NEW DRUG APPROVAL

Brand Name	Camcevi™
Generic Name	leuprolide
Drug Manufacturer	Foresee Pharmaceuticals Co., Ltd.

New Drug Approval

FDA Approval Date: May 25, 2021

Review Designation: Standard

Type of review: Type 2 - New Active Ingredient; New Drug Application (NDA): 211488

Dispensing restriction: N/A

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Prostate cancer is cancer that occurs in the prostate. The prostate is a small walnut-shaped gland in males that produces the seminal fluid that nourishes and transports sperm. When prostate cancer spreads beyond the prostate or returns after treatment, it is often called advanced prostate cancer.

Prostate cancer is often grouped into four stages.

Stages I & II: The tumor has not spread beyond the prostate. This is often called “early stage” or “localized” prostate cancer.

Stage III: Cancer has spread outside the prostate, but only to nearby tissues. This is often called “locally advanced prostate cancer.”

Stage IV: Cancer has spread outside the prostate to other parts such as the lymph nodes, bones, liver or lungs. This stage is often called “advanced prostate cancer.”

In total, there were 3,087,800 new prostate cancer cases diagnosed in the United States between 2003 and 2017. The incidence was highest among men aged 70 to 74 years and among Black men. The vast majority of these cases were localized (77%), followed by regional (11%), metastatic (5%), and unknown (7%). Compared with all other races/ethnicities, White men had the lowest rates of metastatic (5%) and unknown stage (6%) disease at diagnosis.

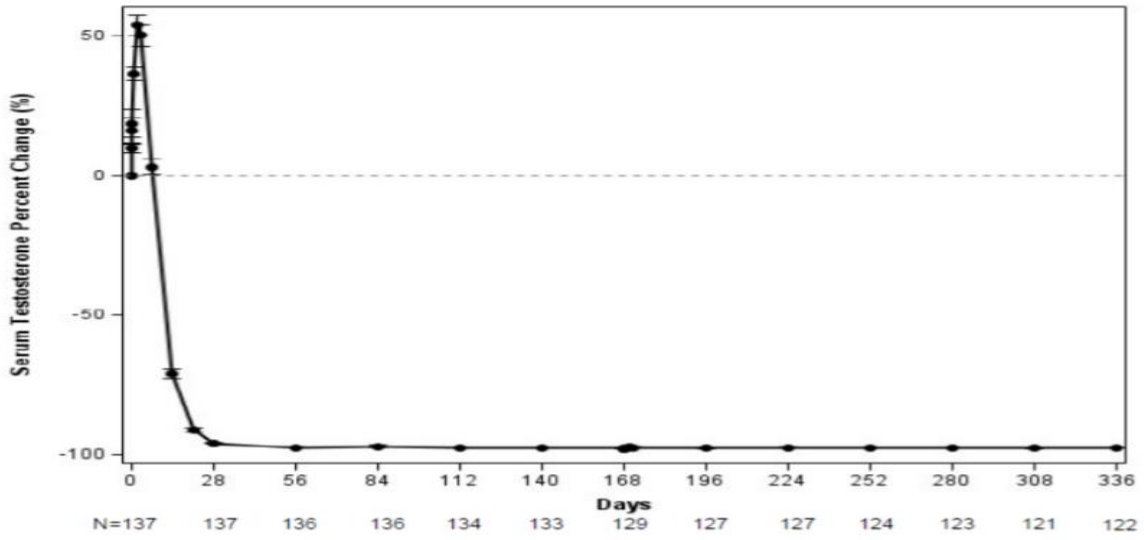
“Although approximately three-fourths of US men with prostate cancer have localized stage at diagnosis, an increasing number and percentage of men have received diagnoses of distant stage prostate cancer,” noted the investigators. “Survival with distant stage prostate cancer has improved, but fewer than one-third of men survive 5 years after diagnosis.”

Efficacy

The efficacy of Camcevi™ was evaluated in an open label, single arm, multinational study FP01C-13 001 (NCT02234115) in patients with advanced prostate carcinoma who have a baseline morning serum testosterone level >150 ng/dL and Eastern Cooperative Oncology Group performance status ≤ 2. Camcevi™ was administered subcutaneously at a dose of 42 mg initially on Day 0 and on Week 24. The population (n = 137) had a median age of 71 years (range 51 to 88) and was 90% White, 6% Black, and 4% Asian. Disease stage was distributed as follows: 23% metastatic (M1), 27% locally advanced (T3/4 NX M0 or any T N1 M0), 26% localized (T1 or T2 N0 M0), and

24% not classifiable. The median testosterone concentration at baseline was 440 ng/dL. The major efficacy outcome measure was medical castration rate, defined as achieving and maintaining serum testosterone suppression to ≤ 50 ng/dL by Week 4 through Week 48 of treatment. Following the first injection of Camcevi™, serum testosterone levels were suppressed to ≤ 50 ng/dL by Week 4 (+/-7 days) in 98.5% of the patients; and from Week 4 through Week 48 in 97.0% of patients (95% CI: 92.2 98.9) estimated using the Kaplan-Meier method. The time course of percent change from baseline in testosterone suppression are shown below. The percentage of patients with testosterone suppression to ≤ 20 ng/dL was 69.3% on Day 28.

Figure 1 CAMCEVI Mean (95% CI) Percentage Change from Baseline in Serum Testosterone Concentration Over Time (N =137)



In the clinical trial, PSA levels were monitored and were lowered on average by 51% after 4 weeks after administration of Camcevi™, 83% after 3 months and remained suppressed throughout the 48 weeks of treatment. These PSA results should be interpreted with caution because of the heterogeneity of the patient population studied. No evidence has shown that the rapidity of PSA decline correlates with clinical benefit.

Safety

ADVERSE EVENTS

The most common (>10%) adverse reactions were hot flush, hypertension, injection site reactions, upper respiratory tract infections, musculoskeletal pain, fatigue, and pain in extremity.

WARNINGS & PRECAUTIONS

Tumor Flare:
Camcevi™, like other GnRH agonists, causes a transient increase in serum levels of testosterone during the first week of treatment, declining thereafter to baseline levels or below by the end of the second week of treatment. Transient worsening of symptoms, or the occurrence of additional signs and symptoms of prostate cancer, may develop during the first few weeks of Camcevi™ treatment. Patients treated with Camcevi™ may experience a temporary increase in bone pain, which can be managed symptomatically. As with other GnRH agonists, cases of ureteral obstruction and spinal cord compression have been observed, which may contribute to paralysis with or without fatal complications. Patients with metastatic vertebral lesions and/or with urinary tract obstruction should be closely observed during the first few weeks of therapy.
Hyperglycemia and Diabetes:

Hyperglycemia and an increased risk of developing diabetes have been reported in men receiving GnRH agonists. Hyperglycemia may represent the development of diabetes mellitus or worsening of glycemic control in patients with diabetes. Monitor blood glucose and/or glycosylated hemoglobin (HbA1c) periodically in patients receiving a GnRH agonist and manage with current practice for treatment of hyperglycemia or diabetes.

Cardiovascular Diseases: Increased risk of developing myocardial infarction, sudden cardiac death, and stroke has been reported in association with use of GnRH agonists in men. The risk appears low based on the reported odds ratios and should be evaluated carefully along with cardiovascular risk factors when determining a treatment for patients with prostate cancer. Patients receiving a GnRH agonist should be monitored for symptoms and signs suggestive of development of cardiovascular disease and be managed according to current clinical practice.

QT/QTc Prolongation:
Androgen deprivation therapy may prolong the QT/QTc interval. Providers should consider whether the benefits of androgen deprivation therapy outweigh the potential risks in patients with congenital long QT syndrome, congestive heart failure, frequent electrolyte abnormalities, and in patients taking drugs known to prolong the QT interval. Electrolyte abnormalities should be corrected. Consider periodic monitoring of electrocardiograms and electrolytes.

Convulsions:
Convulsions have been reported in patients receiving GnRH agonists, like Camcevi™. Manage patients receiving a GnRH agonist who experience convulsions according to current clinical practice.
Embryo-Fetal Toxicity: Based on findings in animal studies and mechanism of action, Camcevi™ can cause fetal harm when administered to a pregnant woman. In animal developmental and reproductive toxicology studies, administration of a monthly formulation of leuprolide on day 6 of pregnancy (sustained exposure was expected throughout the period of organogenesis) caused adverse embryo-fetal toxicity in animals at doses less than the human dose based on body surface area using an estimated daily dose. Advise pregnant patients and females of reproductive potential of the potential risk to the fetus.

CONTRAINDICATIONS

Hypersensitivity to GnRH, GnRH agonist analogs, or any of the components of Camcevi™.

Clinical Pharmacology

MECHANISMS OF ACTION

As a long-acting GnRH agonist, it acts as a potent inhibitor of gonadotropin secretion (luteinizing hormone [LH] and follicle stimulating hormone [FSH]) when given continuously in therapeutic doses.

Dose & Administration

ADULTS

42 mg subcutaneously every 6 months

PEDIATRICS

The safety and efficacy of Camcevi™ in pediatric patients have not been established.

GERIATRICS

Refer to adult dosing

RENAL IMPAIRMENT

No dosage adjustments are required.

HEPATIC IMPAIRMENT

No dosage adjustments are required.

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Injectable emulsion: 42 mg