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Uses of Medicines for Prevention and Treatment of Post-partum Hemorrhage and Other Obstetric Indications

A Summary of Information on Indications, Contraindications, and Supply Chain Considerations for Program Managers

INTRODUCTION

Maternal health practitioners and program managers now have more medication options than before to assist them in preventing and treating post-partum hemorrhage (PPH). However, there is still no single solution for preventing and treating PPH. Countries must determine the appropriate combination of uterotonics, tranexamic acid (TXA), and other life-saving PPH prevention and treatment interventions for use at community, primary, and referral levels. Additionally, these medicines have other important obstetric uses which must be considered.

This brief highlights key characteristics and supply chain considerations for individual uterotonic medicines and TXA that will be used to help program managers determine the most appropriate combination of medicines for prevention and treatment of PPH and other obstetric indications at community, primary, and referral levels.

BACKGROUND

Post-partum hemorrhage (PPH) – or excessive bleeding after childbirth – continues to be one of the major causes of maternal mortality in low- and middle-income countries, accounting for over a quarter of maternal deaths worldwide. WHO recommends the administration of a prophylactic uterotonic immediately after birth for every woman to help prevent PPH caused by uterine atony (non-contracted uterus). WHO also recommends treatment of PPH with a therapeutic uterotonic and intravenous tranexamic acid (TXA), supplemented by additional interventions based on the cause of the bleeding and the woman's clinical status (e.g., removal of retained placenta, repair of laceration, blood transfusion, aortic compression, and surgical intervention if bleeding is not controlled.)

Some uterotonic medicines for prevention and treatment of PPH have been well-known for decades (i.e., oxytocin, ergometrine, and misoprostol) while others are more recent additions. In 2018, WHO updated its PPH treatment recommendations to include the administration of tranexamic acid (TXA) via intravenous route within 3 hours of birth in women with PPH (regardless of the underlying cause of PPH). Also, in 2018, WHO updated its PPH prevention recommendations to include the use of heat-stable carbetocin (HSC). Some of the uterotonic medicines (oxytocin and misoprostol) have other obstetric uses such as induction and augmentation of labor, while others are actually contraindicated for these uses and may cause harm if used inappropriately.

With an expanding “toolkit” of uterotonic medicines and TXA to prevent and treat PPH and for other obstetric uses, program managers need clear information in one place on the indications, contraindications, safety profile, and health system requirements for individual medicines to help them make strategic decisions about which medicine to deploy at different levels of the health system based on their country context.

PURPOSE

This brief is intended to serve as a summary of information on the range of medicines that can be used for the management of post-partum hemorrhage and other obstetric indications. This brief summarizes the recommended uses for the medicines currently available and proven effective for prevention or treatment of PPH, other obstetric indications, and the special characteristics of each. The document also includes specific elements that may influence procurement and supply chain management decisions. This brief will be part of a larger document to guide decision-making around procurement of the appropriate medicines.

RECOMMENDED AUDIENCE

This information summary is intended for use by program managers, including supply chain managers, for consultation as they consider future procurement and supply chain needs.

This summary is also intended for maternal and child health advocates who are communicating with government policymakers, civil society, and other stakeholders pivotal to the decision-making process around policy, procurement, and distribution. This may include health practitioners, technical experts, government leaders, civil society, and community representatives who are concerned about the quality of maternity care and women's health.

SUMMARY OF RECOMMENDED USES AND HEALTH SYSTEM CONSIDERATIONS






This following table summarizes the uses and health system requirements of individual uterotonic medicines and TXA proven to be effective for the prevention or treatment of PPH and other common obstetric indications. For greater detail on each medicine, including contraindications, characteristics, and safety considerations, please see pages 5-9.

Indications & Health System Factors	Medicines proven effective for prevention or treatment of PPH				
	Oxytocin	Misoprostol	Heat-stable Carbetocin	Ergometrine	Tranexamic Acid
Prevention of PPH	✓	✓	✓	✓	✗
Treatment of PPH	✓	✓	✗	✓	✓
Induction of Labor	✓	✓	✗	✗	✗
Augmentation of Labor	✓	✗	✗	✗	✗
Post-abortion Care	✗	✓	✗	✗	✗
Administration Route	IV, IM	Oral, Sublingual, Rectal	IV, IM	IV, IM	IV
Cold Chain Requirement	Yes	No	No	Yes	No
Cost	+	+	++++	+	++
Skilled Provider Required	Yes	No Can be used in community health centers	Yes	Yes	Yes

+ Low IV Intravenous
 ++ Medium IM Intramuscular
 ++++ High

OXYTOCIN

RECOMMENDED USES

Prevention of PPH		Recommended as the first-line drug of choice of prevention of PPH
Treatment of PPH		Intravenous oxytocin alone is the recommended uterotonic drug for the treatment of PPH
Induction of labor		If misoprostol is not available, intravenous oxytocin alone should be used for induction of labor
Augmentation of labor		Recommended for the treatment for delay of labor - inappropriate use can contribute to serious maternal morbidities, including uterine rupture, fetal asphyxia or fetal demise.
Post-abortion care		Not recommended

PRODUCT CHARACTERISTICS

Presentation	<ul style="list-style-type: none"> • 10 IU ampoule
Administration	<ul style="list-style-type: none"> • Intramuscularly or intravenously • IV: immediate action; IM: slower action, longer lasting clinical effect
Storage	<ul style="list-style-type: none"> • 2 to 8 degrees Celsius
Cost per unit	<ul style="list-style-type: none"> • International Medical Products Price Guide (IMPPG): USD 0.16 per ampoule; UNFPA catalogue: USD 0.275 per ampoule
Supplies required	<ul style="list-style-type: none"> • Syringes, needles, and IV infusion set (for IV only)
Availability	<ul style="list-style-type: none"> • Present on most countries' Essential Medicines Lists • Currently included in most countries' standard treatment guidelines • Over 100 manufacturers worldwide, but high prevalence of poor quality

HEALTH SYSTEM IMPLICATIONS

Type of Health Facility	<ul style="list-style-type: none"> • Oxytocin should only be administered at health facilities where appropriately skilled providers are present.
Supply Chain	<ul style="list-style-type: none"> • Should be procured in 10 IU ampoules, not 5 IU ampoules (costly and can be misused) • Requires a functional cold chain – from the manufacturer to the point of entry and during distribution to, and storage at, health facilities. • Care should be taken to procure quality-assured oxytocin, as there is high prevalence of poor quality in the public and private sector.
Administration Concerns	<ul style="list-style-type: none"> • For PPH treatment: If the bleeding does not respond to oxytocin, WHO recommends the use of intravenous ergometrine, oxytocin-ergometrine fixed dose or a prostaglandin (including sublingual misoprostol, 800 micrograms).

MISOPROSTOL

RECOMMENDED USES

Prevention of PPH	✓	Recommended where skilled birth attendants are not available and in settings where oxytocin is not available
Treatment of PPH	✓	Recommended when oxytocin is not available.
Induction of labor	✓	Recommended for induction of labor, with 25 mcg presentation - inappropriate use can contribute to serious maternal morbidities
Augmentation of labor	✗	Not recommended - inappropriate use can contribute to serious maternal morbidities, including uterine rupture, fetal asphyxia or fetal demise.
Post-abortion care	✓	Recommended for post-abortion care

PRODUCT CHARACTERISTICS

Presentation	<ul style="list-style-type: none"> • 200 mcg oral tablets for PPH and post-abortion care • 25 mcg oral or vaginal tablets for induction of labor
Administration	<ul style="list-style-type: none"> • Orally for PPH prevention; sublingually for PPH treatment • Orally / sublingually / vaginally for post-abortion care • Orally or vaginally for induction of labor
Storage	<ul style="list-style-type: none"> • Misoprostol is sensitive to moisture.
Cost per unit	<ul style="list-style-type: none"> • IMPPG: USD 0.180 per 200 mcg tablet; no price listed for 25 mcg presentation • UNFPA catalogue: USD 0.25 per oral tablet of 200 mcg; no price listed in catalogue for 25 mcg presentation
Supplies required	<ul style="list-style-type: none"> • None
Availability	<ul style="list-style-type: none"> • Both presentations listed on most recent WHO Essential Medicines List • Present on most national Essential Medicines Lists, although sometimes not for obstetric purposes • 200 mcg presentation widely available; 25 mcg presentation not widely available and high prevalence of poor quality

HEALTH SYSTEM IMPLICATIONS

Type of Health Facility	<ul style="list-style-type: none"> • Can be administered in community health centers without the presence of skilled birth attendants.
Supply Chain	<ul style="list-style-type: none"> • Care should be taken to procure misoprostol packaged in aluminum blisters to reduce the risk of exposure to moisture. • Care should be taken to procure quality-assured misoprostol, as there is high prevalence of poor quality in the public and private sector.
Administration Concerns	<ul style="list-style-type: none"> • The lack of availability of the 25 mcg may cause providers to attempt to cut a 200 mcg tablet into the appropriate dose. This practice should be avoided as achieving a 25 mcg “piece” of a 200 mcg tablet is virtually impossible when done by hand. • Sensitivity around the potential use of misoprostol for other purposes continues to impede its scale-up, even when it would be advantageous due to lack of availability of oxytocin and/or when skilled labor or reliable cold chains for appropriate storage of oxytocin are not in place.

HEAT-STABLE CARBETOCIN

RECOMMENDED USES

Prevention of PPH	✓	Recommended when cost is comparable to other effective uterotonics and/or when a cold chain is not available; recent trials show non-inferiority to oxytocin
Treatment of PPH	✗	Not recommended
Induction of labor	✗	Not recommended
Augmentation of labor	✗	Not recommended - inappropriate use can contribute to serious maternal morbidities, including uterine rupture, fetal asphyxia or fetal demise.
Post-abortion care	✗	Not recommended

PRODUCT CHARACTERISTICS

Presentation	<ul style="list-style-type: none"> 100 µg in 1-ml ampoule
Administration	<ul style="list-style-type: none"> Intramuscularly or intravenously
Storage	<ul style="list-style-type: none"> Heat-stable carbetocin may be stored at 25 degrees Celsius
Cost per unit	<ul style="list-style-type: none"> Current market price ranges from approximately USD 13 to 25. WHO and manufacturer working on an agreement to make the product affordable at a sustainable price
Supplies required	<ul style="list-style-type: none"> Syringes, needles, and IV infusion set (for IV only)
Availability	<ul style="list-style-type: none"> Currently only 1 sole manufacturer

HEALTH SYSTEM IMPLICATIONS

Type of Health Facility	<ul style="list-style-type: none"> Heat-stable carbetocin (HSC) should only be administered at health facilities where appropriately skilled providers are present.
Supply Chain	<ul style="list-style-type: none"> Concern of supply constraints, as there is currently only 1 manufacturer.
Administration Concerns	<ul style="list-style-type: none"> Since the use of HSC for prevention of post-partum hemorrhage is a new recommendation, the product will need to go through the process of introduction and scale-up in the health system, including registration of HSC products; inclusion of HSC in the national Essential Medicines List; revision of standard treatment guidelines to include HSC for the prevention of PPH; forecasting and supply planning, including strategic decision making around where HSC will be made available Due to its longer half-life, special care must be taken to ensure safe use of HSC for PPH prevention only.

ERGOMETRINE

RECOMMENDED USES

Prevention of PPH	✓	Recommended option when oxytocin is not available and in women without hypertensive disorders
Treatment of PPH	✓	Recommended when oxytocin is not available, or when bleeding does not respond to oxytocin (in women without hypertensive disorders)
Induction of labor	✗	Not recommended
Augmentation of labor	✗	Not recommended - inappropriate use can contribute to serious maternal morbidities, including uterine rupture, fetal asphyxia or fetal demise.
Post-abortion care	✗	Not recommended

PRODUCT CHARACTERISTICS

Presentation	<ul style="list-style-type: none"> Ergometrine maleate 0.2mg/ml injection in 1ml ampoule Methylethergometrine maleate 0.2mg/ml injection in 1 ml ampoule
Administration	<ul style="list-style-type: none"> Intramuscularly or intravenously
Storage	<ul style="list-style-type: none"> Ergometrine requires cold storage and protection from light; it is more heat sensitive than oxytocin
Cost per unit	<ul style="list-style-type: none"> IMPPG: USD 0.182 per ampoule; UNFPA catalogue: USD 0.219 per ampoule
Supplies required	<ul style="list-style-type: none"> Syringes, needles, and IV infusion set (for IV only)
Availability	<ul style="list-style-type: none"> Present on most countries' Essential Medicines Lists Present on most recent WHO Essential Medicines List Widely available, but high prevalence of poor quality

HEALTH SYSTEM IMPLICATIONS

Type of Health Facility	<ul style="list-style-type: none"> Ergometrine should only be administered at health facilities where appropriately skilled providers are present.
Supply Chain	<ul style="list-style-type: none"> Requires a functional cold chain – from the manufacturer to the point of entry and during distribution to, and storage at, health facilities. Critical that the medicine is protected from light. Care should be taken to procure quality-assured ergometrine, as there is high prevalence of poor quality in the public and private sector.
Administration Concerns	<ul style="list-style-type: none"> Use of ergometrine in women with hypertensive disorders is contraindicated.

TRANEXAMIC ACID

RECOMMENDED USES

Prevention of PPH	✗	Not recommended
Treatment of PPH	✓	Early use of IV TXA (as early as possible after clinical diagnosis of PPH, and only within 3 hours of birth) in addition to standard care is recommended for women with clinically diagnosed PPH following vaginal birth or caesarean section.
Induction of labor	✗	Not recommended
Augmentation of labor	✗	Not recommended
Post-abortion care	✗	Not recommended

PRODUCT CHARACTERISTICS

Presentation	<ul style="list-style-type: none"> • 100 mg / ml
Administration	<ul style="list-style-type: none"> • Intravenously, in complement with other uterotonics
Storage	<ul style="list-style-type: none"> • Stored at 25 degrees Celsius
Cost per unit	<ul style="list-style-type: none"> • No price listed in UNFPA catalogue • Only buyer price listed in IMPPG: USD 1.06 per ampoule
Supplies required	<ul style="list-style-type: none"> • IV infusion set, syringes and needles
Availability	<ul style="list-style-type: none"> • Many manufacturers worldwide

HEALTH SYSTEM IMPLICATIONS

Type of Health Facility	<ul style="list-style-type: none"> • Tranexamic acid should only be available at health facilities where appropriately skilled providers are present.
Supply Chain	<ul style="list-style-type: none"> • TXA is available in many countries' essential medicine list (EML), with trauma as the clinical indication; Countries should update their EML to specify PPH as one of the indications for administration of IV TXA.
Administration Concerns	<ul style="list-style-type: none"> • Tranexamic acid complements other uterotonics – it is not a substitute • Administration of TXA via the oral route has not been shown thus far to be effective for PPH prevention.

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