University Hospitals Sussex
NHS Foundation Trust

Guideline for use of Carbetocin to prevent postpartum haemorrhage (PPH) in caesarean birth

Summary statement: How does the document support patient care?	Enables efficient care to facilitate safe patient flow through the maternity service.
Staff / stakeholders involved in development:	Consultant Anaesthetists Consultant obstetricians Midwives L east & west Pharmacy
Division:	Women and Childrens
Department:	Maternity / theatres
Responsible Person:	Governance lead Midwife
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For use by:	Consultant Anaesthetist
Purpose:	Provide guidance for use of Carbetocin in the context of caesarean birth.
This document supports:	Caesarean Birth guideline
Approved by: **Divisional Governance / Management Group**	JOGG: 16th August 2023 MGC: May 2023 Date uploaded to Staffnet: 22nd August 2023
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Version	date	Author	Status	Comment
1.0	May 2023	Consultant Anaesthetists / Pharmacist lead Women & Childrens	Archived	New Trust wide guideline.
1.1	Aug 2023	Consultant Anaesthetist	LIVE	Correction to contraindications and cautions. Section 5.1 Severe PET is a contraindication (where concern for cardiovascular stability exists) Section 5.2 PET is a caution for use.

The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician.
If in doubt contact a senior colleague or expert.

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1.0 Introduction

Carbetocin is a synthetic analogue of oxytocin, with a significantly longer duration of action. Carbetocin is intended for use only in well-equipped specialist obstetric units with experienced and qualified staff available.

2.0 Purpose

Carbetocin is recommended to prevent post-partum haemorrhage following caesarean birth in theatre. It may be used instead of, not in addition to, oxytocin. Carbetocin should be offered to all patients undergoing caesarean birth, unless contra-indicated (see section 5.1).

It is licensed in the uk for prevention of postpartum haemorrhage due to uterine atony in patients having a caesarean birth under epidural or spinal anaesthesia.

3.0 Definitions

PPH postpartum haemorrhage
ED90 Effective dose in 90% of people

4.0 Responsibilities, accountabilities and duties

- Theatre/ODP team – maintenance of stock levels and storage.
- Anaesthetist – appropriate preparation, administration and documentation on anaesthetic and drug charts when used. Further management of uterine atony/post partum haemorrhage if applicable.
- Obstetrician – management of 3rd stage of birth, monitoring uterine tone, management of uterine atony/post partum haemorrhage if applicable, documentation of findings and plan.
- Midwife – monitoring uterine tone and lochia, escalation of concerns, initial management of uterine atony/post partum haemorrhage if applicable. Documentation of findings.

5.0 How to give Carbetocin

Carbetocin must only be administered after the birth of the baby and as soon as possible after umbilical cord clamping.

Dose is 100 micrograms to be given over 1 minute. It is recommended to dilute 1 ml Carbetocin with 9 mls 0.9% sodium chloride making it up to 10mls total volume for administration; flush cannula after administration.

Caesarean following labour augmented with oxytocin infusion: Ensure any intrapartum oxytocin infusion has been discontinued then give 100 microgram dose as above.

Low risk elective caesarean only: Consider dose reduction to 20-50 micrograms (2-5 mls)

- (ED90 ≤ 20 mcgs if not in labour with low risk of PPH)
- May still give up to 100mcgs if required.

DO NOT exceed 100mcgs dose, if further uterotonic required use second agent.
DO NOT give oxytocin bolus or infusion within 4 hours of Carbetocin administration.
DO NOT give Carbetocin prior to the birth of the baby.

5.1 Contraindications

- During pregnancy and labour before birth of the baby.
- Carbetocin must not be used for the induction of labour.
- Hypersensitivity to Carbetocin, oxytocin or to any of the excipients.
- Hepatic or renal disease
- Serious cardiovascular disorders
- Epilepsy
- Severe eclampsia, pre-eclampsia (where concern for cardiovascular stability exists)

5.2 Cautions for use

- Cardiovascular disease (avoid if severe)
- Severe hypotension
- Hyponatraemia or water intoxication*
- Pre-eclampsia or eclampsia*
- General Anaesthesia
- Hyponatraemia
- Migraine
- Asthma

Elimination half-life of Carbetocin is >40 minutes (compared with 1-6 minutes for oxytocin), clinical effect apparent for up to 4 hours, therefore no need for bolus or infusion of oxytocin and if uterine tone remains inadequate following administration of 100mcgs, 2nd line agent should be used.

Initial studies for the efficacy of Carbetocin excluded women and people under GA and therefore its license does not include GA.

* Oxytocin use has been linked to water intoxication and hyponatraemia. This may manifest with neurological symptoms including seizures hence the cautions in these groups of women and people. Although this risk could theoretically exist for Carbetocin, its in vitro affinity for the human vasopressin V2 receptor is much lower than that of oxytocin, and to date there have been no cases in the literature linking Carbetocin with hyponatraemia and water intoxication.

The use of Carbetocin at any stage before birth of the baby is not appropriate because its uterotonic activity persists for several hours. This is in marked contrast to the rapid reduction of effect observed after discontinuation of an oxytocin infusion.

In case of persistent vaginal or uterine bleeding after administration of Carbetocin the cause must be determined. Consideration should be given to causes such as retained placental fragments, perineal, vaginal and cervix lacerations, inadequate repair of the uterus, or disorders of blood coagulation.

Carbetocin is intended for single administration only, intramuscular or intravenous. In case of intravenous administration, it must be administered slowly over 1 minute. In case of persisting uterine hypotonia or atonia and the consequent excessive bleeding, additional therapy with uterotonic should be considered.

Animal studies have shown carbetocin to possess some antidiuretic activity (vasopressin activity: <0,025 IU/vial) and therefore the possibility of hyponatraemia cannot be excluded, particularly in patients also receiving large volumes of intravenous fluids. The early signs of drowsiness, listlessness and headache should be recognised to prevent convulsions and coma.

In general, Carbetocin should be used cautiously in the presence of migraine, asthma and cardiovascular disease or any state in which a rapid addition to extracellular water may produce hazard for an already overburdened system.

5.3 Drug interactions

During clinical trials, Carbetocin has been administered in association with a number of analgesics, spasmolytics and agents used for epidural or spinal anaesthesia, and no drug interactions have been identified. However specific interaction studies have not been undertaken.

Since Carbetocin is closely related in structure to oxytocin, the occurrence of interactions known to be associated with oxytocin cannot be excluded. Severe hypertension has been reported when oxytocin was given 3 to 4 hours following prophylactic administration of a vasoconstrictor in conjunction with caudal-block anaesthesia.

During combination with ergot-alkaloids, such as methylergometrine, oxytocin and Carbetocin may enhance the blood pressure enhancing effect of these agents. If oxytocin or methylergometrine are administered after Carbetocin there may be a risk of cumulative exposure.

Since it has been found that prostaglandins potentiate the effect of oxytocin, it is expected that this can also occur with Carbetocin. Therefore, it is not recommended that prostaglandins and Carbetocin be used together. If they are concomitantly administered, the patient should be carefully monitored.

Some inhalation-anaesthetics, such as halothane and cyclopropane may enhance the hypotensive effect and weaken the effect of Carbetocin on the uterus. Arrhythmias have been reported for oxytocin during concomitant use.

5.4 Common adverse effects

System	Very Common 1/10	Common >1/100 and < 1/10
Blood/lymphatic system		Anaemia
CNS	Headache, tremor	Dizziness
GI	nausea	
Vascular disorders	Hypotension, flushing	
Respiratory		Chest pain, dyspnoea
Skin/subcutaneous	Pruritis	
Musculoskeletal		Back pain
General	Feeling of warmth	Chills, pain

Carbetocin has some antidiuretic action so could lead to hyponatraemia in patients receiving large volumes of fluid. Watch for signs of drowsiness, headache which are early warning signs of potential convulsion or coma.

6.0 Training implications

Suggested resources for information on medicines:

- BNF accessed April 2023
- SPC Carbetocin https://www.medicines.org.uk/emc Accessed April 2023
- Medusa NHS Injectable Medicines Guide. https://nww.bsuh.nhs.uk/clinical/teams-and-departments/pharmacy/

7.0 Monitoring arrangements

Element to be Monitored	Lead	Tool for Monitoring	Frequency	Responsible Individual/ Group/ Committee for review of results/report	Responsible individual/ group/ committee for acting on recommendations/ action plan	Responsible individual/group/ committee for ensuring action plan/lessons learnt are Implemented
Compliance with the guidelines	Clinical Governance Manager Lead Consultant Obstetrician for audit lead	Audit	Every 3 years Or 6-9 months after a practice change.	Obstetrics and gynaecology audit meetings and any other appropriate meetings	Clinical Services Managers Midwifery matrons Clinical unit Obstetrics lead	Consultant Oobstetrician or Aanaesthetic Lead Audit lead
Review cases of incidents	Risk Lead Midwife + relevant service lead	Datix	Weekly	Datix review meetings, lessons learnt to be disseminated via departmental meetings	Clinical Services Managers Midwifery Matrons Clinical Unit Obstetrics lead	Lead Obstetrician/Anaesthetist Audit/ Risk Lead Midwife

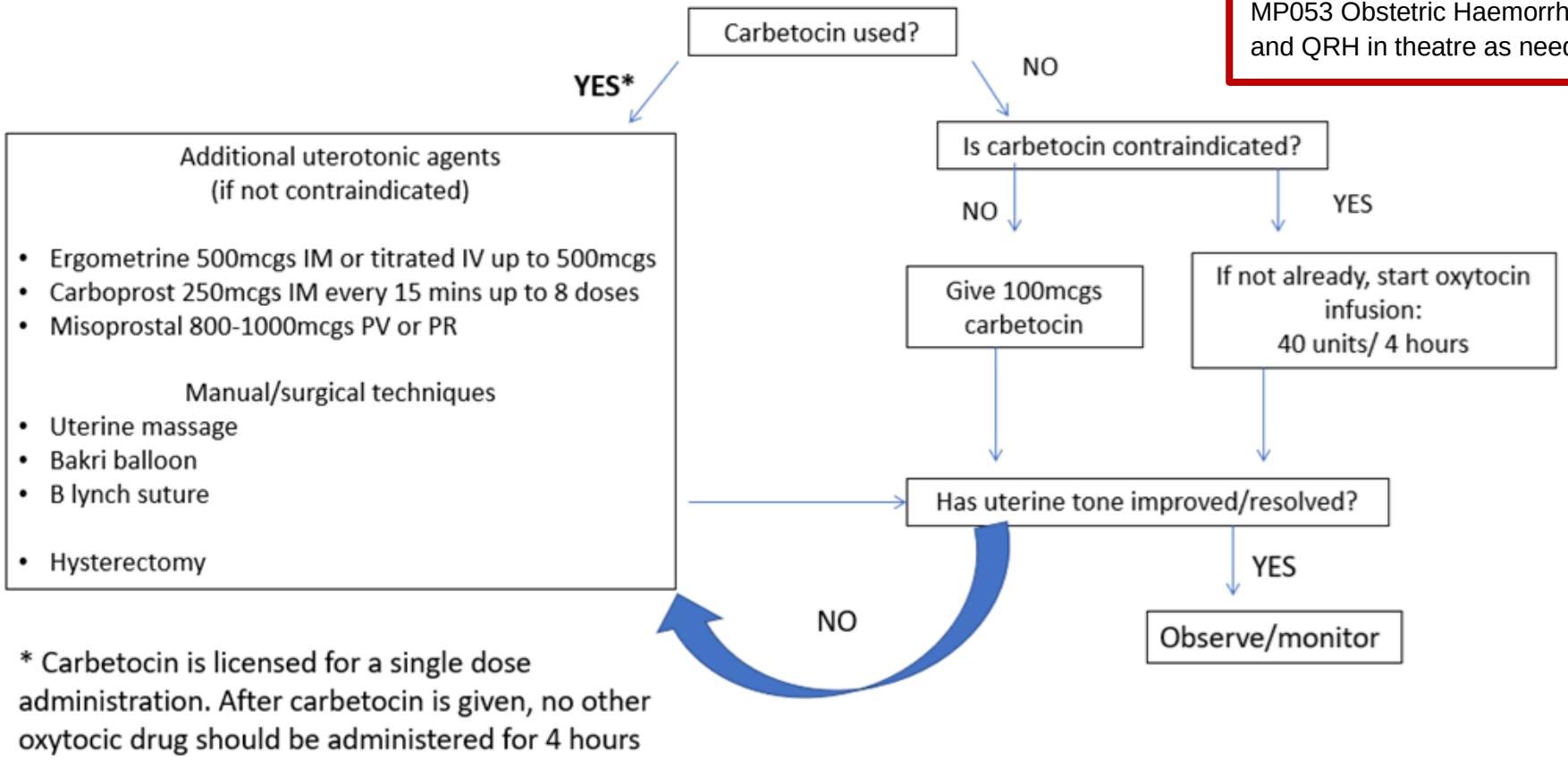
8.0 References

1. BNF accessed April 2023
2. SPC carbetocin https://www.medicines.org.uk/emc Accessed April 2023
3. Anaesthesia 2019, 74, 1305–1319 Heesen et al. | Consensus statement on uterotonic agents during caesarean section

Appendix 1: Management of Inadequate uterine tone during or after caesarean

SRH & WH:
Please also refer to CG12029 Postpartum Haemorrhage

RSCH & PRH:
Please also refer to MP053 Obstetric Haemorrhage and QRH in theatre as needed.



* Carbetocin is licensed for a single dose administration. After carbetocin is given, no other oxytocic drug should be administered for 4 hours