Claims:

1. Use of an aldose reductase inhibitor in the manufacture of a medicament for the treatment of a genetic and/or metabolic disorder that alters sorbitol metabolism or causes over production of sorbitol.

2. The use of claim 1, wherein the treatment decreases sorbitol accumulation.

3. The use claim 1 or 2, wherein the disorder is a genetic disorder that alters metabolism of sorbitol or causes over-production of sorbitol.

4. The use of any one of claims 1-3, wherein the disorder is sorbitol dehydrogenase deficiency.

5. The use of any one of claims 1-4, wherein the disorder is genetic sorbitol dehydrogenase deficiency.

6. The use of any one of claims 1-5, wherein the disorder includes clinical features or complications selected from the group consisting of cataracts, neuropathy, retinopathy, cardiomyopathy, nephropathy, microvascular complications, atherosclerosis and other cardiovascular complications, albuminuria, and diabetes.

7. The use of any one of claims 1-6, wherein the disorder is hereditary neuropathy.

8. The use of claim 7, wherein the hereditary neuropathy is associated with sorbitol dehydrogenase deficiency.

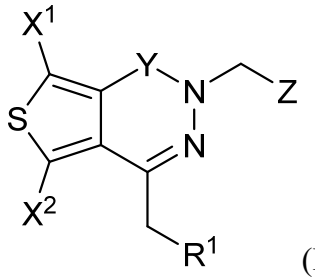
9. The use of claim 7 or 8, wherein the hereditary neuropathy is Charcot–Marie–Tooth disease (CMT).

10. The use of claim 9, wherein the CMT disease is CMT neuropathy type 1 (CMT-1).

11. The use of claim 9, wherein the CMT disease is CMT neuropathy type 2 (CMT-2).

12. The use of any one of claims 1-7, wherein the disorder is distal hereditary motor neuronopathy (dHMN).

13. The use of any one of claims 1-12, wherein the aldose reductase inhibitor is a compound of Formula (III)



(III),

or a salt thereof, wherein

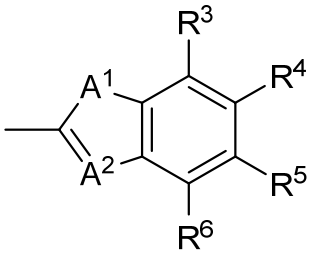
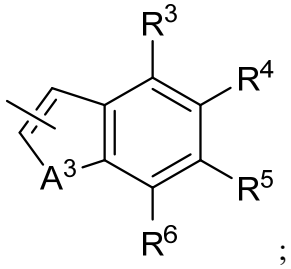
R^1 is CO_2R^2;

R^2 is hydrogen, (C_1-C_6)-alkyl, (C_1-C_6)-hydroxyalkyl, or (C_1-C_6)-aminoalkyl;

X^1 is hydrogen or halogen;

X^2 is hydrogen or halogen;

Y is a bond, C=O, C=S, C=NH, or C=N(C_1-C_4)-alkyl;

Z is  or ;

A^1 is NR^7, O, S or CH_2;

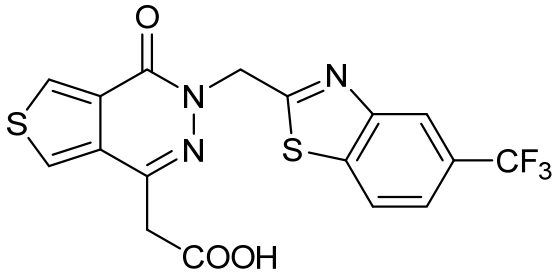
A^2 is N or CH;

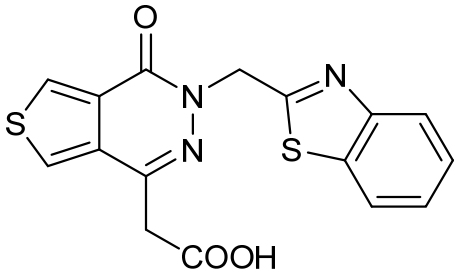
A^3 is NR^7, O, or S;

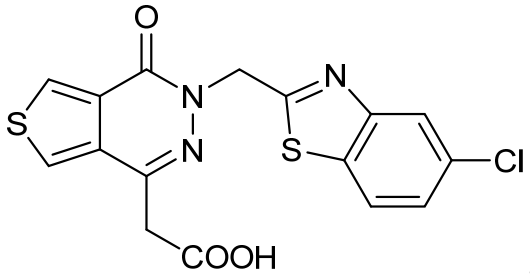
R^3, R^4, R^5, and R^6 are independently hydrogen, halogen, cyano, acyl, haloalkyl, haloalkoxy, haloalkylthio, trifluoroacetyl, (C_1-C_4)-alkyl, (C_1-C_4)-alkoxy, (C_1-C_4)-alkylthio, (C_1-C_4)-alkylsulfinyl, or (C_1-C_4)-alkylsulfonyl; and

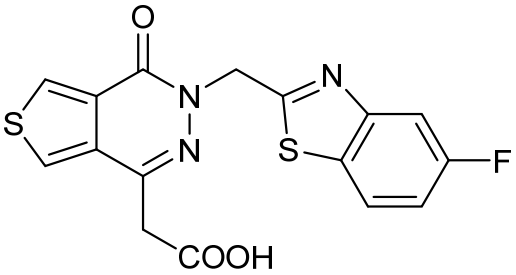
R^7 is hydrogen, C_1-C_4 alkyl, or C(O)O-(C_1-C_4)-alkyl.

14. The use of claim 13, wherein the aldose reductase inhibitor is selected from the group consisting of



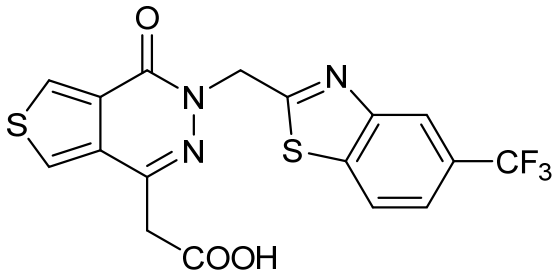
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, and salts thereof.

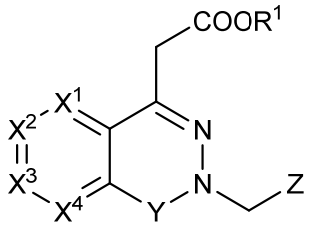
15. The use of any one of claims 1-14, wherein the aldose reductase inhibitor is Compound B:



or a salt thereof.

16. The use of any one of claims 1-12, wherein the aldose reductase inhibitor is zopolrestat or a salt thereof, or epalrestat or a salt thereof.

17. The use of any one of claims 1-12, wherein the aldose reductase inhibitor is a compound of Formula (I):



or a salt thereof, wherein

R^1 is H, (C_1-C_6)-alkyl, (C_1-C_6)-hydroxyalkyl, or (C_1-C_6)-aminoalkyl;

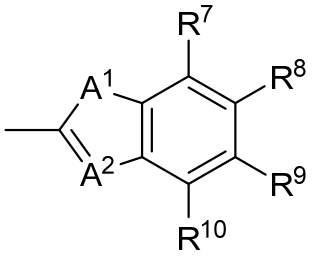
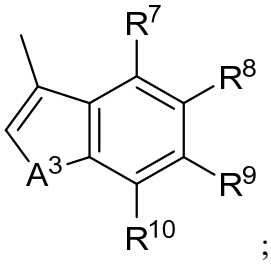
X^1 is N or CR^3;

X^2 is N or CR^4;

X^3 is N or CR^5;

X^4 is N or CR^6; with the proviso that two or three of X^1, X^2, X^3, or X^4 are N;

Y is a bond, C═O, C═S, C═NH, or C═N(C_1-C_4)-alkyl;

Z is  or ;

A^1 is NR^{11}, O, S, or CH_2;

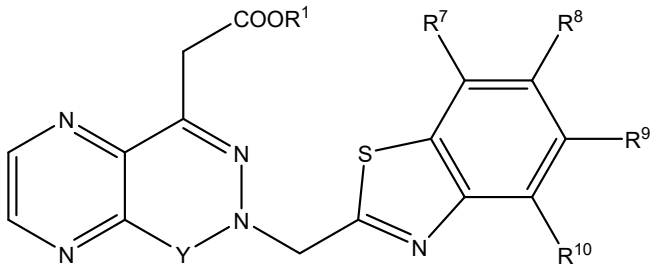
A^2 is N or CH;

A^3 is NR^{11}, O, or S;

R^3 through R^{10} are independently hydrogen, halogen, cyano, acyl, haloalkyl, haloalkoxy, haloalkylthio, trifluoroacetyl, (C_1-C_4)-alkyl, (C_1-C_4)-alkoxy, (C_1-C_4)-alkylthio, (C_1-C_4)-alkylsulfinyl, or (C_1-C_4)-alkylsulfonyl; or two of R^3 through R^6 or two of R^7 through R^{10} taken together are (C_1-C_4)-alkylenedioxy; and

R^{11} is hydrogen, C_1-C_4 alkyl, or C(O)O-(C_1-C_4)-alkyl.

18. The use of any one of claims 1-12 or 17, wherein the aldose reductase inhibitor is a compound of Formula (II):



(II)

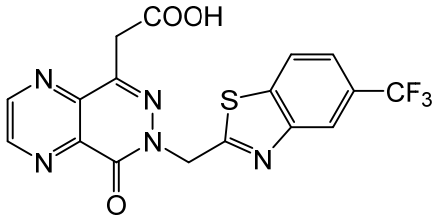
or a salt thereof, wherein

R^1 is H, (C_1-C_6)-alkyl, (C_1-C_6)-hydroxyalkyl, or (C_1-C_6)-aminoalkyl;

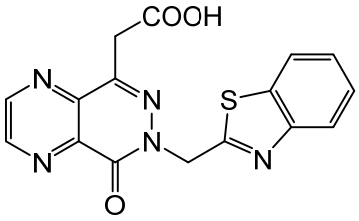
Y is a bond, C═O, C═S, C═NH, or C═N(C_1-C_4)-alkyl; and

R^7 through R^{10} are independently hydrogen, halogen, cyano, acyl, haloalkyl, haloalkoxy, haloalkylthio, trifluoroacetyl, (C_1-C_4)-alkyl, (C_1-C_4)-alkoxy, (C_1-C_4)-alkylthio, (C_1-C_4)-alkylsulfinyl, or (C_1-C_4)-alkylsulfonyl; or two of R^7 through R^{10} taken together are (C_1-C_4)-alkylenedioxy.

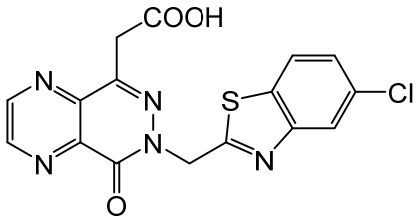
19. The use of claim 17 or 18, wherein the aldose reductase inhibitor is selected from the group consisting of



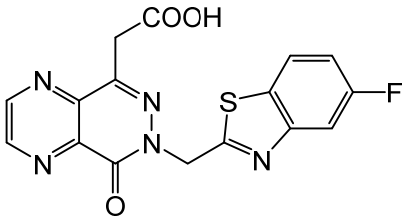
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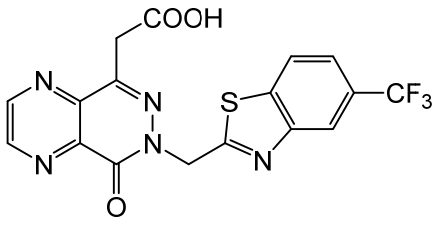


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, and salts thereof.

20. The use of any one of claims 1-12 or 17-19, wherein the aldose reductase inhibitor is Compound A



or a salt thereof.

21. The use of any one of claims 1-20, wherein the disorder is in a human.

22. The use of claim 21, wherein the human has diabetes.

23. The use of claim 21 or 22, wherein the human has a complication of diabetes.