1. Purpose

This document outlines the procedure details for the preparation and administration of carboprost (Hemabate®) as third line management of a major primary postpartum haemorrhage (PPH). This procedure is linked to the ‘Postpartum Haemorrhage’ guideline and the ‘Postpartum Haemorrhage: Immediate and Ongoing Postnatal Management after Major PPH’ procedure.

Where processes differ between campuses, those that refer to the Sandringham campus are differentiated by pink text or have the heading Sandringham campus.

2. Definitions

Primary postpartum haemorrhage (PPH) is traditionally defined as blood loss greater than or equal to 500 mL, within 24 hours of delivery.

Secondary PPH is defined as a blood loss of >500mL after 24 hours and up to 6 weeks postpartum

A major PPH is defined as continued bleeding and failure to respond to first-line management and cases where blood loss is approaching or exceeding 1000mL

Carboprost tromethamine (Hemabate®) is a prostaglandin analogue used to control severe PPH caused by uterine atony that is not responsive to oxytocin, ergometrine or uterine massage.¹ Carboprost is an alternative medicine to dinoprost (Prostin F2 alpha®) which has been discontinued.

3. Responsibilities

- Obstetric and midwifery staff
- Senior medical staff (including the on-call Obstetric Consultant) are responsible for attending all cases of major PPH or on request
- Anaesthetic staff are responsible for providing and advising on clinical care in cases of major PPH when intensive monitoring and resuscitation are required
- The Haematology Consultant should be consulted early to prevent development of disseminated intravascular coagulation (DIC). For all cases of developing or actual coagulopathies, resuscitation with blood products may be required
- Other available specialists such as the Gynae/Oncology Consultant should be consulted early when bleeding is intractable, or where hysterectomy or ligation/embolisation of uterine arteries are being considered
- Pharmacists.

4. Procedure

<table>
<thead>
<tr>
<th>Medicine name</th>
<th>Carboprost</th>
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<tr>
<td>Brand name</td>
<td>Hemabate®</td>
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Presentation
250 micrograms in 1mL ampoules

Storage
Store in fridge: 2 to 8°C

Route of administration
- Intramuscular (IM) injection; once–only in the Birth Centre. Repeated doses only in operating theatre.
- Intramyometrial injection: in operating theatre only*

*The manufacturer does not recommend carboprost for intramyometrial administration. However, the off-label use of this medicine is considered routine for the treatment of PPH with high quality supporting evidence.2, 3, 4

Restrictions
Carboprost is Special Access Scheme (SAS) Category A medicine
An SAS form must be completed by the prescribing doctor before use.
Please forward the completed SAS form the Pharmacy Department as soon as possible.

4.1 Indication
Carboprost is used in the management of severe PPH due to uterine atony that is unresponsive to conventional PPH therapy i.e. oxytocin, ergometrine or uterine massage.

4.2 Contraindications
- Hypersensitivity to any component of the preparation: carboprost, tromethamine, sodium chloride, benzyl alcohol
- Patients with known active cardiac, pulmonary, renal or hepatic disease
- Acute pelvic inflammatory disease.

4.3 Precautions
Carboprost should be used with caution in women with:
- a history of hypotension or hypertension
- a history of or currently diagnosed with diabetes
- a history of anaemia
- a history of hepatic disease or jaundice
- chorioamnionitis
- a history of epilepsy
- previously compromised (scarred) uteri
- a history of glaucoma or raised intraocular pressure.

4.4 Adverse effects
- Bronchopulmonary: bronchospasm, pulmonary oedema due to raised pulmonary artery pressures, hypoxia due to pulmonary shunting
- Cardiovascular: acute hypertension (usually transient and requiring no treatment), acute hypotension, cardiac arrhythmia including ventricular tachycardia (rarely), flushing, syncope and palpitations
- Gastrointestinal: abdominal cramps, diarrhoea and vomiting
- Other: an increase in temperature greater than 1.1°C, convulsions (rarely), flushing, shivering, uterine rupture, headache (usually mild and transient).

4.5 Prerequisites
Experienced anaesthetist on standby:
- Intravenous (IV) access x 2 using 16 gauge cannulas
- Pulse oximetry and oxygen administration
4.6 Administration

After a vaginal birth in Birth Centre

If bleeding is intractable after administration of first and second line management in the Birth Centre, a once-only dose of carboprost 250 micrograms (1mL) by deep intramuscular (IM) injection may be administered. The duty consultant must be informed. If further doses are required the woman must be transferred to theatre and the consultant asked to attend.

Administer concomittent ondansetron 4mg IV for management of side-effects (if not already administered).

If the woman is unlikely to have postnatal opioid analgesia, consider concomittent administration of loperamide 4mg orally, for management of diarrhoea. (Note: contraindicated in women with cardiac disease, long QT syndrome).

At laparotomy / LUSCS

Administer 250 micrograms (1mL) by deep intramuscular (IM) injection. It may be repeated at intervals of no less than 15 minutes. The total dose should not exceed 2mg (8 doses).^{2}

OR

Consultant decision: Infiltrate 500 micrograms (2mL) of carboprost directly into the myometrium using a 21 gauge spinal needle, aspirating intermittently to avoid direct systemic injection. Repeat 15 minutes later if necessary, to a maximum of 2mg of carboprost.^{3}

Avoid cervical injection because of an increased risk of direct systemic uptake.

After vaginal birth and with woman in the operating theatre

Administer 250 micrograms (1mL) by deep intramuscular (IM) injection. It may be repeated at intervals of no less than 15 minutes. The total dose should not exceed 2mg (8 doses).^{2}

OR

Consultant decision: Using a 22 gauge spinal needle, inject 1mL (250 micrograms) of carboprost through the anterior abdominal wall into the myometrium on each side of the uterine fundus.

Alternatively, inject 2mL (500 micrograms) into the uterine fundus, aspirating to avoid direct systemic injection. Repeat if required to a maximum dose of 2mg.^{3}

Ultrasound guidance may be useful.

4.7 Unsuccessful responses

Proceed to alternative management regimens which may include:

- balloon tamponade
- uterine packing
- B-Lynch suture
- uterine artery and internal iliac artery ligation
- pelvic arterial embolisation
- hysterectomy.

5. Evaluation, monitoring and reporting of compliance to this procedure

Compliance to this procedure will be monitored, evaluated and reported through the notification of clinical incidents on VHIMS and by monthly clinical audit of PPHs greater than 1500mL.
6. References


7. Legislation related to this procedure


8. Appendices

Appendix 1: PPH Algorithm: Parkville

Please ensure that you adhere to the below disclaimer:

PGP Disclaimer Statement

The Royal Women's Hospital Clinical Guidelines present statements of 'Best Practice' based on thorough evaluation of evidence and are intended for health professionals only. For practitioners outside the Women's this material is made available in good faith as a resource for use by health professionals to draw on in developing their own protocols, guided by published medical evidence. In doing so, practitioners should themselves be familiar with the literature and make their own interpretations of it.

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PPH recognised

Summon HELP and simultaneously:
- Reassure the woman
- Massage uterus (rub up)
- IV and IM ergometrine 0.25mg & IV ondansetron 4mg
- Indwelling urinary catheter

Resuscitation including:
- Insert large bore IV (≥16G)
- Collect blood for group & cross match, FBE,
- Continue to measure blood loss
- Commence Fluid Balance Chart
- Anaesthetist help

Ensure third stage drug management has been completed

First line uterotonic management

- IV ergometrine 0.25mg and IM ergometrine 0.25mg plus IV ondansetron 4mg, if not already given

OR

- IV oxytocin 10 units if blood pressure elevated

PLUS

Commence IV OXYTOCIN INFUSION (40 UNITS) 1 litre in Hartmann's or Normal Saline Via infusion pump @250mL/hr

Inadequate response

Second line uterotonic management

1. 250 micrograms (1mL) deep IM injection carboprost (Hemabate®) at no less than 15 min intervals to max 20mg. First dose may be given on Birth Centre.

2. Misoprostol 400 micrograms (2 tabs) sublingually OR rectally as per woman's condition

3. Tranexamic acid 1 ampoule (1g/10mL) IV via syringe pump @1mL/minute, over 10 minutes

ESCALATE

On-call consultant to attend when:
- Inadequate response to management
- Bleeding continues
- Blood loss approaching or exceeding 1000 mL

CONSIDER the multidisciplinary team, including anaesthetist, haematologist, gynaecology fellow/consultant, operating department staff.

CONSIDER implementing the Massive Transfusion Protocol

Inadequate response

Transfer to Operating Suite

ABC (Airway/Breathing/Circulation)
- Continue to Replace Fluid
  -Volume expanders
  -Packed cells
  -Clotting factors
- Analgesia
- Massage uterus

CONSIDER
- Bimanual uterine compression
- Aortic compression

Third line uterotonic management

- Carboprost 250mg (1mL) as deep IM injection 250mg as intramyometrial injection into each cornu or 500mcg into the fundus, at intervals no less than 15mins and to a max 2mg (8 doses)

CONSIDER (if not already given)
- Misoprostol 400 micrograms (2 tabs) sublingually if condition permits
- Tranexamic acid 1 ampoule (1g/10mL) IV via syringe pump @1mL/minute over 10 minutes.

CONSIDER implementing the Massive Transfusion Protocol