PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

PrCAMCEVI®

Leuprolide extended-release injectable emulsion

For subcutaneous use

21 mg leuprolide (as leuprolide mesylate) (3-Month)

Gonadotropin Releasing Hormone Analogue

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Kirkland, QC, H9H 5B9
Canada

Date of Authorization:
2026-03-31

Submission Control Number: 295847

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Part 1: Healthcare Professional Information

1 Indications

CAMCEVI (leuprolide mesylate) is indicated for:

- treatment of adult patients with advanced prostate cancer.

1.1 Pediatrics

- No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2 Geriatrics

- The mean age of the male patients studied in the clinical trials was 69.8 years (range 51–89 years). The safety and efficacy of CAMCEVI was established in this population (see 14 Clinical Trials).

2 Contraindications

CAMCEVI is contraindicated in:

- patients with hypersensitivity to gonadotropin releasing hormone (GnRH) analogues, or any of the components of CAMCEVI. Anaphylactic reactions including anaphylactic shock to synthetic GnRH or GnRH analogues have been reported in post-marketing surveillance. For a complete listing, see the section 6 Dosage Forms, Strengths, Composition, and Packaging.
- women and paediatric patients.
- women who are or may become pregnant.
- women who are nursing.

3 Serious Warnings and Precautions Box

Serious Warnings and Precautions

CAMCEVI (leuprolide mesylate) should be prescribed by a qualified physician experienced in the use of hormonal therapy in prostate cancer.

The following are clinically significant adverse events:

- Clinical testosterone flare reaction in men with prostate cancer (see **7 Warnings and Precautions,** General)
- Pituitary apoplexy (see **7 Warnings and Precautions,** Endocrine and Metabolism)
- Osteoporosis (see **7 Warnings and Precautions**, Endocrine and Metabolism).

4 Dosage and Administration

4.1 Dosing Considerations

- CAMCEVI should be administered by a healthcare professional.

- CAMCEVI, 21 mg administered subcutaneously is designed to provide continuous extended release of leuprolide for 3 months.

4.2 Recommended Dose and Dosage Adjustment

- CAMCEVI
  The recommended dose of CAMCEVI is 21 mg administered every three months as a single subcutaneous injection (see 4.4 Administration).

4.4 Administration

CAMCEVI is administered by subcutaneous injection, whereupon it forms a solid drug delivery depot releasing leuprolide mesylate over 3 months. The injectable emulsion contains approximately 21 mg of leuprolide base (equivalent to approximately 24 mg leuprolide mesylate). The recommended dosing is 1 subcutaneous injection every 12 weeks.

As with other drugs administered by subcutaneous injection, the injection site should vary periodically. The specific injection location chosen should be an area with sufficient soft or loose subcutaneous tissue. In clinical trials, the injection was administered in the upper- or mid-abdominal area. Areas with brawny or fibrous subcutaneous tissue or locations that can be rubbed or compressed (i.e., with a belt or clothing waistband) should be avoided.

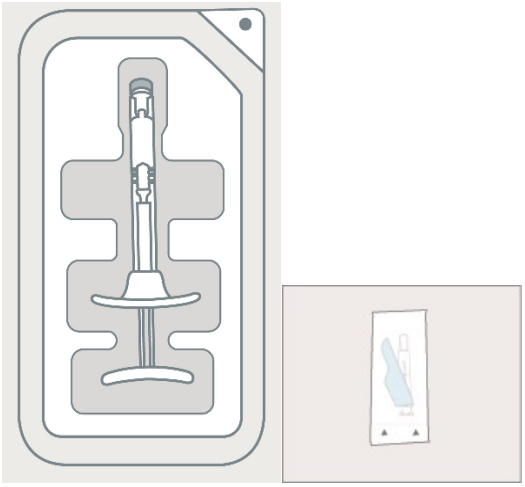
Administration Procedure

IMPORTANT: Allow the product to reach room temperature before using. The use of gloves is recommended during administration [Occupational Health and Safety (OH&S)].

Follow the instructions as directed to ensure proper preparation of CAMCEVI prior to administration:

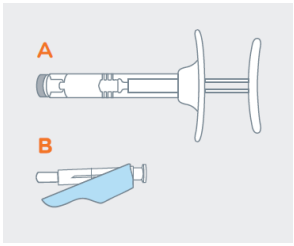
CAMCEVI kit contains:

- One sterile pre-filled plastic syringe closed with elastomeric grey tip cap, plunger and finger grip
- One sterile 18-gauge SurGuard®3 safety needle, 5/8 inch needle

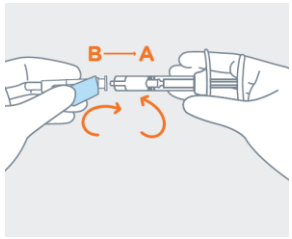


Syringe Assembly

Remove contents

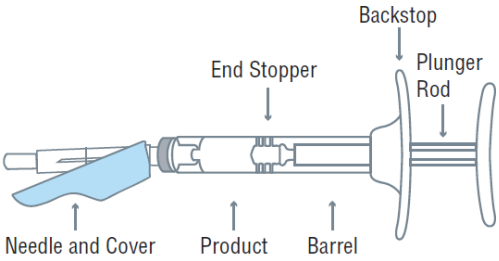


Assemble the Needle

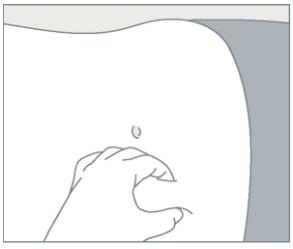
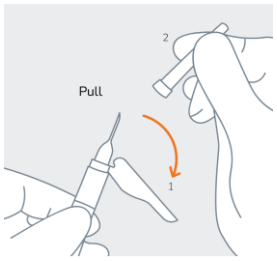
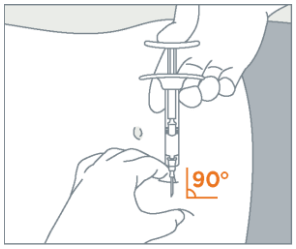
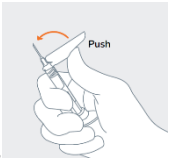
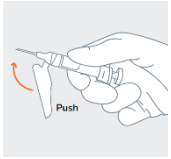
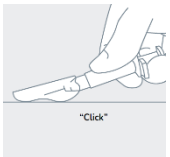


1. Keep contents in their original, sealed blister container and allow pre-filled syringe to sit at room temperature for 30 minutes prior to subcutaneous injection.
2. On a clean, dry surface, remove pre-filled CAMCEVI syringe (A) from the blister container and remove needle cartridge (B) from the carton box. Visually inspect the contents prior to use.
3. Remove pre-filled syringe (A) from blister tray and open the safety needle (B) package by peeling back the paper tab.
4. Remove the gray cap from syringe (A).
5. Attach the needle (B) to the end of the syringe (A) by gently screwing clockwise with approximately a three-quarter turn until the needle is secure. **Do not overtighten, as the**

needle hub may become damaged resulting in leakage of the product during injection. The safety sheath may also be damaged if the needle is overtightened onto the syringe.



Administration Procedure

Prepare the Injection Site	Expose Needle	Administer Treatment	Activate Safety Sheath and Discard Needle
			Using finger/thumb: 1.  2.  OR Using flat surface: 1.  2. 

1. Choose an injection site on the upper- or mid-abdominal area that has not recently been used. Clean the injection site with an alcohol swab. Do **NOT** inject in areas with brawny or

fibrous subcutaneous tissue or locations that can be rubbed or compressed (i.e., with a belt or clothing waistband).

2. (1) Move the safety sheath away from the needle and towards the syringe and (2) remove the clear needle cover immediately before injection.
   Note: Should the needle hub appear to be damaged, or leak, the product should NOT be used. The damaged needle should NOT be replaced and the product should NOT be injected. In the event of damage to the needle hub, use a new replacement CAMCEVI kit.
3. Grab and bunch the skin around the injection site with one hand. Insert the needle at a 90° angle, then release the bunched skin.
4. Inject the full contents of the syringe with a slow and steady push, then withdraw the needle at the same 90° angle used for insertion.
5. Immediately following the withdrawal of the needle, activate the safety sheath using a finger/thumb or flat surface and push until it completely covers the needle tip and locks into place. An audible and tactile "click" verifies a locked position. Check to confirm the safety sheath is fully engaged.
6. After use, place the used syringe with needle protected in a suitable sharps container. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

4.5 Missed Dose

Maintaining testosterone suppression is important in treating the symptoms of hormone-dependent prostate cancer. Missing an appointment by a few days should not disrupt the benefits of treatment, but keeping a consistent schedule of leuprolide injections is an important part of treatment. Call your healthcare professional for instructions if you miss a dose.

5 Overdose

There is no clinical experience with the effects of an acute overdose. There is no known antidote for CAMCEVI overdose. In the event of an overdose, stop CAMCEVI, undertake general supportive measures until clinical toxicity has been diminished or resolved.

For the most recent information in the management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

6 Dosage Forms, Strengths, Composition, and Packaging

Table 1 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Subcutaneous	Extended-release emulsion,21 mg	N-methyl-2-pyrrolidone

injection	leuprolide (as leuprolide mesylate) per syringe	Poly(D,L-Lactide-co-Glycolide)

CAMCEVI is available as follows:

Kit Contents
CAMCEVI 21 mg pre-filled syringe and a sterile 18-gauge needle.

- CAMCEVI is a sterile, off-white to pale yellow, viscous and opalescent injectable emulsion.

7 Warnings and Precautions

Please see 3 Serious Warnings and Precautions Box.

General

CAMCEVI, like other GnRH analogues, causes a transient increase in serum concentration of testosterone during the first week of treatment. Patients may experience worsening of symptoms or onset of new symptoms, including bone pain, neuropathy, hematuria, or ureteral or bladder outlet obstruction. Cases of spinal cord compression, which may contribute to paralysis with or without fatal complications, have been reported with GnRH analogues. If spinal cord compression or renal impairment due to ureteral obstruction develops, standard treatment of these complications should be instituted.

Patients with metastatic vertebral lesions and/or with urinary tract obstruction should begin leuprolide therapy under close supervision.

Administration procedure should be followed, as lack of clinical efficacy may occur due to incorrect administration of the product (see 7 Warnings and Precautions, Monitoring and Laboratory Tests and 4.4 Administration, Administration Procedure).

Carcinogenesis and Mutagenesis

No carcinogenicity studies or genotoxicity studies have been conducted specifically with CAMCEVI.

Two-year carcinogenicity studies conducted with leuprolide in rats found increased incidences of pituitary hyperplasia and adenomas, pancreatic islet-cell adenomas, and testicular interstitial cell adenomas (see 16 Non-Clinical Toxicology, Carcinogenicity).

Genotoxicity studies performed with leuprolide using bacterial and mammalian systems found no evidence of genotoxic potential (see 16 Non-Clinical Toxicology, Genotoxicity).

Cardiovascular

Increased risk of developing myocardial infarction, sudden cardiac death and stroke has been reported in association with use of GnRH analogues in men. The risk appears low based on the reported odds ratios, and should be evaluated carefully along with cardiovascular risk factors. Reports of events related to cardiovascular ischemia including myocardial infarction, stroke and cardiovascular-related deaths have been reported in patients treated with GnRH analogues.

Physicians should consider whether the benefits of androgen deprivation therapy outweigh the potential cardiovascular risk.

Patients receiving GnRH analogues should be monitored for symptoms and signs suggestive of development of cardiovascular disease, and management according to current clinical practice and guidelines should be considered (see 7 Warnings and Precautions, Monitoring and Laboratory Tests).

Effect on QT/QTc interval

Androgen deprivation therapy may prolong the QT/QTc interval. In patients with a history of or risk factors for QT prolongation including congenital long QT syndrome, electrolyte abnormalities, or congestive heart failure, and/or in patients receiving concomitant medicinal products that might prolong the QT interval, physicians should assess whether the benefits of androgen deprivation therapy outweigh the potential risks including the potential for Torsade de pointes prior to initiating CAMCEVI.

Driving and Operating Machinery

Fatigue and dizziness have been reported in patients taking CAMCEVI.

Therefore, exercise caution when driving or operating a vehicle or potentially dangerous machinery.

Endocrine and Metabolism

Pituitary apoplexy

During post-marketing surveillance, serious cases of pituitary apoplexy (a clinical syndrome secondary to infarction of the pituitary gland) have been reported after the administration of GnRH analogues, with a majority occurring within 2 weeks of the first dose, and some within the first hour. In these cases, pituitary apoplexy has presented as sudden headache, vomiting, visual changes, ophthalmoplegia, altered mental status, and sometimes cardiovascular collapse. Immediate medical attention is required. Pre-existing gonadotropin-secreting pituitary adenoma was diagnosed in a majority of patients. If the presence of macroadenomas is evidenced by imaging and biochemical assessments, this should be surgically removed prior to

start of GnRH analogues including CAMCEVI treatment.

Hypogonadism
Long-term administration of leuprolide will cause suppression of pituitary gonadotropins and gonadal hormone production with clinical symptoms of hypogonadism. These changes have been observed to reverse on discontinuation of therapy. However, whether the clinical symptoms of induced hypogonadism will reverse in all patients has not yet been established.

Hyperglycemia and Diabetes
Hyperglycaemia and an increased risk of developing diabetes have been reported in men receiving GnRH analogues. Hyperglycaemia may represent development of diabetes mellitus or worsening of glycaemic control in patients with diabetes. Monitor blood glucose and/or glycosylated haemoglobin (HbA1c) periodically in patients receiving a GnRH analogue and manage with current practice for treatment of hyperglycaemia or diabetes.

Hematologic

Anemia is a known physiologic consequence of testosterone suppression. Assessment of anemia risk and management according to local clinical practice and guidelines should be considered.

Hypersensitivity Reactions

Delayed Hypersensitivity Reactions
Delayed hypersensitivity reactions including the severe cutaneous adverse reactions (SCAR) of Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) have been very rarely reported post-marketing in association with leuprorelin therapy (see 8.5 Post-Market Adverse Reactions). Discontinue future leuprorelin therapy at first signs or symptoms of a delayed hypersensitivity reaction, and treat patients according to current clinical practice.

Monitoring and Laboratory Tests

Patients with vertebral and/or brain metastases as well as patients with urinary tract obstruction should be closely monitored during the first few weeks of therapy.

Monitor response to leuprolide by periodically measuring serum concentrations of testosterone and prostate specific antigen. Results of testosterone determinations are dependent on assay methodology. It is advisable to be aware of the type and precision of the assay methodology to make appropriate clinical and therapeutic decisions.

Testosterone levels should also be evaluated in the case of suspected or known handling errors, as lack of efficacy may result from incorrect preparation or administration. Baseline risk factors of cardiovascular diseases should be assessed. Patients receiving leuprolide should be

monitored periodically for risk factors, signs and symptoms of cardiovascular diseases. In addition, baseline ECG recording and serum potassium, calcium, and magnesium levels are recommended. Monitoring of ECG and serum electrolyte levels during treatment should also be considered for those at risk for electrolyte abnormality and QTc prolongation.

Blood glucose levels and/or glycosylated hemoglobin (HbA1c) should be checked periodically in patients treated with GnRH analogues and more frequently in diabetic patients (see 7 Warnings and Precautions, Endocrine and Metabolism).

The effects of leuprolide on bone lesions may be monitored by bone scans, while its effects on prostatic lesions may be monitored by ultrasonography, and/or CT scan in addition to digital rectal examination. Intravenous pyelogram, ultrasonography, or CT scan may also be utilized to diagnose or assess the status of obstructive uropathy.

Musculoskeletal

Decreased bone mineral density can be anticipated with long term use of a GnRH analogue. Androgen deprivation therapy is associated with increased risks of osteoporosis and skeletal bone fractures. The risk of skeletal bone fracture increases with the duration of androgen deprivation therapy. Assessment of osteoporosis risk and management according to clinical practice and guidelines should be considered.

In patients with significant risk factors for decreased bone mineral content and/or bone mass such as chronic alcohol and/or tobacco use, presumed or strong family history of osteoporosis, or chronic use of drugs that can reduce bone mass such as anticonvulsants or corticosteroids, CAMCEVI may pose an additional risk. In these patients, risk versus benefit must be weighed carefully before therapy with CAMCEVI is initiated.

Neurologic

Convulsions have been reported in patients on leuprolide with or without a history of predisposing factors in the post-market setting. Convulsions are to be managed according to the current clinical practice.

Idiopathic Intracranial Hypertension (pseudotumor cerebri)
Idiopathic intracranial hypertension (pseudotumor cerebri) has been reported in adult and pediatric patients receiving GnRH agonists. Monitor patients for signs and symptoms of idiopathic intracranial hypertension, including headache, papilledema, blurred vision, diplopia, loss of vision, pain behind the eye or pain with eye movement, tinnitus, dizziness, and nausea. Refer the patient to an ophthalmologist to confirm the presence of papilledema. Treatment should be discontinued immediately if the patient develops any signs or symptoms suggestive of idiopathic intracranial hypertension.

Tumor Flare

CAMCEVI, like other GnRH analogues, 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 occasionally develop during the first few weeks of CAMCEVI treatment. A small number of patients may experience a temporary increase in bone pain, which can be managed symptomatically.

As with other GnRH analogues, isolated cases of ureteral obstruction and spinal cord compression have been observed, which may contribute to paralysis with or without fatal complications. If spinal cord compression or renal impairment develops, standard treatment of these complications should be instituted.

Patients with metastatic vertebral lesions and/or with urinary tract obstruction should be closely observed during the first few weeks of therapy.

Reproductive Health

- **Fertility**

Based on findings in animals and mechanism of action, CAMCEVI may impair fertility in males of reproductive potential (see 10 Clinical Pharmacology, 16 Non-Clinical Toxicology).

Continuous daily administration of leuprolide results in decreased levels of luteinizing hormone (LH), follicle stimulating hormone (FSH) and reduction of testosterone to castrate levels.

- **Teratogenic Risk**

CAMCEVI is contraindicated in women who are or may become pregnant (see 2 Contraindications). Based on findings in animals, CAMCEVI may cause fetal harm if administered to pregnant women (see 16 Non-Clinical Toxicology, Reproductive and Developmental Toxicology).

Respiratory

There have been post-marketing reports of interstitial pneumonitis associated with leuprolide use. Treatment should be discontinued immediately if the patient develops any signs or symptoms suggestive of interstitial lung disease.

7.1 Special Populations

7.1.1 Pregnancy

Leuprolide is contraindicated in women who are or may become pregnant (see 2 Contraindications). Studies in animals have shown leuprolide can result in embryotoxicity and lethality (see 16 Non-Clinical Pharmacology). CAMCEVI is not indicated for use in women as

safety and efficacy have not been established in this group of patients.

7.1.2 Breastfeeding

CAMCEVI is contraindicated for use in nursing women as safety and efficacy have not been established in this group of patients.

7.1.3 Pediatrics

CAMCEVI is contraindicated for use in children as safety and efficacy have not been established in this group of patients.

7.1.4 Geriatrics

The mean age of the male patients studied in the clinical trials was 69.8 years (range 51–89 years). The safety and efficacy of CAMCEVI was established in this population. (See 14 Clinical Trials).

8 Adverse Reactions

8.1 Adverse Reaction Overview

The safety of CAMCEVI was evaluated in a clinical trial involving patients with advanced prostate cancer who received at least one dose of CAMCEVI. CAMCEVI, like other GnRH analogues, caused a transient increase in serum testosterone concentrations during the first week of treatment, declining thereafter to baseline levels or below by the end of the second week of treatment. Therefore, potential exacerbations in signs and symptoms of the disease during the first weeks of treatment are of concern in patients with vertebral metastases and/or urinary obstruction or hematuria which, if aggravated, may lead to neurological problems (such as weakness and/or paresthesia of the lower limbs) or increase the obstruction (see 7 Warnings and Precautions).

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials therefore may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful for identifying and approximating rates of adverse drug reactions in real-world use.

In an open-label, non-comparative clinical trial (FP01C-17-001), patients with advanced prostate cancer received CAMCEVI administered subcutaneously at a dose of 21 mg on Day 0 and Day 84. Of 144 patients enrolled, 91.7% received both doses of CAMCEVI.

The most common adverse reactions (incidence ≥ 10%) were hot flush and hypertension.

Serious Adverse Events occurred in 6% of patients treated with CAMCEVI. Serious adverse events included acute myocardial infarction, cerebrovascular accident, drug induced liver injury and pancreatitis (each 0.7%)

No death was reported during the study.

Discontinuation occurred in 10.4% of subjects. Only 1 subject discontinued due to an adverse event (stroke).

The following adverse events (all grades) occurred in the clinical trial of CAMCEVI and were reported in ≥5% of patients (Table 2).

Table 2 Summary of Adverse Events Reported in ≥ 5% of Patients Treated with CAMCEVI

Adverse Reaction	N = 144	
	All Grades (%)	Grade 3-4[a] (%)
Hot flush	24	0
Hypertension[a]	15	0.7
Injection site reaction[b]	10	0
Weight increase	8	0

[a] Only includes a grade 3 adverse reaction. Hypertension includes blood pressure increased, essential hypertension, and hypertension.

[b] Injection site reaction includes injection site erythema, hemorrhage, induration, nodule, localized edema; and injection site pain.

8.3 Less Common Clinical Trial Adverse Reactions

The following are selected clinically significant adverse reactions reported in less than 5% of patients receiving CAMCEVI in study FP01C-17-001:

General disorders and administration site conditions:	Asthenia, localized oedema.
Injury, poisoning and procedural complications:	Post procedural complication.
Investigations:	Alanine aminotransferase increased, blood triglycerides increased, aspartate aminotransferase increased, increased weight, electrocardiogram QT prolonged.
Metabolism and nutrition disorders:	Decreased appetite.
Musculoskeletal and connective tissue disorders:	Pain in extremity.
Psychiatric:	Insomnia, libido decreased.
Renal and urinary disorders:	Pollakiuria.
Skin:	Hyperhidrosis

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Laboratory abnormalities were observed, but it was difficult to assess relationship to the drug treatment as most occurred in <3% of patients and most in 1 subject each. The following laboratory abnormalities occurred in the clinical trial for CAMCEVI and were reported in > 1% of patients (

Table 3).

Table 3 Summary of Laboratory Abnormalities

Lowest Level Term	Total (No=144) Grade 1–2 (%)	Total (No=144) Grade 3-4 (%)
Alanine aminotransferase increased	4.9%	0%
Aspartate aminotransferase increased	3.5%	0%
Blood glucose increased	1.4%	0.7%
Urine red blood cell increased	1.4%	0%

The following grade 1–2 laboratory abnormalities occurred in 1 subject each (0.7%): Decreased hemoglobin, blood urea nitrogen increased, blood total bilirubin increased, urine white blood cell increased, blood white blood cell increased, alkaline phosphatase increased, triglycerides increased.

8.5 Post-Market Adverse Reactions

During post-marketing surveillance of other leuprolide dosage forms and other patient populations, the following adverse events were reported.

Cardiovascular System: Hypotension;

Endocrine System: Pituitary apoplexy;

Eye disorders: Photosensitivity reactions;

Gastrointestinal System: Hepatic dysfunction;

General disorders and administration site conditions: Localized reactions including induration and abscess, fibromyalgia (e.g., joint and muscle pain, headaches, sleep disorders, gastrointestinal distress, and shortness of breath);

Hemic and Lymphatic System: Decreased white blood cells;
Integumentary System: Hair growth;

Central/Peripheral Nervous System: Convulsion, spinal fracture/paralysis, hearing disorder;

Miscellaneous: Hard nodule in throat, weight gain, increased uric acid;

Musculoskeletal System: Tenosynovitis-like symptoms, decreased bone density;

Respiratory System: Respiratory disorders; interstitial lung disease, anaphylactoid or asthmatic process

Skin and subcutaneous tissue disorders: Rash, urticarial, severe skin reactions [including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN)].

9 Drug Interactions

9.2 Drug Interactions Overview

No formal drug interaction studies have been conducted with leuprolide.

No data is available on the interaction with alcohol.

9.4 Drug-Drug Interactions

No pharmacokinetic drug interactions were conducted with CAMCEVI.

Interactions with drugs have not been established.

Since androgen deprivation treatment may prolong the QTc interval, the concomitant use of leuprolide with medicinal products known to prolong the QTc interval or medicinal products able to induce torsades de pointes should be carefully evaluated. Such medicinal products include but are not limited to the examples that follow: Class IA (e.g. quinidine, disopyramide), Class III (e.g. amiodarone, sotalol, dofetilide, ibutilide, dronedarone), or Class IC (e.g. flecainide, propafenone) antiarrhythmic medicinal products, antipsychotics (e.g. chlorpromazine), antidepressants (e.g. amitriptyline, nortriptyline), opioids (e.g. methadone), macrolide antibiotics and analogues (e.g. erythromycin, clarithromycin, azithromycin), quinolone antibiotics (e.g. moxifloxacin), antimalarials (e.g. quinine), azole antifungals, 5-hydroxytryptamine (5-HT3) receptor antagonists (e.g. ondansetron), and beta-2 adrenoceptor agonists (e.g. salbutamol).

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Therapy with leuprolide results in suppression of the pituitary-gonadal system. Results of diagnostic tests of pituitary gonadotropic and gonadal functions conducted during and after leuprolide therapy may be affected.

10 Clinical Pharmacology

10.1 Mechanism of Action

Leuprolide, a GnRH analogue, acts as a potent inhibitor of gonadotropin secretion when given continuously and in therapeutic doses. Animal and human studies indicate that following an initial stimulation of gonadotropins, chronic administration of leuprolide results in suppression of ovarian and testicular steroidogenesis. This effect is reversible upon discontinuation of drug therapy.

In humans, subcutaneous administration of single daily doses of leuprolide result in an initial increase in circulating levels of LH and FSH, leading to a transient increase in levels of the gonadal steroids (testosterone and dihydrotestosterone in males, and estrone and estradiol in pre-menopausal females). However, long term administration of leuprolide results in decreased levels of LH and FSH. In males, testosterone is reduced to levels associated with castration (≤50ng/dL in serum). In pre-menopausal females, estrogens are reduced to post-menopausal levels.

10.2 Pharmacodynamics

Following the first dose of CAMCEVI, mean serum testosterone concentrations transiently increased, then fell to below castrate threshold levels (≤ 50 ng/dL) within 4 weeks and remained below castrate levels with continued treatment.

Additional PK/ECG analyses demonstrated that the standard clinical dose of Camcevi 21 mg (3-Month) reduced testosterone to castrate levels with no clinically meaningful changes in ECG parameters, except for the expected increase in QTcF consistent with the known effects of sex hormone suppression on the QT interval. The peak mean increase in ΔQTcF was 15.9 msec on Day 84. No clinically significant effects were observed on heart rate, PR, or QRS intervals. Although PR >200 msec with ≥25% increase was reported in up to 3.6% of subjects, no cases of second-degree AV block were observed. Overall, ECG abnormalities were infrequent and not

considered clinically significant.

10.3 Pharmacokinetics

Table 4 PK Parameters of CAMCEVI in PK population

PK Parameter	First Dose			Second Dose		
	N	Mean	SD	N	Mean	SD
C_{max}, ng/mL	30	43.4	18.7	30	37.8	14.9
T_{max}, h	30	2.00 (2.00, 8.00)		30	2.00 (1.92, 8.00)	
$AUC_{0\text{-week12}}$, day×ng/mL	30	93.5	50.4	30	102	45.3
Vd (L)	8[a]	10300	8110	23[b]	9580	5320
$t_{1/2}$ (h)	8[a]	578	428	23[b]	608	257
CL (L/h)	8[a]	12.0	6.84	23[b]	10.9	4.18

[a] 22 subjects not reported due to the adjusted R^2 value < 0.80 or $AUC_{0\text{-last}}$ /$AUC_{0\text{-inf}}$ ratio < 0.80.

[b] 7 subjects not reported due to the adjusted R^2 value < 0.80 or $AUC_{0\text{-last}}$ /$AUC_{0\text{-inf}}$ ratio < 0.80.

Absorption

The pharmacokinetics were observed during injections of CAMCEVI administered initially (n = 30 patients) and at 12 weeks (n = 30 patients). Following the first and the second doses of CAMCEVI, mean serum leuprolide concentrations rose rapidly to reach the C_{max} of 43.4 and 37.8 ng/mL at 2.00 and 2.00 hours (median T_{max}), respectively. Following the initial rapid increase, leuprolide concentrations declined gradually over the remaining duration of the dosing interval (Day 3 to Day 84). The mean serum concentrations during this "plateau" phase were mostly maintained at 0.40–1.22 (after Day 3 to Day 84) and 0.23–2.02 ng/ml (after Day 87 to Day 182) post the first and the second dose, respectively.

Distribution

The mean steady state volume of distribution of leuprolide following intravenous bolus administration to healthy male volunteers was 27 L. In vitro binding to human plasma proteins ranged from 43% to 49%.

Metabolism

Leuprolide is a peptide that is primarily metabolized by peptidases and not by CYP enzymes.

The major metabolite (M-I) plasma concentrations measured in 5 prostate cancer patients reached maximum concentration 2 to 6 hours after dosing and were approximately 6% of the peak parent drug concentration. One week after dosing, mean plasma M I concentrations were approximately 20% of mean leuprolide concentrations.

Elimination
In healthy male volunteers, a 1 mg bolus of leuprolide administered intravenously revealed that the mean systemic clearance was 7.6 L/h, with a terminal elimination half life of approximately 3 hours based on a 2-compartment model.

No drug excretion study was conducted specifically with CAMCEVI.

Special Populations and Conditions
The pharmacokinetics of the drug have not been determined in patients with hepatic or renal impairment.

- **Pediatrics:** CAMCEVI is contraindicated in pediatric patients (see 2 Contraindications).
- **Geriatrics:** The mean age of the male patients studied in the clinical trials was 69.8 years (range 51–89 years). The safety and efficacy of CAMCEVI was established in this population. (See 14 Clinical Trials).
- **Sex:** Only male patients were included in studies with CAMCEVI.
- No clinically meaningful differences in systemic exposure of leuprolide were observed based on age, race, or body weight.

11 Storage, Stability, and Disposal

Store CAMCEVI at a refrigerated temperature of 2°C to 8°C (35.6 ºF and 46.4 ºF). Protect CAMCEVI from light by storing in the original package until time of use. Do not freeze or shake.

12 Special Handling Instructions

CAMCEVI should be handled following Occupational Health and Safety (OH&S) safety guidelines. The use of gloves is recommended.

Keep contents in their original, sealed blister container and allow pre-filled syringe to sit at room temperature for 30 minutes prior to subcutaneous injection.

Part 2: Scientific Information

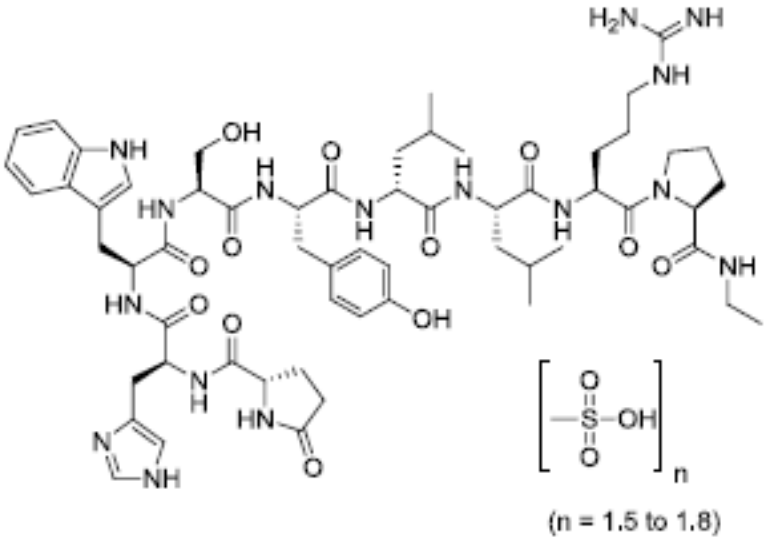
13 Pharmaceutical Information

Drug Substance
Non-proprietary name of the drug substance: Leuprolide mesylate

Chemical name:	5-oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-D-leucyl-L-leucyl-L-arginyl-N-ethyl-L-prolinamide mesylate

Molecular formula and molecular mass: $C_{59}H_{84}N_{16}O_{12} \cdot (CH_4O_3S)n$, n = 1.5–1.8 ; 1209.41 Daltons (free base)

Structural formula:



Physicochemical properties: Leuprolide mesylate is a white to off-white powder, freely soluble in water, dimethyl sulfoxide (DMSO), N-methylpyrrolidone (NMP); insoluble in acetone and acetonitrile; and the pKa is 6.1.

Pharmaceutical standard: Professed.

14 Clinical Trials

14.1 Clinical Trials by Indication

Indication 1: Treatment of Adult Patients with Advanced Prostate Cancer

Table 5 Summary of patient demographics for clinical trials in prostate cancer

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range; in years)	Sex
FP01C-17-001	Open-label, single arm, phase 3, multi-centre, multi-national	CAMCEVI 21mg is an injectable extended release emulsion containing 21 mg leuprolide (equivalent to approximately 24 mg as leuprolide mesylate), administered subcutaneously every 3 months	144	69.8 (51 to 89)	Male

The efficacy of CAMCEVI 21 mg was evaluated in an open-label, single arm, multi-center, multinational phase 3 study in adult patients with histologically confirmed advanced prostate carcinoma (baseline morning serum testosterone level 150 ng/dL; Eastern Cooperative Oncology Group [ECOG] ≤ 2). A total of 144 subjects were enrolled and received at least one dose of the study drug (intent-to-treat [ITT] population), and 132 subjects completed the study without major protocol violations affecting the primary efficacy endpoint (per-protocol [PP] population). Of 144 subjects enrolled, 132 subjects received both doses of CAMCEVI 21 mg (compliance of 91.7%).

The median age of the patients in the study was 70 years and all were male. The population was 88% white, 0.7% black and 11% Asian. The mean and median duration with diagnosed prostate cancer was 842.7 and 109 days, respectively. With regard to disease stage, 8.33% (12/144) subjects had prostate carcinoma stage IV, 42.4% (61/144) subjects had prostate carcinoma stage III, 22.2% (32/144) subject had prostate carcinoma stage II, 13.9% (20/144) subjects had prostate carcinoma stage I, and 13.2% (19/144) subjects had unknown prostate carcinoma stage at baseline. There were 93.8% (135/144) subjects with Grade 0 and 6.25% (9/144) subjects with Grade 1 in ECOG performance status at baseline. The median testosterone concentration at baseline was 423 ng/dL.

The primary endpoint of the study was to determine the percentage of subjects achieving serum testosterone suppression (≤50 ng/dL) by week 4 (day 28), and maintaining that suppression from week 4 through week 24 (day 168) of treatment. To demonstrate clinical efficacy, the lower bound of the 95% confidence interval for the primary endpoint estimate was

prespecified to be greater than 90%. Insufficient suppression of testosterone was defined as suppression that did not occur by Day 28 or the occurrence of a testosterone level > 50 ng/dL between Day 28 and Day 168. The secondary endpoints consisted of post suppression excursions, percentage of patients that achieved and maintained testosterone suppression below 20ng/dL and serum PSA levels.

Study Results

In the ITT population serum testosterone levels were suppressed to castrate levels (≤ 50 ng/dL) by Day 28 following the first injection of CAMCEVI 21 mg in 98.6% of the patients (141/143). The percentage of patients with testosterone suppression (≤ 50 ng/dL) from week 4 through week 24 was 97.9% in the ITT population (Table 6). The percentage of patients with testosterone suppression (≤ 20 ng/dL) was 72% (103/143) on Day 28, and 96.4% (135/140) on Day 168 in the ITT population. In the PP population, the percentage of patients with testosterone suppression (≤ 20 ng/dL) was 71.2% (94/132) on Day 28, and 96.2% (125/130) on Day 168.

Table 6 Primary Endpoint Results for Study FP01C-17-001

Population	# Enrolled/ completed	Percentage of subjects with serum testosterone ≤ 50 ng/dL (95% CI)	
		By Day 28	Day 28–Day 168
ITT[a]	144/143	98.6 (95.04-99.83)	97.9 (93.5-99.3)
PP[b]	144/132	98.5 (94.63-99.82)	97.7 (93.1-99.3)

[a]Any subject who received at least 1 dose of CAMCEVI 21mg

[b]Any subject who received 2 doses of CAMCEVI 21 mg, followed the inclusion/exclusion criteria of the protocol, and had no major protocol violation

CI = confidence interval; ITT = intent-to-treat; PP = per protocol

Source: Main Study FP01C-17-001, Table 11-4, Table 11-5, Table 11-6 and Table 11-7

Two of 143 subjects (1.4%) did not reach castrate levels on Day 28. One subject had a baseline level of 493 ng/dL, and his testosterone level was suppressed to 76 ng/dL on Day 28, and then reached castrate levels at the next measurement (Day 56) of 17.7 ng/dL. This subject stayed below 50 ng/dL for the duration of the study. The second subject had a baseline value of 480 ng/dL, and his testosterone level was suppressed to 84.4 ng/dL on Day 28, and then reached castrate levels at the next measurement (Day 56) of 35 ng/dL. This subject stayed below 50 ng/dL for the duration of the study. Following the second injection of CAMCEVI 21 mg, an additional 1 subjects (1/132; 0.76%) exhibited 1 episode of transient post suppression breakthrough (serum testosterone > 50 ng/dL). The subject showed 338 ng/dL on Day 84, but returned to castrate level (9.5 ng/dL) on Day 85 and stayed below castrated level through the remainder of the study.

Serum PSA levels were substantially reduced after the first injection, and this effect remained until the end of the study. In the ITT population, the PSA levels were lowered on average by 72.7% after 4 weeks (Day 28) after administration of CAMCEVI 21 mg and lowered by 96.5% at the end of study (Day 168). Similar decreases in PSA levels were observed in the PP population.

15 Microbiology

Not applicable.

16 Non-Clinical Toxicology

General Toxicology

Published studies on a sustained release formulation of leuprolide demonstrated that the product has a low order of acute toxicity in mice and rats, with LD50's above 5000 mg/kg (greater than 400 mg/kg of leuprolide) for oral, subcutaneous and intraperitoneal routes of administration, and above 2000 mg/kg (greater than 160 mg/kg as leuprolide) for intramuscular injection. The only clinical signs observed were related to local effects at the site of injection.

3-Month Single Dose Subcutaneous Toxicity Study in Male Sprague-Dawley Rats

Leuprolide mesylate (3.4, 10.1 and 16.9 mg/body) was administered to 7-week-old male rats via single subcutaneous injection that resulted in sustained release of leuprolide over a 91-day period. Serum testosterone was suppressed to castrate level (<50 ng/dL) throughout the study. No mortality or moribundity were noted in any of the leuprolide mesylate-treated groups or a reference leuprolide-treated group. A shortening of prothrombin time and decreases in the weight of the testis, epididymis, prostate, and seminal vesicles were observed in all leuprolide-treated groups. Pituitary hyperplasia was noted in the high dose leuprolide mesylate-treated group and all leuprolide acetate-treated groups. The no observed adverse effect level (NOAEL) of leuprolide mesylate was above 16.9 mg/body (approximately 39.30-50.60 mg/kg, or 8-10 times the recommended human dose based on body surface area), since pituitary hyperplasia noted at this level and higher was considered adverse.

No studies with repeat administration were conducted. CAMCEVI is an extended-release formulation. Effects of continuous release were observed for a 3-month period.

Single Dose Subcutaneous Toxicity Studies in Dogs

A single SC injection (60 mg in 0.5 mL) of sustained release leuprolide or a supporting formulation in dogs showed no overt toxicities, no body weight abnormalities, and no remarkable observations at the injection sites during the study. In another study, dogs received a single SC injection (45 mg in 0.375 mL) of leuprolide or a supporting formulation. There were no body weight abnormalities during the study. Overt toxicity not related to the test article was observed in two dogs (i.e., seizures and otitis externa). Three dogs demonstrated minimal

edema at the injection site on Day 1, and one dog had slight edema at the injection site on Day 14.

Carcinogenicity

No carcinogenicity studies have been conducted specifically with CAMCEVI.

Two-year carcinogenicity studies with leuprolide were conducted in rats and mice. In rats, a dose-related increase of benign pituitary hyperplasia and benign pituitary adenomas was noted at 24 months when the drug was administered subcutaneously at high daily doses (0.6 to 4 mg/kg). There was a significant but not dose-related increase of pancreatic islet cell adenomas in females and of testicular interstitial cell adenomas in males (highest incidence in the low dose group). In mice, no pituitary abnormalities were observed at a dose as high as 60 mg/kg for 2 years.

Genotoxicity

No mutagenicity, clastogenicity or aneugenicity studies have been conducted specifically with CAMCEVI.

A sustained release formulation of leuprolide was not genotoxic in either an in vitro cytogenetics assay using Chinese hamster lung cells, an in vivo micronucleus assay in mice, or the Ames test with five strains of *Salmonella typhimurium*.

Reproductive and Developmental Toxicology

No reproductive and developmental toxicology studies have been conducted specifically with CAMCEVI.

Reproduction and teratology studies conducted with a sustained release formulation indicate all effects observed are related to consequences of repeated administration of this pharmacologic agent. Fertility studies, where male rats were dosed once every four weeks for three doses prior to mating, showed that the drug produced reversible atrophy of the testes or accessory sex organs at doses as low as 0.024 mg/kg (as leuprolide), and a decrease in LH, FSH and testosterone levels. A reversible decrease in copulation and implantation sites was also observed at the high dose of 2.4 mg/kg. No effects on the fetuses were observed.

Female rats dosed at 2.4 mg leuprolide acetate/kg once, four weeks prior to mating, caused an interruption in the estrus cycle and decreased vaginal size. Weights of the ovaries and uterus were decreased. Following mating, corpora lutea and the number of implantation sites were decreased at 0.24 mg/kg and above; the number of live fetuses was reduced at 2.4 mg/kg and above. No abnormal development was noted in the fetuses.

In the perinatal study, the administration of the sustained release formulation of leuprolide in rats prior to delivery at up to 8 mg/kg showed effects on sex organ weights, but no adverse effects on the fetuses, including weights of their sex organs.

Major fetal malformations were observed in developmental and reproductive toxicology studies in rabbits after a single administration of a monthly formulation of leuprolide administered on day 6 of pregnancy at test dosages of 0.00024, 0.0024, and 0.024 mg/kg (approximately 1/1500 to 1/15 the human dose based on body surface area using an estimated daily dose in animals and humans). Since a depot formulation was utilized in the study, a sustained exposure to leuprolide was expected throughout the period of organogenesis and to the end of gestation. Increased fetal mortality and decreased fetal weights with the two higher doses were observed.

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr]CAMCEVI®

Leuprolide extended-release injectable emulsion, 21 mg

This Patient Medication Information is written for the person who will be taking **CAMCEVI**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This Patient Medication Information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about **CAMCEVI**, talk to a healthcare professional.

Serious warnings and precautions box

CAMCEVI should be prescribed by a healthcare professional experienced with the use of hormonal therapy in prostate cancer.

CAMCEVI may cause:

- Worsening of the symptoms of prostate cancer at the beginning of the treatment. CAMCEVI may cause an increase in blood levels of testosterone during the first week of treatment. This can cause:
  - bone pain, numbness, tingling, muscle weakness
  - bloody urine
  - blockage of your urinary tract or bladder
  - pressure on your spinal cord (spinal cord compression)
- **Pituitary apoplexy** (bleeding or decreased blood flow causing tissue death of the pituitary gland). This might occur within 2 weeks of the first dose, and some within the first hour.
- **Osteoporosis** (bone thinning). CAMCEVI may increase your risk of osteoporosis and bone fractures. Your healthcare professional will monitor your risks for bone thinning and bone fractures during treatment with CAMCEVI.

See the **Serious side effects and what to do about them table**, below, for more information on these and other serious side effects.

What CAMCEVI is used for:
CAMCEVI is used for the treatment of adult patients with advanced prostate cancer.

How CAMCEVI works:
CAMCEVI belongs to a group of medicines called Gonadotropin Releasing Hormone (GnRH) analogues.

CAMCEVI contains leuprolide. It works by blocking the action of androgens (hormones like testosterone). This will shrink or stop the growth of prostate cancer cells which may result in reduced symptoms related to the disease.

The ingredients in CAMCEVI are:
Medicinal ingredients: Leuprolide (as leuprolide mesylate)
Non-medicinal ingredients: N-methyl-2-pyrrolidone; Poly (D, L-lactide-co-Glycolide).

CAMCEVI comes in the following dosage form:
Extended release emulsion: 21 mg leuprolide (as leuprolide mesylate) in a pre-filled syringe.

Do not use CAMCEVI if:
- you are allergic to leuprolide mesylate or any other ingredients in CAMCEVI.
- you have had an allergic reaction to CAMCEVI or other drugs like CAMCEVI, including a severe allergic reaction (anaphylactic shock).
- you are a woman.
- you are pregnant or may become pregnant. Leuprolide may cause miscarriage or may cause harm to an unborn baby.
- you are breast-feeding.
- you are younger than 18 years of age.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take CAMCEVI. Talk about any health conditions or problems you may have, including if you:
- have a history of urinary tract obstruction.
- have had spread of cancer to the bones of the spine (vertebrae).
- have a history of spinal cord compression.
- have risk factors for bone thinning (osteoporosis), such as if you:
  - have a family history of severe osteoporosis
  - have low bone mineral density
  - are taking any medication that can cause thinning of the bones. For example, corticosteroids or anti-convulsive (anti-seizure) medications
  - use alcohol or tobacco.
- have heart disease, or a genetic heart condition called “Long QT syndrome”.

Other warnings you should know about:

CAMCEVI can cause serious side effects, including:

- **Cardiovascular problems**, such as: heart attack, sudden cardiac death (sudden loss of heart function) and stroke. It may also cause changes to your heart rhythm.
- **Hyperglycemia** (increase in blood sugar) and **Diabetes** (high blood sugar).
  - CAMCEVI may increase your blood sugar levels. This may increase your risk of diabetes or worsen the symptoms in patients with diabetes.
  - If you have diabetes, talk to your healthcare professional before you are given CAMCEVI. You may need to test your blood sugar more frequently during treatment.
  - Your healthcare professional may need to give or change your blood sugar medicine. This will help control your blood sugar levels.
- **Anemia** (decreased number of red blood cells)
  - CAMCEVI suppresses the production of testosterone. This may cause a decrease in the number of red blood cells (anemia).
  - If you have anemia, talk to your healthcare professional before you are given CAMCEVI.
- **Skin reactions:**

- Very rare, severe allergic skin reactions such as **Stevens-Johnson Syndrome (SJS)** and **Toxic Epidermal Necrolysis (TEN)** have been reported.
- Symptoms may include: rash with blisters, redness and peeling skin. If you notice these symptoms, tell your healthcare professional right away or get emergency help.

See the Serious side effects and what to do about them table, below, for more information on these and other serious side effects.

- **Hypogonadism** (reduced production of sex hormone)
  Treatment with CAMCEVI may reduce the production of male sex hormones. This can lead to side effects such as loss of sexual desire and inability to maintain erection (impotence).
- **Fertility**
  Treatment with CAMCEVI may reduce your ability to have children. Talk to your healthcare professional if this is a concern for you.
- **Check-ups and testing:**
  You will have regular visits with your healthcare professional during treatment with CAMCEVI to monitor your health. They may do:
  - blood and urine tests,
  - bone scans (such as ultrasonography and/or CT scan) and
  - tests to check your heart (ECG recording).
- **Driving and using machines**
  CAMCEVI can cause fatigue and dizziness. Before you drive or do tasks that require special attention, wait until you know how you respond to CAMCEVI.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with CAMCEVI:
- antiarrhythmic medicines (used to treat abnormal heart rhythm) such as: quinidine, disopyramide, amiodarone, sotalol, dofetilide, ibutilide, dronedarone, flecainide, propafenone
- antipsychotic medicines (used to treat mental disorders) such as: chlorpromazine
- antidepressant medicines (used to treat depression) such as: amitrptyline, nortryptiline
- opioid medicines (used to treat pain), such as methadone
- antibiotics (used to treat bacterial infections), such as: erythromycin, clarithromycin, azithromycin, moxifloxacin
- antifungals (used to treat fungal infections)
- antimalarials (used to treat malaria), such as quinine
- medicines belonging to a class called beta-2 agonists (used to treat asthma), such as salbutamol
- medicines belonging to a class called 5-HT3 antagonists (used to treat nausea), such as ondansetron

How to take CAMCEVI:
CAMCEVI will be given to you by a healthcare professional in a healthcare setting. CAMCEVI is given by injection under the skin (subcutaneously).

Usual dose:
21 mg once every 3 months.

Overdose:

If you think you, or a person you are caring for, have been given too much CAMCEVI, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Missed Dose:

If you miss an appointment to receive your dose of CAMCEVI, contact your health professional as soon as possible.

It is very important that you keep all scheduled appointments with your healthcare professional. If you miss an appointment by a few days, it should not disrupt the benefits of treatment. But you must follow your medicine administration schedules for the therapy to be effective.

Possible side effects from using CAMCEVI:

These are not all the possible side effects you may have when taking CAMCEVI. If you experience any side effects not listed here, tell your healthcare professional.

Side effects include:

- hot flash
- skin reaction at injection site (ex. burning and stinging, pain, redness, itching and/or swelling)
- fatigue
- pain in muscles, ligaments, tendons or bones (musculoskeletal pain)
- pain in extremity
- joint pain
- regularly waking up at night to urinate
- urinary urgency
- dizziness
- upper respiratory tract infection (such as a cold)

CAMCEVI may cause abnormal blood test results. Your healthcare professional will decide when to perform blood tests and will interpret the results.

Serious side effects and what to do about them

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Get immediate medical help
	Only if severe	In all cases	
Very Common			
Hypertension (high blood pressure): severe headaches, nosebleed, vision problems, shortness of breath, fatigue or confusion, dizziness or fainting, chest pain or pressure, swelling in your ankles and legs, bluish colour to your lips and skin, racing pulse or heart palpitations		✓	

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Get immediate medical help
	Only if severe	In all cases	
Common			
Osteoporosis (thin, fragile bones): broken bones, pain, back pain that gets worse when standing or walking		✓	
Prolongation of QT interval (a heart rhythm condition): Irregular heartbeat, fainting, loss of consciousness, seizures			✓
Subdural haematoma (bleeding within the skull): headache that doesn't go away; drowsiness; confusion, memory changes; speech or language problems; paralysis, loss of consciousness			✓
Tumor flare (worsening of the symptoms of prostate cancer at the beginning of the treatment): increase in the severity of side effects or new pain after starting hormone therapy		✓	
Uncommon			
Atrial fibrillation (abnormal heart rhythm which is rapid and irregular): chest discomfort with unpleasant awareness of your heartbeat, faintness, shortness of breath, weakness			✓
Deep vein thrombosis (blood clot in the deep veins of the leg or arm): swelling, pain, arm or leg may be warm to the touch and may appear red			✓
Diabetes: with symptoms such as excessive thirst, excessive urination, excessive eating, unexplained weight loss, poor wound healing, infections		✓	
Hyperglycemia (high blood sugar): increased thirst, frequent urination, dry skin, headache, blurred vision and fatigue		✓	
Myocardial infarction (heart attack): pressure or squeezing pain between the shoulder blades, in the chest, jaw, left arm or upper abdomen, shortness of breath, dizziness, fatigue, light-headedness, clammy skin, sweating, indigestion, anxiety, feeling faint and possible irregular heartbeat			✓
Very rare			

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Get immediate medical help
	Only if severe	In all cases	
Pituitary apoplexy (bleeding or decreased blood flow to your pituitary gland): sudden headache, vomiting, visual changes			✓
Stroke (bleeding or blood clot in the brain): sudden numbness, weakness or tingling of the face, arm, or leg, particularly on one side of the body, sudden headache, blurry vision, difficulty swallowing or speaking, or lethargy, dizziness, fainting, vomiting, trouble understanding, trouble with walking and loss of balance			✓
Drug induced Liver Injury: pain in the right abdomen, fever, fatigue, weakness, nausea, vomiting, loss of appetite, yellowing of the skin or eyes, dark urine			✓
Pancreatitis (inflammation of the pancreas): upper abdominal pain, fever, rapid heart beat, nausea, vomiting, tenderness when touching the abdomen			✓
Unknown			
Anemia (decreased number of red blood cells): fatigue, loss of energy, looking pale, shortness of breath, weakness		✓	
Convulsion: seizure, spasms, shaking or fits			✓
Pneumonitis (inflammation of the lung tissue): shortness of breath, cough, fatigue, loss of appetite, unintentional weight loss			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:
CAMCEVI will be managed and stored by healthcare professionals. The information below on how to store CAMCEVI is meant for your healthcare professional.

- CAMCEVI should be stored refrigerated between 2°C to 8°C. Do NOT freeze.
- Store in the original package and protect from light.

If you want more information about CAMCEVI:
- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); or by calling Accord Healthcare Inc. at 1-866-296-0354.

This leaflet was prepared by: Accord Healthcare Inc.

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