Implanon is a subdermal implant containing etonogestrel, which is a metabolite of desogestrel, a third generation progestagen which has been available in a combined oral contraceptive in Australia for approximately 10 years. Etonogestrel has poor affinity for androgen receptors and therefore gives fewer androgenic side effects compared to the older second generation progestagens, such as levonorgestrel. Implanon is an effective form of contraception, with a Pearl Index of 0.00-0.07, i.e. pregnancy risk is lower than that seen after tubal occlusion or vasectomy.

The flexible rod is a matrix design with the etonogestrel crystals dispersed in a polymer of ethylenevinylacetate (EVA) surrounded by an EVA membrane (Figure 1). The release of the hormone is steady, with slightly higher serum levels seen in the first few weeks. There is a very gradual fall in serum levels over the three years of use. Serum levels are reduced in women who are taking liver enzyme inducing drugs such as rifampicin, griseofulvin, phenytoin and carbimazapine. Serum levels are not affected by concurrent use of oral antibiotics or by gastrointestinal upsets.

Serum levels in women over 70 kg are in the lower range, however, the clinical significance of this is uncertain. In clinical trials, a number of women weighed over 70 kg but no pregnancies were seen in this group. Steady release of the hormone directly into the blood stream avoids the first pass effect on the liver.

Implanon comes in a ready loaded disposable...

Figure 1. The Implanon rod
sterile applicator. The needle on the applicator is designed to penetrate the skin readily but is able to tunnel under the skin without puncturing the skin from below. This enables placement of the rod in the superficial subdermal plane, so that the rod is easily palpable.

The device is Pharmaceutical Benefits Scheme listed for the cost of one prescription price to the user (although the cost to the taxpayer is $220).

How does Implanon work?
Etonogestrel inhibits ovulation by the suppression of luteinising hormone release from the pituitary. Serum levels of etonogestrel sufficient to inhibit ovulation are achieved within the first day after insertion of Implanon.

Etonogestrel does not completely inhibit follicle stimulating hormone secretion from the pituitary. Some follicular activity is seen in the ovaries, resulting in physiological levels of serum oestradiol. Etonogestrel also produces thickening of the cervical mucus, preventing sperm penetration. Progestagenic changes are also seen in the endometrium, with a decrease in endometrial thickness.

Is it readily reversible?
The implant can be removed at any time at the woman’s request but must be removed at three years. Serum etonogestrel levels become undetectable within a few days after removal of the implant. Studies have shown that pre-existing levels of fertility return rapidly, with 94% of women having ovulated within one month of rod removal.3

Return to ovulation is sometimes rapid because of the follicular development seen in the ovary with the etonogestrel implant. Women who do not wish to become pregnant will therefore need to commence another form of contraception immediately after removal of the implant.

What are the possible side effects?
The incidence of side effects varies according to the woman’s sensitivity to progestagens. As Implanon is the first hormonal contraceptive implant marketed in Australia, it is difficult to compare it directly with other hormonal contraceptives currently available. It may be helpful to look at the side effects reported with depomedroxyprogesterone acetate compared to those reported with Implanon (Table 1).3,4

Changes to menstrual pattern
Changes to usual menstrual pattern will be seen in all women who use the implant. It is not possible to predict what the new pattern will be for any individual. Neither is it possible to predict the bleeding pattern from a woman’s previous experience with another progestagen only method such as depot medroxyprogesterone acetate. Table 2 shows the range of bleeding patterns seen with the etonogestrel implant.5

Dysmenorrhoea
Pain occurring at the time of menstruation is seen in 40% of women having natural menstrual cycles. In 88% of these women, the pain disappears or is significantly reduced during Implanon use. In 2% of Implanon users, dysmenorrhoea becomes worse.5

Body weight
Studies have shown an increase of 2.6% in body weight over a two year period of Implanon use. This was not significantly different from controls who were using nonhormonal methods of contraception.6
Acne
Overall, the incidence of acne is similar in the general population (24%) as it is in users of the etonogestrel implant (21%). Of women who suffered from acne in their natural cycles, 58% noted an improvement with etonogestrel implant use. A new acne- occurred for the first time in 14% of women using the etonogestrel implant.6

Lipid metabolism
There have been no clinically significant changes to total cholesterol, HDL cholesterol, LDL cholesterol, or triglycerides in Implanon users.7,8

Carbohydrate metabolism
Common to other steroid hormones, etonogestrel use causes a slight insulin resistance, with slightly elevated glucose levels during the two hours after a glucose load. However, in studies these were only occasionally outside of the normal range. Caution is advised in the use of etonogestrel in women who suffer from poorly controlled diabetes mellitus.

Bone mass
A two year study comparing the bone mineral density of etonogestrel implant users to that of controls who were not using hormonal contraception has shown no adverse effects.9

Venous thromboembolism
There appears to be no change to the balance between coagulation and fibrinolysis. This is in common with other progestagen only contraceptive methods currently available. It needs to be noted however, that it is a Therapeutic Goods Administration requirement that all progestagen only contraceptive product information carry the same precautions as that carried on oestrogen containing contraceptives. This may cause an apparent conflict between the information given to the woman by her doctor and the product information.

Blood pressure
There were no changes to mean systolic and diastolic pressures seen in Implanon users over a two year period.6 FPA Health is currently surveying users of the etonogestrel implant to obtain an Australian perspective. Common side effects are similar to those reported in the original studies, i.e. there are reports of acne, weight gain and mood changes, as well as irregular bleeding patterns.

Can Implanon be used during lactation?
The etonogestrel implant appears to cause no changes to the quality or quantity of breast milk in lactating women. The growth and development of infants is similarly not affected although a small amount of etonogestrel can be detected in the breast milk of mothers using Implanon.9

Despite these findings, the product carries a precaution for use in lactation. The lactating woman needs to make an informed decision on whether to use the implant after discussion with her doctor.

The importance of training
Training enables the doctor to counsel women on the benefits and side effects associated with Implanon use, to select appropriate users and to correctly time insertion of the implant.

The technique of insertion, although simple, is different from that used with other hormone implants and needs to be learned by all doctors before they attempt their first insertion. Correct superficial placement of the rod ensures easy removal in the future.

It has been recommended by the Therapeutics Goods Administration and the Royal Australian and New Zealand College of Obstetrics and Gynaecology that doctors undergo a recognised training course in the use of the etonogestrel implant. Information about training sessions can be obtained from the manufacturer.

Insertion and removal
Insertion of an etonogestrel implant should be scheduled for a time when you can be as sure as possible that the woman is not pregnant (Table 3). It is important that the technique is learned under supervision, so this issue will not be covered in this article.

Most of the insertions undertaken have been

Table 3. Timing of insertion

<table>
<thead>
<tr>
<th>Implanon is immediately effective when inserted following:</th>
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<tbody>
<tr>
<td>• no use of hormones: cycle day 1-5</td>
</tr>
<tr>
<td>• COCs: after last active tablet (until day following pill free interval)</td>
</tr>
<tr>
<td>• POP/injectable/implant: straight away</td>
</tr>
<tr>
<td>• delivery: day 21-28 after delivery</td>
</tr>
<tr>
<td>- with later insertion, exclude pregnancy and use additional contraception for seven days</td>
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problem free. Problems seen are usually due to poor insertion technique or to incorrect timing of insertion, with the woman being pregnant at the time of insertion.

The rods are not radio opaque. Localisation of impalpable rods needs to be done using ultrasound. Ensure the radiologist to whom you refer the woman is skilled in localisation (information is available on the manufacturer’s website www.organon.com/implanonlocalization).

Removal of an implant that has been inserted too deeply should only be attempted by a doctor experienced with difficult removals. If the woman wants to continue using the implant system, a new rod can be inserted through the incision made for removal of the old rod during the same procedure.

Conclusion
Implanon has been enthusiastically welcomed by Australian women, with Australia having the highest per capita uptake of Implanon than any other country in which it has been released. It is highly likely therefore, that all general practitioners, obstetricians and gynaecologists will see women in their surgeries requesting information on this new method of contraception.

Conflict of interest: Dr Cherry is a consultant to Organon Australia, providing medical education in the use of Implanon.

References