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Patient Information Leaflet and Consent

The Use of Micronised Progesterone for Women with Early Pregnancy Bleeding and Previous Miscarriage

Background information

The information below is to help you decide whether or not to have this treatment and to let you know any reasons why we might advise you not to have it.

What is the treatment?

Progesterone is an important pregnancy hormone that reduces the bleeding and cramping that can occur in threatened miscarriage. It is naturally produced by the mother's ovary until around 9 weeks after that the developing placenta takes over.

Micronised progesterone is like the progesterone made by our body. Currently Cyclogest® and Utrogestan® are the only available micronised preparations. These preparations are not licensed for use in pregnancy, but can be used for specific patients after discussion with your midwife, nurse or doctor in the early pregnancy unit.

Why is the treatment being offered or recommended?

The NICE guideline produced in November 2021 by NHS England recommended offering extra progesterone to women with early pregnancy bleeding and at least one previous miscarriage.

This guideline was the result of a large UK-wide research study (the PRISM trial). Women with early pregnancy bleeding were divided into two groups. One group was given progesterone and the other group had placebo (dummy) treatment.

Overall the women who had progesterone had a 75% chance of having a baby, compared with 72% of those who had placebo treatment. This difference may have been due to chance.

When the number of previous miscarriages was looked at more closely, in the women who had progesterone, the chances of a having a baby increased by 2% in the group of women with one previous miscarriage; by 6.6% in the two previous miscarriages group; and by up to 15% in the group who had three or more previous miscarriages.

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In the last group this would **not** have been due to chance; progesterone was shown to be of some benefit.

No benefit was seen in women who had early pregnancy bleeding with **no** previous miscarriage.

How long do I need to take the progesterone?

The maximum benefits of progesterone are seen by 12 weeks. Therefore this unit recommends stopping treatment at this gestation.

The NICE recommendation is to continue treatment to 16 weeks, as this is the duration of treatment used in the PRISM trial. However, there is no scientific evidence to support the use of progesterone from 12-16 weeks.

The trial showed little benefit if progesterone was started **after** 9 weeks of pregnancy.

I have not experienced bleeding so can I take progesterone?

Another trial called the PROMISE trial looked at whether women with recurrent miscarriage (3 or more miscarriages) and **no** vaginal bleeding, would benefit from progesterone.

Again women were divided into two groups, one given progesterone and the other placebo treatment. This trial found that in women with 3 or less previous miscarriages, progesterone did **not** increase the chance of a pregnancy continuing. Two-thirds of the women in the trial however went on to have a baby whether they had progesterone or not.

In women with 4 or more previous miscarriages, there was a small increase seen. It was not possible to say if this was due to chance or not.

Could the treatment be harmful to me or my baby?

Micronised progesterone is the only progesterone recommended for this use. The trial showed that there was no increase in harm for mothers or babies in the womb from using it. There was no increase in abnormalities seen in the babies born to mothers in the trial which is reassuring. However abnormalities that are rare may not be seen in trials.

There is no information at the moment about the long-term health of children exposed to progesterone treatment in particular, the 12-16 weeks interval of pregnancy. This will not be known for several years.

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What do I have to do?

The progesterone is a bullet shaped pessary which you put into your vagina twice a day, until you are 12 weeks pregnant. It can be started once a scan shows that you have a pregnancy growing inside your womb. It should be started **before** 9 weeks of pregnancy to have the best effect.

Are there any side effects?

You may experience headache, dizziness, mood change, breast pain, constipation, vaginal soreness, vaginal bleeding, itching around the vulva (the area outside the vagina) and oily discharge from the pessary. Contact your Early Pregnancy Unit if you have any concerns.

What conditions or illnesses might mean the treatment is ***not*** recommended?

Progesterone cannot be given if you have or have had any of the following conditions: genital or breast cancer; liver tumours; severe kidney disease; angina; heart attack; stroke/'mini-stroke'; high blood pressure; pregnancy itch and or jaundice (cholestasis); severe pregnancy rash (pemphigoid gestationalis); uncontrolled diabetes or other medical disorders such as thyroid; blood disorder (porphyria); blood clots in your vein or lungs; inflammation of the veins (thrombophlebitis); **allergy** to any of the components in the pessary*.

*Cyclogest® components: vegetable fat, Mexican yam root.

*Utrogestan® components: Sunflower oil, **soya/bean,** Mexican yam root**, peanuts**, gelatine (unknown if porcine or bovine), glycerol and titanium dioxide.

What conditions or illnesses might mean the treatment ***may not*** be recommended?

Progesterone can only be given after discussion of the risks for: epilepsy; uncontrolled asthma; conditions increasing risk of blood clots; severe migraines or migraine with aura or paralysis; overweight; heavy smoker; depression needing medication; previous intolerance to progesterone (eg. contraception).

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Could I still have a miscarriage despite treatment?

Although progesterone may slightly reduce the chance of miscarriage it will not prevent all miscarriages. If the pregnancy stops growing when you are taking the progesterone the natural process of miscarriage may be delayed, and therefore may not be diagnosed until your booking scan around 12 weeks. The progesterone treatment would need to be stopped for a minimum of 4 days to allow a natural miscarriage to take place or before medical management of miscarriage could be offered.

The Consent Form (Two copies – one to patient, one into patient records)

I understand:

- ◯ That research has shown that some women with early pregnancy bleeding and 3 or more previous miscarriages are less likely to miscarry if they have progesterone.
- ◯ That research has shown the benefit is less clear for those with less than three miscarriages who have early pregnancy bleeding
- ◯ That there is no benefit for women who have not have a previous miscarriage.
- ◯ That there is no benefit for women who are not bleeding in early pregnancy even if they have had three or more previous miscarriages.
- ◯ That progesterone will only be started after I have a scan that shows I have a pregnancy in my womb
- ◯ That micronised progesterone vaginal pessaries are inserted twice a day, unless the pregnancy stops growing or I miscarry
- ◯ That there is no long term information on the effects to the children born to mothers who used extra progesterone in pregnancy, particularly between 12 and 16 weeks of pregnancy
- ◯ That the maximum benefit of progesterone treatment is achieved by 12 weeks of gestation.

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I confirm:

- ◯ That I have none of the conditions stated above which would prevent me from using progesterone
- ◯ That my questions have been answered to my satisfaction

Name of patient	Signature	Date
Name of staff	Signature	Date
GMC/NMC No.	Grade	