CAVERJECT IMPULSE- alprostadil injection, powder, lyophilized, for solution
Pharmacia and Upjohn Company LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use CAVERJECT IMPULSE safely and effectively. See full prescribing information for CAVERJECT IMPULSE.

CAVERJECT IMPULSE® (alprostadil) for injection, for intracavernosal use
Initial U.S. Approval: 1981

RECENT MAJOR CHANGES

Warnings and Precautions, Needle Breakage (5.7)	05/2016
Warnings and Precautions, Benzyl Alcohol (5.8)	10/2016

INDICATIONS AND USAGE

CAVERJECT IMPULSE is a prostaglandin E1 agonist indicated
- For the treatment of erectile dysfunction (1.1)
- As an adjunct to other diagnostic tests in the diagnosis of erectile dysfunction (1.2).

DOSAGE AND ADMINISTRATION

- Determine the most suitable dose and formulation of CAVERJECT to use (2.1)
- Administer first intracavernosal injections in the physician's office and titrate the dose for each patient to the lowest effective dose (2.1)
- Dosage for erectile dysfunction (2.2):
  - Erectile dysfunction of vasculogenic, psychogenic, or mixed etiology:
    Initiate dosing with 2.5 mcg
  - Erectile dysfunction of pure neurogenic etiology (spinal cord injury):
    Initiate dosing with 1.25 mcg
- Follow dose titration procedures for each type of erectile dysfunction and determine the maintenance dosage for erectile dysfunction for patient home use in the physician's office (2.2)
- The recommended frequency of injection is no more than 3 times weekly, with at least 24 hours between each dose (2.2)
- While on self-injection treatment, the patient should visit the prescribing physician's office every 3 months to assess the efficacy and safety of the therapy (2.2)
- Instruct the patient on proper use and assess that they are well trained in the self-injection technique prior to initiation of at-home use (2.3)
- To diagnose erectile dysfunction (pharmacologic testing), inject CAVERJECT IMPULSE intracavernosally and monitor patients for the occurrence of an erection (2.4)
- Follow procedure for CAVERJECT IMPULSE syringe preparation (2.5)

DOSAGE FORMS AND STRENGTHS

For injection: 10 mcg or 20 mcg freeze-dried powder for reconstitution in a dual-chamber syringe (3)

CONTRAINDICATIONS

- Known hypersensitivity to the drug (4)
- Men who have conditions that predispose them to priapism, such as sickle cell anemia or sickle cell trait, multiple myeloma, or leukemia (4)
- Treatment of erectile dysfunction in men with fibrotic conditions of the penis, such as anatomical deformation, angulation, cavernosal fibrosis, or Peyronie's disease (4)
- Men with penile implants (4)

WARNINGS AND PRECAUTIONS

- Prolonged erection and priapism have occurred in patients receiving CAVERJECT. To minimize the chances of this occurring, titrate CAVERJECT IMPULSE slowly to the lowest effective dose (2.1). Advise patients to seek immediate medical assistance for an erection that persists longer than 4 hours (5.1)
- Penile fibrosis has occurred in patients receiving CAVERJECT. Follow patients regularly to detect signs of penile fibrosis. Discontinue in patients who develop penile angulation or cavernosal fibrosis (5.2)
- Hypotension - injections of CAVERJECT IMPULSE can lead to increased peripheral blood levels of alprostadil,

especially in patients with significant corpora cavernosa venous leakage. Avoid use in patients with known cavernosal venous leakage (5.3)

- Injection site bleeding may occur in patients taking anticoagulants, such as warfarin or heparin. Compress the site of injection with an alcohol swab or sterile gauze for 5 minutes (5.4)
- Cardiovascular risk related to underlying medical conditions - Underlying treatable medical causes of erectile dysfunction should be diagnosed and treated prior to initiation of therapy (5.5)
- Risks of use in combination with other vasoactive medications injected intracavernosally - Safety and efficacy of combinations of CAVERJECT and other vasoactive agents have not been systematically studied. Use of such combinations is not recommended (5.6)
- Risk of needle breakage – CAVERJECT IMPULSE uses a superfine needle and cases of needle breakage have been reported. Careful instruction in proper patient handling and injection techniques may minimize this risk (5.7)
- Benzyl alcohol – CAVERJECT IMPULSE contains benzyl alcohol as a preservative (5.8)
- Counseling patients about sexually transmitted diseases. Counseling of patients about the protective measures necessary to guard against sexually transmitted disease including the Human Immunodeficiency Virus (HIV) is advised. (5.9)

ADVERSE REACTIONS

Most common (≥10%) adverse reactions: penile pain (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer at (1-800-438-1985 and *www.pfizer.com*) or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*
See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 10/2016

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
1.1 Erectile Dysfunction
1.2 Diagnostic Test
2 DOSAGE AND ADMINISTRATION
2.1 Dosage and Administration Information Overview
2.2 Dosage for Erectile Dysfunction
2.3 Patient Instruction for Self-Injection Technique for Treatment of Erectile Dysfunction
2.4 Adjunct to the Diagnosis of Erectile Dysfunction
2.5 CAVERJECT IMPULSE Syringe Preparation
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Prolonged Erection and Priapism
5.2 Penile Fibrosis
5.3 Hypotension
5.4 Injection Site Bleeding When Used With Anticoagulants
5.5 Cardiovascular Risk Related to Underlying Medical Conditions
5.6 Risks Of Use in Combination With Other Vasoactive Medications Injected Intracavernosally
5.7 Needle Breakage
5.8 Benzyl Alcohol
5.9 Counseling Patients About Sexually Transmitted Diseases
6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
6.2 Post-marketing Experience
7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation

8.4 Pediatric Use
8.5 Geriatric Use
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
14 CLINICAL STUDIES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION
* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Erectile Dysfunction

CAVERJECT IMPULSE is indicated for the treatment of erectile dysfunction.

1.2 Diagnostic Test

CAVERJECT IMPULSE is indicated as an adjunct to other diagnostic tests in the diagnosis of erectile dysfunction.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage and Administration Information Overview

- Determine the most suitable dose and formulation of CAVERJECT (CAVERJECT IMPULSE or CAVERJECT Sterile Powder) for each patient.
- Administration of the first injections of CAVERJECT IMPULSE should be done in the physician's office by medically trained personnel.
- Carefully titrate the dose of CAVERJECT IMPULSE for each patient to the lowest effective dose.
- The site of injection is usually along the dorso-lateral aspect of the proximal third of the penis.
- Wipe the intended injection site with an alcohol swab prior to injection.
- Avoid visible veins during injection.
- Alternate the side of the penis that is injected and the site of injection.
- Compress the site of injection with an alcohol swab or sterile gauze for 5 minutes.
- CAVERJECT IMPULSE is intended for single use only and should be discarded after use.
- Safety and efficacy of CAVERJECT doses greater than 60 mcg have not been established.

2.2 Dosage for Erectile Dysfunction

Starting Dosage for Erectile Dysfunction of Vasculogenic, Psychogenic, or Mixed Etiology.

Initiate dosing with 2.5 mcg of alprostadil. If there is a partial response at 2.5 mcg, the dose may be increased to 5 mcg within 1 hour. During titration, no more than 2 doses should be given within a 24-hour period. The optimal dose should produce an erection suitable for intercourse that does not exceed

a duration of 1 hour. The patient must stay in the physician's office until complete detumescence occurs.

If additional titration is required, doses in increments of 5 to 10 mcg may be given at least 24 hours apart. Repeat the titration as necessary until the optimal dose is achieved.

Starting Dosage for Erectile Dysfunction of Pure Neurogenic Etiology (Spinal Cord Injury):

Initiate dosing with 1.25 mcg of alprostadil using CAVERJECT Sterile Powder. If there is a partial response, the dose may be increased to 2.5 mcg within 1 hour. No more than 2 doses during initial titration should be given within a 24-hour period. The optimal dose should produce an erection suitable for intercourse that does not exceed a duration of 1 hour. The patient must stay in the physician's office until complete detumescence occurs.

If additional titration is required, a dose of 5 mcg may be given during the next 24 hours. Thereafter, doses in increments of 5 mcg may be given at least 24 hours apart until the optimal dose is reached.

Maintenance Dosage for Erectile Dysfunction for Patient Home Use:

Once the dose of CAVERJECT IMPULSE has been determined in the physician's office, additional dose adjustment may be required after consultation with the physician. Adjust the dose in accordance with the titration guidelines described above. The recommended frequency of injection is no more than 3 times weekly, with at least 24 hours between each dose.

While on self-injection treatment, it is recommended that the patient visit the prescribing physician's office every 3 months to assess the efficacy and safety of the therapy and to adjust the dose of CAVERJECT IMPULSE, if needed.

2.3 Patient Instruction for Self-Injection Technique for Treatment of Erectile Dysfunction

Instruct the patient on proper use and assess that they are well trained in the self-injection technique prior to initiation of at-home use. Advise the patient to read the Patient Information and Instructions for Use for detailed instructions on use of the product (*see FDA-approved patient labeling [Patient Information and Instructions for Use]*).

2.4 Adjunct to the Diagnosis of Erectile Dysfunction

To diagnose erectile dysfunction (pharmacologic testing), inject CAVERJECT IMPULSE intracavernosally and monitor patients for the occurrence of an erection. Extensions of this testing are the use of CAVERJECT as an adjunct to laboratory investigations, such as duplex or Doppler imaging. For any of these tests, use a single dose of CAVERJECT IMPULSE that induces a rigid erection.

2.5 CAVERJECT IMPULSE Syringe Preparation

1. Select the CAVERJECT IMPULSE syringe based upon dose to be administered.

Syringe Strength	Reconstituted Concentration	Dosages Available for Delivery after Reconstitution			
10 mcg	10 mcg/0.5 mL	2.5 mcg	5 mcg	7.5 mcg	10 mcg
20 mcg	20 mcg/0.5 mL	5 mcg	10 mcg	15 mcg	20 mcg

2. Open the sealed plastic tray. Remove the syringe, the needle assembly, and the alcohol swabs from the tray. The syringe has a dose window and a plunger. The needle assembly is a sealed unit that contains the outer protective cap, the inner protective cap, and the superfine needle.
3. Use the alcohol swab to wipe the rubber membrane at the tip of the syringe. Pick up the needle assembly, grasp the paper tab, and peel off the paper cover (the lid).

4. Hold the needle assembly by the cap and press the needle assembly onto the tip of the syringe. Turn it clockwise until the needle assembly is firmly locked into place.
5. Remove the outer protective cap from the needle by twisting it clockwise. Do not yet remove the inner protective cap, the thin plastic tube that directly covers the needle.
6. Hold the syringe system with the needle pointing upward. The plunger rod should still be in the fully extended position, with all of the threads visible. Slowly rotate the plunger rod clockwise until it goes all the way in and stops. Do not push on the plunger while trying to rotate it.
7. Turn the syringe upside down several times to make sure the solution is evenly mixed. The solution should be clear. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. The product should not be used if particulate matter or discoloration are present.
8. Hold the syringe with the needle upward and carefully remove the inner protective cap from the needle. Lightly tap the glass cartridge a few times with your finger until any large bubbles disappear up into the tip. With the syringe pointed upward, push in the plunger rod until it stops to push any air out.
9. To set the dose: locate the dose window on the syringe and then slowly turn the plunger rod clockwise until the correct dose number appears in the center of the window. The syringe is now ready for use. If you pass the correct number, keep turning the plunger in the same direction until the correct number comes around again – do not try to turn it backward.
10. After reconstitution, the syringe should be used within 24 hours when stored between 36–77°F (2°C to 25°C). Do not freeze. CAVERJECT IMPULSE is for single use only. Discard the injection delivery system and any remaining solution after use.

3 DOSAGE FORMS AND STRENGTHS

Caverject Impulse (alprostadil) for injection contains sterile, freeze-dried alprostadil for reconstitution and sterile bacteriostatic water in a prefilled dual chamber glass cartridge. It is available in 10 mcg and 20 mcg strengths.

4 CONTRAINDICATIONS

CAVERJECT IMPULSE should not be used:

- in men who have a known hypersensitivity to the drug *[see Adverse Reactions (6.1)]*
- in men who have conditions that predispose them to priapism, such as sickle cell anemia or sickle cell trait, multiple myeloma, or leukemia *[see Warnings and Precautions (5.1)]*
- for the treatment of erectile dysfunction in men with fibrotic conditions of the penis, such as anatomical deformation, angulation, cavernosal fibrosis, or Peyronie's disease *[see Warnings and Precautions (5.2)]*
- in men with penile implants.

5 WARNINGS AND PRECAUTIONS

5.1 Prolonged Erection and Priapism

Prolonged erection defined as erection lasting between 4 to 6 hours in duration occurred in 4% of 1,861 patients treated up to 18 months in studies of CAVERJECT Sterile Powder. The incidence of priapism (erections lasting more than 6 hours in duration) was 0.4%. In the event of an erection that persists longer than 4 hours, the patient should seek immediate medical assistance. If priapism is not treated immediately, penile tissue damage and permanent loss of potency may result.

To minimize the chances of prolonged erection or priapism, CAVERJECT IMPULSE should be titrated slowly to the lowest effective dose *[see Dosage and Administration (2.1]*. In addition, do not use CAVERJECT IMPULSE in patients who have conditions that predispose them to priapism, such as

sickle cell anemia or sickle cell trait, multiple myeloma, or leukemia *[see Contraindications (4)]*.

5.2 Penile Fibrosis

The overall incidence of penile fibrosis, reported in clinical studies with CAVERJECT Sterile Powder was 3%. In one self-injection clinical study where duration of use was up to 18 months, the incidence of penile fibrosis was 7.8%.

Physical examination of the penis, should be performed periodically to detect signs of penile fibrosis. Treatment with CAVERJECT IMPULSE should be discontinued in patients who develop penile angulation or cavernosal fibrosis.

5.3 Hypotension

Intracavernous injections of CAVERJECT IMPULSE can increase peripheral blood levels of alprostadil which can result in hypotension. Avoid use of CAVERJECT IMPULSE in patients with known cavernosal venous leakage.

5.4 Injection Site Bleeding When Used With Anticoagulants

Patients on anticoagulants, such as warfarin or heparin, may have increased propensity for injection site bleeding after intracavernosal injection with CAVERJECT IMPULSE. Compress the site of injection with an alcohol swab or sterile gauze for 5 minutes.

5.5 Cardiovascular Risk Related to Underlying Medical Conditions

There is a potential for cardiac risk of sexual activity in patients with preexisting cardiovascular disease. Therefore, treatments for erectile dysfunction, including CAVERJECT IMPULSE, generally should not be used in men for whom sexual activity is inadvisable because of their underlying cardiovascular status. In addition, the evaluation of erectile dysfunction should include a determination of potential underlying causes and the identification of appropriate treatment following a complete medical assessment.

5.6 Risks Of Use in Combination With Other Vasoactive Medications Injected Intracavernosally

The safety and efficacy of combinations of CAVERJECT IMPULSE and other vasoactive agents injected intracavernosally have not been established in clinical studies. The risks of prolonged erection, priapism, and hypotension may be increased.

5.7 Needle Breakage

CAVERJECT IMPULSE uses a superfine (29 gauge) needle for administration. As with all superfine needles, the possibility of needle breakage exists and cases of needle breakage have been reported. Needle breakage, with a portion of the needle remaining in the penis, has been reported and, in some cases, required hospitalization and surgical removal. Careful instruction in proper patient handling and injection techniques may minimize the potential for needle breakage.

5.8 Benzyl Alcohol

The preservative benzyl alcohol contained in CAVERJECT IMPULSE has been associated with serious adverse events, including the "gasping syndrome", and death in pediatric patients. The minimum amount of benzyl alcohol at which toxicity may occur is not known. The risk of benzyl alcohol toxicity depends on the quantity administered and the liver and kidneys' capacity to detoxify the chemical. Premature and low-birth weight infants may be more likely to develop toxicity. CAVERJECT IMPULSE is not indicated for pediatric patients.

5.9 Counseling Patients About Sexually Transmitted Diseases

The use of CAVERJECT IMPULSE offers no protection against sexually transmitted diseases.

Counseling of patients about the protective measures necessary to guard against sexually transmitted diseases, including the Human Immunodeficiency Virus (HIV) is advised.

6 ADVERSE REACTIONS

The following are discussed in more detail in other sections of the labeling:

- Prolonged Erection and Priapism *[see Warnings and Precautions (5.1)]*
- Penile Fibrosis *[see Warnings and Precautions (5.2)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

CAVERJECT IMPULSE was evaluated in 87 patients in an open-label crossover study of 6 weeks treatment duration that compared the formulation of alprostadil for injection contained in CAVERJECT IMPULSE with the formulation contained in CAVERJECT Sterile Powder. Doses used in this study ranged from 2.5 mcg to 20 mcg. Adverse reactions reported for the CAVERJECT IMPULSE formulation included: penis disorder (4.6%), prolonged erection (1.1%), injection site erythema (1.1%), rash (1.1%), dizziness (1.1%), and hematospermia (1.1%). Penis disorder included penile pain, post-injection pain, and pain with erection.

CAVERJECT IMPULSE was also evaluated in 63 patients in a single-dose, double-blind, crossover study that compared CAVERJECT IMPULSE with CAVERJECT Sterile Powder. Doses used in this study ranged from 2.5 mcg to 20 mcg. Adverse reactions reported for the CAVERJECT IMPULSE formulation included: penile pain (1.6%) and pruritus (1.6%).

In addition to the adverse reactions observed for CAVERJECT IMPULSE in these two studies, the following adverse reactions have been reported in clinical studies of CAVERJECT Sterile Powder:

Local Adverse Reactions: Local adverse reactions derived from 1861 patients in clinical studies of CAVERJECT Sterile Powder, including an 18-month, open-label study, are shown in Table 1.

Table 1. Local Adverse Reactions Reported by ≥ 1% of Patients Treated with CAVERJECT Sterile Powder for up to 18 Months

Penile pain	37%
Prolonged erection	4%
Penile fibrosis	3%
Injection site hematoma	3%
Penis disorder*	3%
Injection site ecchymosis	2%
Penile rash	1%
Penile edema	1%

* Penis disorder includes: numbness, irritation, sensitivity, pruritus, erythema, skin tear, discoloration, itching.

The following local adverse reactions were reported in < 1% of patients: injection site hemorrhage, injection site inflammation, injection site itching, injection site swelling, injection site edema, urethral bleeding, penile warmth, numbness, irritation, sensitivity, pruritus, erythema, painful erection, and abnormal ejaculation.

In these studies, no local adverse reactions were reported in the 294 patients who received placebo,

except for penile pain (2%).

Penile Pain: In the majority of the cases, penile pain was rated mild or moderate in intensity. Three percent of patients discontinued treatment because of penile pain

Prolonged Erection/Priapism: Prolonged erection was defined as an erection that lasted for 4 to 6 hours; priapism was defined as an erection that lasted 6 hours or longer. In clinical studies, the frequency of prolonged erection after intracavernosal administration of CAVERJECT Sterile Powder was 4%, while the frequency of priapism was 0.4% *[see Warnings and Precautions (5.1)]*.

Penile Hematoma/Ecchymosis: In clinical studies the frequency of penile hematoma and ecchymosis was 3% and 2%, respectively.

Systemic Adverse Reactions**:** Systemic adverse reactions reported by ≥ 1% of subjects in clinical studies of CAVERJECT Sterile Powder included: dizziness (1%).

The following systemic adverse reactions, were reported in < 1% of patients: testicular pain, scrotal edema, hematuria, pelvic pain, hypotension, vasodilation, vasovagal reaction, diaphoresis, rash, and non-application site pruritus. Three patients (0.2%) discontinued due to symptomatic hypotension.

No systemic adverse reactions were reported in the 294 patients who received placebo.

6.2 Post-marketing Experience

The following additional adverse reactions have been reported: device malfunction/failure, drug ineffective and drug effect decreased.

7 DRUG INTERACTIONS

The potential for pharmacokinetic drug-drug interactions between alprostadil and other agents administered orally or intracavernosally has not been formally studied *[see Warnings and Precautions (5.6)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

CAVERJECT IMPULSE is not indicated for use in females.

8.2 Lactation

CAVERJECT IMPULSE is not indicated for use in females.

8.4 Pediatric Use

CAVERJECT IMPULSE is not indicated for use in pediatric patients *[see Warnings and Precautions (5.8)]*.

8.5 Geriatric Use

A total of 341 subjects included in clinical studies were 65 and older. No overall differences in safety and effectiveness were observed between these subjects and younger subjects, and the other reported clinical experience has not identified differences in responses between elderly and younger patients.

10 OVERDOSAGE

Overdosage was not observed in clinical trials with CAVERJECT IMPULSE. If intracavernous overdose of CAVERJECT IMPULSE occurs, the patient should be under medical supervision until any systemic effects have resolved and/or until penile detumescence has occurred. Treatment of any

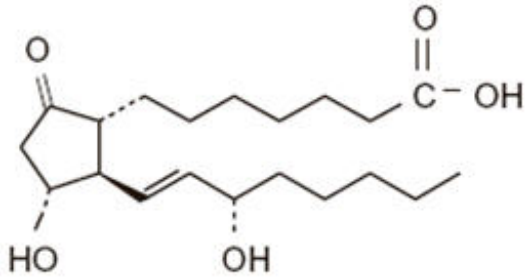
systemic symptoms (e.g., hypotension) would be appropriate.

11 DESCRIPTION

CAVERJECT IMPULSE contains alprostadil a synthetic form of prostaglandin E_1 (PGE_1) and is designated chemically as (11α,13E,15S)-11,15-dihydroxy-9-oxoprost-13-en-1-oic acid. The molecular weight is 354.49.

Alprostadil is a white to off-white crystalline powder with a melting point between 115° and 116°C. Its solubility at 35°C is 8000 micrograms (mcg) per 100 milliliter double distilled water.

The structural formula of alprostadil is represented below:



CAVERJECT IMPULSE is available as a disposable, single-dose, dual chamber syringe system. The system includes a glass cartridge which contains sterile, freeze-dried alprostadil in the front chamber and sterile bacteriostatic water for injection in the rear chamber. The alprostadil is reconstituted with the sterile bacteriostatic water just before injection. CAVERJECT IMPULSE is available in two strengths for intracavernosal administration:

10 microgram – The reconstituted solution has a volume of 0.64 mL. The delivered volume, 0.5 mL, contains 10 micrograms (mcg) of alprostadil, 324.7 mcg of alpha cyclodextrin, 45.4 mg of lactose, 23.5 mcg of sodium citrate, and 4.45 mg of benzyl alcohol.

20 microgram – The reconstituted solution has a volume of 0.64 mL. The delivered volume, 0.5 mL, contains 20 micrograms (mcg) of alprostadil, 649.3 mcg of alpha cyclodextrin, 45.4 mg of lactose, 23.5 mcg of sodium citrate, and 4.45 mg of benzyl alcohol.

During manufacture, the pH of the alprostadil for injection was adjusted with hydrochloric acid and/or sodium hydroxide before lyophilization.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Alprostadil induces erection by relaxation of trabecular smooth muscle and by dilation of cavernosal arteries. This leads to expansion of lacunar spaces and entrapment of blood by compressing the venules against the tunica albuginea, a process referred to as the corporal veno-occlusive mechanism.

12.2 Pharmacodynamics

There are no results from pharmacodynamic studies in humans.

12.3 Pharmacokinetics

Absorption: For the treatment of erectile dysfunction, alprostadil is administered by injection into the corpora cavernosa. The absolute bioavailability of alprostadil has not been determined.

Distribution: Following intracavernosal injection of 20 mcg alprostadil, mean peripheral plasma concentrations of alprostadil at 30 and 60 minutes after injection (89 and 102 picograms/mL, respectively) were not significantly greater than baseline levels of endogenous alprostadil (96

picograms/mL). Plasma levels of alprostadil were measured using a radioimmunoassay method. Alprostadil is bound in plasma primarily to albumin (81% bound) and to a lesser extent α-globulin IV-4 fraction (55% bound). No significant binding to erythrocytes or white blood cells was observed.

Metabolism: Alprostadil is converted to compounds, which are further metabolized prior to excretion. Following intravenous administration, approximately 80% of circulating alprostadil is metabolized in one pass through the lungs, primarily by beta- and omega-oxidation. Following intracavernosal injection of 20 mcg alprostadil, peripheral levels of the major circulating metabolite, 13, 14-dihydro-15-oxo-PGE_1, increased to reach a peak 30 minutes after injection and returned to pre-dose levels by 60 minutes after injection.

Excretion: The metabolites of alprostadil are excreted primarily by the kidney, with almost 90% of an administered intravenous dose excreted in urine within 24 hours post-dose. The remainder of the dose is excreted in the feces. There is no evidence of tissue retention of alprostadil or its metabolites following intravenous administration.

Pharmacokinetics in Specific Populations

Geriatric: The potential effect of age on the pharmacokinetics of alprostadil has not been formally evaluated.

Race: The potential effect of race on the pharmacokinetics of alprostadil has not been formally evaluated.

Renal and Hepatic Insufficiency: The pharmacokinetics of alprostadil have not been formally studied in patients with renal or hepatic insufficiency.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term carcinogenicity studies have not been conducted. The following battery of mutagenicity assays revealed no potential for mutagenesis: bacterial mutation (Ames), alkaline elution, rat micronucleus, sister chromatid exchange, CHO/HGPRT mammalian cell forward gene mutation, and unscheduled DNA synthesis (UDS). Rat reproductive studies indicate that alprostadil at doses of up to 0.2 mg/kg/day does not adversely affect or alter rat spermatogenesis, providing a 200-fold margin of safety compared with the usual human doses.

14 CLINICAL STUDIES

The efficacy of CAVERJECT Sterile Powder was investigated in men with a diagnosis of erectile dysfunction due to psychogenic, vasculogenic, neurogenic, and/or mixed etiology in two double-blind placebo controlled studies (Study 1 and Study 2) and in one 6-month open-label study (Study 3). In clinical studies (Study 1 and Study 3), over 80% of patients experienced an erection sufficient for sexual intercourse after intracavernosal injection of CAVERJECT Sterile Powder.

Study 1: A total of 153 men with ED with a mean age of 53 years (range 23–69 years) were enrolled. The study had three phases: a 2.5 week, randomized, double-blind, placebo-controlled crossover phase in which each man received in-office injections of placebo or 2.5 mcg, 5 mcg, 7.5 mcg, or 10 mcg of CAVERJECT Sterile Powder; a 2 week, open-label, in-office dose-titration phase to identify the optimum home-use dose (the latter dose was defined as a dose inducing an erection sufficient for intercourse and lasting ≤ 60 minutes); and a 4-week open-label, at-home phase. In the double-blind placebo-controlled, crossover phase, each dose of CAVERJECT was significantly more effective than placebo by clinical evaluation ("full penile rigidity") and by RigiScan criteria (≥ 70% rigidity for at least 10 minutes); there was no response to placebo. The percentage of responders increased with increasing doses of CAVERJECT. The overall response rates in the crossover and dose-titration phases were 76% (117/153) by clinical evaluation and 51% (78/152) by RigiScan criteria. Seventy-three

percent of the injections in 102 men who used CAVERJECT in the at-home phase resulted in satisfactory intercourse. Seventy-five percent of the men who used CAVERJECT in the at-home phase remained on the dose identified as optimum for them during the dose-titration phase; 17% and 8% of the men decreased or increased their dose, respectively. The mean duration of erection per injection was 70.8 minutes.

Study 2: A total of 296 men with ED with a mean age of 54 years (range 21–74 years) were enrolled in this double-blind, placebo controlled, parallel-arm design study. The men were randomly assigned to one of five groups and received either a single dose of placebo, 2.5 mcg, 5 mcg, 10 mcg, or 20 mcg of CAVERJECT Sterile Powder. No patient responded to placebo. The differences in the response rates in both the clinical and the RigiScan evaluations between each of the doses of CAVERJECT and placebo were statistically significant. There was also a statistically significant dose-response relationship with higher clinical response rates and higher RigiScan response rates with increasing doses of CAVERJECT (with exception of the 10-mcg dose). The mean duration of erection after injection ranged from 12 minutes after the 2.5-mcg dose to 44 minutes after the 20-mcg dose and the relationship was linear (p = .025, linear regression analysis).

Study 3: The efficacy of CAVERJECT Sterile Powder was further evaluated in a 6-month, open-label, at-home study in 683 men with ED with a mean age of 58 years (range 20–79 years). The optimum dose of CAVERJECT was established by titration in 89% of men (606/683). A total of 471/683 men (69%) completed the 6-month study. Eighty-seven percent of the 13,762 injections of CAVERJECT administered resulted in satisfactory sexual activity. The mean duration of erection was 67.5 minutes.

The formulation of alprostadil contained in CAVERJECT IMPULSE was compared to CAVERJECT Sterile Powder in 87 men with ED in a single-blind, crossover study. The doses used by the patients in the study ranged from 2.5 mcg to 20 mcg and were the same for both formulations. The efficacy of the two formulations was shown to be comparable, as assessed by the 30-point erectile function (EF) domain score from the International Index of Erectile Function (IIEF) and by a physician-assessment score for erectile response. The mean EF domain scores for CAVERJECT Sterile Powder and the formulation contained in CAVERJECT IMPULSE were 26.6 (SD=5.3) and 27.6 (SD=3.8), respectively. The mean physician's assessment scores for CAVERJECT Sterile Powder and the formulation contained in CAVERJECT IMPULSE were 2.6 (SD=0.6) and 2.7 (SD=0.5), respectively, based on a scale of 0 (no tumescence) to 3 (full rigidity).

16 HOW SUPPLIED/STORAGE AND HANDLING

CAVERJECT IMPULSE is supplied as a disposable, single-dose, dual chamber syringe system. The system includes a glass cartridge, which contains sterile, freeze-dried alprostadil in the front chamber and sterile bacteriostatic water for reconstitution in the rear chamber. The syringes contain either 12.8 or 25.6 mcg of alprostadil to allow delivery of a maximum of 10 or 20 mcg/0.5mL. Store the unreconstituted product at 68°F to 77°F (20°C to 25°C); excursions permitted to 59°F to 86°F (15°C to 30°C) [see USP Controlled Room Temperature].

When reconstituted and used as directed, the deliverable amount for the 10 mcg strength is 10 mcg/0.5 mL or an increment of 10 mcg/0.5 mL: 2.5 mcg/0.125 mL, 5 mcg/0.25 mL, or 7.5 mcg/0.375 mL of alprostadil. The deliverable amount for the 20 microgram strength is 20 mcg/0.5 mL or an increment of 20 mcg/0.5 mL: 5 mcg/ 0.125 mL, 10 mcg/0.250 mL, or 15 mcg/0.375 mL of alprostadil. The reconstituted solution should be used within 24 hours when stored between 36–77°F (2°C to 25°C). Do not freeze.

CAVERJECT IMPULSE is supplied in a carton containing 2 blister trays. Each blister tray contains one dual chamber syringe system, one needle and 2 alcohol swabs. It is available in the following strengths:

10 mcg	NDC 0009-5181-01
	NDC 0009-5182-

20 mcg	NDC 0009-5182-01

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use)

Dosing and Self-Administration

To ensure safe and effective use of CAVERJECT IMPULSE, instruct and train the patient in the self-injection technique before he begins intracavernosal treatment with CAVERJECT IMPULSE, at home. Inform the patient the initial dose administration and dose titration will take place in the physician's office.

Once the home dose of CAVERJECT IMPULSE has been established instruct the patient not to change the dose without consulting their physician.

The patient may expect an erection to occur within 5 to 20 minutes and it should last no longer than 1 hour. CAVERJECT IMPULSE should be used no more than 3 times per week, with at least 24 hours between each use.

Inform the patient that they must visit the physician's office for regular check-ups for assessment of the therapeutic benefit and safety of treatment with CAVERJECT IMPULSE.

When self-administering the patient should be instructed to:

- Discard any reconstituted solution with precipitates or discoloration
- Administer the injection along the dorso-lateral aspect of the proximal third of the penis
- Wipe the intended injection site with an alcohol swab prior to injection
- Avoid visible veins during injection
- Alternate the side of the penis that is injected and the site of injection
- Compress the site of injection with an alcohol swab or sterile gauze for 5 minutes
- Use each CAVERJECT IMPULSE system only once and discard after use
- Do not use a bent needle. If the needle is bent, it must not be used; they should also not attempt to straighten a bent needle. They should remove the needle from the syringe, discard it, and attach a new, unused sterile needle to the syringe.
- Not re-use or share needles and to properly discard after use

Penile Pain

Advise patients that the most frequently occurring side-effect is penile pain after injection, and is usually mild to moderate in severity *[see Adverse Reactions (6.1)]*.

Priapism

A potentially serious adverse reaction with intracavernosal therapy of CAVERJECT IMPULSE is priapism. Instruct the patient to seek immediate medical assistance if an erection persists for longer than 4 hours *[see Warnings and Precautions (5.1)]*.

Penile Fibrosis

Penile fibrosis has been reported in clinical studies with CAVERJECT. Advise the patient to report any penile pain that was not present before or that increased in intensity, as well as the occurrence of nodules or hard tissue in the penis or curvature of the erect penis to his physician as soon as possible. *[see Warnings and Precautions (5.2)]*.

Injection Site Reactions

Inform the patient that injection of CAVERJECT IMPULSE can induce a small amount of bleeding at the site of injection and that hematoma and ecchymosis may occur. Advise the patient to report any persistent

redness, tenderness or swelling.

Sexually Transmitted Disease

Use of intracavernosal CAVERJECT IMPULSE offers no protection from the transmission of sexually transmitted diseases. Advise the patient about the protective measures that are necessary to guard against the spread of sexually transmitted diseases, including the human immunodeficiency virus (HIV).

This product's label may have been updated. For current full prescribing information, please visit www.pfizer.com

Distributed by

Pfizer

Pharmacia & Upjohn Co

Division of Pfizer Inc, NY, NY 10017

LAB-0007-9.0

Patient Information

CAVERJECT IMPULSE® [KAV-er-jeckt]

(alprostadil)
for injection, for intracavernosal use

Read this Patient Information before you start using CAVERJECT IMPULSE and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

What is CAVERJECT IMPULSE?

CAVERJECT IMPULSE is a prescription medicine used:

- to treat erectile dysfunction (ED).
- with other medical tests to diagnose ED.

CAVERJECT IMPULSE is not meant for use in women or children under 18 years of age.

Who should not use CAVERJECT IMPULSE?

Do not use CAVERJECT IMPULSE if you have:

- certain medical problems that might cause you to have an erection that lasts for more than 4 hours, such as sickle cell anemia, sickle cell trait, multiple myeloma, leukemia.
- a deformed penis shape
- a penile implant

What should I tell my healthcare provider before using CAVERJECT IMPULSE?

Before you use CAVERJECT IMPULSE, tell your healthcare provider if you:

- have had an erection that lasted more than 4 hours
- have sickle cell trait or sickle cell anemia
- have or have had a blood cell cancer called multiple myeloma or leukemia
- have a deformed penis shape
- have a penile implant
- have low blood pressure (hypotension)
- have bleeding problems
- have or have had heart problems such as a heart attack, irregular heartbeat, angina, chest pain, narrowing of the aortic valve or heart failure
- have any other medical conditions

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

CAVERJECT IMPULSE may affect the way other medicines work, and other medicines may affect the way CAVERJECT IMPULSE works causing side effects.

Especially tell your healthcare provider if you take any other medicines that are injected into your penis (intracavernosally) or certain medicines called anticoagulant medicines (such as heparin or warfarin).

Ask your healthcare provider or pharmacist for a list of these medicines, if you are not sure.

Know the medicines you take. Keep a list of them to show to your healthcare provider and pharmacist when you get a new medicine.

How should I use CAVERJECT IMPULSE?

- See the detailed **Instructions for Use** that comes with your CAVERJECT IMPULSE for information about how to prepare and inject CAVERJECT IMPULSE the right way.
- Use CAVERJECT IMPULSE exactly as your healthcare provider tells you to.
- Your healthcare provider will tell you how much CAVERJECT IMPULSE to use and when to use it.
- Your healthcare provider may change your dose if needed. **Do not** change your dose of CAVERJECT IMPULSE without first talking to your healthcare provider.
- **Your healthcare provider should show you how to prepare and inject CAVERJECT IMPULSE the right way before you inject it for the first time.**
- CAVERJECT IMPULSE should not be used more than 3 times per week.
- CAVERJECT IMPULSE should not be used more than 1 time every 24 hours.
- Change the exact place and side of the penis that you inject Caverject Impulse each time you use it.
- CAVERJECT IMPULSE is for one use only and should be thrown away properly after a single use.

You should see your healthcare provider every 3 months for check-ups to be sure that CAVERJECT IMPULSE is working the right way and to change your CAVERJECT IMPULSE dose if needed.

What are the possible side effects of CAVERJECT IMPULSE?

CAVERJECT IMPULSE may cause serious side effects, including:

- **an erection that will not go away .** If you have an erection that lasts more than 4 hours, get medical help right away. If it is not treated right away, this condition can permanently damage your penis.
- **deformed penis shape (penile fibrosis).** Your healthcare provider should check your penis regularly for signs of penile fibrosis. You should not continue to use CAVERJECT IMPULSE if you get penile fibrosis.
- **low blood pressure (hypotension)**
- **injection site bleeding.** People who take certain medicines called anticoagulants (such as heparin or warfarin) may have a risk for increased bleeding at the injection site.
- **increased risk of heart problems.** Sexual activity can put an extra strain on your heart, especially if your heart is weak from a heart attack or heart disease. Ask your healthcare provider if your heart is healthy enough to handle the extra strain of having sex. Stop sexual activity and get medical help right away if you get symptoms of a heart problem such as chest pain, dizziness or nausea.
- **needle breakage**. There is a possibility of needle breakage with use of CAVERJECT IMPULSE. To best avoid breaking the needle, you should pay careful attention to your healthcare provider's instructions and try to handle the syringe and needle properly. If the needle is bent at any time, do not attempt to straighten it and do not use it. A bent and re-straightened needle is predisposed to breakage. Remove the needle from the syringe, discard, and attach a new, unused sterile needle to the syringe. If the needle breaks during injection and you are able to see and grasp the broken end, you should remove it and contact your healthcare provider. If you cannot see or cannot grasp the broken end, you should promptly contact your healthcare provider

- **benzyl alcohol toxicity.** Benzyl alcohol is a preservative in CAVERJECT IMPULSE. Benzyl alcohol has caused serious side effects, including death, in children, especially premature and low-birth weight infants, who have received the preservative benzyl alcohol. CAVERJECT IMPULSE is not meant for use in children.

CAVERJECT IMPULSE does not protect you or your partner from getting sexually transmitted infections, including HIV-the virus that causes AIDS.

The most common side effects of CAVERJECT IMPULSE include:

- penile pain
- erection lasting 4 to 6 hours (prolonged erection)
- penile fibrosis (deformed penis shape)
- bruising at the injection site
- penile numbness, irritation, sensitivity, itching, swelling and discoloration
- skin tears of the penis
- penile rash

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of CAVERJECT IMPULSE. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of CAVERJECT IMPULSE

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information Leaflet. Do not use CAVERJECT IMPULSE for a condition for which it was not prescribed. Do not give CAVERJECT IMPULSE to other people even if they have the same symptoms that you have. It may harm them.

This Patient Information summarizes the most important information about CAVERJECT IMPULSE. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about CAVERJECT IMPULSE that is written for health professionals.

For more information, go to www.pfizer.com or call 1-800-438-1985.

What are the Ingredients in CAVERJECT IMPULSE?

Active ingredient: alprostadil

Inactive ingredients: alpha cyclodextrin, lactose, sodium citrate, benzyl alcohol and hydrochloric and/or sodium hydroxide for pH adjustment.

What are the causes of and treatments for ED?

There are several causes of ED. These include medications that you may be taking for other conditions, poor blood circulation in the penis, nerve damage, emotional problems, too much smoking or alcohol use, use of street drugs, and hormonal problems. Often, ED is due to more than one cause.

Treatments for ED include switching medications if you are taking a medication that causes erectile dysfunction, prescription medications, medical devices that produce an erection, surgical procedures to correct blood flow in the penis, penile implants, and psychological counseling.

You should not stop taking any prescription medications, unless told to do so by your doctor.

The use of other medical treatments for ED in combination with CAVERJECT is not recommended. Discuss any concerns you may have about combination treatment with your doctor.

INSTRUCTIONS FOR USE

Before you use CAVERJECT, your doctor must train you in how to prepare and give the injection properly.

Before using CAVERJECT, talk to your doctor about what to expect when using it, possible side effects, and what to do if side effects occur. Your dose has been selected for your individual needs. Do not change your dose without consulting your doctor. If you are not sure of the volume or dose to be used, talk to your doctor or pharmacist.

Follow these instructions exactly to properly prepare the syringe for use, and to correctly inject a sterile (germ-free) dose of CAVERJECT.

Supplies Needed

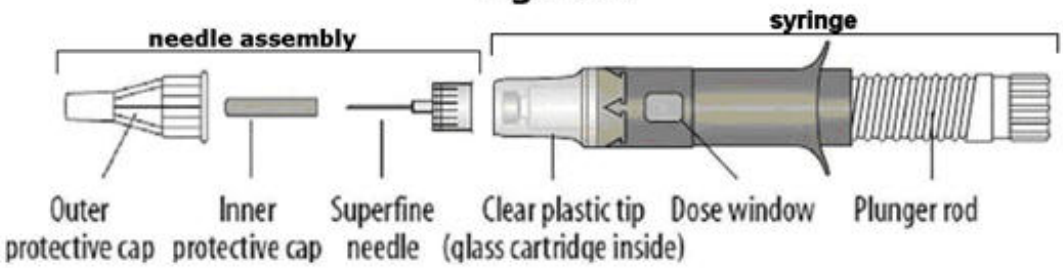
The CAVERJECT IMPULSE carton contains two (2) sealed plastic trays, with one dose of Caverject in each tray.

Each tray contains: (a) a syringe, (b) a separate needle assembly and (c) two alcohol swabs. The syringe and the needle assembly are shown in Figure A (below). Please note that the needle assembly is packaged as a single piece and is sealed with a paper cover on the bottom.

DO NOT try to assemble the syringe until you have read ALL of the instructions.

First-read through ALL of the instructions (Step 1 through Step 12) before trying to assemble the syringe. Then go back to Step 1 and begin to prepare the syringe for use.

Figure A



CAVERJECT IMPULSE is available in two versions: the 10 mcg strength (white plunger) and the 20 mcg strength (blue plunger). Each syringe is designed to be used only one time, but you can select the dose that will be delivered:

- The 10 mcg strength syringe (white plunger) can deliver 10 mcg (the full dose), or one of three partial doses: 7.5 mcg, or 5 mcg, or 2.5 mcg.
- The 20 mcg strength syringe (blue plunger) can deliver 20 mcg (the full dose), or one of three partial doses: 15 mcg, or 10 mcg, or 5 mcg.

If you deliver a partial dose there will be left-over solution in the syringe – this is normal.

MAKE SURE YOU HAVE THE CORRECT STRENGTH OF CAVERJECT IMPULSE to deliver your assigned dose

INSTRUCTIONS for PREPARING the SYRINGE (Step 1 through Step 12)

Wash your hands thoroughly and dry them with a clean towel.

STEP 1. Open the sealed plastic tray. Remove the syringe, the needle assembly, and the alcohol swabs from the tray. All items should be present.

Look at the needle assembly. The needle assembly is a sealed unit that contains the outer protective cap, the inner protective cap, and the superfine needle, as shown in Figure A. It is sealed with a small round paper cover (not shown in Figure A).

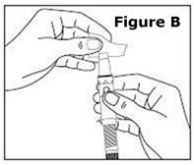
Do not open the needle assembly at this point – leave it sealed inside the outer protective cap.

Next, examine the syringe. Find the location of the dose window. Right now you will not see anything in this window, but at a later Step, a number will appear in this window (the dose to be delivered).

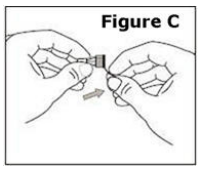
Finally, look at the Plunger, but do not move it at this time. During the assembly process, some Steps may ask you to ROTATE the plunger and other steps may ask you to PUSH the plunger.

It is important to only rotate the plunger – or only push – as directed in each Step, but DO NOT do both at the same time.

Never PUSH on the plunger – even slightly – while trying to rotate it. This can cause the plastic threads on the plunger rod to stick.



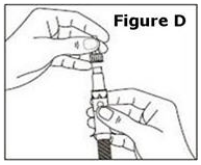
STEP 2. Open the packet containing the alcohol swab, and then pick up the syringe. Use the alcohol swab to wipe the rubber membrane at the tip of the syringe (Figure B). Discard the alcohol swab.



STEP 3. Pick up the Needle Assembly. Grab the paper tab and peel off the paper cover (lid) from the bottom of the needle assembly (Figure C).

Hold the needle assembly by the cap. Pick up the syringe with your other hand.

Press the needle assembly onto the tip of the syringe and turn it clockwise (like tightening a screw) until the needle assembly is firmly locked into place.

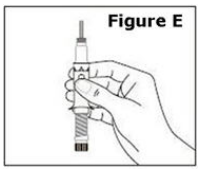


STEP 4. Remove (twist off - clockwise) the outer protective cap from the needle (Figure D), but DO NOT REMOVE the inner protective cap at this time. The inner protective cap is the thin plastic tube that directly covers the needle. It will be

removed later.

If you are not sure which piece is the inner protective cap, see Figure A (Step 1) to identify the inner protective cap.

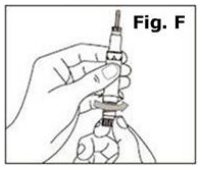
The next few steps will mix the powder and the fluid to make the Caverject Impulse solution.



STEP 5.

Hold the syringe system with the needle pointing upward.

The plunger rod should still be in the fully extended position, with all of the threads visible, as shown in Figure E.



STEP 6.

Slowly **ROTATE** the plunger rod clockwise (like tightening a screw,) **until it goes all the way in and stops** (Figure F).

This automatically combines the drug powder and the fluid.

DO NOT turn the plunger rod counter-clockwise (do not try to "unscrew" the plunger rod).

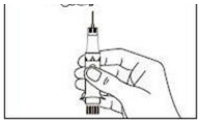
DO NOT PUSH on the plunger while trying to rotate it. This can cause the plastic threads on the plunger rod to stick.

STEP 7.

Turn the syringe upside down several times to make sure the solution is evenly mixed. The solution should be clear. Do not use it if it is cloudy or contains particles.

STEP 8.

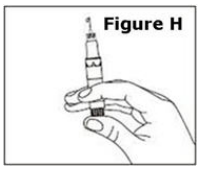
Hold the syringe with the needle upward and carefully remove the inner protective cap from the needle (Figure G). Do not touch the exposed needle because it is sterile.



STEP 9.

Next, you need to remove any large bubbles from the solution.

Lightly tap the glass cartridge a few times with your finger until any large bubbles disappear up into the tip. Very small bubbles may remain.



STEP 10.

With the syringe pointed upward (Figure H), use your thumb to **push in the plunger rod until it stops**.

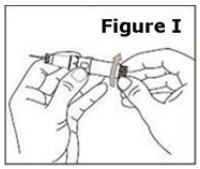
This will push the air out. Some liquid will appear at the needle point.

After pressing the plunger you may still see some small bubbles on the wall of the glass cartridge. This is normal.

If you can't press the plunger rod in, check that the plunger rod is rotated all the way: turn it clockwise until it stops, and then repeat Step 10.

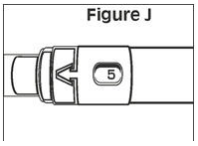
After the plunger is pushed in – Do Not rotate the plunger. That will be done in the next step.

PLEASE READ the following before going on.



STEP 11.

In Step 11, you will need to set the dose by ROTATING the plunger until the correct dose appears in the small oval Dose Window on the syringe. The plunger must be rotated "clock-wise" – like tightening a screw.



DO NOT PUSH on the plunger while trying to rotate it. This can cause the plastic threads on the plunger rod to stick.

If the plunger does stick, you can try

to free it by gently turning it backward ("unscrewing it") and trying again.

TO SET THE DOSE:

Locate the Dose Window on the syringe. This small oval window (above the left thumb in Figure I) is where the dose number will appear when the plunger is rotated.

Then – holding the syringe as shown in Figure I, **slowly turn the plunger rod clockwise** (like tightening a screw – see arrow in Figure I) until the correct dose number appears **in the center of the window** (Figure J).

If you pass the correct number, keep turning the plunger in the same direction until the correct number comes around again – do not try to turn it backward

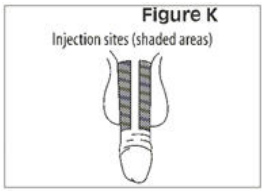
The syringe is now ready for use.

STEP 12. Set the syringe down on a flat level surface.

The needle is sterile .Make sure the needle does not touch the surface or anything else.

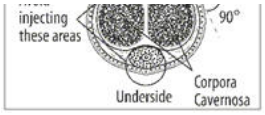
How to give the injection

- Make yourself comfortable. Take some time to relax yourself and your partner. If your doctor has recommended you use an alcohol cleansing swab, open one now.
- Make sure that the needle is **not** bent. If it is, **do not** use it. **Do not** attempt to straighten the needle out. Properly discard it.



1. The injection will go into the part of the penis shown as the shaded area in Figure K. Do not inject into the white areas because there may be blood vessels in the white areas. Also see Figure L.

2. The correct injection angle is shown in Figure L.



3. If your doctor has recommended that you use an alcohol swab, wipe over the area for injection and let it dry. Reconfirm that the correct dose is visible in the dose window. If the correct dose is not in the dose window, repeat Step 11.

4. Take hold of the penis from the front, with the first two fingers underneath close to the testicles and the thumb on top (Figure M).

5. Gently squeeze the penis between your thumb and finger so that the injection site bulges out. If there is a foreskin on the penis, make sure it is stretched.

6. Keeping a firm grip on the penis and taking the syringe in your free hand, push the needle straight through the skin all the way into the bulgy part (corpora cavernosa). Avoid veins or other obvious blood vessels (Figures K and L).

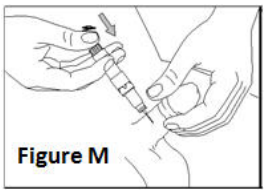


Figure M

7. Push the plunger firmly and steadily until it no longer moves. **Plunger movement may be very small or undetectable if administering a partial dose.**

8. If the plunger does not move easily adjust the needle depth slightly and try again. **Do not** force the solution from the syringe.

9. After completing the injection, carefully pull the needle out. A drop of liquid may remain on the tip of the needle. Press gently on the injection site with the alcohol swab. Massage the penis to help the Caverject Impulse solution spread through it.

Some liquid will remain in the syringe if you delivered a PARTIAL dose. This is expected. Do not try to inject left-over liquid from a partial dose. Syringes used to inject a partial dose must be discarded since each syringe can only be used one time. Discard syringes with left-over liquid.

- A partial dose is 5 mcg, 10 mcg or 15 mcg for the BLUE plunger syringe.
- A partial dose is 2.5 mcg, 5 mcg, or 7.5 mcg for the WHITE plunger syringe.

Do not keep any solution in the cartridge to use for a second injection. When you have finished with the

syringe, discard it carefully as recommended by your doctor, so no one will use it or stick themselves with it.

After your injection:

Dispose of your used CAVERJECT IMPULSE syringes and needle.

- Put your used CAVERJECT IMPULSE syringe and needle in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and syringes in your household trash.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out
  - upright and stable during use
  - leak-resistant
  - properly labeled to warn of hazardous waste inside the container
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. Do not reuse or share your needles or syringes with other people. For more information about the safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.
- Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

How should I store CAVERJECT IMPULSE?

1. Store **unmixed** CAVERJECT IMPULSE at room temperature between 68°F to 77°F (20°C to 25°C).
2. Store **mixed** CAVERJECT IMPULSE between 36–77°F (2°C to 25°C). Do not freeze.
3. CAVERJECT IMPULSE should be used within 24 hours after it is mixed.

Keep CAVERJECT IMPULSE and all medicines out of the reach of children.

This Patient Information and Instructions for Use has been approved by the U.S Food and Drug Administration.

This product's label may have been updated. For current full prescribing information, please visit www.pfizer.com.

Rx only

Manufactured by:

Distributed by

Pfizer

Pharmacia & Upjohn Co

Division of Pfizer Inc, NY, NY 10017

LAB-0641-6.0
October 2016

PRINCIPAL DISPLAY PANEL - 10 microgram Syringe Label

Caverject Impulse®

Dual Chamber System

alprostadil for injection

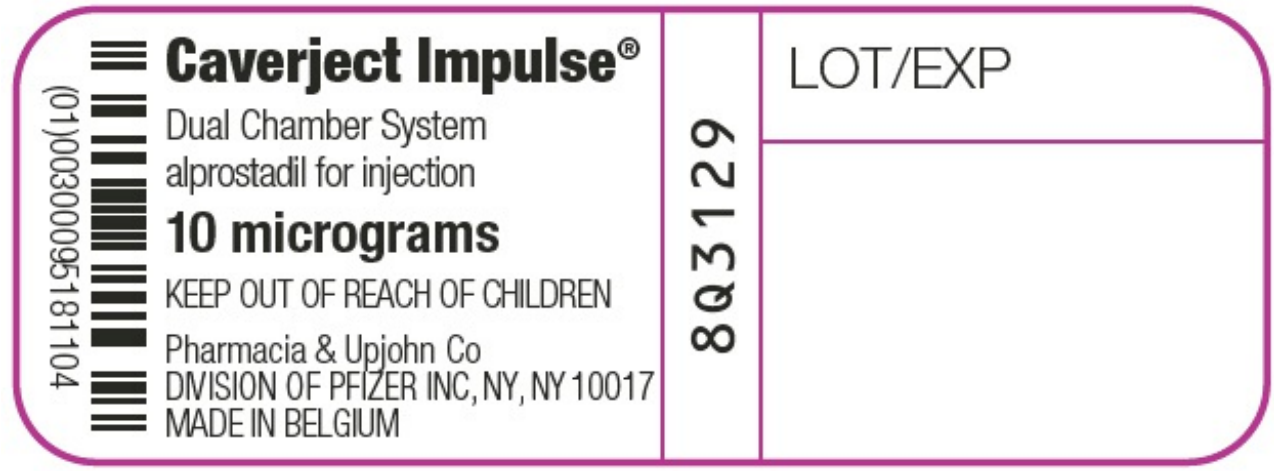
10 micrograms

KEEP OUT OF REACH OF CHILDREN

Pharmacia & Upjohn Co
DIVISION OF PFIZER INC, NY, NY 10017
MADE IN BELGIUM

8Q3129

LOT/EXP



PRINCIPAL DISPLAY PANEL - 10 micrograms Syringe Carton

Pfizer

Caverject Impulse®
alprostadil for injection

10 micrograms

NDC 0009-5181-01
Contains 2 of NDC 0009-5181-10

For intracavernosal use only
Dual Chamber System

Contains 2 single dose injection systems
Diluent Contains Benzyl Alcohol

Rx only

PAA
084401

NO TEXT AREA

Distributed by
Pharmacia & Upjohn Co
Division of Pfizer Inc
NY, NY 10017

PAA084401

MADE IN BELGIUM

Store between 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

Reconstituted solution should be used within 24 hours when stored between 2°C to 25°C (36°F - 77°F).

DOSAGE AND USE

See accompanying prescribing information.

Lyophilized in container.

Each injection system contains: a pre-filled dual chamber syringe, a needle and two alcohol swabs.

KEEP OUT OF REACH OF CHILDREN

Caution: Federal law restricts the device to sale by or on the order of a physician.

The maximum deliverable volume is 0.5 mL.

Each 0.5 mL contains:

Alprostadil	10 mcg
Alpha cyclodextrin	324.7 mcg
Lactose	45.4 mg
Sodium citrate	23.5 mcg
Benzyl alcohol	4.45 mg

When necessary, the pH of the alprostadil for injection was adjusted with hydrochloric acid and/or sodium hydroxide, before lyophilization.

Each dual chamber syringe contains:
(front chamber) 12.8 mcg alprostadil, 415.5 mcg alpha cyclodextrin, 30.08 mcg sodium citrate, 58.14 mg lactose;
(rear chamber) 6.05 mg benzyl alcohol.
Reconstitution according to directions produces a volume of 0.64 mL.

Pfizer

Caverject Impulse®

10 micrograms

alprostadil for injection

NDC 0009-5181-01
Contains 2 of NDC 0009-5181-10

For intracavernosal use only
Dual Chamber System

Contains 2 single dose injection systems
Diluent Contains Benzyl Alcohol

Rx only

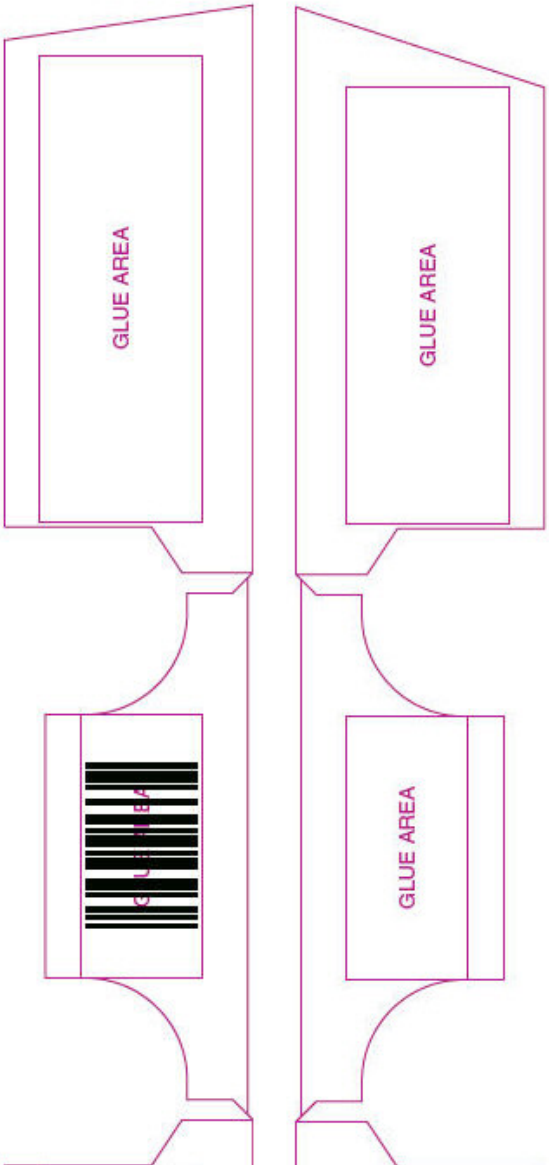
Caverject Impulse®

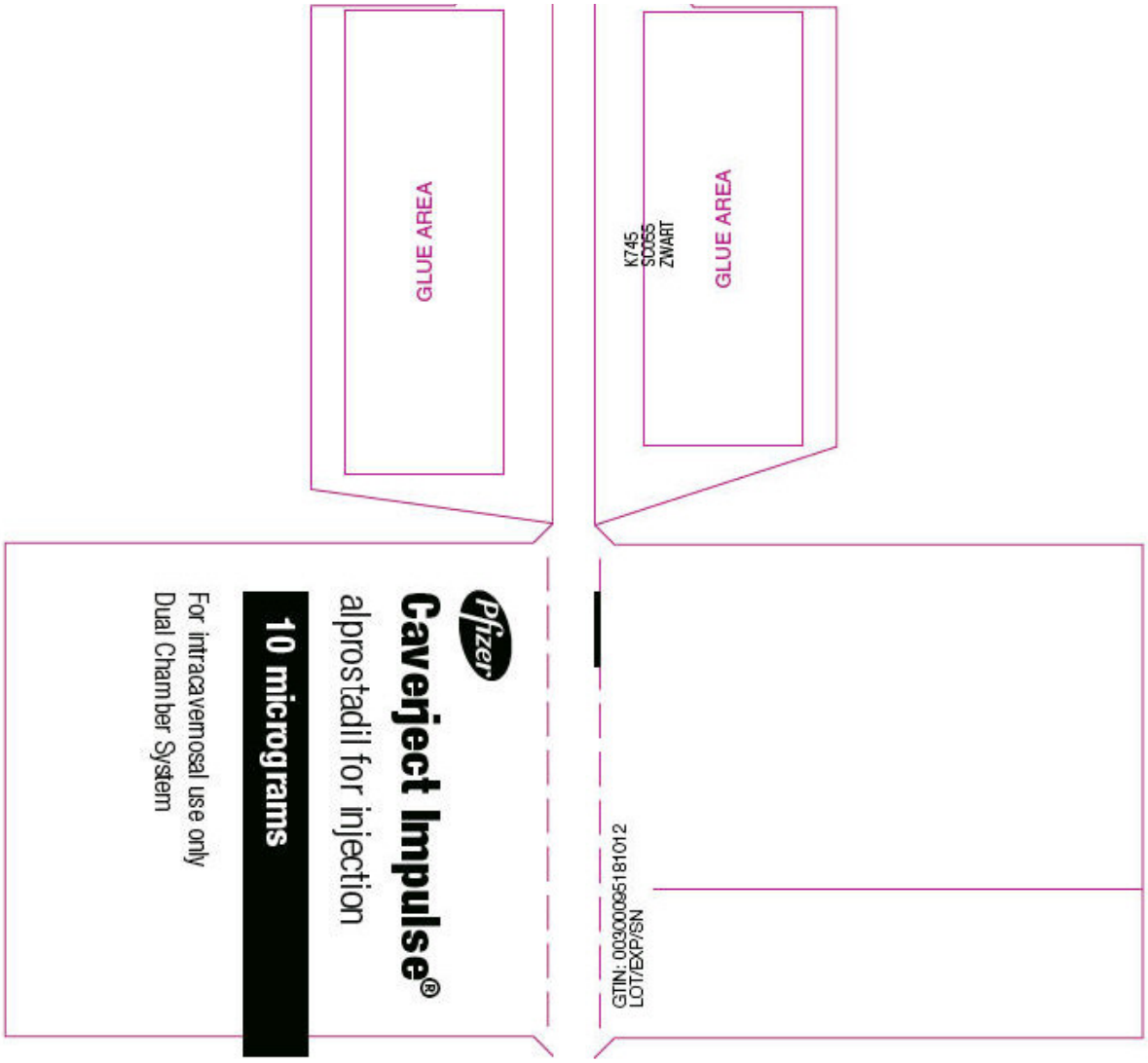
10 micrograms

alprostadil for injection

For intracavernosal use only

Contains 2 single dose injection systems
Diluent Contains Benzyl Alcohol





PRINCIPAL DISPLAY PANEL - 20 microgram Syringe Label

Caverject Impulse®

Dual Chamber System
alprostadil for injection

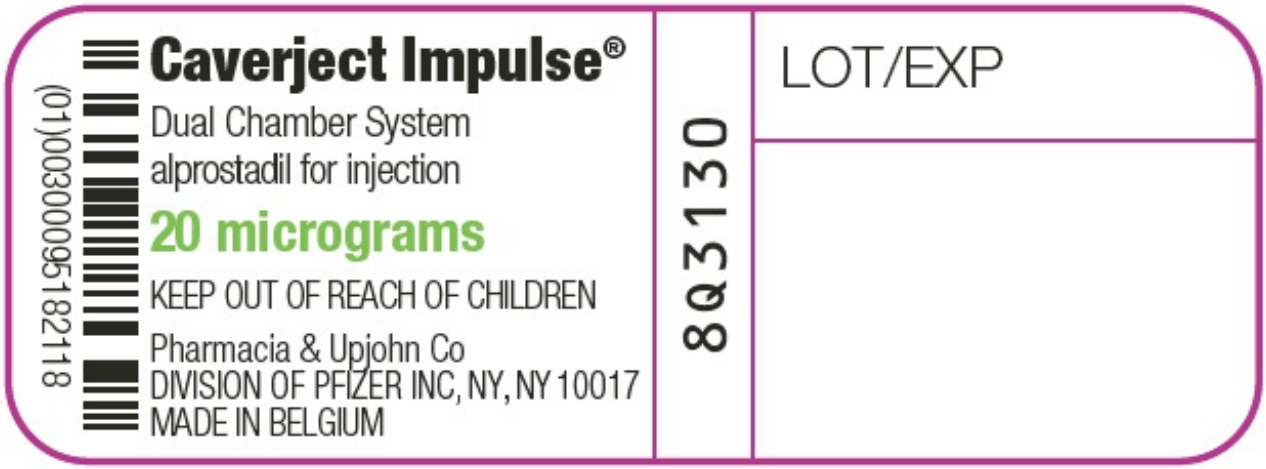
20 micrograms

KEEP OUT OF REACH OF CHILDREN

Pharmacia & Upjohn Co
DIVISION OF PFIZER INC, NY, NY 10017
MADE IN BELGIUM

8Q3130

LOT/EXP



PRINCIPAL DISPLAY PANEL - 20 micrograms Syringe Carton

Pfizer

Caverject Impulse®
alprostadil for injection

20 micrograms

NDC 0009-5182-01
Contains 2 of NDC 0009-5182-11

For intracavernosal use only
Dual Chamber System

Contains 2 single dose injection systems
Diluent Contains Benzyl Alcohol

Rx only

Caverject Impulse®

20 micrograms

alprostadil for injection

NDC 0009-5182-01
Contains 2 of NDC 0009-5182-11

Store between 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

Reconstituted solution should be used within 24 hours when stored between 2°C to 25°C (36°F - 77°F).

DOSAGE AND USE

See accompanying prescribing information.

Lyophilized in container.

Each injection system contains: a pre-filled dual chamber syringe, a needle and two alcohol swabs.

KEEP OUT OF REACH OF CHILDREN

Caution: Federal law restricts the device to sale by or on the order of a physician.

MADE IN BELGIUM

The maximum deliverable volume is 0.5 mL.

Each 0.5 mL contains:

Alprostadil	20 mcg
Alpha cyclodextrin	649.3 mcg
Lactose	45.4 mg
Sodium citrate	23.5 mcg
Benzyl alcohol	4.45 mg

When necessary, the pH of the alprostadil for injection was adjusted with hydrochloric acid and/or sodium hydroxide, before lyophilization.

Each dual chamber syringe contains:
(front chamber) 25.6 mcg alprostadil, 831.0 mcg alpha cyclodextrin, 30.08 mcg sodium citrate, 58.14 mg lactose;
(rear chamber) 6.05 mg benzyl alcohol.
Reconstitution according to directions produces a volume of 0.64 mL.

PAA084402

Distributed by
Pharmacia & Upjohn Co
Division of Pfizer Inc, NY, 10017

N 3 0009-5182-01 9

NO TEXT AREA

PAA 084402

For intracavernosal use only
Dual Chamber System

Contains 2 single dose injection systems
Diluent Contains Benzyl Alcohol

Rx only

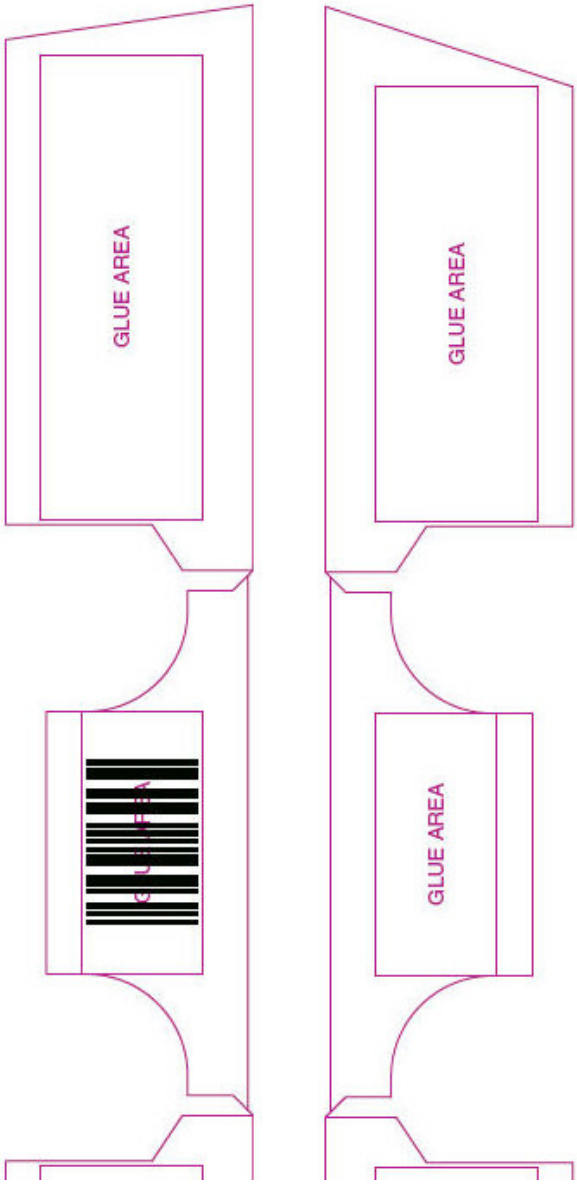
Caverject Impulse®

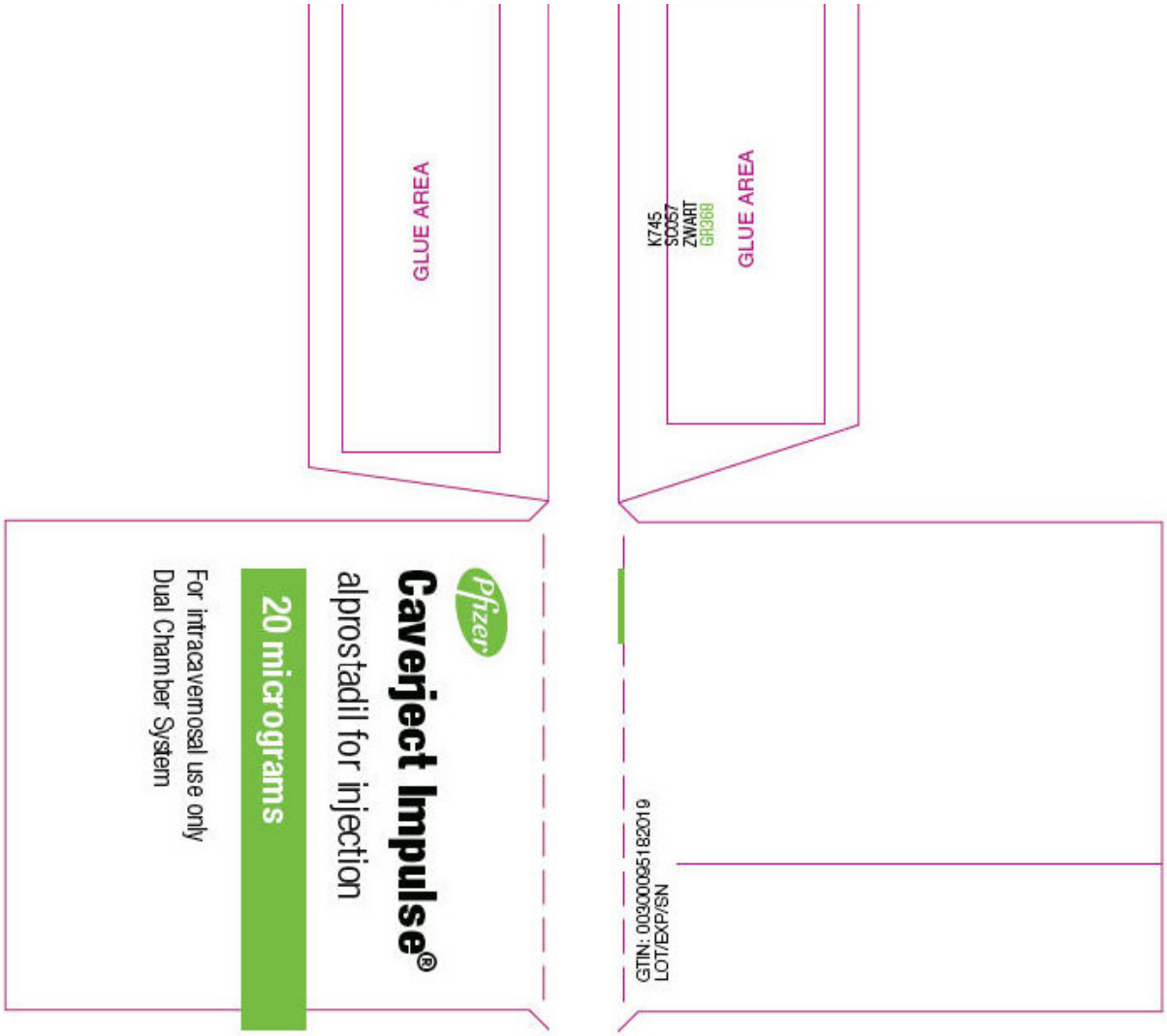
20 micrograms

alprostadil for injection

For intracavernosal use only

Contains 2 single dose injection systems
Diluent Contains Benzyl Alcohol





CAVERJECT IMPULSE

alprostadil injection, powder, lyophilized, for solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0009-5181
Route of Administration	INTRACAVERNOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
ALPROSTADIL (UNII: F5TD010360) (ALPROSTADIL - UNII:F5TD010360)	ALPROSTADIL	10 ug in 0.5 mL

Inactive Ingredients

Ingredient Name	Strength
ALFADEX (UNII: Z1LH97KTRM)	324.7 ug in 0.5 mL
LACTOSE, UNSPECIFIED FORM (UNII: J2B2A4N98G)	45.4 mg in 0.5 mL
SODIUM CITRATE, UNSPECIFIED FORM (UNII: 1Q73Q2JULR)	23.5 ug in 0.5 mL
BENZYL ALCOHOL (UNII: LKG8494WBH)	4.45 mg in 0.5 mL

HYDROCHLORIC ACID (UNII: QTT17582CB)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0009-5181-01	2 in 1 CARTON	06/11/2002	
1	NDC:0009-5181-10	0.5 mL in 1 SYRINGE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021212	06/11/2002	

CAVERJECT IMPULSE

alprostadil injection, powder, lyophilized, for solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0009-5182
Route of Administration	INTRACAVERNOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
ALPROSTADIL (UNII: F5TD010360) (ALPROSTADIL - UNII:F5TD010360)	ALPROSTADIL	20 ug in 0.5 mL

Inactive Ingredients

Ingredient Name	Strength
ALFADEX (UNII: Z1LH97KTRM)	649.3 ug in 0.5 mL
LACTOSE, UNSPECIFIED FORM (UNII: J2B2A4N98G)	45.4 mg in 0.5 mL
SODIUM CITRATE, UNSPECIFIED FORM (UNII: 1Q73Q2JULR)	23.5 ug in 0.5 mL
BENZYL ALCOHOL (UNII: LKG8494WBH)	4.45 mg in 0.5 mL
HYDROCHLORIC ACID (UNII: QTT17582CB)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0009-	2 in 1 CARTON	06/11/2002	

1	5182-01	2 in 1 CARTON	06/11/2002	
1	NDC:0009-5182-11	0.5 mL in 1 SYRINGE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021212	06/11/2002	

Labeler - Pharmacia and Upjohn Company LLC (618054084)

Establishment

Name	Address	ID/FEI	Business Operations
Pfizer Manufacturing Belgium NV		370156507	ANALYSIS(0009-5181, 0009-5182) , MANUFACTURE(0009-5181, 0009-5182) , PACK(0009-5181, 0009-5182)

Establishment

Name	Address	ID/FEI	Business Operations
Pharmacia and Upjohn Company LLC		618054084	API MANUFACTURE(0009-5181, 0009-5182)

Revised: 5/2019 Pharmacia and Upjohn Company LLC