Progesterone Protocols for The Attempted Reversal of Mifepristone

Oral Protocol

1. Prometrium brand or progesterone generic micronized oral capsules 200 mg, two capsules (400 mg) by mouth ASAP and bedtime on day 1 (must be at least 5 hours apart). 200mg, two capsules (400 mg) AM and PM on day 2 and 3.

2. Continue progesterone 200mg, two capsules (400mg) at bedtime for a minimum of two weeks or according to your clinical judgment.

Vaginal Protocol (Capsules per vagina)

1. If the patient is unable to take oral capsules or intramuscular injections, consider vaginal administration of oral capsules Prometrium brand or progesterone generic micronized oral capsules 200 mg, two capsules (400 mg) inserted vaginally ASAP AND at bedtime day 1 (must be at least 5 hours apart). 200mg, two capsules (400 mg) AM and PM on day 2 and 3.

2. Continue progesterone 200mg, two capsules (400 mg) inserted vaginally daily at bedtime for a minimum of two weeks or according to your clinical judgment.

Intramuscular Protocol

1. Compounded progesterone in oil 200mg (100mg/ml or 50mg/ml) intramuscularly (IM) upper outer quadrant of gluteal muscle, slowly over 2-3 minutes as soon as possible after the ingestion of mifepristone.

2. Continue progesterone in oil, 200 mg IM once a day for two more days.

3. Continue progesterone in oil, 200mg IM every other day until day 14 after mifepristone ingestion.

4. Continue progesterone in oil, 200 mg IM twice a week for a minimum of two weeks or according to your clinical judgment.

Additional Instructions for the Reversal Provider:

- Do not prescribe Prometrium based in peanut oil if the patient is allergic to peanuts.
- If prescribing oral, prescribe enough for 1 week at a time with refills. One month's supply may be unaffordable if the patient's insurance doesn't cover.
- Provide ultrasound per Clinic Protocol as soon as possible to confirm embryonic viability and intrauterine location. If less than 6 weeks after LMP, consider monitoring serial HCG levels and simply do ultrasound at 6 weeks.
- If bleeding or cramping occurs and an intrauterine location of pregnancy has not been confirmed, treat as an ectopic pregnancy and appropriately refer until an intrauterine location is confirmed.
- For an ectopic pregnancy or an incomplete abortion, seek consultation as necessary.
- Provide an ultrasound every 1-2 weeks during the first trimester to confirm continued viability.
- The physician, midwife, PA or NP who prescribes should see patient within 72 hours or ensure a plan for ongoing care.
- Providers should use their own professional judgement based on experience prescribing progesterone. Some providers have successfully prescribed 600 mg twice a day for two days, followed by 400 mg twice a day for two days and then 400 mg at bedtime. Other doctors, particularly in Europe have used even higher doses.

Reversal in Second and Third Trimester:

- If the patient has had laminaria inserted and been given mifepristone, but still has a living fetus, progesterone should be prescribed, the laminaria removed, and she should be evaluated for rupture of the membranes. The patient should also be assessed for the need for antibiotics, as laminaria will increase the chance for chorioamnionitis in a pregnancy that continues after their use.
- A minimum of two weeks of progesterone treatment is recommended in second and third trimesters of pregnancy for reversal of mifepristone. The individual prescribing provider should use his or her clinical judgement for dose and duration of progesterone treatment.

Approved by:
George Delgado, M.D., Medical Advisor, APR Medical Advisory Team
Dr. Brent Boles, M.D., Medical Director, Heartbeat International