September 13, 2024

Epitomee Medical Ltd.
% Janice Hogan
Regulatory Counsel
Hogan Lovells US LLP
1735 Market Street Suite 2300
Philadelphia, Pennsylvania 19103

Re: K240544
Trade/Device Name: Epitomee
Regulation Number: 21 CFR 876.5982
Regulation Name: Ingested, Transient, Space Occupying Device For Weight Management And/Or Weight Loss
Regulatory Class: Class II
Product Code: QFQ
Dated: February 27, 2024
Received: August 16, 2024

Dear Janice Hogan:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-

assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Anthony Lee -S

Anthony C. Lee, Ph.D., M.B.A.
Assistant Director
DHT3A: Division of Renal, Gastrointestinal, Obesity, and Transplant Devices
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Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

Submission Number *(if known)*

K240544

Device Name

Epitomee

Indications for Use *(Describe)*

Epitomee is indicated to aid in weight management in overweight and obese adults with a Body Mass Index (BMI) of 25 - 40 kg/m2, when used in conjunction with diet and exercise.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(K) SUMMARY

Epitomee Medical's Epitomee

Submitter

Epitomee Medical Ltd.
17 Hatochen St.
Caesarea
Israel

Contact Person: Ruthie Amir

Date Prepared: September 12, 2024

Name of Device: Epitomee

Common Name: Weight management device

Regulation Number: 21 CFR 876.5982

Classification Name: Ingested, transient, space occupying device for weight management and/or weight loss

Product Code: QFQ

Regulatory Class: II

Predicate Device: Gelesis Inc.'s Plenity (DEN180060)

Device Description

The subject device of this 510(k) notification, Epitomee, is comprised of two components: The outer component is a capsule and the inner component contains superabsorbent hydrogel particles. Each particle is approximately 250 microns in size. The particles are enclosed in pH sensitive compartments. Once Epitomee is swallowed, the capsule disintegrates in the stomach and releases the pH sensitive compartments. By absorption of water in the stomach fluid, the superabsorbent particles within the compartments swell to form a three-dimensional matrix designed to occupy volume in the stomach that creates a sensation of fullness, enabling weight loss. Epitomee mechanism of action is purely mechanical and does not involve any chemical activity. Epitomee works directly in the gastrointestinal (GI) tract. Epitomee is provided non-sterile.

Intended Use / Indications for Use

Epitomee is intended to aid in weight management in overweight and obese adults with a Body Mass Index (BMI) of 25 - 40 kg/m^2, when used in conjunction with diet and exercise.

Summary of Technological Characteristics

Epitomee has very similar technological characteristics compared to the predicate device. Both devices are composed of two major components: an outer capsule and an inner expendable component occupying space in the stomach. Both devices are ingestible, transient, space occupying devices designed as a standard capsule for oral intake. For both devices the oral capsule encloses self-expandable particles that form a three-dimensional matrix designed to occupy volume in the stomach, to create a sensation of fullness. The capsule of both devices disintegrates in the stomach and releases the enclosed self-expanded particles. For both devices the hydrogel particles increase their weight and dimensions after absorbing water from the stomach and both devices interact with the stomach by occupying volume. Both devices are self-disintegrated to enable natural evacuation through gastric emptying.

Although the subject device consists of a triangular arrangement and has a smaller net volume than the predicate, the triangular shape of the compartments was designed to attain relatively large dimensions, creating a space occupying tree-dimensional structure and the difference does not raise new questions of safety or effectiveness as both devices achieve their intended use by occupying volume in the stomach, thereby creating sensation of fullness. Clinical study results showed that the subject device is as safe and effective as the predicate device. In addition, despite the different materials used by the two devices, both devices utilize hydrogel materials to expand with water. Both devices have been demonstrated to be biocompatible. Furthermore, both devices are intended to degrade within the user's GI tract and be eliminated through normal bowel movements emptying.

A table comparing the key features of the subject and predicate device is provided below.

Epitomee Substantial Equivalence Chart

	Epitomee Medical's Epitomee **(Subject Device)**	**Gelesis Inc/'s Plenity** **(DEN180060)** **(Predicate Device)**
Regulatory Class	II	II
CFR Regulation	21 CFR 876.5982	21 CFR 876.5982
Product Code	QFQ	QFQ
Intended Use	Epitomee is indicated to aid in weight management in overweight and obese adults with a Body Mass Index (BMI) of 25 - 40 kg/m^2, when used in conjunction with diet and exercise.	Plenity is indicated to aid in weight management in overweight and obese adults with a Body Mass Index (BMI) of 25 - 40 kg/m^2 , when used in conjunction with diet and exercise.

	Epitomee Medical's Epitomee **(Subject Device)**	**Gelesis Inc/'s Plenity** **(DEN180060)** **(Predicate Device)**
Treated area/Site of application in the body	Non-systemic and works directly in the gastrointestinal (GI) tract (stomach)	Non-systemic and works directly in the gastrointestinal (GI) tract (stomach)
System components	An outer capsule that is swallowed by the patients and an inner expendable device occupying space in the stomach	An outer capsule that is swallowed by the patients and an inner expendable device occupying space in the stomach
Administration	Standard capsule for oral intake; 2 capsules per day (one capsule before lunch and one capsule before dinner) with water	Standard capsule for oral intake; 6 capsules per day (3 capsules before lunch and 3 capsules before dinner) with water
Duration of Use	6 months	6 months
Device Design/Mode of Action	The device is an ingestible, transient, space occupying device designed as a standard capsule for oral intake. The oral capsule contains thousands of particles. The particles are contained in compartments and can each hydrate up to 100 times their original weight, to form a three-dimensional matrix designed to occupy volume in the stomach..	The device is an ingestible, transient, space occupying device designed as a standard capsule for oral intake. The oral capsule contains thousands of Plenity particles. The particles are non-clustering and can each hydrate up to 100 times their original weight, to form a three-dimensional matrix designed to occupy volume in the stomach.
Capsule Material	Pharmaceutical grade hydroxypropyl methylcellulose (HPMC) capsule	Porcine gelatin capsule
Biocompatibility	Biocompatible	Biocompatible

	Epitomee Medical's Epitomee **(Subject Device)**	**Gelesis Inc/'s Plenity** **(DEN180060)** **(Predicate Device)**
Compartment Size Deployed	Particles contained in three compartments that form a three-dimensional triangular matrix once hydrated in the stomach. The total net volume in the stomach is 17cc, with each edge of triangular matrix having a dimension of 62 mm	The Plenity device does not contain a compartment. It contains thousands of particles that form a non-clustering three-dimensional matrix in the stomach once hydrated. The total volume is approximately one quarter of the stomach volume
Self-Expanding	Self-expanding when hydrated	Self-expanding when hydrated
Principles of Operation	The capsule disintegrates in the stomach, allowing water to penetrate the envelope and hydrate the gel particles. The expansion of the particles results in unfolding of the device into a three-dimensional matrix composed of 3 identical compartments occupying volume in the stomach. The hydrogel particles increase their weight and volume after absorbing the water from the stomach. When fully hydrated, the Epitome structure occupies only about 17cc net volume in the stomach, with each edge of the triangular matrix having a dimension of 62 mm, generating a space occupying tree-dimensional structure to create a sensation of fullness.	The capsule disintegrates in the stomach allowing water to hydrate the gel particles. The gel particles spread and form a three-dimensional matrix occupying volume in the stomach. The hydrogel particles increase their weight and volume after absorbing the water from the stomach. When fully hydrated, the Plenity particles occupy about quarter of average stomach volume to create a sensation of fullness.
Release characteristics of substances	The capsule disintegrates in the stomach and releases the particles enclosed in the compartments	The capsule disintegrates in the stomach and releases the contained particles.

	Epitomee Medical's Epitomee **(Subject Device)**	**Gelesis Inc/'s Plenity** **(DEN180060)** **(Predicate Device)**
Degradation mechanism and profile	Epitomee self-disintegrates. Epitomee passes through the pylorus and device breaks down in the small intestine where the hydrogel particles are free to flow with the mix outside the body.	The Plenity device self-disintegrates. Plenity passes through the digestive system maintaining its three-dimensional structure in the stomach and small intestine before breaking down in the colon and flowing freely with the mix outside the body. The water is then released and reabsorbed by the body. Plenity particles are eliminated through normal bowel movements.

Performance Data

Nonclinical and clinical studies have been conducted to demonstrate the performance of Epitomee.

Biocompatibility

Epitomee underwent biocompatibility assessment according to ISO 10993-1 requirements for a device having permanent (> 30 days) surface contact with mucosal membranes. All the biological endpoints have been addressed by biocompatibility studies and/or rationales as the device components have long and documented history of safe use. Endpoints considered are:

- Cytotoxicity
- Sensitization
- Irritation
- Acute Systemic Toxicity
- Genotoxicity
- Sub-chronic Toxicity
- Chronic Toxicity
- Carcinogenicity
- Material Mediated Pyrogenicity
- Implantation

Nonclinical Testing

Bench testing has been conducted to demonstrate that the Epitomee meets its specification as functions as intended. The testing includes:

- Device dimensional verification
- Device inflation
- Device functional performance
- Device mechanical Integrity
- Device loss of rigidity
- Device inflation with different beverages and food mediums
- Shape retention
- Device clearance from stomach
- Device degradation in intestine
- Device irregular surface test
- Device interaction with medication

The *in vitro* tests of inflation and degradation were verified by *ex vivo* studies. In addition, potential interaction between the Epitomee and Metformin was evaluated. GLP animal studies were conducted to demonstrate the device safety in vivo.

Clinical Data

The performance of Epitomee is supported by multiple clinical studies.

Pivotal Clinical Study (RESET Study)

The RESET study was a prospective, randomized, double-blind, placebo-controlled, multicenter trial to support the use of Epitomee for weight reductions in patients. The study enrolled 279 men and non-pregnant, non-lactating women, 18 years of age or older, who are overweight (body mass index [BMI] of 25-30 kg/m^2) or obese (BMI of 30-40 kg/m^2), with and without prediabetes. All 9 sites enrolled in the study were in the US, located across 9 different states.

The subjects were evenly matched for gender and age groups with females constituting 80.4% and 79.4% of the Epitomee and placebo groups, respectively, and the majority of subjects being between 40 and 65 years of age (66.7% and 67.4% in the Epitomee and placebo groups, respectively). Mean BMI was 34.1 in Epitomee group and 33.7 in the placebo group. The majority of the study subjects were Caucasian, with 70.3% and 65.2% of the recruited in the Epitomee and placebo groups, respectively. Black or African American subjects constituted 21.0% and 24.1% of the total sample in the Epitomee and placebo groups, respectively.

Eligible subjects were randomized to test or placebo arms. Subjects were to take one capsule of the investigational device or placebo twice daily, with 2 cups of water half-hour before the main meals, for 24 weeks. Subjects in both groups received the same program of diet, physical activity, and behavior therapy. Efficacy and safety assessments were conducted up to week 24 since start of the study treatment. An additional safety assessment was conducted at week 28.

The study demonstrated that both co-primary endpoints were successfully met. Epitomee treatment group total body weight (TBW) reduction at 24-weeks post randomization was significantly greater (mean, 6.6%; SD, 6.5) than the placebo group (mean, 4.6%; SD, 4.7) (P<0.0001). The co-primary endpoint of treatment responders was also achieved: the rate of Epitomee treatment group subjects whose total body weight was reduced by at least 5% at 24-weeks post randomization was 55.5% (CI; 46.1-64.6), significantly exceeding the threshold of >35% (P<0.0001).

Subgroup analyses were performed to evaluate total body weight loss at week 24 in clinically relevant subgroups of patients (gender, baseline BMI categories, subjects with %TBW≥0) and showed higher TBW reduction in the Epitomee arm than the placebo arm. The differences between the arms ranged from approximately 2%-5%.

Epitomee capsule treatment efficacy is further supported by the analysis of secondary endpoints. Epitomee capsule treatment resulted in a significantly higher percentage of responders losing between 7.5-12.5% of TBW as compared to the placebo treatment. Specifically, 38.7% of Epitomee treated patients achieved ≥ 7.5%, 26.9% achieved ≥ 10%, and, 16.8%, ≥ 12.5% of TBW loss compared to 21.5%, 10.7% and 6.6% in the placebo group. Consistent with the weight reduction results, Epitomee treatment achieved a greater reduction in Excess Weight Loss (EWL) and higher BMI reduction over time resulting in more subjects shifting from obesity Class II to a lower obesity category.

Finally, subjects treated with Epitomee showed better improvement in quality of life in several items of the IWQOL-Lite-CT questionnaire as well as the physical function relative to the placebo group, with physical function score being statistically meaningful and both physical score and total score being marginally significance.

The study demonstrated a favorable safety profile of Epitomee treatment throughout the study duration. Epitomee treatment was well tolerated, with fewer patient dropouts in Epitomee group than the control group 19 (13.8%) and 20 (14.2%), respectively. There were no serious adverse device effects (SADEs) in the study.

There were no differences in the incidence of treatment-emergent AEs between the study groups. Adverse events were equally distributed between the groups when assessed by severity. There were no differences in the incidence of treatment-emergent AEs between the groups in relation to causality, AE outcome, and action taken. In both groups, almost all adverse events were assessed by the investigator as mild or moderate in intensity (>95%). The overall incidence of treatment-emergent gastrointestinal adverse events was no different in the Epitomee group vs. the control group.

Notably, the safety and efficacy performance of Epitomee as shown in the RESET study was very similar to that of the predicate device.

Extended Study (ELECT Study)

The ELECT study assessed the effect of Epitomee on body weight after an additional exposure of 24 weeks in subjects from the RESET pivotal study. Subjects from Epitomee and Placebo

groups in the RESET study who completed the 24-week treatment period and had at least 3% weight loss were offered to participate in this extended study. The ELECT study is an open-label, one arm extension study and all subjects were treated with Epitomee, twice daily. Sixteen (16) subjects who were assigned to the placebo during RESET crossed over to the Epitomee group (Placebo-Epitomee) and 17 subjects who were assigned to the Epitomee group during the RESET continued Epitomee for an additional 24 weeks (Epitomee-Epitomee).

Safety results from the ELECT study showed that the overall incidence of AEs was no different between the Epitomee subjects who were exposed for an entire year (27 AEs in 12 [70.6%] subjects) versus the Placebo subjects who were switched to Epitomee and were exposed to Epitomee for the first time for a period of 24 weeks (17 AEs in 10 [62.5%] subjects). All AEs in the ELECT study were mild gastrointestinal (GI) events, and all recovered. There were no deaths or SAEs.

Gastric Emptying Study

Epitomee Medical has conducted a prospective, single center, open-label, single-arm study to examine the effect of the Epitomee device on gastric emptying rate in healthy subjects. Ten (10) healthy subjects were enrolled in the study. Subjects completed a gastric emptying test using gastric scintigraphy before taking Epitomee (baseline). Following the baseline scintigraphy, the subjects received the Epitomee device treatment for 10 consecutive days, and underwent another gastric emptying test with capsule intake prior to the test meal.

The results showed that Epitomee was well-tolerated and had a favorable safety profile with no SAEs. There was no significant effect on gastric emptying with Epitomee.

Conclusions

Epitomee is as safe and effective as its predicate device. Epitomee has the same intended use and indications for use, and similar technological characteristics as its predicate device. The minor technological differences between Epitomee and its predicate device raise no new issues of safety or effectiveness. Performance data demonstrate that Epitomee is as safe and effective as the predicate device. Thus, Epitomee is substantially equivalent.