

**MR JULIAN PAMPIGLIONE  
DORSET FERTILITY**

**TAMOXIFEN CITRATE**

Tamoxifen citrate created in 1967 is chemically very similar to Clomiphene citrate, which was first used to induce ovulation in 1961 and is still used today as the first line of drug treatment for ovulation. Although the side effects are similar patients who experience significant effects with Clomiphene citrate often have less severe effects with Tamoxifen citrate (and vice versa). This is especially so with rare depressive side effects.

Tamoxifen citrate acts on both the hypothalamus and the pituitary gland to competitively block oestrogen. The pituitary gland senses this as a reduction in oestrogen levels in the blood (and therefore reduction in ovarian activity). The effect is that the amount of Follicle Stimulating Hormone (FSH) and Luteinising Hormone (LH) is increased. This increase then stimulates ovarian follicular development. The tablets are stopped after five days and by then the follicle is secreting increased amounts of oestrogen. When the amount of oestrogen reaches the appropriate level a mid-cycle surge of LH results and ovulation occurs.

Antidepressants such as paroxetine (Paxil), fluoxetine (Prozac), and sertraline (Zoloft) can decrease the effectiveness of tamoxifen.

Although there are theoretically less anti oestrogen effects on cervical mucus and the endometrium this is not born out in practice and pregnancy rates are similar with both drugs.

There is significantly more clinical experience using Clomiphene citrate and for this reason we use Tamoxifen citrate as a second line drug

**Dosage**

Tamoxifen citrate is taken in 20 mgs tablets. The usual course of treatment lasts five days, starting on the second day of the period. A blood test is usually done on the 21<sup>st</sup> day of the cycle just to confirm that ovulation is taking place. If ovulation has not occurred, then the dosage is increased to 40 or 60 mgs daily.

**Side Effects**

Tamoxifen citrate has a few side effects and these occur infrequently. The most common is vaginal dryness.

Some women who take Tamoxifen citrate experience hot flushes. Some women develop ovarian cysts. These cysts are not dangerous and disappear once treatment has stopped.

Other symptoms can include abdominal bloating, breast discomfort, nausea, skin rash, dizziness and depression.

Very rarely, the patient may experience blurring of vision, if this occurs, treatment must be stopped immediately.

Tamoxifen citrate causes twin pregnancy in about 5-8% of cases. Extremely rarely it causes triplet or higher order multiple pregnancy.

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Tamoxifen citrate is an oral preparation that is simpler to administer than other injectable treatments for ovulation induction. There are a number of methods of monitoring treatment with Tamoxifen citrate. The simplest is a Progesterone blood test, usually performed on Day 21 of the cycle. This will determine whether ovulation is taking place or not. It will not, however, differentiate between single ovulation and an exaggerated response from multiple follicles. This latter response might result in multiple pregnancy.

**TAMOXIFEN CITRATE AND MULTIPLE PREGNANCY**

In order to identify patients who produce multiple follicles, it is possible to perform an ultrasound scan. If an excess response exists, the individual would be advised not to try for a pregnancy in that treatment cycle and the dose of Tamoxifen would be reduced, unless the patient was at the minimum dose.

We have developed a monitoring scheme that would allow those who wished to have a single ultrasound scan during the first Tamoxifen citrate cycle. This would be carried out between day 10 and day 12 of the cycle at the Royal Bournemouth Hospital. Scans are performed between 9am and 10.30am.

It is by no means essential that everyone should have monitoring, but it is important that ovarian ultrasound monitoring is available. When considering whether to have ultrasound monitoring, patient should consider the following:-

1. An ultrasound scan will identify patients who over-respond to Tamoxifen citrate, especially the higher doses.
2. There is no treatment in that cycle, other than to make a decision whether to take the risk in terms of multiple pregnancy, or avoid sexual intercourse for that cycle.
3. Ultrasound scans will also identify under-response, but a single progesterone blood test on day 21 will do the same.
4. It may be necessary in the case of poor responders to have more than one ultrasound scan and this may take up a protracted amount of time.
5. If you are prepared to take the risk of multiple pregnancy, currently 5-8% in an ovulation induction programme, you could start the treatment with Tamoxifen citrate without worrying about an ultrasound scan.
6. You may need more than one ultrasound

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