

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Sensor, glucose, implanted, non-adjunctive use

Device Trade Name: Eversense Continuous Glucose Monitoring System

Device Procode: QHJ

Applicant's Name and Address: Senseonics, Incorporated
20451 Seneca Meadows Pkwy
Germantown, MD 20876

Date of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P160048/S006

Priority Review: *Not Applicable*

Date of FDA Notice of Approval: June 6, 2019

An original PMA (P160048) was approved on June 21, 2018 with the following indications:

The Eversense CGM System is indicated for continually measuring glucose levels in adults (age 18 and older) with diabetes for up to 90 days. The system is intended to:

- *Provide real-time glucose readings*
- *Provide glucose trend information.*
- *Provide alerts for the detection and prediction of episodes of low blood glucose (hypoglycemia) and high blood glucose (hyperglycemia).*

The system is a prescription device. Historical data from the system can be interpreted to aid in providing therapy adjustments. These adjustments should be based on patterns seen over time.

The system is indicated for use as an adjunctive device to complement, not replace, information obtained from standard home blood glucose monitoring devices.

The current supplement was submitted to expand the indications for the Eversense CGM System as described below.

II. INDICATIONS FOR USE

The Eversense CGM System is indicated for continually measuring glucose levels in adults (age 18 and older) with diabetes for up to 90 days. The system is indicated for use to replace fingerstick blood glucose measurements for diabetes treatment decisions.

The system is intended to:

- Provide real-time glucose readings.
- Provide glucose trend information.
- Provide alerts for the detection and prediction of episodes of low blood glucose (hypoglycemia) and high blood glucose (hyperglycemia).

The system is a prescription device. Historical data from the system can be interpreted to aid in providing therapy adjustments. These adjustments should be based on patterns seen over time. The system is intended for single patient use.

III. CONTRAINDICATIONS

The following contraindications are included in the labeling:

- The Smart Transmitter is incompatible with magnetic resonance imaging (MRI) procedures. The Smart Transmitter is MR unsafe and **MUST BE REMOVED** before undergoing an MRI (magnetic resonance imaging) procedure. For information on the Sensor, please see MRI Safety Information.
- The system is contraindicated in people for whom dexamethasone or dexamethasone acetate may be contraindicated.
- Mannitol or sorbitol, when administered intravenously, or as a component of an irrigation solution or peritoneal dialysis solution, may increase blood mannitol or sorbitol concentrations and cause falsely elevated readings of your sensor glucose results. Sorbitol is used in some artificial sweeteners, and concentration levels from typical dietary intake do not impact sensor glucose results.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Eversense Continuous Glucose Monitoring System labeling.

V. DEVICE DESCRIPTION

The Eversense Continuous Glucose Monitoring System (Eversense System, or System) provides continuous glucose measurements over a 40-400 mg/dL range. The system provides real-time glucose values, glucose trends, and alerts for high and low glucose through a mobile application installed on a compatible mobile device platform (e.g.,

Android or iOS device). The Eversense System consists of a fluorescence-based glucose sensor (Eversense Sensor) that is inserted under the skin by a Health Care Provider with Insertion Tools; an externally worn Eversense Smart Transmitter (Transmitter); and the Eversense Mobile Medical Application (MMA), which runs on a compatible mobile device. The inserted Sensor is a radiofrequency (RF) powered device that collects readings and sends them to the Transmitter. The Transmitter calculates, stores, and transmits the glucose data via Bluetooth Low Energy (BLE) to the MMA on the mobile device.

The System consists of four principal components:

- 1. Sensor:** The Sensor uses a fluorescence sensing mechanism to detect glucose in the interstitial fluid (ISF). The Sensor is inserted subcutaneously by a Health Care Provider and receives RF-power from the Transmitter to measure interstitial fluid glucose every 5 minutes. The Sensor sends fluorescence measurements to the Transmitter for calculation and storage of glucose values. The Sensor has a silicone collar component that contains 1.75 mg of an anti-inflammatory steroid drug (dexamethasone acetate) that elutes locally to reduce tissue inflammation around the Sensor. The Sensor operating life is the lesser of 90 days or until the device's end-of-life is reached. The Sensor is provided sterile to the Health Care Provider, for single use in a Sensor holder. The Sensor is inserted by a qualified Health Care Provider using the provided Insertion Tools.
- 2. Transmitter:** The Transmitter, worn externally over the inserted Sensor, is a device that powers the Sensor, calculates the glucose values from the Sensor-measured fluorescence readings, and using secure BLE wirelessly sends the glucose information to the MMA for display on the handheld device (HHD). An adhesive patch holds the transmitter in place. The Transmitter contains a rechargeable battery which is charged with a charging cradle powered by a USB connection. The Transmitter also provides vibration signals for alerts and notifications, such as low glucose levels, irrespective of whether the MMA is in the vicinity or not.
- 3. MMA:** The MMA is a software application that runs on a compatible mobile device for display of glucose information provided by the Transmitter. The MMA receives and displays the calculated glucose information from the Transmitter, including glucose trend information and glucose alerts. The MMA also allows the user to calibrate the CGM System by input of blood glucose measurements. It also communicates with the Senseonics server for a one-time download of calibration parameters specific for each Sensor. The MMA also provides the user an option to upload the data to Senseonics Data Management System (DMS) for historic viewing and storing of glucose data.
- 4. Insertion Tools:** Insertion Tools (a Blunt Dissector and Insertion Tool) are provided to the Health Care Provider for Sensor insertion. The Blunt Dissector is used to create the subcutaneous space in which the Sensor is placed. The Sensor holder in which the Sensor is stored during transport and sterilization is used to transfer the Sensor to

Insertion Tool. The Insertion Tool is used to place the Sensor into the subcutaneous space.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are a number of alternative practices used for managing diabetes, and often more than one practice is recommended by Health Care Providers. This includes oral and/or injectable medications, as well as self-monitoring of blood glucose using home blood glucose monitoring devices. Self-monitoring blood glucose meters and test strips provide a blood glucose measurement at a single point in time, whereas CGM provides continuous glucose measurements. Additionally, behavior changes related to physical activity and healthy eating can aid in successful diabetes management.

Each alternative has its own advantages and disadvantages. Patients should thoroughly discuss the alternatives with their Health Care Provider to choose the method that best suits individual expectations and lifestyles.

VII. MARKETING HISTORY

The Eversense Continuous Glucose Monitoring System has been approved for commercial distribution in the United States since June 21, 2018.

A different version of the Eversense CGM System has been approved for commercial distribution in the European Union and European Economic Area countries requiring CE Mark since May 2016, and subsequently in other countries outside of European Union.

The Eversense CGM System has not been withdrawn from commercial distribution in any geography for any reason related to safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with use of the device.

Potential adverse effects related to insertion, removal and wear of the sensor include:

- Allergic reaction to adhesives
- Bleeding
- Bruising
- Infection
- Pain or discomfort
- Scarring or skin discoloration
- Sensor fracture during removal
- Skin inflammation, thinning, discoloration or redness

There are risks relating to difficulty with Sensor removal, and potential risks associated

with subsequent procedures required for Sensor removal. Five instances of difficulty with Sensor removal, one of which was reported as a serious adverse event in which the subjects was referred to a general surgeon for successful Sensor removal, were documented in the clinical studies reviewed. Based on postmarket data available from Europe, and the results observed in these clinical studies, the occurrence of these events is low.

There is a risk of Sensor breakage leaving a Sensor fragment under the skin. Two instances of Sensor breakage were documented in the clinical studies reviewed. Based on postmarket data available from Europe and the results observed in these clinical studies, the occurrence and severity of these events is low.

There may be potential risks relating to repeated insertion and removal procedures, including buildup of scar tissue over time at the sensor insertion site, in a small range of locations on the outside surface of the upper arms. Based on postmarket data available and the results observed in these clinical studies, these risks are not expected to occur.

The Eversense CGM System has a drug component, consisting of 1.75 mg of dexamethasone acetate (DXA), contained in a dexamethasone eluting silicone collar placed on the outside of the Eversense Sensor. Based on information and clinical evaluations performed, the sponsor has demonstrated that risks relating to both local and potential systemic exposures to the dexamethasone component of the device, as well as repeated exposure to the dexamethasone component of the device, are not expected to occur.

These risks appear to be remote based on the results observed in these clinical studies, although these clinical studies did not include subjects taking dexamethasone (or other glucocorticoid medications).

There is a minor risk of skin irritation, inflammation, or infection due to either the Sensor or the adhesive.

There are potential adverse effects associated with making diabetes treatment decision when glucose values and rates of change provided by the device are inaccurate, as follows:

The risks of making treatment decisions based on falsely high readings include inappropriate or excessive administration of insulin. These inappropriate treatments could increase the risk of hypoglycemia or prolong existing hypoglycemia which can result in seizures, loss of consciousness, and rarely, death.

The risks of making treatment decisions based on falsely low readings include inappropriate administration of carbohydrates. These inappropriate treatments could increase the risk of hyperglycemia or prolong existing hyperglycemia, increasing exposure to long-term microvascular complications of diabetes (eye, kidney, nerve and heart disease) and acute diabetic ketoacidosis (DKA) which can result in weakness,

seizures, and death.

The risks of making treatment decisions based on inaccurate calculation of the rate of change of glucose could increase the risk of serious hypoglycemia or hyperglycemia if treatment is influenced by the inaccurate rate of change. Inaccurate calculation of the rate of change of glucose could also prevent a patient from taking measures to prevent a sustained increase or decrease in glucose levels, which could lead to serious hypoglycemia or hyperglycemia.

The device also provides glucose alerts; these alerts may cause a user to take action to prevent potential future glycemic events. Potential adverse events may therefore also result from inaccuracies that cause a failure to trigger alerts, or cause false alerts. This may cause users to take an inappropriate action, or incorrectly take no action, and result in increased risk or prolongation of hyperglycemia or hypoglycemia.

There are potential risks associated with making acute and long-term therapy adjustments when glucose values and rates of change provided by the device are inaccurate. The risks of making therapy adjustments based on inaccurate device information include inappropriate adjustment of diabetes medication regimens. This could increase the risk of hypoglycemia and corresponding risk of seizures, loss of consciousness, and rarely, death; it may also increase the risk of hyperglycemia, increasing exposure to long-term microvascular complications of diabetes (eye, kidney, nerve and heart disease) and risk of acute diabetic ketoacidosis (DKA) which can cause weakness, seizures, and death.

The body-worn Transmitter component of the system provides an alternate means of delivering alerts to users through vibratory feedback. The level of information necessary to understand the safety aspects of the user interface, and how it supports the user and reduces the potential for use error was provided by the sponsor and found to be adequate. There may be an additional risk that the display, or alerts related to the CGM device may not be able to override other applications or functions (phone, camera, SMS) within the mobile device. This risk could potentially result in missed alerts, or temporary loss of access to the display. Missed alerts, or inability to access the display could result in missed opportunities to detect or prevent hypoglycemia or hyperglycemia and are discussed above. Human factors studies conducted assessed the safety of the user interface of the mobile app (sole display) for this device, and the ability for users to receive and understand alerts and notifications via the Transmitter vibration feature. The human factors studies sufficiently assessed the potential for user error associated with comprehension of the impact of mobile device and app settings on notifications and Bluetooth communications, as well as use of the audio override feature.

IX. SUMMARY OF PRECLINICAL STUDIES

Non-clinical performance characteristics and preclinical validation of the Eversense CGM System was established in preclinical studies summarized in the SSED for P160048. The changes from the approved Eversense CGM System are limited to software changes to the user interface intended to support non-adjunctive use and which

would not affect non-clinical performance of the device. Therefore, new preclinical studies, other than software verification and validation studies and human factors studies for non-adjunctive use, were not needed.

A. Laboratory Studies

Bench testing that was conducted to support safety and effectiveness of the Eversense CGM System was provided in the SSED for P160048. Additional testing to support device modifications related to the change in the indications is described below:

Software: Software verification and validation testing of the modified user interface software (mobile app) was performed in accordance with the FDA guidance document entitled “Guidance for the Contents of Premarket Submissions for Software Contained in Medical Devices,” dated May 11, 2005. Verification and validation testing included units test, system level verification tests (which included functional testing to demonstrate the device meet its requirements), code review, traceability linking and validation testing to ensure the software conforms to user needs and intended uses. Specific test methods, acceptance criteria, and test results were reviewed and found acceptable.

Human Factors/Usability: Human factors validation testing was conducted per the FDA guidance entitled “Applying Human Factors and Usability Engineering to Medical Devices” dated February 3, 2016. Human factors testing was conducted to support the non-adjunctive use, including human factors studies with patient users and caregiver users. The human factors validation evaluation and testing demonstrates that the device can be used by the intended users without serious use errors or problems, for the intended uses and under the expected use conditions.

B. Animal Studies

No new animal studies were needed to support this PMA supplement. Please refer to SSED P160048 for the animal studies supporting the original PMA application.

C. Additional Studies

No additional studies were performed to support this PMA Supplement. Please refer to SSED P160048 for the additional studies supporting the original PMA application.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

No new clinical studies were conducted to support the change in the indications for the device. The applicant previously performed clinical studies to establish the clinical measurement performance characteristics of the device, including accuracy across the claimed measuring range (40 to 400 mg/dL glucose), precision, claimed calibration frequency (every 12 hours), the wear period for the sensor (90 days), and performance of the alerts and notifications. Information obtained in those studies was used to support a

determination of safety and effectiveness of the device for use as an adjunctive device to complement, not replace, information obtained from standard home glucose monitoring devices. These clinical studies were conducted under IDE #G150165 and a summary of these studies is provided in SSED for P160048.

This same clinical study information was also used to support a reasonable assurance of safety and effectiveness of the Eversense Continuous Glucose Monitoring System for replacement of fingerstick blood glucose monitoring for diabetes treatment decisions in the US.

As a condition of approval, the applicant will conduct a post-approval study. The study will be a non-blinded, prospective, multi-center, single arm longitudinal cohort study, to evaluate the safety and effectiveness of diabetes management with the Eversense CGM System non-adjunctively compared to self-monitoring of blood glucose using a blood glucose meter in participants with either Type 1 or Type 2 diabetes. Subjects will serve as their own control, with their baseline based on using SMBG to manage their diabetes for the first 6 months of the study followed by using the Eversense CGM System non-adjunctively for the next 6 months. Total follow-up duration is 12 months.

Approximately 925 subjects will be screened to achieve approximately 740 subjects at the end of the study. The investigation will include both clinic visits and home use of Eversense CGM System. The non- adjunctive phase will include insertion and wear of two sensors, up to 90-day duration each, inserted sequentially. All care decisions specific to diabetes will be based on blood glucose (BG) values in the first phase and the Eversense CGM system values (in accordance with device labeling) in the second phase.

The primary study endpoint will be the incidence of severe hypoglycemia and diabetic ketoacidosis events. Secondary endpoints will include (1) rate of all device-related and insertion and removal procedure-related adverse events, (2) rate of adverse events related to use of the user interface, patient training or labeling materials, (3) Change in HbA1c from baseline at 6 and 12 months, (4) average hours of use per day, and (5) serious adverse events regardless of causality.

A. Study Design

A summary of the clinical study designs is provided in SSED for P160048.

B. Accountability of PMA Cohort

A summary of the cohort accountability is provided in SSED for P160048.

C. Study Population Demographics and Baseline Parameters

A summary of the study population demographics and baseline parameters is provided in SSED for P160048.

D. Safety and Effectiveness Results

1. Safety Results

A summary of safety results is provided in SSED for P160048. For other information considered for this PMA supplement, see Sections XI and XII, below.

2. Effectiveness Results

A summary of effectiveness results is provided in SSED for P160048. For other information considered for this PMA supplement, see Sections XI and XII, below.

E. Financial Disclosure

A summary of financial disclosure information is provided in SSED for P160048.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA Supplement was not referred to the Clinical Chemistry and Toxicology Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The results of the clinical studies performed by the applicant establish a reasonable assurance of effectiveness of the Eversense CGM System to be used as intended in the intended use population. The primary effectiveness measurements for the clinical studies were based on the performance evaluation of the Eversense CGM System compared to the blood glucose values measured by the laboratory glucose analyzer during the in-clinic sessions that spanned the wear period of the device (days 1, 7, 14, 30, 60, and 90).

The clinical measurement performance data are also comparable to currently approved CGM devices approved for non-adjunctive use. The data support acceptable accuracy and performance across the claimed measuring range (40 to 400 mg/dL), precision, 90-day wear period claims for the Sensor, and effective alerts for detection and prediction episodes of hypoglycemia and hyperglycemia.

The clinical and analytical studies demonstrate that the Eversense CGM System is effective in the study population designed to be representative of the intended use population.

B. Safety Conclusions

The risks of the device are based on the adverse events observed in the clinical studies described in section X above, and the potential adverse effects of the device on health as described in the SSED for P160048.

The following related adverse events were observed from using the Eversense CGM System: pain/discomfort, bruising, erythema, retained Sensor fragment, failure to remove Sensor on first attempt, skin hyperpigmentation, dermatitis at patch location, paresthesia, and syncope-vasovagal.

There are potential adverse effects associated with making diabetes treatment decisions when glucose values and rates of change provided by the device are inaccurate, as follows:

The risks of making treatment decisions based on falsely high readings include inappropriate or excessive administration of insulin. These inappropriate treatments could increase the risk of hypoglycemia or prolong existing hypoglycemia which can result in seizures, loss of consciousness, and rarely, death.

The risks of making treatment decisions based on falsely low readings include inappropriate administration of carbohydrates. These inappropriate treatments could increase the risk of hyperglycemia or prolong existing hyperglycemia, increasing exposure to long-term microvascular complications of diabetes (eye, kidney, nerve and heart disease) and acute diabetic ketoacidosis (DKA) which can result in weakness, seizures, and death.

Inaccurate calculation of the rate of change of glucose by the device could increase the risk of serious hypoglycemia or hyperglycemia if treatment is influenced by the inaccurate rate of change. Inaccurate calculation of the rate of change of glucose by the device could also prevent a patient from taking measures to prevent a sustained increase or decrease in glucose levels, which could lead to serious hypoglycemia or hyperglycemia.

There are potential adverse effects associated with making acute and long-term therapy adjustments when glucose values and rates of change provided by the device are inaccurate. The risks of making therapy adjustments based on inaccurate device information include inappropriate adjustment of diabetes medication regimens. This could increase the risk of hypoglycemia and corresponding risk of seizures, loss of consciousness, and rarely, death; it may also increase the risk of hyperglycemia, increasing exposure to long-term microvascular complications of diabetes (eye, kidney, nerve and heart disease) and risk of acute diabetic ketoacidosis (DKA) which can cause weakness, seizures, and death.

The device also provides glucose alerts; these alerts may cause a user to take action to prevent potential future glycemic events. Potential adverse events may therefore also

result from inaccuracies that cause a failure to trigger alerts, or cause false alerts. This may cause users to take an inappropriate action, or incorrectly take no action, and result in increased risk or prolongation of hyperglycemia or hypoglycemia.

C. Benefit-Risk Conclusions

The probable benefits and risks of the device are based on data collected in clinical studies conducted to support PMA approval as described in the SSED for P160048, and based on human factors studies conducted to support approval of this supplement. Potential adverse effects of the device on health are described in Section VIII above. A summary of the Benefits and Risks of the device is presented below.

This submission is for a change to the indications for use to allow the device to be used to replace self-monitoring of blood glucose in making diabetes treatment decisions (non-adjunctive use). The device provides users with an updated glucose value every 5 minutes and information on the direction and rate of change of glucose levels based on recent measurements. The adjustable hypoglycemia and hyperglycemia alerts, and rate of change alerts, are intended to warn users that they may need to take action to treat or prevent a hypoglycemic or hyperglycemic event.

Continuous glucose measurement and real-time passive alert functionality is not available using traditional blood glucose monitoring. Blood glucose meters only provide information about discrete, intermittent blood glucose levels in response to a user-initiated action, and therefore are unable to passively monitor and provide information about patterns of glycemic excursions throughout the day and night when patients are unable to test their blood glucose. Furthermore, real time knowledge of whether blood glucose is increasing or decreasing adds information unavailable from traditional discrete monitoring and has the potential to improve therapeutic decision making relative to intermittent blood glucose monitoring. For example, information regarding glucose level direction and rate of change can alert users to take action to prevent hypoglycemia or hyperglycemia, and to modify therapeutic decision making to account not only for a glucose value but also for how glucose levels are changing. The availability of continuous glucose monitoring and accompanying alerts is especially helpful for individuals with hypoglycemia unawareness (these individuals may develop severe hypoglycemia with loss of consciousness, seizures, or rarely death without the normal warning symptoms), during times when patients are unable to easily check their blood glucose using a traditional blood glucose meter, and during the night when patients may have prolonged hypoglycemia that does not waken them and which could proceed to severe hypoglycemia if not treated in time. Traditional blood glucose monitoring is not able to capture these potentially dangerous episodes of asymptomatic hypoglycemia or alert users to hyperglycemia or hypoglycemia in the absence of user action. Use of a mobile device as the display is beneficial to patients, as it offers convenience in terms of decreasing the number of devices required to be with the patient to utilize this CGM device. Therefore, this device provides significant benefits to users not possible with traditional glucose monitoring.

Non-adjunctive use of the Eversense CGM System is expected to provide the benefit of decreased pain relative to fingerstick measurements. Non-adjunctive use of the Eversense CGM System is expected to be associated with increased access to glucose information and decreased burden of self-monitoring blood glucose (SMBG) based diabetes treatment decisions. The decreased daily burden of use of the Eversense CGM System to replace fingerstick glucose measurements can additionally have psychosocial benefit (e.g. reduced burnout and perceived stigma). SMBG adherence is known to be suboptimal, and non-adjunctive use of the Eversense CGM System could increase adoption of continuous glucose monitor use and provide opportunities for easier and more convenient glucose monitoring to patients with diabetes, while providing the added benefits of this device.

Compared to other currently marketed CGM Systems, this device has potential additional advantages associated with a significantly longer wear period (90 days) compared to the wear periods of currently marketed (6-14 day) CGM Systems. The longer-term sensor eliminates the need for patients to insert a new sensor every 7-14 days, and the transmitter can be removed without ending the sensor life. The longer-term sensor could result in increased utilization of CGM technology by patients. A subcutaneously implanted sensor provides the potential benefits of not being susceptible to being accidentally removed, which is known to occur with other currently marketed CGM systems. Because the body-worn transmitter can be removed and replaced at any time, this may also provide some patients with the benefit of increased discretion regarding use of a CGM system. The transmitter adhesive, designed to allow daily removal and re-application, may also provide benefit to patients who experience skin sensitivity to the adhesives used in other currently marketed CGM systems. Further, the transmitter itself provides vibratory alerts, in contrast to other currently marketed CGM Systems.

Similar to other marketed CGM Systems with a similar indications for use, this device has the following risks:

Risks of treatment decisions made from falsely high CGM readings include inappropriate or excessive administration of insulin. These inappropriate treatments could increase the risk of hypoglycemia or prolonged hypoglycemia which can result in seizures, loss of consciousness, or rarely, death. Risks of treatment decisions made from falsely low CGM readings include inappropriate administration of carbohydrate. These inappropriate treatments could increase the risk of hyperglycemia or prolonged hyperglycemia, which can progress to diabetic ketoacidosis, and result in loss of consciousness, or rarely, death.

Inaccurate calculation of the rate of change of glucose by the device could prevent a patient from taking measures to stop a trend of increasing or decreasing glucose levels which could lead to serious hypoglycemia or hyperglycemia. This could also lead patients to make inappropriate adjustments to their treatment, resulting in serious hypoglycemia or hyperglycemia. also increase the risk of serious hypoglycemia or

hyperglycemia if treatment is influenced by the inaccurate rate of change. With non-adjunctive use of the Eversense CGM System, there are risks due to missed alerts and false negative hypoglycemia and hyperglycemic readings related to patients not being alerted of potential hypoglycemia or hyperglycemia, particularly since users of this device may rely on these alerts in certain situations to guide their self-treatment strategy (e.g., to alert them to potential nighttime hypoglycemia).

Compared to other marketed CGM Systems with similar indications for use, this device has additional potential risks, which do not differ from the currently marketed version (for adjunctive use) of the Eversense CGM System (P160048, approved in June 2018). A description of these potential risks follows:

There are potential risks relating to the insertion and removal procedures required for use of the Eversense CGM System, which involves an outpatient based procedure. Designation of specific healthcare providers, required training for the insertion and removal procedures, as well as adequate labeling, is helpful to mitigate these risks. Potential risks relating to insertion and removal procedures include pain, inflammation, infection, and sensor breakage leaving a sensor fragment under the skin in the subcutaneous tissue. There are also risks relating to difficulty with sensor removal, and risks associated with subsequent procedures (i.e., anesthesia, pain, infection) to attempt sensor removal. In addition, there may be potential risks relating to repeated insertion and removal procedures including scar tissue buildup, as the outside side of the upper arms is the only sensor insertion site. A post-approval study is currently in progress to confirm the safety of the insertion and removal procedures relating to the currently marketed device.

The Eversense CGM System has a drug component, consisting of 1.75mg of dexamethasone acetate (DXA), contained in a dexamethasone eluting silicone collar to the outside of the Eversense Sensor. The sponsor has provided sufficient information and evaluation to reasonably demonstrate that the risks relating to the dexamethasone component of the device are not expected to occur. The sponsor has demonstrated that clinically significant systemic exposure to the dexamethasone component of the device are not expected to occur. The sponsor has also provided information to indicate that wound healing as well as the local area surrounding the device insertion site are not adversely affected. Further, there may be a potential risk relating to repeated exposure to dexamethasone, but these risks seem to be unlikely, given the lack of systemic or local effects relating to a single exposure to dexamethasone.

The sponsor did not conduct a new clinical study to support the approval of this new indication for use. Instead, a post-approval clinical study will be used to confirm the safety and effectiveness of the Eversense CGM System. This is necessary considering the non-adjunctive (high-risk) claim, high-risk patient population intended to use the device, and residual uncertainty relating to real-world performance of this device, considerations relating to this device constituting relatively new technology, as well as confirmation of safety relating to usability of the device for the new indication for

use, and the updates to the user interface.

Patient Perspective:

Patient perspectives considered during the review included patients' preference for CGMs that can be used non-adjunctively, longer CGM sensor wear times, elimination of frequent self-insertion, and a totally subcutaneous sensor. The comparatively short sensor life of 6-14 days for other non-adjunctive CGM systems, the need to self-insert the sensor, the need for the transmitter to remain adhered to the skin for the sensor duration, and the inconveniences of wearing a percutaneous sensor that can be dislodged during normal activities have been noted as sources of patient dissatisfaction with other non-adjunctive CGM systems. The benefits of the Eversense CGM System may result in increased utilization of CGM technology.

D. Overall Conclusions

In conclusion, the Eversense CGM has demonstrated effectiveness and safety in bench, pre-clinical, and clinical studies. The data in this application support the reasonable assurance of the safety and effectiveness of this device when used in accordance with the indication for use.

The benefits of using the System, as discussed above, outweigh the risks.

XVI. CDRH DECISION

CDRH issued an approval order on June 6, 2019. The final conditions of approval cited in the approval order are described below.

The applicant is required to conduct a Post Approval Study (PAS) meeting the following criteria: The Post Approval Study to Evaluate the Safety and Effectiveness of the Eversense Continuous Glucose Monitoring (CGM) System Used Non-Adjunctively is a non-blinded, prospective, multi-center, single arm longitudinal cohort study (patient serving as their own control), to evaluate the safety and effectiveness of diabetes management with the Eversense CGM System non-adjunctively compared to self-monitoring of blood glucose (SMBG) using a blood glucose (BG) meter in participants with either Type 1 or Type 2 diabetes. Subjects will serve as their own control, with their baseline based on using SMBG to manage their diabetes for the first 6 months followed by using Eversense CGM System non-adjunctively for the second 6 months. Total follow-up duration is 12 months.

Approximately 925 subjects will be screened to achieve approximately 740 subjects at the end of the study. The investigation will include both clinic visits and home use of Eversense CGM System. The non- adjunctive phase will have two sensors, up to 90-day duration, inserted sequentially. All care decisions specific to diabetes will be based on blood glucose (BG) values in the first phase and the Eversense CGM system values in the second phase.

The primary study endpoint will be the incidence of severe hypoglycemia and diabetic ketoacidosis events. Secondary endpoints will include (1) rate of all device-related and insertion and removal procedure-related adverse events, (2) rate of adverse events related to use of the user interface, patient training or labeling materials, (3) Change in HbA1c from baseline at 6 and 12 months, (4) average hours of use per day, and (5) serious adverse events regardless of causality.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.