

# South Australian Perinatal Practice Guidelines

## Prostaglandin analogues for postpartum haemorrhage

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### Misoprostol (Prostaglandin E<sub>1</sub> analogue)

#### Introduction

- > Misoprostol (Cytotec®) a prostaglandin E<sub>1</sub> analogue is an inexpensive tablet and is stable at room temperature if kept dry
- > Systematic reviews of randomized controlled trials show that misoprostol is less effective than oxytocin and other injectable uterotonics in preventing postpartum haemorrhage and has side-effects, such as high temperature and shivering (Gülmezoglu 2007; WHO 2009)
- > The most recent Cochrane systematic review states that there is insufficient evidence to show that the addition of misoprostol is superior to the combination of oxytocin and ergometrine alone for the treatment of primary PPH (Mousa & Alfrevic 2007)

#### Dosage and route of administration

- > The most common misoprostol regimens reported for the treatment of PPH are 600, 800 or 1,000 micrograms rectally (Hofmeyr et al. 2004; Gülmezoglu et al. 2007)
- > However, doses reported in recent published clinical trials range from 400 micrograms to 1,000 micrograms and have been provided sublingually, rectally and orally (Derman 2006; Hemmerling 2006)
- > The buccal or sublingual route has rapid uptake, prolonged duration and greatest total bioavailability. The rectal route has slow uptake but prolonged duration. The oral route has the most rapid uptake, but the shortest duration
- > In order to improve the rapidity of onset of action and overall bioavailability misoprostol regimens may be modified by administering 200 micrograms orally, 400 micrograms sublingually and 400 micrograms rectally or similar (Hofmeyr et al. 2004)

#### Side effects

- > Shivering and fever up to 40° C are common (especially via oral and sublingual routes)
- > Diarrhoea, headache and vomiting

### Prostaglandin F<sub>2α</sub> (Dinoprost)

#### Introduction

- > Intramyometrial prostaglandin F<sub>2α</sub> is an established 2<sup>nd</sup> line treatment for postpartum haemorrhage unresponsive to oxytocic agents along with ongoing bimanual compression and uterine massage (Belfort & Dildy in James et al. 2011)
- > Case series show prostaglandin F<sub>2α</sub> is effective in 88 % of cases refractory to oxytocics (Oleen & Mariano 1990)
- > **This preparation is not suitable for intramuscular injection**

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### Pharmacology

- > Prostaglandin  $F_{2\alpha}$  ( $PGF_{2\alpha}$ ) is a potent smooth muscle contractor which is 90 % metabolised on first passage through the lungs
- > A large bolus of  $PGF_{2\alpha}$  can overload the lung metabolic pathways and allow unmetabolised  $PGF_{2\alpha}$  into the systemic arterial system, with resultant cardiovascular effects

### Indications

- > To control severe PPH caused by uterine atony that is not responsive to oxytocin, ergometrine or uterine massage
- > Note - Management of severe postpartum haemorrhage requiring  $PGF_{2\alpha}$  requires senior obstetrician involvement

### Contraindications

- > Prostaglandin  $F_{2\alpha}$  ( $PGF_{2\alpha}$ ) is a potent smooth muscle contractor which is 90 % metabolised on first passage through the lungs
- > A large bolus of  $PGF_{2\alpha}$  can overload the lung metabolic pathways and allow unmetabolised  $PGF_{2\alpha}$  into the systemic arterial system, with resultant cardiovascular effects

### Relative contra-indications

- > Severe asthma, lung disease and cardiovascular disease

### Side Effects

The following adverse side effects have been reported:

- > Respiratory: bronchospasm, pulmonary oedema due to raised pulmonary artery pressures, hypoxia due to pulmonary shunting
- > Cardiovascular: acute hypertension- usually transient. Hypotension secondary to myocardial failure, cardiac arrhythmia including ventricular tachycardia
- > Gastrointestinal: abdominal cramps, diarrhoea and vomiting
- > Other: convulsions (rarely), flushing, shivering, uterine rupture, headache – usually mild and transient

### Prerequisites

- > Experienced anaesthetist on standby
- > Intravenous access x 2 using 16 gauge cannulas
- > Pulse oximetry and oxygen administration
- > Resuscitation equipment on hand
- > Usually used in a controlled environment (e.g. in theatre at caesarean section) where misoprostol is unable to be administered

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## Prostaglandin F<sub>2α</sub> (Dinoprost) preparation and administration

### Presentation:

- > PGF<sub>2α</sub> 5 mg in one mL ampoule

### Preparation of Solution

- > Dilute (5 mg) 1 mL of PGF<sub>2α</sub> to 10 mL with sodium chloride 0.9 % to give 0.5 mg PGF<sub>2α</sub> per mL (NSW Health 2010)
- > Discard 4 mL from 10 mL to leave the maximum dose of 3 mg (6 mL). This procedure decreases the chance of overdose

### Administration

#### At laparotomy / LSCS:

- > Infiltrate 2 mL of prepared solution (1 mg) directly into myometrium using a 21 gauge spinal needle, aspirating intermittently to avoid direct systemic injection.
- > Repeat 10-15 minutes later if necessary. Avoid cervical injection because of increased risk of direct systemic uptake

#### After vaginal delivery:

- > Using 22 gauge spinal needle, the medical officer injects 1 mL (0.5 mg) of diluted PGF<sub>2α</sub> through the anterior abdominal wall into the myometrium on each side of the uterine fundus, or 2 mL (1 mg) into the uterine fundus, aspirating to avoid direct systemic injection
- > Repeat if required to a maximum dose of 3 mg
- > Ultrasound guidance may be useful

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### Unsuccessful response

- > Proceed to alternative surgical management e.g. balloon tamponade, uterine packing, B-Lynch suture, uterine artery and internal iliac artery ligation, pelvic arterial embolization and hysterectomy

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### References

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9. NSW Health. Prevention, early recognition and management of postpartum haemorrhage. Policy Directive Document No PD2010\_064, October 2010. Available from URL: [http://www.health.nsw.gov.au/policies/pd/2010/pdf/PD2010\\_064.pdf](http://www.health.nsw.gov.au/policies/pd/2010/pdf/PD2010_064.pdf)

### Useful references

RANZCOG College statements. Available from URL: <http://www.ranzcog.edu.au/womens-health/statements-a-guidelines/college-statements.html?start=1>

- > C-Obs 12: The use of misoprostol in obstetrics and gynaecology
- > C-Obs 43: Management of postpartum haemorrhage

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## Abbreviations

C	Celsius
e.g.	For example
et al.	And others
IV	Intravenous
LSCS	Lower segment caesarean section
mg	Milligram(s)
mL	Millilitre(s)
NSW	New South Wales
%	Percent
PPH	Postpartum haemorrhage
PG	Prostaglandin
®	Registered trademark

## Version control and change history

**PDS reference:** OCE use only

Version	Date from	Date to	Amendment
1.0	03 Sept 07	17 July 12	Original version
2.0	17 July 12	current	