NEW ZEALAND DATA SHEET

1. PRODUCT NAME
CARBOPROST-REACH 250 microgram (µg)/mL Solution for Injection

2. QUALITATIVE AND QUANTITIATIVE COMPOSITION
Each 1 mL contains 250 µg carboprost or 332 µg carboprost (as tromethamine).

Excipient(s) with known effect
Each 1 mL contains 9.45 mg/mL benzyl alcohol (added as preservative). For the full list of excipients, see section 6.1.

3. PHARMACEUTIAL FORM
Solution for Injection.

CARBOPROST-REACH is a clear colourless solution.

4. CLINCAL PARTICUALRS
4.1 Therapeutic indications
CARBOPROST-REACH is indicated for the treatment of postpartum haemorrhage due to uterine atony which has not responded to conventional methods of management.

Prior treatment should include the use of intravenously administered oxytocin, manipulative techniques such as uterine massage and, unless contraindicated, intramuscular ergot preparations. Studies have shown that in such cases, the use of CARBOPROST-REACH has resulted in satisfactory control of haemorrhage, although it is unclear whether or not ongoing or delayed effects of previously administered embolic agents have contributed to the outcome. In a high proportion of cases, CARBOPROST-REACH used in this manner has resulted in the cessation of life-threatening bleeding and the avoidance of emergency surgical intervention.

4.2 Dose and method of administration
Dose
An initial dose of 250 µg (1 mL) is to be given by deep intramuscular injection.

In clinical trials, it was found that the majority of successful cases (73%) responded to single injections. In some selected cases, however, multiple dosing at intervals of 15 to 90 minutes was carried out with successful outcome. The need for additional injections and the interval at which these should be given can be determined only by the attending physicians as dictated by the course of clinical events. The total dose of CARBOPROST-REACH should not exceed 2 mg (8 doses).

Method of administration
CARBOPROST-REACH **MUST NOT** be given intravenously. CARBOPROST-REACH is to be given by deep intramuscular injection.

4.3 Contraindications
Hypersensitivity to carboprost tromethamine or any of the excipients in CARBOPROST-REACH. Acute pelvic inflammatory disease.

Patients with active cardiac, pulmonary, renal or hepatic disease.

4.4 Special warnings and precautions for use

CARBOPROST-REACH must not be given intravenously.

This preparation should not be used for induction of labour.

CARBOPROST-REACH, as with other potent oxytocic agents, should be used only with strict adherence to recommended dosages. CARBOPROST-REACH should be used by medically trained personnel and is available only to hospitals and clinics with specialised obstetric units where 24 hour resident medical cover is provided.

Since prostaglandins may potentiate the effect of oxytocin, it is recommended that the use of these drugs simultaneously or in sequence should be carefully monitored.

Very rare cases of cardiovascular collapse have been reported following the use of prostaglandins. This should always be considered when using CARBOPROST-REACH.

CARBOPROST-REACH should be used with caution in patients with a history of glaucoma or raised intra-ocular pressure, asthma, hypertension or hypotension, cardiovascular disease, renal disease, hepatic disease (see section 4.3 Contraindications), anaemia, jaundice, diabetes or past history of epilepsy.

During the clinical trials with carboprost tromethamine, 5/115 (4%) patients had an increase in blood pressure reported as a side effect. The degree of hypertension was moderate. The cases reported did not require specific therapy for the elevated blood pressure.

During the clinical trials with carboprost, chorioamnionitis was identified as a complication contributing to postpartum uterine atony and haemorrhage in 8/115 (7%) of cases, 3 of which failed to respond to carboprost tromethamine. This complication during labour may have an inhibitory effect on the uterine response to carboprost tromethamine similar to what has been reported for other oxytocic agents.

As with other oxytocic agents, CARBOPROST-REACH should be used with care in patients with compromised (scarred) uteri. The possibility of uterine rupture should be borne in mind where high tone myometrial contractions are sustained.

Animal studies lasting several weeks at high doses have shown that prostaglandins of the E and F series can induce proliferation of bone. Such effects have also been noted in newborn infants who have received prostaglandin E1 during prolonged treatment. There is no evidence that short-term administration of CARBOPROST-REACH can cause similar bone effects.

Decreases in maternal arterial oxygen content have been observed in patients treated with carboprost tromethamine. A causal relationship to carboprost tromethamine has not been established, however, it is recommended that patients with pre-existing cardio-pulmonary problems receiving CARBOPROST-REACH are monitored during treatment and given additional oxygen if necessary.

CARBOPROST-REACH contains benzyl alcohol which is associated with severe adverse effects, including fatal “gasping syndrome”, in paediatric patient. The minimum amount of benzyl alcohol at which toxicity may occur is unknown. The risk of benzyl alcohol toxicity depends on the quantity administered and the capacity of the liver and

kidneys to detoxify the chemical. Premature and low birth weight infants may be more likely to develop toxicity.

Paediatric population
CARBOPROST-REACH should not be used in paediatrics patients.

4.5 Interaction with other medicines and other forms of interaction
CARBOPROST-REACH may augment the activity of other oxytocic agents. Concomitant use with other oxytocic agents is not recommended.

4.6 Fertility, pregnancy and lactation
Fertility
No data available.

Pregnancy - Australian Pregnancy Category D
Administration of prostaglandins such as carboprost during pregnancy stimulates the uterus and may cause inability to sustain pregnancy and irreversible foetal damage or death. CARBOPROST-REACH is indicated in the postpartum period. It is not indicated for use during pregnancy.

Carboprost has been found to cross the placenta and distribute to the foetus in pregnant women. Any dose of carboprost that produces increased uterine tone could put the fetus at risk.

In animal studies, administration of carboprost for 3 or more days during gestation caused a high incidence of resorptions in rats and rabbits and embryotoxic effects in rats. The lowest dose of carboprost which caused these effects was approximately 6 and 36 times lower, in rats and rabbits respectively, than the recommended maximum dose in humans (based on surface area comparisons).

Administration of carboprost to rats for 7 - 8 days prior to delivery was associated with shortened gestation length, dystocia, increased incidence of still births and decreased offspring body weight. The lowest dose of carboprost which caused these effects was approximately 100 times lower than the recommended maximum dose in humans (based on surface area comparisons).

Administration of carboprost at doses up to 3 times the expected maximum human dose (based on surface area) for 3 or 6 days prior to mating had no effect on male or female fertility in rats, although other carboprost-like drugs are known to disrupt fertility.

CARBOPROST-REACH contains benzyl alcohol which can cross the placenta (see Section 4.4 Special warnings and precautions for use).

Lactation
It is not known if carboprost is secreted into breast milk, however, this possibility cannot be ruled out.

Administration of carboprost to rats during the pre- and post-natal period resulted in failure of dams to lactate. The lowest dose of carboprost which caused these effects was approximately 100 times lower than the recommended maximum dose in humans (based on surface area comparisons). The effect was reversible.

The relevance of these findings to lactation in humans treated with carboprost is unclear. However, based on plasma clearance rates it is recommended that breast feeding does not occur for at least 6 hours after administration.

4.7 Effects on ability to drive and use machinery

No data available.

4.8 Undesirable effects

On rare occasions, cardiovascular collapse has been reported with some of the prostaglandins, so this should always be considered when using CARBOPROST-REACH.

The adverse effects of carboprost are generally transient and reversible when therapy ends.

The most frequent side effects observed with the use of carboprost are related to its contractile effect on smooth muscle. Thus, nausea, vomiting and diarrhoea have been reported as very commonly encountered. The incidence of vomiting and diarrhoea may be decreased by pre-treatment and concomitant use during treatment of anti-emetic and antidiarrhoeal agents.

Hyperthermia and flushing have been observed after intramuscular carboprost, but if not complicated by endometritis, the temperature elevation will usually return to normal within several hours of the last injection.

The table below lists the adverse effects identified through clinical trials and post-marketing surveillance by System Organ Class (SOC) and frequency. Within each frequency grouping, adverse events are presented in order of decreasing seriousness.

System Organ Class	**Very common (≥10%)**	**Common (≥ 1% to < 10%)**	**Uncommon (≥ 0.1% to < 1%)**
Infections and infestations		Endometritis	Septic shock, urinary tract infection
Psychiatric			Sleep disorder
Nervous system disorders		Headache	Syncope vasovagal, pre-syncope, lethargy, dystonia, paraesthesia, dysgeusia, dizziness, somnolence
Eye disorders			Eye pain, vision blurred
Ear and labyrinth disorders			Tinnitus, vertigo
Cardiac disorders			Tachycardia
Vascular disorders		Flushing, hot flush, Elevated blood	Hypertension
Respiratory, thoracic and mediastinal disorders		Cough	Pulmonary oedema, respiratory distress, hyperventilation, dyspnoea asthma, wheezing, hiccups
Gastrointestinal disorders	Diarrhoea, vomiting, nausea		Haematemesis, epigastric pain, abdominal pain, cramps, dry
Skin and subcutaneous tissue disorders			Diaphoresis, sweating, perspiration,

Musculoskeletal and connective tissue disorders			Back pain, myalgia, torticollis
Reproductive system and breast disorders		Retained placenta or membranes, uterine haemorrhage	Uterine rupture, perforation of uterus, pelvic pain, breast tenderness
General disorders and administration site conditions	Retrosternal discomfort	Chills, shivering	Tightness in chest, injection site pain, injection site erythema
Investigations	Body temperature increased	Fever	

Post-marketing Experience

Infections and infestations
Upper respiratory tract infection.

Immune system disorders
Hypersensitivity reactions (e.g., anaphylactic reaction, anaphylactic shock, anaphylactoid reaction, angioedema).

Endocrine disorders
Thyrotoxic crisis.

Psychiatric disorders
Anxiety, nervousness.

Nervous system disorders
Syncope.

Cardiac disorders
Palpitations.

Respiratory, thoracic and mediastinal disorders
Throat tightness, choking sensation, epistaxis, dry throat.

Gastrointestinal disorders
Gastralgia, retching.

Skin and subcutaneous tissue disorders
Rash.

Musculoskeletal and connective tissue disorders
Leg cramps, blepharospasm.

Reproductive system and breast disorders
Uterine sacculation.

General disorders and administration site conditions
Chest pain, excessive thirst, asthenia.

Reporting of Suspected Adverse Reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/

4.9 Overdose

Symptoms

Hypertension, increased body temperature.

Treatment

Treatment of overdosage must be symptomatic at this time, as clinical studies with prostaglandin antagonists have not progressed to the point where recommendations may be made. If evidence of adverse effects appears, the frequency of administration of CARBOPROST-REACH should be decreased or administration discontinued.

For risk assessment and advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of Action

Carboprost tromethamine administered intramuscularly stimulates in the gravid uterus myometrial contractions similar to labour contractions at the end of a full-term pregnancy. Whether or not these contractions result from a direct effect of carboprost on the myometrium has not been determined. Post-partum, the resultant myometrial contractions provide haemostasis at the site of placentation.

Carboprost tromethamine also stimulates the smooth muscle of the human gastrointestinal tract. This activity may commonly produce vomiting or diarrhoea or both when used to terminate pregnancy and for use postpartum. In laboratory animals and also in humans, carboprost tromethamine can elevate body temperature. With the clinical doses of carboprost tromethamine for use postpartum, some patients do experience transient temperature increases.

In laboratory animals and in humans, large doses of carboprost tromethamine can raise blood pressure, probably by contracting the vascular smooth muscle. In some patients, carboprost tromethamine may cause transient bronchoconstriction.

5.2 Pharmacokinetic properties

Drug plasma concentrations were determined by radioimmunoassay in peripheral blood samples collected by different investigators from 10 patients undergoing abortion. The patients had been injected intramuscularly with 250 µg of carboprost at two hour intervals. Blood levels of drug peaked at an average of 2060 picograms/mL one-half hour after the first injection then declined to an average concentration of 770 picograms/mL two hours after the first injection just before the second injection. The average plasma concentration one-half hour after the second injection was slightly higher (2663 picograms/mL) than that after the first injection and decreased again to an average of 1047 picograms/mL by two hours after the second injection. Plasma samples were collected from 5 of these 10 patients following additional injections of the prostaglandin. The average peak concentrations of drug were slightly higher following each successive injection of the prostaglandin, but always decreased to levels less than the preceding peak values by two hours after each injection.

Five women who had delivery spontaneously at term were treated immediately postpartum with a single injection of 250 µg of carboprost tromethamine. Peripheral blood samples were collected at several times during the four hours following treatment and carboprost tromethamine levels were determined by radioimmunoassay. The highest concentration of carboprost tromethamine was observed at 15 minutes in 2 patients (3009 and 2916 picograms/mL), at 30 minutes in 2 patients (3097 and 2792 picograms/mL), and at 60 minutes in 1 patient (2718 picograms/mL).

5.3 Preclinical safety data
No data available.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Trometamol
Sodium chloride
Sodium hydroxide or hydrochloric acid (for pH adjustment)
Water for injection
Benzyl alcohol (added as preservative).

6.2 Incompatibilities
No data available.

6.3 Shelf life
30 months

6.4 Special precautions for storage
Store at 2° - 8°C. Refrigerate. Do not freeze.

6.5 Nature and contents of container
CARBOPROST-REACH is available in Type 1 glass vials of 1 mL solution, stoppered with 13 mm gray chlorobutyl rubber stoppers and sealed with 13 mm flip top blue grain finish aluminium seals, packed in cartons.

6.6 Special precautions for disposal
Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE
Prescription Medicine.

8. SPONSOR
CARSL Consulting
PO Box 766
Hastings 4156
Ph: 0275086002

For:
Reach Pharmaceuticals Pty Ltd
Ground Floor, Corporate One
84 Hotham Rd,

Preston VIC 3072
medical@reach-pharma.com

9. DATE OF FIRST APPROVAL

23 January 2025

10. DATE OF REVISION OF THE TEXT

18 February 2026

Summary of table of changes

Section changed	Summary of new information
6.3	Shelf life update
8	Sponsor address updated