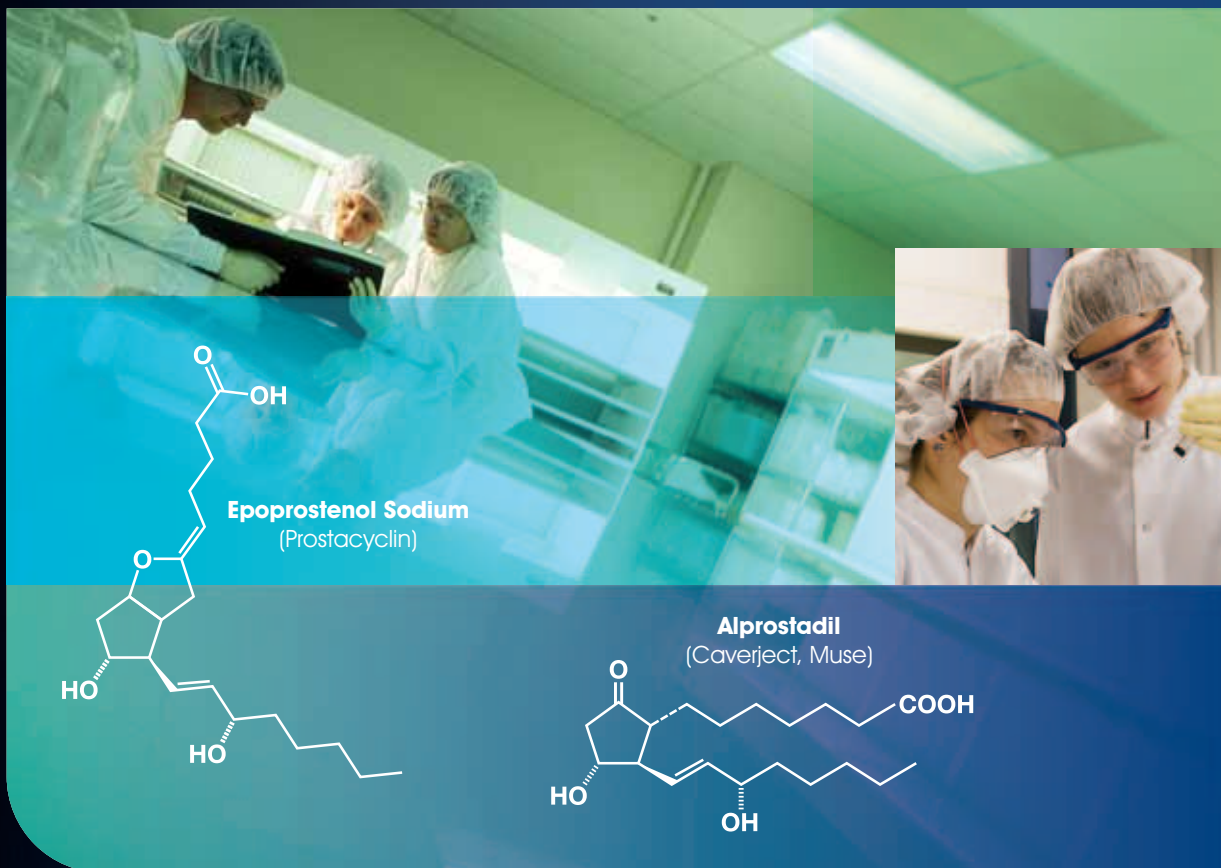


Select Prostaglandins

Epoprostenol Sodium (Prostacyclin)
Alprostadil (Caverject, Muse)



Epoprostenol Sodium
(Prostacyclin)

CCCCC/C=C/C1C(O)C(O)O1C(=O)O

Alprostadil
(Caverject, Muse)

CCCCC/C=C/C1C(O)C(=O)O1C(=O)O

Johnson Matthey
Pharmaceutical Materials

Promoted in conjunction with

Alfa Aesar[®]
A Johnson Matthey Company

Select Prostaglandins

From Johnson Matthey



Johnson Matthey

Johnson Matthey Pharmaceutical Materials has amassed an unparalleled level of expertise in the complex field of prostaglandins and related high potency molecules.

Epoprostenol

Epoprostenol, an eicosanoid lipid, is used for the long-term intravenous treatment of primary pulmonary hypertension and pulmonary hypertension associated with the scleroderma spectrum of disease in NYHA Class III and Class IV patients who do not respond adequately to conventional therapy.

Alprostadil

Alprostadil, is used as a drug in the treatment of erectile dysfunction and has vasodilatory properties.

For each product, we offer a complete technical package, reference standards, and impurity markers, supported by a program of DMF filings.



Alprostadil

Alprostadil

Background

Alprostadil is the pharmaceutical name for prostaglandin E₁. It is used as a drug in the treatment of erectile dysfunction and has vasodilatory properties.

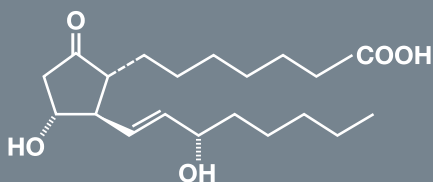
Alprostadil is also used in maintaining a patent ductus arteriosus in the fetus. This is primarily useful when there is threat of premature closure of the ductus arteriosus.

Pharmacology

Its pharmacology includes vasodilation, hypotension, and anti-platelet activities. The IC₅₀ of PGE₁ for the inhibition of ADP-induced human platelet aggregation is 40 nM.

The vasorelaxant and anti-hypertensive effects of PGE₁ are used to treat male erectile dysfunction and to provide emergency vasodilation of the patent ductus arteriosus in infants whose cardiac anomalies require pulmonary shunting for survival.

In human males, the intracavernosal effective dose range for PGE₁ is 2 to 80 µg, and the transurethral range is 125 to 1,000 µg



Alprostadil Systematic (IUPAC) Name

7-[3-hydroxy-2-(3-hydroxyoct-1-enyl)-5-oxo-cyclopentyl] heptanoic acid

IDENTIFIERS

CAS Number	745-65-3
ATC Code	C01EA01, G04BE01
PubChem	149351
DrugBank	APRD00785

CHEMICAL DATA

Formula	C ₂₀ H ₃₄ O ₅
Mol. mass	354.481 g/mol

References:

Kobzar, G., Mardla, V., Järving, I., et al. Antiaggregating potency of E-type prostaglandins in human and rabbit platelets. *Proc Estonian Acad Sci Chem* 40 179-180 (1991).

Okada, F., Nukada, T., Yamauchi, Y., et al. The hypotensive effect of prostaglandin E₁ on hypertensive cases of various types. *Prostaglandins* 7 99-106 (1974).

Padma-Nathan, H., Hellstrom, W.J.G., Kaiser, F.E., et al. Treatment of men with erectile dysfunction with transurethral alprostadil. *N Engl J Med* 336 1-7 (1997).

Olley, P.M., Coceani, F. Prostaglandins and the ductus arteriosus. *Annu Rev Med* 32 375-3785 (1981).

Alprostadil is not currently offered by Johnson Matthey in the US territory.

Alprostadil Based Drugs

Alprostadil Base

Caverject®

Indication

Caverject (Alprostadil) is a drug manufactured by Pfizer® for the treatment of erectile dysfunction.

Dosage

Caverject is available as a sterile freeze-dried powder for intracavernosal use in four sizes: 5, 10, 20 and 40 micrograms per vial--When reconstituted as directed with 1 milliliter of bacteriostatic water for injection or sterile water, both preserved with benzyl alcohol 0.945% w/v, gives 1.13 milliliters of reconstituted solution. This is then administered by injection.

Clinical Pharmacology

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.

Sales and Consumption

In 2004 sales of Caverject reached \$17 million in the US alone.

Caverject is an injectable form of Alprostadil marketed by Pfizer.



d Drugs

Muse®

Indication

Muse (Alprostadil) is a drug manufactured by Vivus® for the treatment of erectile dysfunction.

Dosage

Muse is a FDA approved prescription treatment consisting of a small medicated pellet about half the size of a grain of rice that is placed in the urinary opening using a plastic applicator. No needles are used with Muse administration.

Clinical Pharmacology

Muse works by opening blood vessels to increase blood flow into the penis.

Sales and Consumption

In 1997 sales of Muse reached \$128 million worldwide. Muse is administered as a pellet of Alprostadil marketed by Vivus.

There are a number of other forms of Alprostadil using similar delivery systems. However a number of customers are developing transdermal gel applicators for the future.



Epoprostenol Sodium

Epoprostenol So

Background

Epoprostenol sodium is otherwise known as Prostacyclin, which is a member of the family of lipids known as eicosanoids. It is produced in endothelial cells from Prostaglandin H2 by enzyme prostacyclin synthase.

GSK are the innovators of this drug and the branded compound is known as Flolan®. Despite patent expiring in 1999, there is no generic available. There are alternative drugs to Flolan, such as Ilomedin®, Remodulin® and Tracleer®, but Flolan® is considered the gold standard for PPH treatments.



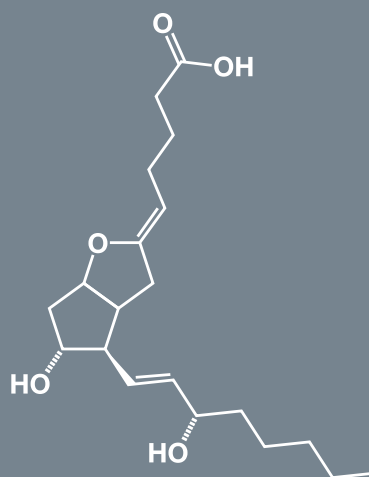
Indicated Uses

Epoprostenol is used for the long-term intravenous treatment of primary pulmonary hypertension and pulmonary hypertension associated with the scleroderma spectrum of disease in NYHA Class III and Class IV patients who do not respond adequately to conventional therapy.

Epoprostenol has two major pharmacological actions: (1) direct vasodilation of pulmonary and systemic arterial vascular beds, and (2) inhibition of platelet aggregation. In animals, the vasodilatory effects reduce right and left ventricular afterload and increase cardiac output and stroke volume. The effect of epoprostenol on heart rate in animals varies with dose. At low doses, there is vagally mediated bradycardia, but at higher doses, epoprostenol causes reflex tachycardia in response to direct vasodilation and hypotension. No major effects on cardiac conduction have been observed. Additional pharmacologic effects of epoprostenol in animals include bronchodilation, inhibition of gastric acid secretion, and decreased gastric emptying. No available chemical assay is sufficiently sensitive and specific to assess the in vivo human pharmacokinetics of epoprostenol.

FLOLAN (epoprostenol sodium) for Injection is a sterile sodium salt formulated for intravenous (IV) administration. Each vial of FLOLAN contains epoprostenol sodium equivalent to either 0.5 mg (500,000 ng) or 1.5 mg (1,500,000 ng) epoprostenol, 3.76 mg glycine, 2.93 mg sodium chloride, and 50 mg mannitol. Sodium hydroxide may have been added to adjust pH.

Epoprostenol is not currently offered by Johnson Matthey in the US territory.



Prostacyclin Systematic (IUPAC) Name

5-[7-hydroxy-8-(3-hydroxyoct-1-enyl)-4-oxabicyclo[3.3.0]oct-3-ylidene] pentanoic acid

PHARMACOKINETIC DATA

Metabolism	Epoprostenol is metabolized to 6-keto-PGF1 α and 6, 15-diketo-13, 14-dihydro-PGF1 α
Half Life	The in vitro half-life of epoprostenol in human blood at 37°C and pH 7.4 is approximately 6 minutes

CHEMICAL DATA

Formula	C ₂₀ H ₃₂ O ₅
Mol. mass	352.465 g/mol
SMILES	search in eMolecules PubChem

Select Prostaglandins

Epoprostenol Sodium (Prostacyclin)

Alprostadil (Coverject, Muse)

**Johnson Matthey
Pharmaceutical Materials – Ireland**

Unit 4, OC Commercial Park
Little Island, Cork
Ireland

Tel: +353 (0)21 435 3969
Fax: +353 (0)21 435 3944
Email: prostaglandins@matthey.com

www.jmpharmaireland.com

Alprostadil and Epoprostenol are not currently offered
by Johnson Matthey in the US territory.



Johnson Matthey
Pharmaceutical Materials

Promoted in conjunction with

Alfa Aesar[®]
A Johnson Matthey Company