c, an improvement in time in range, and low incidence rates of severe hypoglycemia.
- Bekiari et al. (2018) performed a meta-analysis including 40 studies (1,027 participants) to understand the efficacy and safety of hybrid closed-loop (artificial pancreas) systems in nonpregnant adults with type 1 diabetes mellitus (T1DM). The primary outcome was the proportion of time that sensor glucose level was within the near normoglycemic range (3.9-10 mmol/L). Secondary outcomes included the proportion of time that sensor glucose level was above 10 mmol/L or below 3.9 mmol/L, low blood glucose index overnight, mean sensor glucose level, total daily

insulin needs, and HbA1c level. The analysis found that proportion of time in the near normoglycemic range was significantly higher with artificial pancreas use, both overnight (weighted mean difference 15.15%, 95% confidence interval 12.21% to 18.09%) and over a 24-hour period (9.62%, 7.54% to 11.7%). Moreover, artificial pancreas systems had a favorable effect on the proportion of time with sensor glucose level above 10 mmol/L (−8.52%, −11.14% to −5.9%) or below 3.9 mmol/L (−1.49%, −1.86% to −1.11%) over 24 hours, compared with control treatment. Thus, the authors concluded that artificial pancreas systems were an efficacious and safe approach for treating outpatients with T1DM.

- In 2022, Choudhary and colleagues reported on a multicenter, randomized controlled trial (The Advanced Hybrid Closed Loop Study in Adult Population with Type 1 Diabetes (ADAPT) trial) to assess the efficacy of advanced hybrid closed loop (AHCL) systems compared with current therapy. Eighty-two adults with T1DM using multiple daily injections of insulin and intermittently scanned continuous glucose monitoring (isCGM) with HbA1c of at least 8% were randomized to one of two cohorts: multiple daily injections of insulin plus isCGM (cohort A), or real time continuous glucose monitoring (cohort B). At six-month follow-up, mean HbA1c level had decreased by 1.54% (from 9.00% to 7.32%) in the AHCL group and by 0.20% (9.07% to 8.91%) in the multiple daily injections of insulin plus isCGM group. Thus, the authors concluded that in individuals with T1DM using multiple daily injections of insulin plus isCGM and with HbA1c of at least 8%, the use of AHCL conferred benefits in terms of glycemic control beyond those that could be achieved with multiple daily injections of insulin plus isCGM.

Insulin pump use in individuals with type 2 diabetes mellitus (T2DM):

- A multicenter, randomized controlled trial (OpT2mise) (Reznik et al., 2014) compared the efficacy of pump treatment and multiple daily injections for lowering glucose in insulin-treated individuals with type 2 diabetes mellitus (T2DM). The study randomized 331 individuals with T2DM with poor glycemic control to insulin pump treatment or continued multiple daily injections of insulin. The primary endpoint was change in mean glycated hemoglobin (HbA1c) level between baseline and end of the randomized phase for the intention-to-treat population. At six months, individuals treated with an insulin pump had a mean reduction in HbA1c of 1.1%, as compared with a reduction of 0.4% in the multiple daily injection group ($p<0.0001$); moreover, there was not an associated increase in hypoglycemia. Two diabetes-related serious adverse events (hyperglycemia or ketosis without acidosis) resulting in hospital admission occurred in the pump treatment group compared with one in the multiple daily injection group. No ketoacidosis occurred in either group and one episode of severe hypoglycemia occurred in the multiple daily injection group. Thus, the authors concluded that in individuals whose T2DM is poorly controlled despite using multiple daily injections of insulin, pump treatment could be considered as a safe and valuable treatment option.

- On follow-up from the OpT2mise randomized trial, Aronson et al. (2016) transitioned the multiple daily injection group to insulin pump therapy after six months. The primary endpoint was the between-group difference in change in mean glycated hemoglobin (HbA1c) level from baseline to the end of 12 months. The mean HbA1c at baseline was 9% in both groups. At six months, the reduction in HbA1c was significantly greater with pump therapy than with MDI ($p<0.001$). The participants initially randomized to insulin pump treatment maintained the improvement in glycemic control at 12 months, and the final mean HbA1c levels were identical in both groups. There were no differences in weight gain or ketoacidosis between groups. In addition, one participant in each group experienced severe hypoglycemia. In summary, the investigators concluded that insulin pump therapy had a durable effect on glycemic control in T2DM.
- Pickup et al. (2017) conducted a systematic review and meta-analysis to compare glycemic control during continuous subcutaneous insulin infusion (CSII) and multiple daily insulin injections (MDI) in individuals with type 2 diabetes mellitus (T2DM). The authors identified five randomized trials that compared mean glycated hemoglobin (HbA1c) level during CSII versus MDI in individuals with T2DM. The primary outcome was glycemic control at study completion, as measured by HbA1c level. The authors reported that insulin pump therapy achieves better glycemic control than MDI in participants with poorly controlled T2DM at baseline; moreover, the greatest effect was noted in individuals with the highest baseline HbA1c levels and insulin doses.

Bihormonal, fully automated system (bionic pancreas):

- In a crossover trial, El-Khatib et al. (2017) aimed to assess whether a bihormonal bionic pancreas initialized only with body mass index (BMI) can safely reduce mean glycemic level in adults with type 1 diabetes mellitus (T1DM). Forty-three adults received therapy with automated, bihormonal, closed-loop system for 11 days and therapy with their own insulin pump for 11 days. The primary outcomes were the mean glucose concentration and time with continuous glucose monitoring (CGM) glucose concentration less than 3.3 mmol/L, analyzed over days two through 11. The mean CGM glucose concentration was 7.8 mmol/L in the bionic pancreas period versus 9.0 mmol/L in the comparator period ($p<0.0001$). The mean time with CGM glucose concentration less than 3.3 mmol/L was 0.6% in the bionic pancreas period versus 1.9% in the comparator period ($p<0.0001$). There were no serious or unexpected adverse events in the bionic pancreas period of the study. The authors concluded that relative to conventional and SAP therapy, the bihormonal bionic pancreas was able to achieve superior glycemic regulation without the need for carbohydrate counting. However, the authors noted that additional studies were needed to establish the long-term benefits and risks of automated glycemic management with a bihormonal bionic pancreas.
- Russell et al. (2016) performed a randomized cross-over study to compare the safety and efficacy of a bihormonal bionic pancreas versus conventional insulin

pump therapy in children aged six to 11 years with type 1 diabetes mellitus (T1DM). Nineteen participants were randomly assigned to either five days with the bionic pancreas or conventional insulin pump therapy (control) as the first intervention, followed by a three-day washout period, and then five days with the other intervention. The bionic pancreas period was associated with a lower mean CGM-measured glucose concentration ($p=0.00037$) and a lower proportion of time with a CGM-measured glucose concentration below 3.3 mmol/L ($p<0.0001$) than was the control period on days two through five. The median number of carbohydrate interventions given per participant for hypoglycemia on days one through five was lower during the bionic pancreas period than during the control period ($p=0.037$). No episodes of severe hypoglycemia were recorded. In summary, the authors concluded that the bionic pancreas reduced episodes of hypoglycemia relative to insulin pump therapy in children with T1DM. The authors noted that future studies should investigate the long-term use of the bionic pancreas in real-world settings.

- An observational study in 2014 by Hanazaki and colleagues examined whether perioperative intensive insulin therapy using an artificial pancreas with a closed-loop glycemic control system can be used to prevent hypoglycemia in surgical patients. The study included 305 patients undergoing hepatic, pancreatic, or esophageal resections using an artificial pancreas. Data were collected prospectively and were reviewed or analyzed retrospectively. Perioperative mean blood glucose level and achievement rates in target blood glucose range of 80 to 110 mg/dL were 100.5 ± 11.9 mg/dL and 88.1% ± 16.0%, respectively. There were no significant differences in glycemic control between the type of surgery performed. In addition, no patients had hypoglycemia. In conclusion, the authors opined that perioperative insulin therapy using an artificial pancreas with a closed-loop glycemic control system could be used to prevent hypoglycemia and maintain stable glycemic control with less variability of blood glucose concentration.

Professional organizations/societies:

- The 2024 American Diabetes Association (ADA)'s "Standards of Care in Diabetes-2024" clinical practice recommendations for the treatment and management of diabetes mellitus recommended:
  - "AID systems should be offered for diabetes management to youth and adults with type 1 diabetes mellitus and other types of insulin-deficient diabetes who are capable of using the device safely (either by themselves or with a caregiver). The choice of device should be made based on the individual's circumstances, preferences, and needs."
  - "Insulin pump therapy alone with or without a sensor-augmented pump low-glucose suspend feature should be offered for diabetes management to youth and adults on MDI with type 1 diabetes mellitus or other types of insulin-deficient diabetes who are capable of using the device safely (either by themselves or with a caregiver), and who are not able to use or do not choose an AID system.

The choice of device should be made based on the individual's circumstances, preferences, and needs."
    - "Insulin pump therapy can be offered for diabetes management to youth and adults on MDI with type 2 diabetes mellitus who are capable of using the device safely (either by themselves or with a caregiver). The choice of device should be made based on the individual's circumstances, preferences, and needs."
- The 2021 "American Association of Clinical Endocrinology Clinical Practice Guideline: The use of Advanced Technology in the Management of Persons with Diabetes Mellitus" (Grunberger et al.) recommended:
    - "The use of an insulin pump without CGM could be used to manage persons with diabetes mellitus who were achieving glycemic targets with minimal time below range (TBR), who reported infrequent episodes of symptomatic hypoglycemia, and who were using SMBG on a regular basis (at least 4 times per day for persons with T1DM)." Grade B; Intermediate-High Strength of Evidence;
    - "The use of an insulin pump with CGM or SAP was recommended to manage all persons with diabetes mellitus treated with intensive insulin management who preferred not to use automated insulin suspension/dosing systems or had no access to them." Grade A; Intermediate-High Strength of Evidence;
    - "Low-glucose suspend (LGS) was strongly recommended for all persons with T1DM to reduce the severity and duration of hypoglycemia, whereas predictive low-glucose suspend (PLGS) was strongly recommended for all persons with T1DM to mitigate hypoglycemia. Both systems did not lead to a rise in mean glucose, but did lead to increased confidence and trust in the technology, more flexibility around mealtimes, and reduced diabetes mellitus distress for persons with diabetes and caregivers. Therefore, anyone with frequent hypoglycemia, impaired hypoglycemia awareness, and those who feared hypoglycemia leading to permissive hyperglycemia should be considered for this method of insulin delivery." Grade A; High Strength of Evidence;
    - "AID systems were strongly recommended for all persons with T1DM, since their use has been shown to increase TIR, especially in the overnight period, without causing an increased risk of hypoglycemia. Given the improvement in TIR and the reduction in hyperglycemia with AID, this method of insulin delivery was preferred above other modalities. For persons with diabetes mellitus with suboptimal glycemia, significant glycemic variability, impaired hypoglycemia awareness, or who allowed for permissive hyperglycemia due to the fear of hypoglycemia, such AID systems should be considered." Grade A; High Strength of Evidence.

Codes

The inclusion of any code in this table does not imply that the code is under management or requires prior authorization. Refer to the applicable health plan for

management details. Prior authorization of a code listed in this table is not a guarantee of payment. The Certificate of Coverage or Evidence of Coverage policy outlines the terms and conditions of the member's health insurance policy

HCPCS Code	Description
A4224	Supplies for maintenance of insulin infusion catheter, per week
A4225	Supplies for external insulin infusion pump, syringe type cartridge, sterile, each
A4230	Infusion set for external insulin pump, non-needle cannulas type
A4231	Infusion set for external insulin pump, needle cannulas type
A4232	Syringe with needle for external insulin pump, sterile, 3 cc
A4238	Supply allowance for adjunctive, non-implanted continuous glucose monitor (cgm), includes all supplies and accessories, 1 month supply = 1 unit of service
A4239	Supply allowance for non-adjunctive, non-implanted continuous glucose monitor (cgm), includes all supplies and accessories, 1 month supply = 1 unit of service
A9274	External ambulatory insulin delivery system, disposable, each, includes all supplies and accessories
E0782	Infusion pump, implantable, non-programmable (includes all components, e.g., pump, catheter, connectors, etc.)
E0784	External ambulatory infusion pump, insulin
E0785	Implantable intraspinal (epidural/intrathecal) catheter used with implantable infusion pump, replacement
E0786	Implantable programmable infusion pump, replacement (excludes implantable intraspinal catheter)

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