Advisory Committee for Reproductive Health Drugs
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Non-U.S. Clinical Studies

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Proposed Regimen

- Single oral dose of three 200 mg tablets of mifepristone
- In two days, two 200 ug tablets of misoprostol, unless confirmed termination

Studies 14 and 24: Design

	Study 14	Study 24
No. patients	1286	1194
Duration of gestation	$\leq$ 49 d	$\leq$ 63 d
Day 1: Mifepristone	600 mg	600 mg
Day 3: Misoprostol	400μg	400 μg; if no abortion in 3 hours, additional 200 μg
Follow-up	Day 8-15	Day 10-18

Exclusion Criteria

- Smoke $\geq$ 10 cigarettes/day
- Cardiovascular disease
- Asthma
- Glaucoma or high intraocular pressure
- Diabetes
- Hyperlipidemia
- Renal, adrenal, or hepatic insufficiency
- Anemia

Treatment Outcome: Definition

- **Successful: complete expulsion without need for surgery**

- **Failure:**
  - **incomplete expulsion**
  - **pregnancy continued**
  - **surgery required for hemostasis**

Efficacy Evaluable Population

- **Pregnancy confirmed**

	n/N	%
Study 14	1205/1286	93.7
Study 24	1104/1194	92.5

Study 14: Treatment Outcome

Efficacy Evaluable Population

	N	Rate (%)
Complete expulsion	1149	95.4
Incomplete expulsion	34	2.8
Ongoing Pregnancy	18	1.5
Surgery to stop bleeding	4	0.3
Total	**1205**	

Study 14

Complete Expulsion Rate for Efficacy Evaluable Population by Gestational Age

Gestational Age (days)	Events/N	Rate (%)
< 36	117/119	98.3
36-42	447/463	96.5
43-49	570/607	93.9
50-56	12/13	92.3
57-63	3/3	100.0
≤ 49	1134/1189	95.4

Study 24

Complete Expulsion Rate for Efficacy Evaluable Population by Gestational Age

Gestational Age (days)	Events/N	Rate (%)
< 36	15/15	100.00
36-42	163/171	95.3
43-49	293/306	95.7
50-56	358/389	92.0
57-63	196/223	87.9
≤ 49	471/492	95.7

Study 24: Treatment Outcome

Evaluable Patients with Gestational Age ≤ 49 Days

	n	Rate (%)
Total	**210**	
Misoprostol not administered		
Complete expulsion	19	100.0
Single dose misoprostol		
Complete expulsion	189	99.0
Incomplete expulsion	1	0.5
Surgery to stop bleeding	1	0.5
Complete expulsion rate	**208/210**	**99.0**

Analysis of Success Rates for Subgroups:
Studies 14 and 24

Subgroup	Study 14 n/N (%)	Study 24 n/N (%)
If GA≤ 49 days	1134/1189 (95.4)	471/492 (95.7)
. . and took ≤ 1 misoprostol dose	1134/1189 (95.4)	208/210 (99.0)
. . and known outcome	1160/1216 (95.4)	227/230 (98.7)
. . and if unknown outcome = failure	1160/1264 (91.8)	227/239 (95.0)

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Success Rates:

Studies 14 and 24

	Study 14 (N=1286)	Study 24 (N=1194)
Evaluable (N)	1205	1104
No. of Patients with Success	1149	1025
Rate (%)	95.4	92.8

Adverse Events with Incidence >2%: Studies 14 and 24

Adverse Event	Incidence (%)	
	Study 14	Study 24
Painful contraction of uterus	78.5	85.6
Nausea	40.7	49.9
Vomiting	16.8	29.1
Diarrhea	12.3	15.4
Headache	2.6	3.1
Dizziness	1.2	2.6
Metrorrhagia	N/A	3.4
Anemia	N/A	2.9

Cardiovascular Adverse Events

- **Mild to moderate**
  - **tachycardia and palpitations**
  - **hypotension**
  - **hypertension**
  - **syncope**

- **Severe**
  - **1 case hypotension**

+3
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Serious Adverse Events: Studies 14 and 24

- **Enrolled** 2480
- **Hospitalizations** 21 (1%)
- **Heavy bleeding** 52 (2%)
  - **surgical intervention** 15 (1%)
  - **blood transfusion** 4 (<1%)