February 2021 Tweetorial JPP

**[Dr Sharon Rees](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)**[@reesprescribe](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)

[#tamoxifen](https://twitter.com/search?q=%23tamoxifen) is a synthetic derivative of estrogen discovered in 1960s. Originally developed as a contraceptive (worked in rats) but had opposite effect in humans, stimulating ovulation! Licensed 1970’s as a selective estrogen receptor modulator (SERM) for breast cancer

[](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)

**[Dr Sharon Rees](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)**[@reesprescribe](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)

Day 2: Main uses for [#tamoxifen](https://twitter.com/search?q=%23tamoxifen) include estrogen receptor (ER) +ve breast cancer, recurrence & prevention of breast cancer & infertility. Dose usually 20mg daily, but can increase to 80mg for anovulatory infertility. Duration of treatment is 5 years for primary prevention breast cancer

[](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)

**[Dr Sharon Rees](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)**[@reesprescribe](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)

Day 3: [#tamoxifen](https://twitter.com/search?q=%23tamoxifen) is an oral prodrug with over 99% protein binding. Liver metabolism produces active metabolites & excretion is faecal. CYP3A4 breakdown leads to the metabolite endoxifen & there is further CYP2D6 breakdown to afimoxifene. CYP2D6 polymorphisms & drug inhibitors can alter active drug concentrations. t½ of the main metabolite is 14 days.

[](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)

**[Dr Sharon Rees](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)**[@reesprescribe](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)

Day 4: [#tamoxifen](https://twitter.com/search?q=%23tamoxifen) is a non-steroidal SERM with complex tissue-dependent binding. At tumour level, active metabolites block the estrogen receptor (ER) & also cause apoptosis in ER +ve cells. Agonist activity in the endometrium increases the risk endometrial cancer, but as an ER agonist in bone tissue, tamoxifen can prevent osteoporosis

[](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)

**[Dr Sharon Rees](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)**[@reesprescribe](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)

Day 4 (cont):[#tamoxifen](https://twitter.com/search?q=%23tamoxifen) resistance is intrinsic to a high percentage of advanced breast cancer cases & in 30-40% resistance can be acquired. Theories include altered estrogen receptor signaling, down-regulation of the estrogen receptor, or functional variations in the tamoxifen-ER complex, affecting gene regulation

[](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)

**[Dr Sharon Rees](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)**[@reesprescribe](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)

Day 5: Common adverse drug reactions for [#tamoxifen](https://twitter.com/search?q=%23tamoxifen) include alopecia, constipation, hot flush, fatigue, nausea, rash. Serious or rare; endometrial cancer, increased risk VTE, agranulocytosis, ocular toxicity. Long-term therapy can lead to hepatotoxicity (not exhaustive)

[](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)

**[Dr Sharon Rees](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)**[@reesprescribe](https://twitter.com/reesprescribe%22%20%5Ct%20%22_blank)

Day 6: [#tamoxifen](https://twitter.com/search?q=%23tamoxifen) has severe drug-drug interactions with CYP2D6 inhibitors, which lead to reduced efficacy e.g paroxetine, fluoxetine, cinacalcet, terbinafine. [#tamoxifen](https://twitter.com/search?q=%23tamoxifen) also increases the effect of warfarin possibly by reducing CYP2C9 activity. Multiple moderate DDIs (not exhaustive)



[**Dr Sharon Rees**](https://twitter.com/reesprescribe)

[@reesprescribe](https://twitter.com/reesprescribe)

Day 7: Interesting fact; some foods & herbs could alter efficacy e.g oranges/citrus fruits which contain tangeretin (mainly peel) & grapefruit (CYP3A4 inhibitor) can all reduce efficacy of [#tamoxifen](https://twitter.com/search?q=%23tamoxifen). Valerian & turmeric may inhibit breakdown too (the PIL just refers to ‘herbs’)

CPD: in addition to the tweets, read the BNF section on Hormone responsive malignancy (breast cancer) and the monograph on Tamoxifen

Another useful source is the Summary of Product Characteristics for tamoxifen – see links below

<https://bnf.nice.org.uk/treatment-summary/breast-cancer.html>

<https://bnf.nice.org.uk/drug/tamoxifen.html#drugAction>

<https://www.medicines.org.uk/emc/product/2248/smpc#PRODUCTINFO>

CPD questions (most but not all answers will be in the tweets). There is only one correct answer per question

1. Tamoxifen is a naturally occurring form of estrogen?

TRUE or FALSE

1. Which is True?
2. Tamoxifen is a pro-drug
3. Tamoxifen was originally developed to prevent hot flushes
4. Tamoxifen was licensed for use in the USA in the 1960s
5. The main indication for use is polycystic ovarian syndrome
6. Tamoxifen is usually given for a duration of 10 years for primary prevention of breast cancer

 TRUE or FALSE

1. Tamoxifen is only helpful if the type of breast cancer is estrogen receptor positive

 TRUE or FALSE

1. Which is true?
2. Tamoxifen has a very short half-life
3. 80mg is the standard dose for breast cancer
4. More than 1 CYP450 enzyme family is needed to release the active metabolites
5. There is no resistance to tamoxifen
6. Tamoxifen acts purely as an antagonist at the estrogen receptor in all tissues

TRUE or FALSE

1. Which is NOT a common adverse drug reaction (ADR)?
2. Fatigue
3. Nausea
4. Constipation
5. Ocular toxicity
6. CYP2D6 inhibitors such as paroxetine and terbinafine can reduce the efficacy of tamoxifen

TRUE or FALSE

1. Long-term therapy with tamoxifen can cause cancers and liver disease

TRUE or FALSE

1. The drug-drug interaction (DDI) between tamoxifen and warfarin is classified as moderate

TRUE or FALSE