

Pfizer Inc.	PF-05019702 (PRA-027)
Mechanism of Action	Progesterone receptor (PR) antagonist/nuclear receptor 3C3C (NRC3C) antagonist http://iuphar-db.org/DATABASE/ObjectDisplayForward?familyId=98&objectId=627 http://www.ncbi.nlm.nih.gov/gene/5241
Overview	PF-05019702 is a non-steroidal, selective progesterone receptor (PR) antagonist. Its potency (IC ₅₀ = 3.1 nM) was determined in antagonist mode, while no PR agonist activity was observed up to 10 μM. In the agonist mode, PF-05019702 had no activity on the estrogen (ER), glucocorticoid (GR), androgen (AR), or mineralocorticoid (MR) receptors up to 10 μM. In the antagonist mode, PF-05019702 had no activity on GR or ER up to 10 μM, but moderate activity on MR (IC ₅₀ = 2.1 μM) and AR (IC ₅₀ = 1.1 μM).
Safety/Tolerability	PF-05019702 was generally safe and well tolerated following doses up to 500 mg QD for 28 days in cycling and postmenopausal women. Nonclinical toxicology data support clinical studies up to 28 days in duration.
Additional Information	In preclinical studies following oral dosing, PR antagonism by PF-05019702 is distinguished from steroidal PR antagonists by a lack of ovulation inhibition while maintaining PR antagonist activity on reproductive tract endpoints including endometrial thickness, markers of proliferation, and steroid receptor expression. It showed no PR agonist-like activity.
Suitable for and Exclusions	Clinical studies up to 28 days duration where a PR or PR pathway dependent mechanism has a role in disease.
Clinical Trials	http://www.clinicaltrials.gov/ct2/results?term=pra-027
Publications	http://oasys2.confex.com/acs/236nm/techprogram/P1193440.HTM