POUR ELLE

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Why explore new indications for mifepristone?

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Reproductive Health SUPPLIES COALITION

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Legal status of abortion in SSA region

www.worldsabortionlaws.com

RH uses of mifepristone and misoprostol

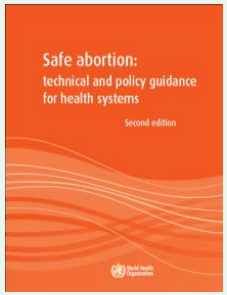
Indication	Clinical advantage to adding mife?	Registered indication (Mifeprex or Mifegyne only)	Registered indication (misoprostol)	WHO EML Listing for indication
Early pregnancy termination	✓	✓ (all mife)	✓ (w/mife)	✓(mife+miso)
Later pregnancy termination*	✓	X	X	✓(mife+miso)
Missed abortion*	✓	X	X	X
IUFD*	✓	X	X	X
Cervical ripening	✓	✓ (Mifegyne)	X	X
Labor induction	X	X	✓	✓ (miso)
Incomplete abortion	X	X	✓	✓ (miso)
PPH	X	X	✓	✓(miso)

Missed abortion and Intra-uterine fetal death (IUFD)

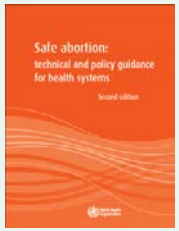
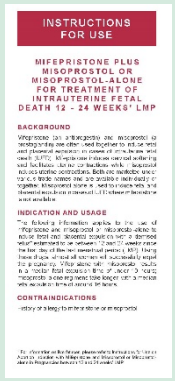
What are we talking about?

- A **missed abortion** is embryonic demise with no symptoms
- An **intra-uterine fetal death (IUFD)** is fetal death occurring from 14 – 28 weeks gestation, can be diagnosed symptomatically
- Both can be diagnosed with ultrasound

Level of evidence: Miso only

	Missed abortion	IUFD
FIGO INTERNATIONAL FEDERATION OF GYNECOLOGY & OBSTETRICS	800 mcg vaginal or 600 mcg sublingual, every 3 hrs (X2)	200 mcg vainal, sublingual or buccal every 4 – 6 hrs
	No formal recommendation	No formal recommendation

Level of evidence: Mife+Miso

	Missed abortion	IUFD
	No formal recommendation	No formal recommendation
	No formal recommendation	No formal recommendation
	No formal recommendation, research ongoing	200 mg mifepristone followed 12-48 hrs by 400 mcg buccal, sublingual or vaginal misoprostol every 3 hrs

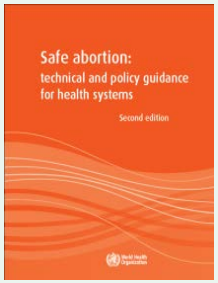
Summary of evidence

- Mifepristone increases sensitivity of the uterus to prostaglandins and ripens the cervix allowing for lower doses of misoprostol for expulsion
- Available evidence shows that while misoprostol alone works well; mife+miso is a promising treatment that may:
  - Shorten time to expulsion, reduce amount of misoprostol required, increase comfort for woman
  - New data on mife-miso combined regimens forthcoming for both indications

Second trimester abortion

- 10-15% of all abortions occur in 2nd trimester (> 12 wks gestational age) and are permitted for medical reasons in most jurisdictions
- Can be managed medically or surgically
- Account for more than 2/3 of major abortion complications
- Wide variation in practice, policy, regulation

Level of evidence: Second trimester abortion

	Mife-miso	Miso alone
FIGO INTERNATIONAL FEDERATION OF GYNECOLOGY & OBSTETRICS	200 mg oral mifepristone followed 36-48 h later with repeated doses of misoprostol • mifepristone + 800 mcg vaginal miso + 400 mcg vaginal/oral/sublingual misoprostol every 3 hrs	400 mcg oral miso + 400 mcg vaginal, buccal or sublingual miso every 3 hrs, no max dose (2017)
	200 mg oral mifepristone followed 36-48 h later with repeated doses of misoprostol • mifepristone + 800 mcg vaginal or 400 mcg oral miso + 400 mcg vaginal or sublingual miso every 3 hrs (2012)	400 mcg oral miso + 400 mcg vaginal or sublingual miso every 3 hrs up to 5 doses (2012)

Summary of evidence

- Pre-treatment will mifepristone shortens time to fetal expulsion
- May result in fewer side effects and improved quality care of care by creating evidence-base to support outpatient, day-procedure care
- As second tri services often medically indicated, the service is often legally permitted, thereby creating a pathway to formal registration of mifepristone

Why this all matters

- Promising ways to improve care for women and legally register mifepristone; offers opportunities for advocacy, training and registration in countries w/no legal indication for elective abortion
- Having approved non-abortion indications (e.g. missed abortion and IUFD) reduces the stigma associated with stocking mifepristone (and misoprostol) and impacts where within the health system/hospital these commodities are stored (e.g. ER, FP clinic, obs/gyn, etc)
- Additional indications help normalize place of these medicines within national registries (budgets) and on country-level EMLs
- Registered indications can facilitative efforts to integrate clinical evidence-base into practice guidelines and foster efforts to train providers on appropriate use of the medicines for all indications
- Formal registration and marketing of products also helps to ensure access to high quality medications

Thank you! Any questions?

www.gynuity.org

FIGO's updated recommendations for misoprostol used alone in gynecology and obstetrics

FIGO
INTERNATIONAL FEDERATION OF GYNECOLOGY & OBSTETRICS
www.figo.org

MISOPROSTOL-ONLY RECOMMENDED REGIMENS 2017

<13 weeks' gestation	13–26 weeks' gestation	>26 weeks' gestation[8]	Postpartum use
Pregnancy termination[a,b,1] 800µg sl every 3 hours *or* pv*/bucc every 3–12 hours (2–3 doses)	**Pregnancy termination**[1,5,6] 13–24 weeks: 400µg pv*/sl/bucc every 3 hours[a,e] 25–26 weeks: 200µg pv*/sl/bucc every 4 hours[f]	**Pregnancy termination**[1,5,9] 27–28 weeks: 200µg pv*/sl/bucc every 4 hours[f,g] >28 weeks: 100µg pv*/sl/bucc every 6 hours	**Postpartum hemorrhage (PPH) prophylaxis**[i,2,10] 600µg po (x1) *or* **PPH secondary prevention**[j,11] (approx. ≥350ml blood loss) 800µg sl (x1)
Missed abortion[c,2] 800µg pv* every 3 hours (x2) *or* 600µg sl every 3 hours (x2)	**Fetal death**[f,g,1,5,6] 200µg pv*/sl/bucc every 4–6 hours	**Fetal death**[2,9] 27–28 weeks: 100µg pv*/sl/bucc every 4 hours[f] >28 weeks: 25µg pv* every 6 hours *or* 25µg po every 2 hours[h]	**PPH treatment**[k,2,10] 800µg sl (x1)
Incomplete abortion[a,2,3,4] 600µg po (x1) *or* 400µg sl (x1) *or* 400–800µg pv* (x1)	**Inevitable abortion**[g,2,3,5,6,7] 200µg pv*/sl/bucc every 6 hours	**Induction of labor**[h,2,9] 25µg pv* every 6 hours *or* 25µg po every 2 hours	
Cervical preparation for surgical abortion[d] 400µg sl 1 hour before procedure *or* pv* 3 hours before procedure	**Cervical preparation for surgical abortion**[a] 13–19 weeks: 400µg pv 3–4 hours before procedure >19 weeks: needs to be combined with other modalities		

References

a WHO Clinical practice handbook for safe abortion, 2014
b von Hertzen et al. Lancet, 2007; Sheldon et al. 2016 FIAPAC abstract
c Gemzell-Danielsson et al. IJGO, 2007
d Sääv et al. Human Reproduction, 2015; Kapp et al. Cochrane Database of Systematic Reviews, 2010
e Dabash et al. IJGO, 2015
f Perritt et al. Contraception, 2013
g Mark et al. IJGO, 2015
h WHO recommendations for induction of labour, 2011
i FIGO Guidelines: Prevention of PPH with misoprostol, 2012
j Raghavan et al. BJOG, 2015
k FIGO Guidelines: Treatment of PPH with misoprostol, 2012

Notes

1 If mifepristone is available (preferable), follow the regimen prescribed for mifepristone + misoprostol[a]
2 Included in the WHO Model List of Essential Medicines
3 For incomplete/inevitable abortion women should be treated based on their uterine size rather than last menstrual period (LMP) dating
4 Leave to take effect over 1–2 weeks unless excessive bleeding or infection
5 An additional dose can be offered if the placenta has not been expelled 30 minutes after fetal expulsion
6 Several studies limited dosing to 5 times; most women have complete expulsion before use of 5 doses, but other studies continued beyond 5 and achieved a higher total success rate with no safety issues
7 Including ruptured membranes where delivery indicated
8 Follow local protocol if previous cesarean or transmural uterine scar
9 If only 200µg tablets are available, smaller doses can be made by dissolving in water (see www.misoprostol.org)
10 Where oxytocin is not available or storage conditions are inadequate
11 Option for community based programs

Route of Administration

pv – vaginal administration
sl – sublingual (under the tongue)
po – oral
bucc – buccal (in the cheek)

* Avoid pv (vaginal route) if bleeding and/or signs of infection

Rectal route is not included as a recommended route because the pharmacokinetic profile is not associated with the best efficacy

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