Tamoxifen (TAM) is a chemical widely used in hormone therapy to treat hormone receptor-positive breast cancer (BC). Humans are regularly exposed to xenoestrogens, chemicals like bisphenol A (BPA) and endosulfan (END), which mimic the natural endogenous estrogens in many pathways and may potentiate (at least in theory) BC risk. BPA is one of the most produced chemicals worldwide used in polycarbonate plastic in food and drink packaging. END is an organochlorine pesticide that, although considered probable carcinogenic to humans, is still illegally used in some countries. Both xenoestrogens share similar routes of exposure to humans through ingestion, and we wonder if such exposure may model the TAM impacts against BC cells. Therefore, in this study, we aimed to investigate the in vitro cytotoxicity effects of TAM, BPA, and END in single-exposures, followed by the effects of co-exposures (TAM+BPA and TAM+END) on the MCF7 cell line (representative of hormone-positive BC). We intended to study the impact of TAM's therapy outcome in ER-positive BC cells when simultaneously exposed to the referred xenoestrogens. The cytotoxic effects were assessed by MTT and SRB assays, and monitoring and photographing cells' morphology were conducted during the experiments. Overall, TAM, BPA, and END showed a reduction in cell viability relative to the control. The combinations of TAM with BPA and END showed a statistically significant decrease in cell viability compared to the control and the compounds alone. The results support that BPA and END can be cytotoxic to MCF7 alone but also interfere with the TAM effects. The current data calls for further research to investigate the modulation of these ubiquitous and xenoestrogenic pollutants over established endocrine therapies for BC.