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சுகாதார அமைச்சு
Ministry of Health

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My No.) FHB/MCU/Misoprostol /2021

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Circular No. 01-20/2021

Provincial Directors of Health Services,
Regional Directors of Health Services,
All Heads of Institutions,

National Guideline on Use of Misoprostol in Gynaecology and Obstetrics

This document outlines the best practice guidelines of Ministry of Health for proper and safe use of Misoprostol tablets in gynaecology and obstetrics care. Recommendations of the Sri Lanka College of Obstetricians and Gynaecologists (SLCOG) were obtained in the formulation of these guidelines.

Misoprostol is a synthetic analogue of prostaglandin E1. At the recommended dosages, misoprostol induces contractions of the smooth muscle fibres in the myometrium and relaxation of the uterine cervix. The uterotonic properties of misoprostol facilitate cervical dilation and evacuation of intrauterine contents.

Preparation - 200mcgm tablet.

1. Use in first and second trimesters
Evidence demonstrate advantages of Misoprostol over available other alternatives in the management of miscarriage in first and second trimesters. The advantages include similar effectiveness as alternatives, fewer side effects, more practical to use and low cost.

Because of its abortive properties, **Misoprostol should not be used until a non-viable status of a pregnancy is confirmed.**

It is not recommended to use Misoprostol after 20 Weeks of Gestation in the presence of a uterine scar (suspected perforation, past Caesarean section or myomectomy)

2. Use in the third trimester
Misoprostol is used extensively in the third trimester in many countries. Advantages include the low cost, feasibility for storage at room temperature and long shelf life.
However, caution should be exercised as the dosage used in the third trimester is much less than the dosage used in the first trimester.

There is significant literature evaluating the use of Misoprostol for cervical ripening and induction of labour. The potential risks and benefits in each individual case should be carefully evaluated and attention paid to the published information regarding minimization of dosage, as with the other prostaglandin misoprostol can cause uterine hypertonicity.

The Ministry of Health recommends, based on the guidance of SLCOG, **the use of Misoprostol in the third trimester only in women with foetuses dead in utero. It is contraindicated in the presence of a uterine scar.** At present, when the baby is alive, the use of misoprostol for induction of labour at the appropriate dosage is only recommended in a research setting. The Ministry of Health will review this decision from time to time.

3. Use of Misoprostol for retained placenta

The use of misoprostol for the treatment of retained placenta following a live birth has not shown any benefit over placebo. Therefore, the use of misoprostol in the management of retained placenta in late pregnancy is not recommended.

4. Use in the post-partum period

Misoprostol is an effective uterotonic and sustained uterine contraction can be achieved in the third stage. However, there is insufficient evidence to recommend misoprostol over conventional injectable uterotonics in the management of the third stage of labour.

Misoprostol may be used for the management of postpartum haemorrhage to compliment the action of standard oxytocic drugs (oxytocin and ergometrine) but not as a substitute for the above drugs.

Particular care has to be taken in the use of misoprostol according to the regimens in each trimester for which evidence is available. Appropriate informed consent should be obtained from women prior to administration of the drug.

5. Procedure for use of Misoprostol:

I. The decision to use the relevant drug (eg: Misoprostol) and the responsibility for the administration of it will be with the Consultant Obstetrician and Gynaecologist.

II. The dosage and the route of administration should be instructed by the Consultant Obstetrician and Gynaecologist and such instructions should be documented clearly.

III. The patient should have the informed choice of its use following adequate counselling on the use of the index drug including the indication and methodology of its use, adverse effects etc. This should be followed by obtaining written informed consent for its use.

IV. Adequate separate records should be maintained on the use of the drug including the presence of any serious adverse effects.

V. Any adverse effects should be reported to the National Medicines Regulatory Authority and Medical Supplies Division of Ministry of Health.

VI. The hospital drug supply system should monitor the supply and usage of Misoprostol in the wards with appropriate record keeping.

VII. The patient should be informed to stay close proximity to the hospital where the drug is administered until complete expulsion of the products of conception is confirmed by an ultrasound scan.

VIII. The woman should receive precise instructions on the actions to be taken in the event of developing any problems following the administration of Misoprostol, particularly, heavy vaginal bleeding.

6. Recommended dosage in different conditions and Trimesters

The following table includes the recommended dosages of Misoprostol in different conditions and trimesters;

	Indication	Dosage	Notes
First Trimester < 13 weeks gestation	Silent / Delayed miscarriage -1st Trimester	800mcg vaginally 3hrly (max * 2 doses) or sublingual 600mcg 3hrly (max*2 doses)	Give 2 doses and leave for 2 weeks unless there is heavy bleeding or infection.
	Incomplete miscarriage - 1st Trimester	600mcg orally single dose or 400mcg sublingual single dose OR 400-600mcg vaginally single dose	Leave for 2 weeks unless heavy bleeding or infection.
	Cervical preparation – pre-instrumentation Eg: resection of myomas	400mcg vaginally 3hrs before OR sublingually I hr before procedure	Use in selected cases for insertion of intrauterine devices Dilatation and curettage in hysteroscopy
Second Trimester 13-26 weeks	Mid trimester foetal death	Intrauterine fetal death: 400mcg vaginally / sublingually / buccal (in the cheek) 4- 6 hourly maximum 4 doses	Reduce doses in women with history of previous section For fetal death in the third Trimester: see induction of labour and death in utero below
Second Trimester 13-26 Weeks	Inevitable miscarriage	200mcg vaginally 8hrly / sublingually / buccal (in the cheek) 6 hourly Maximum 4 doses	
Over 26 weeks	Pre induction ripening of cervix and induction of labour (IOL) for a live viable fetus at term	25mcg orally 2 hourly or 25mcg vaginally 6 hourly	Research on feasibility and generalizability is recommended. Not recommended for routine use currently until further evidence is available. Do not use in a scarred uterus or in a grand multipara.
	Pre induction ripening of cervix and IOL for death in utero after 26 weeks gestation.	25mcg orally 2 hourly or 25mcg vaginally 6 hourly.	Research on feasibility and generalizability is strongly recommended. Not recommended for routine use currently until further evidence is available. Do not use in a scarred uterus or in a grand multipara.

Postpartum	Post-Partum Haemorrhage (PPH) Prophylaxis	600mcg orally single dose	Not recommended in Sri Lanka as it is not as effective as Oxytocin.
	Post-Partum Haemorrhage (PPH) Treatment	800mcg sublingually single dose	As an adjunct / second line drug for the total care of such women.

Notes:
The use of a loading dose of misoprostol is not necessary. There is no advantage to the use of moistened over dry misoprostol.

7. Precautions

- Misoprostol should not be administered if an intrauterine contraceptive device is present. It should be removed first.
- Uterine hyperstimulation and rupture have been reported beyond the first trimester. Therefore, lower dosage of Misoprostol is required in second and third trimester.
- Rare serious cardiovascular accidents have been reported following the administration of the prostaglandin including Misoprostol. For this reason, women with risk factors for cardiovascular disease or established cardiovascular disease should be treated with caution.
- Epileptic seizures have been reported with the use of prostaglandin and prostaglandin analogues. This possibility should be born in mind if Misoprostol is administered in patients with a history of epilepsy.
- Bronchospasms may occur with the use of some prostaglandins and prostaglandin analogues. The possibility of this complication should be born in mind in patients with history of asthma.
- Misoprostol should not be used in the presence of infection. Cases of serious bacterial infection, including very rare cases of fatal septic shock have been reported following the use of misoprostol.
- Misoprostol use should be avoided in cases of confirmed or suspected molar pregnancy.

8. Teratogenicity

- Use of Misoprostol has been associated with birth defects. Suspected anomalies include malformation of limb and cranial nerve defects.

9. Use during lactation

- Misoprostol is rapidly metabolized to misoprostol acid in the mother. Misoprostol acid is biologically active and is excreted in breast milk. Misoprostol should not be administered to breastfeeding mothers because the excretion of misoprostol acid could cause undesirable effects such as diarrhoea in breastfeeding infants.

10. Contraindications

- Known hypersensitivity to misoprostol or any other prostaglandin.
- Known or suspected coagulation disorders and during treatment with anticoagulants.
- Uncertainty about pregnancy viability.
- Suspected ectopic pregnancy.

11. Adverse effects

- Gastrointestinal disorders; nausea (transient and mild), vomiting, diarrhea, abdominal pain.
- Reproductive system disorders; very frequent uterine contractions with pain observed in the hours following Misoprostol intake; vaginal bleeding, sometimes heavy and prolonged.
- General disorders; headache, dizziness, and chills with fever

Considering above facts, you are requested the following:

1.1) To maintain reasonable buffer stock considering consumption of the drug in all specialized institutions
1.2) To submit details of usage of the drug in the attached form to the MSD when requesting to replenish the stock supplied as buffer stock.

In order to ensure proper implementation of above procedure you are kindly requested to bring the content of the circular to all concerned in your province/district/ institution.

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Dr. Asela Gunawardena
Director General of Health Services,

Dr. ASELA GUNAWARDENA
Director General of Health Services
Ministry of Health
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Cc: DDG/MSD –f.i. & n.a.
DDG/MSI- f.i.
Director/ NMRA -f.i. & n.a.
Director (Stock verific) MOH-f.i.
Director MCH- f.i.
Chief Internal Auditor/MoH- f.i
Chairman/SPC-f.i& n.a.
All C.P./Teaching Hospitals- f.i& n.a
DDG/PHS 11-f.i.
DDG(L/S)-f.i.
Director/MSD- f.i. & n.a.
Director/NMQAL- f.i. & n.a.
All Provincial CCPs-f.i.
Secretary/ DEC- f.i
DD/ICT Unit- f.i& n.a
All OIC/RMSD- f.i& n.a

My No: .....

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Director,
Medical Supplies Division

RETURN FORM ON USAGE OF MISOPROSTOL

Name of Institution.....

No	Name of the patient	Ward / BHT	Diagnosis	Dose	Adverse events observed	Consultant's Signature

Stock in hand .....

Required Quantity .....

Signature of Pharmacist..... Date of request.....

Name of Pharmacist .....

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Head of the Institution,