South African National Essential Medicine List
Adult Hospital Level Medication Review Process
Component: Gynaecology

1. Executive Summary

Date: 20 October 2017 (update of initial review, 16 June 2009)
Medicine (INN): Mifepristone
Medicine (ATC): G03XB01
Indication (ICD10 code): Medical termination of pregnancy (TOP) (O04.9)
Patient population: Medical TOP for gestation up to 20 weeks.
Level of Care: Secondary level of care
Prescriber Level: Medical officer, doctor
NNT: i) First trimester TOP: 13 i.e. 13 more women need to be treated with combination treatment (mifepristone with misoprostol) to terminate one more pregnancy compared to misoprostol monotherapy[8]; ii) Mid-trimester TOP: 4 (low quality of evidence[17])
Current standard of Care: Mifepristone + misoprostol (M/M)
Motivator/reviewer name(s): Dr E Bera, Ms TD Leong
PTC affiliation: Dr Bera - Rahima Moosa Mother-and-Child Hospital PTC

2. Name of author(s)/motivator(s)

Dr E Bera, Ms TD Leong.

3. Author affiliation and conflict of interest details

Dr E Bera: Department of Obstetrics & Gynaecology, University of the Witwatersrand; Member of the Adult Hospital Level Committee (2017-2020); no conflicts of interest.
Ms TD Leong: National Department of Health, Essential Drugs Programme; Secretariat to the Adult Hospital Level Committee(2017-2020); no conflicts of interest.

4. Introduction

Mifepristone (RU 486) is an anti-progesterone steroid registered for use in first and second trimester termination of pregnancy (TOP). It sensitizes the myometrium to uterine contractions induced by prostaglandins.

Approximately 85 600 pregnancy terminations are performed upon request annually in South Africa, of which 24% are second trimester TOP's.[1,2]Current practice involves the use of manual vacuum aspiration (MVA) for first trimester TOP, or alternatively medical treatment with vaginal/sublingual misoprostol. Second trimester TOP's are managed medically with vaginal and/or sublingual misoprostol, or a catheter bulb and oxytocin, followed by MVA if abortion is incomplete.
The optimal, safest, and least expensive method for TOP is presently unknown. The aim of this review is to evaluate the effectiveness of mifepristone/misoprostol (M/M), and the cost of including mifepristone in the adult EDL.

5. Purpose/Objective i.e. PICO question

P - Women undergoing termination of pregnancy< 20 weeks' gestation
I - Mifepristone, misoprostol
C -Misoprostol only
O -Complete termination of pregnancy

6. Methods

i. Search strategy A:

The Cochrane Database of Systematic Reviews. Additionally an electronic literature survey using the following terminology (was performed: "mifepristone" [Substance Name] OR "mifepristone [Text Word] AND "termination" [Text Word] OR "termination" [MeSH Terms] AND (("1989/12/31" [PDAT] : "2009/06/01" [PDAT]) AND "human" [MeSH Terms] AND English [lang]) AND (randomized controlled trial [Publication Type] OR (randomized [Title/Abstract] AND controlled [Title/Abstract] AND trial [Title/Abstract]))

Selection of studies: 4 relevant Cochrane Reviews and a RCOG guideline were identified. 64 studies were retrieved from the survey. 39 studies were excluded for the following reasons: outcomes other than abortion (14); comparisons with gemeprost (6); comparisons for cervical ripening prior to MVA (4); mifepristone versus MVA (5); gemeprost vs. misoprostol (6); duration between mifepristone and prostaglandin administration (4).

Evidence synthesis:

<u>First trimester TOP</u>

A Cochrane review (Say et al, 2002) compared medical versus surgical first trimester TOP.[3] In 2 studies involving 472 participants suction curettage ended in significantly higher rates of complete abortions compared with prostaglandins (OR 2.67; 95% CI 1.06-6.75) and was less painful, but the trials did not include the commonly used medical regimens of mifepristone/misoprostol (M/M).

In a subsequently published randomized study of 400 women where M/M was used, the failure rate was 5.4% with M/M vs. 2.1% with MVA (p=NS).[4]

In another recent study involving 1033 women, success rates were higher with surgery compared with M/M (97.7% vs. 94.1%; p< 0.01). Satisfaction was high with both procedures in this study, although significantly higher with surgical than medical (98% vs. 82%; p< 0.0001).[5]

The RCOG recommends medical first trimester TOP as the most effective method up to 7 weeks gestation, and states that medical treatment continues to be an appropriate method for TOP up to 9 weeks.[6]The recommended regimen is: mifepristone 200mg, oral, followed by misoprostol 800mcg vaginally 1-3 days later. For 9-13 weeks, medical treatment is a "safe, acceptable, and effective alternative to surgery from 9-13 weeks", using the same regimen plus a maximum of 4 further doses of 400mcg oral/vaginal at 3-hourly intervals.

Another Cochrane review examined different medical methods for 1st trimester abortion.[7]This review included 39 trials, in which mifepristone 600mg was found to be as effective as 200mg, and oral misoprostol was found less effective with more side-effects than vaginal misoprostol. Combined M/M was more effective than prostaglandins alone, but the results were not pooled due to trials using different doses of misoprostol (95% CI 1.4 to 3.75).In one of the included studies (250 women), the difference in successful abortion was significant: 95.7% vs. 88% (p =

0.047).[8] In a more recent quasi-randomized study involving 100 Nepalese women the success rate with M/M was 94% compared with 86% following 1600 mcg vaginal misoprostol.[9]
Given the degree of uncertainty around success rates with relatively small numbers for medical TOP, a larger review (uncontrolled) of 4132 consecutive cases by Ashok et al, confirms the overall success rate for M/M at 97.7%.[10] The success rates were consistent with several cohorts reviewed by RCOG in their guideline.[6] Misoprostol alone in the 1st trimester has a success rate as low as 47% and at best 88%.[8,11-14]
A very recent RCT compared mifepristone 200mg vs. 100 mg followed by vaginal misoprostol in 2181 women undergoing TOP < 9 weeks, and found success rates of 93.2% and 92% respectively (RD 1.2; 95% CI -1.0 to 3.5), suggesting that the dose of mifepristone can be reduced even further to 100mg for TOP's < 9 weeks.[15] Doses of mifepristone < 100mg appear less effective.[6]

Second trimester TOP (13 – 20 weeks)
The dose requirements of misoprostol decrease with advancing gestation, making direct comparisons between studies of different gestations difficult to interpret. For mid-trimester TOP (13–20 weeks), mifepristone 200mg oral, followed 36-48 hours later by misoprostol 800 mcg vaginally, then 400mcg oral 3-hourly for a maximum of 4 doses is recommended by RCOG.[6] A Cochrane review evaluated 2nd trimester dilatation and evacuation versus mifepristone/misoprostol (M/M), but the numbers were too limited (18 patients) for meaningful conclusions to be made on efficacy or safety.[16]
In a separate RCT of 64 women, addition of mifepristone to misoprostol reduced the duration of complete abortion from 18 hours to 10 hours (p< 0.01), and a corresponding reduction in rates of placental retention from 6.3% to 3.1% was seen, although not statistically significant (p= 0.61).[17] Despite limited comparative data in the 2nd trimester, complete expulsion rates with M/M are around 90% - 97%, compared with 76% - 91% using misoprostol alone.[11-13,17,18]

Safety concerns: contra-indicated in severe asthma, long-term corticosteroid therapy.

Additional search for the period: 2009/06/02 to 2017/10/20
ii. Search strategy B
Cochrane Library:
2 of 5 were selected using the following search strategy:
"mifepristone AND termination of pregnancy"; Publication Year from 2009 to 2017 (Word variations searched). One Cochrane review was not considered relevant to the PICO question and the authors of the review update by Say et al (2009) found no change to conclusions previously made (See initial evidence search and synthesis, above).

iii. Search strategy C
PUBMED database:89 studies were retrieved using the following search strategy:
((((("mifepristone"[MeSH Terms] OR "mifepristone"[All Fields]) AND ("abortion, induced"[MeSH Terms] OR ("abortion"[All Fields] AND "induced"[All Fields]) OR "induced abortion"[All Fields] OR ("termination"[All Fields] AND "pregnancy"[All Fields]) OR "termination of pregnancy"[All Fields])) AND ("randomized controlled trial"[Publication Type] OR "randomized controlled trials as topic"[MeSH Terms] OR "randomised controlled trials"[All Fields] OR "randomized controlled trials"[All Fields])) AND english[All Fields]) AND ("humans"[MeSH Terms] OR "humans"[All Fields]) AND (("2009/06/02"[PDAT] : "2017/10/20"[PDAT]) AND "humans"[MeSH Terms] AND English[lang])

Author, date	*Type of study*	n	Population	Comparators	Primary outcome	Effect sizes	Comments
Wildschut *et al*, 2011[19]	Systematic review and metaanalysis.	40 RCTs: various methods &agents for medical TOP in mid trimester	Pregnant women - medical TOP of a singleton living fetus - 12-28 weeks' gestation	• mifepristone+misoprostolvs. placebo+misoprostol. • mifepristone+misoprostol vs. placebo+misoprostol	• Abortion within 24 hours • Need for surgical evacuation	• OR 12.13 (1.43 to 102.61); p=0.022 • OR 0.23 (0.02 to 2.14); p=0.19	Mifepristone+misoprostol more effective vs. misoprostol alone. However, RCT evidence is limited. (Only one small RCT; Kapp, 2007; low risk of bias: adequate blinding; allocation concealment)
				• Dose of mifepristone, before misoprostol administration: 200 vs. 600 mg	• Abortion within 24h • Need for surgical evacuation	• OR 2.06 (0.18 to 23.83), p=0.56 • OR 0.56 (0.12 to 2.56) , p=0.46	No statistical significant difference found; though evidence limited (1 RCT - Webster, 1996).
Kuiler *et al,* 2011[20]	Systematic review and metaanalysis.	48 RCTs	Pregnant women during the first trimester, undergoing medical TOP	• Mifepristone/prostaglandin regimen: mifepristone 600 mg vs. 200 mg	• Failure to achieve complete abortion.	• RR 1.07, (0.87 to 1.32), I2=0%, p=0.52 i.e. similar effectiveness in achieving complete abortion; 4 RCTs (n=3494),	Combined mifepristone regimens more effective vs. monotherapy; with low dose mifepristone 200 mg demonstrating effectiveness. However, some results limited by small RCTs and high heterogeneity. It is noted that most RCTs "*conducted in settings with good access to emergency services, which may limit the generalisability of these results*".
				• Mifepristone vs. mifepristone + prostaglandin		• RR 3.76 (2.30 to 6.15), I2 =83%; p<0.00001 i.e. combined regimen more effective; 3 RCTs (n=273)	
Dabash et al, 2015[21] ABSTRACT	RCT, double-blind, placebo-controlled	120	Pregnant women - 14-21 weeks' gestation	• mifepristone + misoprostol, buccal vs. placebo + misoprostol, buccal	• Complete uterine evacuation at 48 hours • Mean time to complete abortion	• 55 (91.7%) vs. 43 (71.7%); RR 1.28 (1.07 to 1.53) • 10.4±6.6 hrs vs. 20.6±9.7 hrs; p<0.001 • Side effects reported to be similar in both groups	Small RCT suggests that combination mifepristone regimen more effective and faster vs. misoprostol, buccal alone in terminating 2nd trimester pregnancy.

LI *et al*, 2015[22]	RCT, blinded, placebo controlled.	2500	Pregnant women - ≤ 35 days gestation	• misoprostol 200 mcg + various doses of mifepristone: 50 mg vs. 75 mg vs. 100 mg vs. 125 mg vs. 150 mg.	• Complete abortion • Average days of bleeding	• 472(98.13%) vs. 478 (98.35%) vs. 475 (97.54%) vs. 473 (97.93%) vs. 476 (98.35%); p=0.8801, respectively. 5.69±1.24 vs. 6.78±1.69 vs. 7.92±2.44 vs. 8.04±1.91 vs. 8.25±2.47; p<0.0001, respectively	Per protocol analyses with attrition bias. Allocation concealment inadequate. Lower doses of mifepristone with misoprostol 200 mg are as effective and safe as higher doses for TOP ≤ 35 days, with reduced or shorter vaginal bleeding and fewer ADRs with 50 or 75 mg dose. It is noted that comparison to standard regimen of 200 mg was not investigated. Ectopic pregnancy may be a concern.
Kapoor *et al*, 2014[23] ABSTRACT	Prospective RCT	80	Pregnant women - ≤ 56 days gestation	• mifepristone + misoprostol 800 mcg with repeat dose (400 mcg):dose of mifepristone 100 mg vs. 200 mg	Complete abortion	• 1st dose of misoprostol: 85% vs. 87.5% • Repeat dose of misoprostol: 97.5% vs. 100%.	Small RCT suggests that lower dose mifepristone, 100 mg, as effective as standard dose 200 mcg in combination with misoprostol for medical TOP in early pregnancy ≤ 56 days gestation.

Cost Analysis: Using reasonable estimated success rates for TOP, a (basic) cost analysis was undertaken for each method, stratified by trimester. Direct costs reflect costs accessed on 23 October 2017 [23, 24, 25, 26, 27, 28] (Note: Unless indicated, procedure costs are for level 1 facilities managed by general practitioner). This costing analysis is from the payer's perspective and discounting was not considered to be necessary).

Direct costs

1st trimester manual vacuum aspiration (MVA)
Blood group (Rh) = R32.36
Ultrasound examination (General practitioner) = R386.00
Misoprostol 400mcg 3 hours prior to MVA = R9.41 (R282.25 for 60 tablets, 200 mcg)
Pethidine 100mg im/iv = R3.65
MVA = R1880.00
Oxytocin 10 IU im = R5.29
Total costs = R2316.71

Mifepristone/misoprostol (M/M) <13 weeks
Blood group (Rh) = R32.36
Ultrasound examination (General practitioner) = R386.00
Mifepristone 200mg =R239.40 (3 x 200mg tablets = R718.20)
Misoprostol 800mcg = R18.82
Analgesia (ibuprofen, 400 mg 15, & paracetamol, 500 mg 40) = (R6.95 + R4.78) = R11.73
Repeat ultrasound examination (General practitioner) = R386.00
Total costs = R1074.31

Misoprostol alone <13 weeks
Blood group (Rh) = R32.36
Ultrasound examination (General practitioner) = R386.00
Misoprostol 800mcg x 2 doses = R37.63
Analgesia (ibuprofen, 400 mg 15, & paracetamol, 500 mg 40) = (R6.95 + R4.78) = R11.73
Repeat ultrasound exam (General practitioner) = R386.00
Total costs = R853.72

Mifepristone/misoprostol (M/M) 13 – 20 weeks
Ultrasound examination (General practitioner) = R386.00
Mifepristone 200mg = R239.40
Hospitalisation (1 day) = R873.00
Blood group (Rh) = R32.36
Misoprostol 800mcg plus 1600mcg = R56.46
Analgesia (ibuprofen, 400 mg 15, & paracetamol, 500 mg 40) = (R6.95 + R4.78) = R11.73
Repeat ultrasound exam (General practitioner) = R386.00
Total costs = R1984.95

Misoprostol alone 13-20 weeks
Blood group (Rh) = R32.36
Ultrasound examination (General practitioner) = R386.00
Hospitalisation(2 days) = R1746.00
Misoprostol 400mcg x 5 doses = R47.05

Analgesia (pethidine 100mg) = R3.65
Repeat ultrasound exam (General practitioner) = R386.00
Total costs = R2601.05

Indirect costs: short-stay in facility, vitals monitoring, disposables, etc. – not estimated.
Patient costs: loss of earnings, transport costs, etc. – not estimated.

Costs from complications

Failed initial intervention necessitating MVA*(<13 weeks)*
Ultrasound examination (General practitioner) = R386.00
Analgesia (pethidine 100mg) = R3.65
MVA = R1880.00
Oxytocin 10 IU im = R5.29
Total costs = R2274.94

Failed initial intervention necessitating MVA *(13-20 weeks)*
Ultrasound examination (General practitioner) = R386.00
Analgesia (pethidine 100mg) = R3.65
MVA = R2654.00
Oxytocin 10 IU im = R5.29
Total costs = R3048.94

Bleeding requiring transfusion
Hospitalisation (2 days) = R1746.00
Ultrasound examination (General practitioner) = R386.00
Haemoglobin (Hb) = R17.06
Packed cells (2 units) = R14932.44 (R7466.22 per unit)
Total costs = R17081.50

Uterine perforation *(Level 2 facility, assumed to be regional; specialist care)*
Hospitalisation (3 days) = R3549.00
Ultrasound examination (Specialist) = R565.00
CT of the pelvis = R3384.00
Bloods: Hb, WCC, PLT = R54.88
Renal function (CUSP), urine test = (R28.71+R28.71+R28.71+R24.67) = R110.80
Theatre costs, including general anaesthesia = (R545.00+R5997.00) = R6542.00
Total costs = R14205.68

Pelvic infection post TOP *(Level 2 facility, assumed to be regional; specialist care)*
Hospitalisation (2 days) = R2366.00
Ultrasound examination (Specialist) = R565.00
Bloods: Hb, WCC, PLT = R54.88
Renal function (CUSP), urine test = (R28.71+R28.71+R28.71+R24.67) = R110.80
Intravenous Ceftriaxone 1 g+ Metronidazole 500 mg 8 hourly x 3d = (R5.88*3) + (R19.11*9) = R69.85
Oral antibiotics: Azithromycin, 1 g + Amoxicillin/clavulanic acid 875/125 mg 12 hourly x 7d = R8.29+(R2.24*14)=R39.65
Total costs = R3206.14

Cost model based on estimated risk prevalence data

Clinical parameters	Risk per 1000 procedures
MVA< 13 weeks	
Failed initial intervention necessitating MVA	20
Bleeding requiring transfusion	1
Uterine perforation	3
Pelvic infection post TOP	10
Mifeprsistone/misoprostol (M/M) <13 weeks	
Failed initial intervention necessitating MVA	40
Bleeding requiring transfusion	1
Uterine perforation	1
Pelvic infection post TOP	5
Misoprostol alone <13 weeks	
Failed initial intervention necessitating MVA	140
Bleeding requiring transfusion	3
Uterine perforation	1
Pelvic infection post TOP	5
Mifepristone/misoprostol 13-20 weeks	
Failed initial intervention necessitating MVA	30
Bleeding requiring transfusion	3
Uterine perforation	2
Pelvic infection post TOP	5
Misoprostol alone 13-20 weeks	
Failed initial intervention necessitating MVA	190
Bleeding requiring transfusion	4
Uterine perforation	2
Pelvic infection post TOP	5

Cost Evaluation (per 1000 procedures)

	MVA<13 wks	Misoprostol<13 wks	M/M<13 wks	M/M 13-20 wks	Misoprostol alone 13-20 wks
Direct costs	R 2 316 708.34	R 853 723.36	R 1 074 306.68	R 1 984 940.04	R 2 601 051.70
Failure necessitating MVA	R 45 498.80	R 318 491.60	R 90 997.60	R 91 468.20	R 579 298.60
Bleeding requiring transfusion	R 17 081.50	R 51 244.50	R 17 081.50	R 51 244.50	R 68 326.00
Uterine perforation	R 42 617.04	R 14 205.68	R 14 205.68	R 28 411.36	R 28 411.36
Pelvic infection post TOP	R 32 061.40	R 16 030.70	R 16 030.70	R 16 030.70	R 16 030.70
Total Costs	**R 2 453 967.08**	**R 1 253 695.84**	**R 1 212 622.16**	**R 2 172 094.80**	**R 3 293 118.36**

Estimated budget impact

The costing analysis assumes that the total TOPs performed per annum is 85,600, of which that 24% of women (20 500) undergo 2nd trimester TOP (13-20 weeks). This also takes into consideration the likelihood that 10% of women (6 500) in the 1st trimester will opt for, or require misoprostol rather than MVA.

Therefore, the total annual cost to the NDoH for maintaining TOP services in South Africa utilizing the MVA in the 1st trimester, and misoprostol alone for 2nd trimester termination is approximately R219,460,420,228.00

Procedure	Women (n)	Cost
Misoprostol alone 13-20 wks	20500	R 67 508 926 380.00
Misoprostol alone <13 wks	6500	R 8 149 022 960.00
MVA <13 wks	58600	R 143 802 470 888.00
	TOTAL COST	**R 219 460 420 228.00**

The addition of mifepristone 200mg for TOP <13 weeks for the subgroup of 10% of women declining surgery, and mifepristone 200mg from 13 weeks onwards (M/M), will reduce the total cost to R196,212,458,328.00; a 10.59% decrease in TOP costs.

Procedure	Women (n)	Cost
M/M 13-20 wks	20500	R 44 527 943 400.00
M/M<13 wks	6500	R 7 882 044 040.00
MVA <13 wks	58600	R 143 802 470 888.00
	TOTAL COST	**R 196 212 458 328.00**

Restricting the use of mifepristone only for TOP 13-20 weeks would cost the health department R196,479,437,248.00; a 10.47% decrease in TOP costs.

Procedure	Women (n)	Cost
M/M 13-20 wks	20500	R 44 527 943 400.00
Misoprostol alone <13 wks	6500	R 8 149 022 960.00
MVA <13 wks	58600	R 143 802 470 888.00
	TOTAL COST	**R 196 479 437 248.00**

Summary: From the available data, 1st trimester MVA success rates are around 98% compared to 96% with mifepristone/misoprostol (M/M) and around 86% with misoprostol alone. It appears that MVA is superior and results in higher satisfaction rates than M/M, and therefore remains the recommended choice for first trimester TOP. With surgical termination misoprostol 400mcg PV is recommended for cervical ripening 3 hours before MVA.
In settings without appropriate skills or experience, or where a woman declines surgery, medical TOP is a safe and effective alternative to MVA. Mifepristone 100 mg for TOP's up to 9 weeks is as effective as mifepristone 200mg. This is followed by 800mcg misoprostol PV 2 days later.
From 9 – 13 weeks' mifepristone is given as 200mg stat, followed by 800mcg vaginal misoprostol 2 days later. If abortion is not complete, a maximum of 4 further doses of 400mcg oral misoprostol 3-hourly may be required.

Limited data comparing M/M and misoprostol alone in the 2nd trimester suggest that M/M is associated with higher success rates of complete expulsion, and shorter induction-to-complete abortion intervals, thereby reducing in-patient hospital stay. The success rates are applicable for the following regimen: mifepristone 200mg, oral, stat, followed 36-48 hours later by misoprostol, 800mcg PV, followed by oral misoprostol 400mcg 3-hourly for a maximum of 4 doses.
The success rate for M/M is around 97%, while *vaginal* misoprostol alone has a success rate between 80–90%. Oral misoprostol use in the 2nd trimester averages expulsion rates of around 70%.

There are limitations to this review. An assumption is made about equal access and availability of both medical and surgical options, as well as the availability of skilled personnel for MVA at all sites. It also does not consider the uncommon but real possibility of general anaesthesia either for 1st trimester TOP or for MVA following failed initial treatment. Furthermore, risks of uterine rupture and maternal death following TOP were excluded from this costing, since prevalence estimates are not well documented. Uterine rupture however, is associated with the inappropriate use of *misoprostol*, particularly in multiparous women, women with previous caesarean section, or with advanced gestation.

Results from studies on successes and risks in this review carry a margin of uncertainty. It is possible that RCT's tend to underestimate treatment and procedure-related morbidity risks, since they are generally conducted in tertiary facilities by experienced clinicians, and those outcomes may not represent the norm at lower level facilities.
Finally, cost estimates and medicine prices are subject to the NDoH's tender agreements with pharmaceutical companies and suppliers, and may not reflect the above figures.

EVIDENCE TO DECISION FRAMEWORK

<table>
<tr><th></th><th>JUDGEMENT</th><th>SUPPORTING EVIDENCE & ADDITIONAL CONSIDERATIONS</th></tr>
<tr><td>QUALITY OF EVIDENCE</td><td>What is the overall confidence in the evidence of effectiveness?
Confident [X] Not confident [ ] Uncertain [ ]</td><td>See evidence review above.</td></tr>
<tr><td>BENEFITS & HARMS</td><td>Do the desirable effects outweigh the undesirable effects?
Benefits outweigh harms [X] Harms outweigh benefits [ ] Benefits = harms or Uncertain [ ]</td><td>See evidence review above.</td></tr>
<tr><td>THERAPEUTIC INTERCHANGE</td><td>Therapeutic alternatives available:
Yes [ ] No [X]

List the members of the group: n/a</td><td>Rationale for therapeutic alternatives included: n/a

References: n/a</td></tr>
<tr><td>VALUES & PREFERENCES / ACCEPTABILITY</td><td>Is there important uncertainty or variability about how much people value the options?
Minor [ ] Major [ ] Uncertain [X]

Is the option acceptable to key stakeholders?
Yes [X] No [ ] Uncertain [ ]</td><td></td></tr>
<tr><td>RESOURCE USE</td><td>How large are the resource requirements?
More intensive [ ] Less intensive [X] Uncertain [ ]</td><td>Cost of medicines:
<table><tr><th>Medicine</th><th>Cost (ZAR)*</th></tr><tr><td>Mifepristone 200 mg 3 tablets</td><td>R718.20</td></tr><tr><td>Misoprostol 200 mcg 60 tablets</td><td>R282.25</td></tr></table>*Contract circular HP06-2016SD
Additional resources:
Note: See costing analysis above.</td></tr>
<tr><td>EQUITY</td><td>Would there be an impact on health inequity?
Yes [ ] No [X] Uncertain [ ]</td><td></td></tr>
<tr><td>FEASIBILITY</td><td>Is the implementation of this recommendation feasible?
Yes [X] No [ ] Uncertain [ ]</td><td></td></tr>
</table>

Type of recommendation	We recommend against the option and for the alternative	We suggest not to use the option or to use the alternative	We suggest using either the option or the alternative	We suggest using the option	We recommend the option
	☐	☐	☐	☐	X

Recommendation: Based on this evidence review, the Adult Hospital Level Commitee recommends that mifepristone to be retained in the adult EML, in combination with misoprostol for medical TOP for gestation up to 20 weeks.

Rationale: Updated evidence review and costing analysis found no change to previous conclusions that mifepristone/misoprostol combination regimen is more effective and cost-saving than MVA or misoprostol monotherapy for 1st and 2nd trimester TOP.

Level of Evidence: I Systematice review, Metaanalysis, Expert opinion

Review indicator:

Evidence of efficacy	Evidence of harm	Price reduction
X		

VEN status:

Vital	Essential	Necessary
	X	

NEMLC MEETING OF 14 DECEMBER 2017:

NEMLC accepted the proposal as recommended by the Adult Hospital Level Committee, above.

Monitoring and evaluation considerations

Research priorities

RCT's evaluating mifepristone 100mg vs. 200mg beyond 9 weeks' gestation.

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