AUSTRALIAN PRODUCT INFORMATION – CERVAGEM® (GEMEPROST)

1 NAME OF THE MEDICINE

Gemeprost

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

CERVAGEM pessaries each contain 1 mg of gemeprost.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

4 YELLOW-WHITE SPINDLE SHAPED VAGINAL PESSARIES.CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

For the softening and dilatation of the *cervix uteri* prior to transcervical, intrauterine operative procedures in the first trimester of pregnancy. Therapeutic termination of pregnancy in patients in the second trimester of gestation.

4.2 DOSE AND METHOD OF ADMINISTRATION

See Section 4.4 Special warnings and precautions for use especially for use during second trimester.

Before administration the pessary should be allowed to warm to room temperature for 30 min. away from direct heat and sunlight in the unopened foil sachet.

CERVAGEM pessaries are non-sterile.

Adults: Cervical Dilation (first trimester of Pregnancy): One pessary to be inserted into the posterior vaginal fornix three hours before surgery.

Adequate dilatation and softening is generally obtained three hours after insertion and is maintained for another nine hours. A few patients may require additional surgical dilatation.

Beyond the recommended three hour interval the incidence and severity of gastrointestinal adverse effects, uterine pain and bleeding increases. Attention should therefore be given to the logistics of regularly commencing surgery three hours after insertion of the pessary.

Therapeutic Termination (Second Trimester of Pregnancy). One pessary to be inserted into the posterior vagina fornix at three hourly intervals to a maximum of five administrations. If termination is not well established after five pessaries, a second course of treatment may be started 24 hours after the initial commencement of treatment.

Elderly: Not applicable.

Children: Not applicable.

4.3 CONTRAINDICATIONS

CERVAGEM should not be administered to women with known hypersensitivity to prostaglandins or to any ingredients of this drug. CERVAGEM is also contra-indicated in women experiencing uterine fragility related to uterine scarring and in placenta praevia.

CERVAGEM pessaries should not be used for the induction of labour or cervical softening at term.

CERVAGEM is contraindicated in patients at a risk of hemorrhage due to procedures for placenta previa, ectopic pregnancy, etc. Massive hemorrhage may occur because transvaginal labour cannot occur.

CERVAGEM is contraindicated in patients with fever due to pelvic infection. Inflammation and infection may be aggravated.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

There have been reports of uterine ruptures and cervical laceration with gemeprost. Therefore, extreme care must be taken and cervical dilatation and uterine contractions monitored, when using this drug in the termination of pregnancy (whether therapeutic or for intrauterine foetal death) especially during the second trimester and during the second course of therapy. This is particularly important in women who have one or more of the following conditions: multiparity, uterine scarring, cervical stenosis, vaginal bleeding of unknown origin, or twin pregnancy.

Special attention should be paid to the dosage and administration, and precautions for use.

Serious, potentially fatal, cardiovascular accidents (myocardial infarction and/or spasm of the coronary arteries and severe hypotension) have been reported with prostaglandins including gemeprost and cardiac and vascular parameters should be monitored.

There have been reports of uterine rupture following concomitant administration of gemeprost and syntocinon in the second trimester after previous hysterotomy or classical Caesarean section.

If surgery is unavoidably delayed much beyond the recommended three hour interval, the patient should be kept under observation as the incidence and severity of vaginal bleeding and uterine pain increases. The possibility that spontaneous abortion may occur should also be considered.

Adequate follow-up for patients having a pregnancy termination is essential to ensure that the process has been completed as the effect of CERVAGEM on the foetus has not been established.

Clinical trials have suggested that products of conception in the second trimester of termination of pregnancy patients will be retained in many cases. Due to the risk of retention of products of conception which may need to be surgically removed, appropriate facilities should be available.

CERVAGEM should be used with caution in patients with obstructive airways disease, cardiovascular insufficiency, elevated intraocular pressure, cervicitis or vaginitis.

Patients with the following diseases have not been studied: ulcerative colitis, diabetes mellitus, sickle cell anaemia, epilepsy, disorders of blood coagulation.

Use in hepatic impairment

No data available.

Use in renal impairment

No data available.

Use in the elderly

No data available.

Paediatric use

No data available.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

See Section 4.4 Special warnings and precautions for use.

Oxytocin and other labour inducers or accelerators can potentiate the action of gemeprost.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy

Category B3

CERVAGEM pessaries should not be used for the induction of labour or cervical softening at term as foetal effects have not been ascertained.

Every effort should be made to ensure that once gemeprost has been administered to pregnant women, termination of the pregnancy is completed.

Studies in animals have shown evidence of an increased occurrence of foetal damages, the significance of which is considered uncertain in humans.

Use in lactation

No information available.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Serious or Life Threatening Reactions

Should an anaphylactic reaction occur standard therapy should be employed.

As with all oxytoxic drugs, the potential risk of uterine rupture should be borne in mind in the event of prolonged uterine hypertonia or abnormal uterine pain.

In very rare cases, coronary spasms with subsequent myocardial infarctions have been reported.

More Common Reactions

Reproductive: Vaginal bleeding and mild uterine pain similar to menstrual pain have occurred in approximately 30% of patients in the interval between pessary administration and surgical intervention. If this interval is prolonged beyond the recommended three hours the incidence and severity of this increases.

Gastrointestinal: Nausea and vomiting (11%) loose stools and diarrhoea (3%) occur but are rarely severe enough to require treatment. Standard anti-emetic or anti-diarrhoeal agents may be administered if required.

Musculoskeletal: Lower abdominal pain, back pain

General: Headache, mild pyrexia, flushing.

Less Common Reactions

Cardiovascular: Hypotension, chest pain, palpitations, tachycardia.

Musculoskeletal: Muscle weakness.

Respiratory: Dyspnoea

General: Chills, backache, dizziness.

Hypersensitivity-like reactions: Pruritus, rash, angioedema, anaphylactic reaction including anaphylactic shock, dyspnea (incidence unknown).

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems (Australia).

4.9 OVERDOSE

The toxic dose of gemeprost in women has not been established. Cumulative dosage of 10 mg in 24 hours has been well tolerated. In animals the acute toxic effects are similar to PGE_1, i.e. relaxation of smooth muscle, leading to hypotension and depression of the CNS.

Clinically valuable signs of impending toxicity are likely to be sedation; tremor; convulsion; dyspnoea; abdominal pain and diarrhoea, which may be bloody; palpitations or bradycardia.

Treatment should be symptomatic. A vaginal douche may be of value depending on the elapsed time since insertion of the pessary.

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Genito urinary system and sex hormones, Prostaglandins ATC code: G02AD03

Mechanism of action

CERVAGEM is a Prostaglandin E analogue. Its principal effect is to aid the softening and dilatation of the *cervix uteri* prior to transcervical intrauterine operative procedures. It is hypothesised that gemeprost stimulates or mimics the process of cervical ripening which is thought to be initiated, at least in part, at the spontaneous onset of human parturition, by prostaglandins.

Animal studies have demonstrated that Gemeprost is 10-200 times more potent than prostaglandin E_1, prostaglandin E_2 or prostaglandin $F_{2\alpha}$.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Human pharmacokinetic studies have demonstrated that limited systemic absorption occurs from intravaginal administration of CERVAGEM.

Based on the urinary elimination of metabolites it is concluded that approximately 12-28% of the administered dose reached the systemic circulation. Results from studies using I.V. administration of the drug have demonstrated it to be rapidly metabolised with about 50% of the dose eliminated as metabolites in the urine during the first 24 hours.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Ethanol

Hard fat

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

Once the foil has been opened, any pessary not used within 12 hours should be destroyed.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below -10°C (freeze) in the original pack.

Remove only sufficient pessaries from freezer for immediate use. Any pessaries removed from freezer should NOT be refrozen.

6.5 NATURE AND CONTENTS OF CONTAINER

Container of 5 units dose foil sachets.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Gemeprost INN is Methyl-(E)-7-[(1R,2R,3R)-3-hydroxy-2-[(1E,3R)-3 hydroxy-4,4-dimethyloct-1-enyl]-5-oxocyclopentyl]-hept-2-enoate. It is also known as 16,16-dimethyl-trans-Δ2 PGE1 methyl ester.

It is a colourless to pale yellow viscous liquid having no odour.

Molecular formula

$C_{23}H_{38}O_5$

Molecular weight

394.53.

Chemical structure

No data available

CAS number

64318-79-2

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 Prescription Only Medicine

8 SPONSOR

sanofi-aventis australia pty ltd

12-24 Talavera Road

Macquarie Park, NSW 2113

AUSTRALIA

Toll Free Number (medical information): 1800 818 806

Email: medinfo.australia@sanofi.com

9 DATE OF FIRST APPROVAL

5 June 1990

10 DATE OF REVISION

02 August 2022

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.3	Addition of contraindications
4.4	Addition of cervical laceration warning
4.8	Addition of hypersensitivity-like reactions