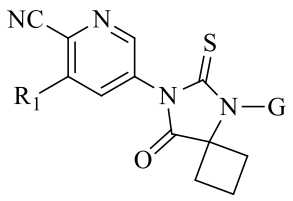
Claims

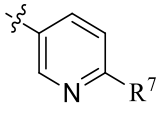
1. A compound of Formula (I)

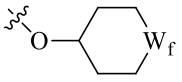


Formula (I)

wherein

R_1 is chloro, methyl, methoxy, difluoromethyl, or trifluoromethyl;

G is  ; wherein

R^7 is  , wherein

W_f is NH, N(methyl), N(2-hydroxyethyl), N(2-methoxyethyl), N(2-fluoroethyl), N(2,2,2-trifluoroethyl), N(cyanomethyl), N(allyl), N(isopentyl), N(prop-2-yn-1-yl), N(3,3-dimethylbutyl), N(3-fluoropropyl), N(3,3,3-trifluoropropyl), N(methoxycarbonylmethyl), N(3-amino-2-hydroxy-propyl), N(3,3-dimethyl-butyl), CH(amino), CH(methylamino), or CH(dimethylamino); or

an N-oxide, enantiomer, diastereomer, or pharmaceutically acceptable salt form thereof.

2. The compound of claim 1, wherein R_1 is chloro, methyl, methoxy, or trifluoromethyl.

3. The compound of claim 2, wherein R_1 is methyl or trifluoromethyl.

4. The compound of claim 1, wherein W_f is NH or N(methyl).

5. The compound of claim 1 that is:

5-[8-[6-[(1-methyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

3-methyl-5-[8-[6-[(1-methyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]pyridine-2-carbonitrile;

3-methoxy-5-[8-[6-[(1-methyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]pyridine-2-carbonitrile;

3-chloro-5-[8-[6-[(1-methyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]pyridine-2-carbonitrile;

5-[5-oxo-8-[6-(4-piperidyloxy)-3-pyridyl]-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[8-[6-[[1-(cyanomethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[8-[6-[[1-(2-methoxyethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

3-methyl-5-[5-oxo-7-thioxo-8-[6-[[1-(2,2,2-trifluoroethyl)-4-piperidyl]oxy]-3-pyridyl]-6,8-diazaspiro[3.4]octan-6-yl]pyridine-2-carbonitrile;

5-[8-[6-[[1-(2-hydroxyethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

3-chloro-5-[5-oxo-8-[6-(4-piperidyloxy)-3-pyridyl]-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]pyridine-2-carbonitrile;

3-chloro-5-[8-[6-[[1-(cyanomethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]pyridine-2-carbonitrile;

5-[5-oxo-7-thioxo-8-[6-[[1-(2,2,2-trifluoroethyl)-4-piperidyl]oxy]-3-pyridyl]-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[8-[6-[[1-(2-fluoroethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

3-chloro-5-[8-[6-[[1-(2-methoxyethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]pyridine-2-carbonitrile;

3-methoxy-5-[5-oxo-8-[6-(4-piperidyloxy)-3-pyridyl]-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]pyridine-2-carbonitrile;

5-[8-[6-[[1-(2-fluoroethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-methyl-pyridine-2-carbonitrile;

3-chloro-5-[8-[6-[[1-(2-hydroxyethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]pyridine-2-carbonitrile;

3-methyl-5-[5-oxo-8-[6-(4-piperidyloxy)-3-pyridyl]-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]pyridine-2-carbonitrile;

5-[8-[6-[(1-allyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[8-[6-[(1-allyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-chloro-pyridine-2-carbonitrile;

5-[8-[6-[[1-(cyanomethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-methyl-pyridine-2-carbonitrile;

5-[8-[6-[[1-(2-methoxyethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-methyl-pyridine-2-carbonitrile;

5-[8-[6-[(1-allyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-methyl-pyridine-2-carbonitrile;

5-[8-[6-[[1-(2-hydroxyethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-methyl-pyridine-2-carbonitrile;

5-[5-oxo-8-[6-[(1-prop-2-ynyl-4-piperidyl)oxy]-3-pyridyl]-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

3-chloro-5-[8-[6-[(1-isopentyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]pyridine-2-carbonitrile;

or a pharmaceutically acceptable salt form thereof.

6. The compound of claim 1 that is:

5-[8-[6-[(1-methyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile; or

3-methyl-5-[8-[6-[(1-methyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]pyridine-2-carbonitrile;

or a pharmaceutically acceptable salt form thereof.

7. The compound of claim 1 that is:

3-methoxy-5-[8-[6-[(1-methyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]pyridine-2-carbonitrile;

3-chloro-5-[8-[6-[(1-methyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]pyridine-2-carbonitrile;

or a pharmaceutically acceptable salt form thereof.

8. The compound of claim 1 that is:

5-[5-oxo-8-[6-(4-piperidyloxy)-3-pyridyl]-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

3-chloro-5-[5-oxo-8-[6-(4-piperidyloxy)-3-pyridyl]-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]pyridine-2-carbonitrile;

3-methoxy-5-[5-oxo-8-[6-(4-piperidyloxy)-3-pyridyl]-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]pyridine-2-carbonitrile;

3-methyl-5-[5-oxo-8-[6-(4-piperidyloxy)-3-pyridyl]-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]pyridine-2-carbonitrile;

or a pharmaceutically acceptable salt form thereof.

9. The compound of claim 1 that is:

5-[8-[6-[(1-methyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

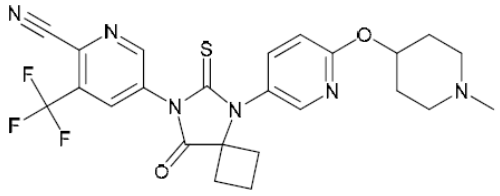
or a pharmaceutically acceptable salt form thereof.

10. The compound of claim 1, that is:

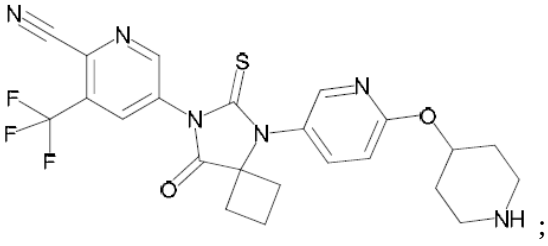
5-[5-oxo-8-[6-(4-piperidyloxy)-3-pyridyl]-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

or a pharmaceutically acceptable salt form thereof.

11. The compound of claim 1, that is:



or



;

or a pharmaceutically acceptable salt form thereof.

12. A pharmaceutical composition comprising a compound of any one of the preceding claims and at least one of a pharmaceutically acceptable carrier, a pharmaceutically acceptable excipient, or a pharmaceutically acceptable diluent.

13. The pharmaceutical composition of claim 12, wherein the compound is:

5-[8-[6-[(1-methyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[5-oxo-8-[6-(4-piperidyloxy)-3-pyridyl]-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[8-[6-[[1-(cyanomethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[8-[6-[[1-(2-methoxyethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[8-[6-[[1-(2-hydroxyethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[5-oxo-7-thioxo-8-[6-[[1-(2,2,2-trifluoroethyl)-4-piperidyl]oxy]-3-pyridyl]-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[8-[6-[[1-(2-fluoroethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[8-[6-[(1-allyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[5-oxo-8-[6-[(1-prop-2-ynyl-4-piperidyl)oxy]-3-pyridyl]-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

or a pharmaceutically acceptable salt form thereof.

14. The pharmaceutical composition of claim 12, wherein the compound is

5-[8-[6-[(1-methyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

or a pharmaceutically acceptable salt form thereof.

15. The pharmaceutical composition of claim 12, wherein the compound is

5-[5-oxo-8-[6-(4-piperidyloxy)-3-pyridyl]-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

or a pharmaceutically acceptable salt form thereof.

16. The pharmaceutical composition of claim 12, wherein the composition is a solid unit dosage form.

17. The pharmaceutical composition of any one of claims 12 to 16 further comprising abiraterone acetate.

18. The pharmaceutical composition of claim 17, further comprising prednisone.

19. The use of a compound according to claim 1, or a pharmaceutically acceptable salt form thereof, in the preparation of a medicament for the treatment of prostate cancer in a human, in which the prostate cancer is affected by the antagonism of one or more androgen receptor types.

20. The use according to claim 19, wherein the compound is:

5-[8-[6-[(1-methyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[5-oxo-8-[6-(4-piperidyloxy)-3-pyridyl]-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[8-[6-[[1-(cyanomethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[8-[6-[[1-(2-methoxyethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[8-[6-[[1-(2-hydroxyethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[5-oxo-7-thioxo-8-[6-[[1-(2,2,2-trifluoroethyl)-4-piperidyl]oxy]-3-pyridyl]-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[8-[6-[[1-(2-fluoroethyl)-4-piperidyl]oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[8-[6-[(1-allyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

5-[5-oxo-8-[6-[(1-prop-2-ynyl-4-piperidyl)oxy]-3-pyridyl]-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

or a pharmaceutically acceptable salt form thereof.

21. The use according to claim 19, wherein the compound is:

5-[8-[6-[(1-methyl-4-piperidyl)oxy]-3-pyridyl]-5-oxo-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

or a pharmaceutically acceptable salt form thereof.

22. The use according to claim 19, wherein the compound is:

5-[5-oxo-8-[6-(4-piperidyloxy)-3-pyridyl]-7-thioxo-6,8-diazaspiro[3.4]octan-6-yl]-3-(trifluoromethyl)pyridine-2-carbonitrile;

or a pharmaceutically acceptable salt form thereof.

23. The use according to any one of claims 19 to 22, wherein the prostate cancer is castration-resistant prostate cancer.

24. The use according to any one of claims 19 to 22, wherein the prostate cancer is metastatic castration-resistant prostate cancer.

25. The use according to any one of claims 19 to 24, in further combination with a therapeutically effective amount of abiraterone acetate.

26. The use according to claim 25, in further combination with a therapeutically effective amount of prednisone.