Progesterone therapy in pregnancy

Target audience	All healthcare professionals caring for pregnant women/people.
Patient group	Pregnant women/people with threatened miscarriage, recurrent early pregnancy loss and/or risk factors for pre-term birth or 2nd trimester loss. The term 'women/pregnant people' is used within this document to include women, girls, trans men, and non-binary and intersex people, who are pregnant or have recently been pregnant.

Summary

- Progesterone therapy has proven benefits in the treatment of the following conditions in pregnancy:
  - Threatened miscarriage and history of one or two previous miscarriages (5% improvement in live birth rates).
  - Threatened miscarriage and history of three or more previous miscarriages (15% improvement in live birth rates).
  - Previous preterm birth or 2nd trimester miscarriage and short cervix.
- There is no proven benefit of progesterone treatment for recurrent miscarriage without bleeding.
- For miscarriage prophylaxis for women/pregnant people fulfilling the criteria, treatment can begin from 6 weeks of gestation after a scan has confirmed the presence of an intrauterine pregnancy.
- For miscarriage prophylaxis, treatment is given in the form of vaginal micronised progesterone 400mg twice a day until 16 weeks of gestation (unless the patient prefers to stop treatment at 12 weeks – see page 5).
  - Prometrium® is licensed for this indication. There are a number of contraindications (see product licence) including allergy to nuts or soya.
  - Cyclogest can also be used for miscarriage prophylaxis. This is unlicensed but is endorsed nationally by the British National Formulary (BNF) and the Royal College of Obstetricians and Gynaecologists (RCOG) therefore does not require the completion of unlicensed paperwork. Can be used in those with a nut allergy.
- For preterm birth prophylaxis, treatment is given in the form of vaginal micronized progesterone 200mg daily until at least 34 weeks of gestation.
  - Cyclogest can be used for this indicaton. This is unlicensed but is endorsed nationally by the BNF and therefore does not require completion of unlicensed paperwork.
  - Utrogestan is licenced for this indication.
- Detailed written consent to progesterone treatment should be completed by patient and prescriber prior to administration using the procedure-specific consent form.

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Abbreviations

BNF	British National Formulary
EPAS	early pregnancy assessment service
IUP	intrauterine pregnancy
NHSL	NHS Lanarkshire
NICE	National Institute for Health and Care Excellence
PROMISE trial	progesterone in recurrent miscarriages trial
RCOG	Royal College of Obstetricians and Gynaecologists
REPL	recurrent early pregnancy loss
TVUSS	transvaginal ultrasound scan
ULM	unlicensed medication

Useful documents

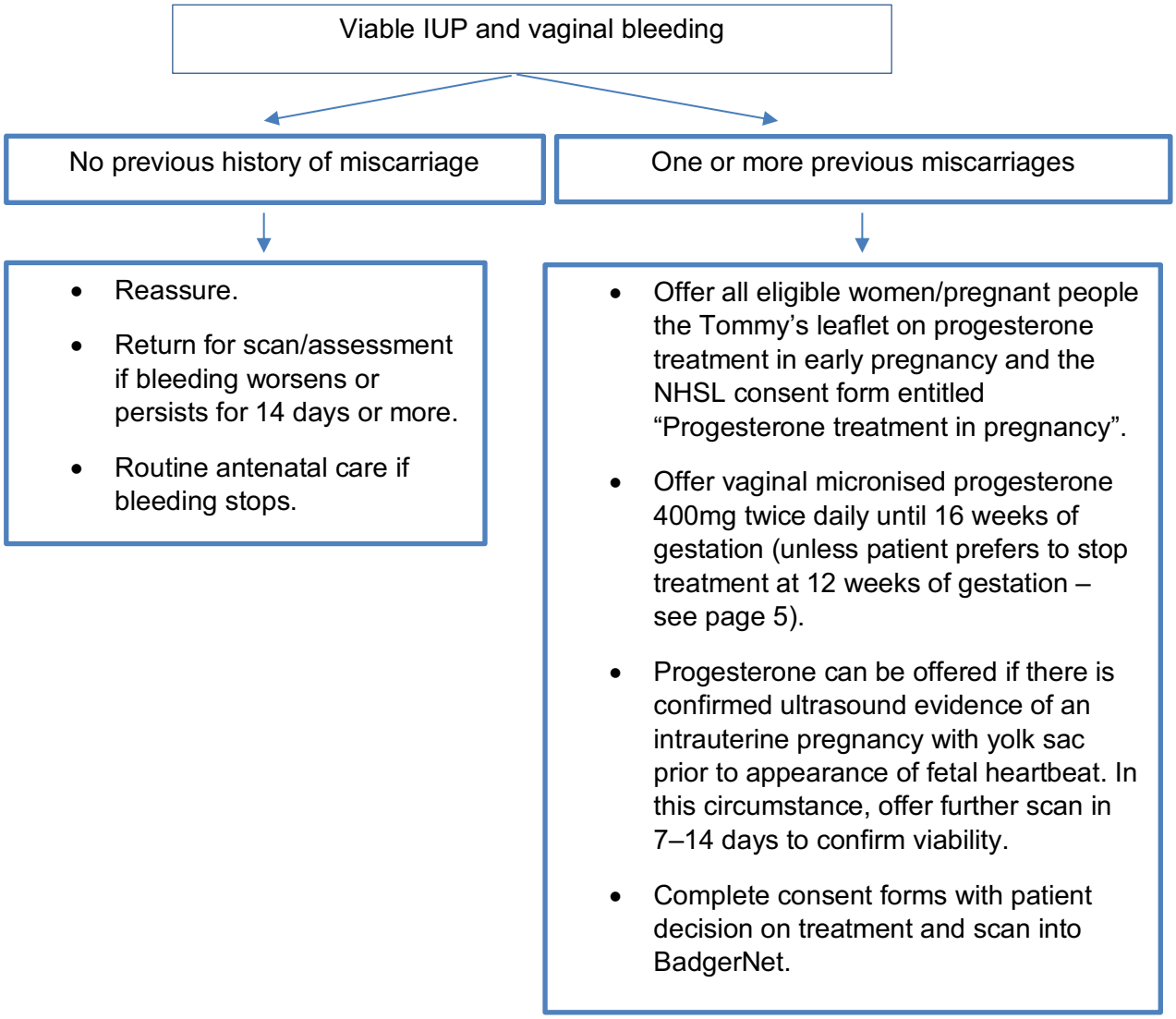
- Consent form for progesterone treatment in pregnancy - Consent to Progesterone Treatment in Early Pregnancy SAMPLE.pdf.
- Patient information leaflet - https://www.tommys.org/pregnancy-information/health-professionals/early-pregnancy-bleeding-and-progesterone-guide-download.
- Unlicensed medicines form - https://www.rightdecisions.scot.nhs.uk/media/tekl134c/appendix-1-individual-unlicensed-high-risk-off-label-application-form-v13.pdf.

Introduction

There is some evidence that progesterone therapy may be of benefit for some women/pregnant people with complications of threatened miscarriage, REPL and prophylaxis against preterm birth or 2nd trimester miscarriage. This guideline outlines clinical situations where progesterone treatment may be of benefit and subsequent management of these patients.

Threatened miscarriage

- Telephone triage all women/pregnant people who present with bleeding in early pregnancy for supportive care or face-to-face review +/- ultrasound scan.
- If a scan is indicated, arrange appointment in the EPAS (early pregnancy assessment service):
    - If the scan is inconclusive, manage according to local protocol.
    - If the scan confirms a viable intrauterine pregnancy, manage as follows:



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- There is evidence in the medical literature[1-4] for the use of progesterone in reducing the risk of miscarriage in women/pregnant people with early pregnancy bleeding and a history of miscarriage.
- Women/pregnant people with bleeding and one or two previous miscarriages who use progesterone increase the likelihood of a livebirth by 5%.
- Women/pregnant people with bleeding with three or more previous miscarriages who use progesterone increase the likelihood of a livebirth by 15%.
- The dose of vaginal micronised progesterone is 400mg twice daily.
- The duration of treatment is recommended in the NICE (National Institute for Health and Care Excellence) guideline until 16 weeks of gestation. There is conflicting opinion in the literature regarding the duration of therapy with some advocating cessation of therapy at 12 weeks of gestation[7]. The risks and benefits of continuing therapy past 12 weeks of gestation should be discussed with the woman/pregnant person as detailed on the progesterone therapy in pregnancy consent form after which an informed decision about duration of treatment should be made and documented on BadgerNet.
- Consent should be taken and a prescription issued by medical staff.

Recurrent early pregnancy loss

- See the guideline entitled “Recurrent miscarriage”.
- Progesterone can increase the livebirth rates for women/pregnant people who experience recurrent miscarriage, in the presence of vaginal bleeding[1-3,5].
- Consider vaginal micronised progesterone 400mg twice daily after ultrasound has confirmed a IUP in women/pregnant people with bleeding.
- Start treatment at time of bleeding and continue until 12 or 16 weeks of gestation.
- Women/pregnant people with REPL and previously successful pregnancy using progesterone treatment, may attend requesting a similar plan in a new pregnancy in the absence of bleeding. There is no evidence that routine progesterone supplementation for women/pregnant people with recurrent miscarriage in the absence of bleeding is of benefit.
- Routine supplementation should be used with caution in asymptomatic women/pregnant people with unexplained recurrent miscarriage (≥3 previous miscarriages, previous successful pregnancy after miscarriage using progesterone). The PROMISE trial did not show any benefit in this scenario. Occasionally, patients who have attended the recurrent miscarriage clinic and received specialist advice, may benefit from treatment and this will be tailored to individual patients through the PEARL clinic.

Prophylaxis of preterm birth or 2nd trimester miscarriage

- See also the guideline entitled “Pre-term birth (with intact membranes)”.
- Women/pregnant people with a history of 2nd trimester spontaneous loss or a history of spontaneous preterm birth up to 34 weeks of gestation, who are between 16-24 weeks of gestation and who have a short cervix (less than 25mm) on transvaginal ultrasound scan should be offered the choice of prophylactic vaginal progesterone or prophylactic cervical cerclage[6].
- Women/pregnant people choosing vaginal progesterone should be offered 200mg micronised progesterone daily until at least 34 weeks of gestation.

References

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22.4.26	E Ferguson	Information about new licensed treatment, change of name of guideline, new guideline format, conversion of appendices/references to new section for useful documents, addition of abbreviations section, clarification about advice regarding duration of therapy.	5
19.8.26	E Ferguson	Clarification about progesterone preparation choice for each indication. Addition of primary care to target audience section.	6