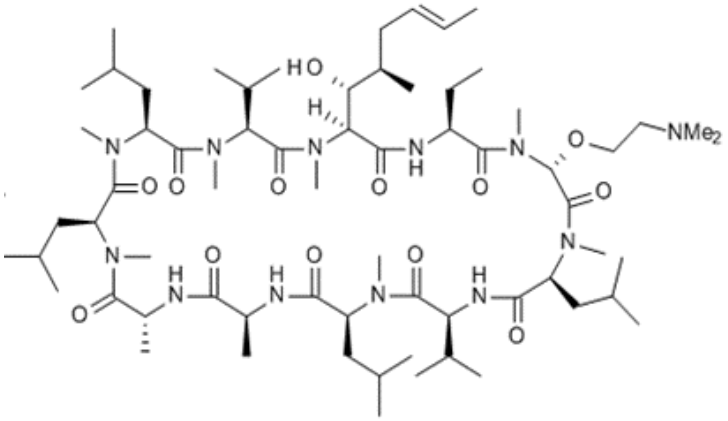
Claims

1. Use of Compound I or a pharmaceutically acceptable salt thereof



Compound I

in the manufacture of a medicament for the prevention and/or treatment of a kidney condition or disease in a subject exposed to a nephrotoxin capable of inducing said kidney condition or disease, wherein the nephrotoxin is

a) a nephrotoxic drug substance selected from the group consisting of antimicrobial agents, cancer chemotherapeutic agents, blood pressure medicines including ACE inhibitors and angiotensin receptor blockers, macrolactone immunosuppressive agents, HIV protease inhibitors, peptic ulcer medicines, non-steroidal anti-inflammatory drugs, proton pump inhibitors, laxatives and contrast agents; or

b) an endogenous nephrotoxin.

2. The use according to claim 1, wherein the nephrotoxin is a nephrotoxic drug substance, wherein the nephrotoxic drug substance is a chemotherapeutic agent selected from the group consisting of platins (e.g. carboplatin, cisplatin, oxaliplatin or nedaplatin), anthracyclines (e.g. daunorubicin, doxorubicin, idarubicin, epirubicin), bleomycins, mitomycins, actinomycins, cyclophosphamides, cytarabine, capecitabine, gemcitabine, ifosfamide, interleukin-2, streptozocin, gemtuzumab ozogamicin, melphalan, methotrexate, pemetrexed, plicamycin, and trimetrexate.

3. The use according to claim 2, wherein the subject is undergoing cancer treatment, wherein said cancer treatment comprises the administration of the chemotherapeutic agent to the subject.

4. The use according to claim 1, wherein the nephrotoxin is a nephrotoxic drug substance, wherein the nephrotoxic drug substance is an antimicrobial agent selected from the group consisting of: aminoglycosides (e.g. gentamicin, tobramycin, amikacin, netilmicin, apramicin, streptomycin, kanamycin, neomycin, sisomycin), beta-lactams (e.g tazobactam, or piperacillin/ tazobactam), polypeptide antibiotics (e.g. polymyxins such as polymyxin A, B, C, D, E (colistin), glycopeptide antibiotics (e.g. vancomycin), outer membrane protein targeting antibiotics, (e.g. murepavadin), antifungal agent (e.g. amphotericin B) and combinations thereof.

5. The use according to claim 4, wherein the antimicrobial agent is gentamicin.

6. The use according to claim 4 , wherein the antimicrobial agent is murepavadin.

7. The use according to any one of claims 4 to 6, wherein the subject is suffering from an infection, and wherein the subject will be, or is undergoing treatment, or has been treated with the antimicrobial agent.

8. The use according to claim 1, wherein the nephrotoxin is a nephrotoxic drug substance, wherein the nephrotoxic drug substance is a blood pressure medicine selected from an ACE inhibitor optionally selected from the group consisting of captopril, benazepril, enalapril, fosinopril, and ramipril; and an angiotensin receptor blocker optionally selected from the group consisting of candesartan, valsartan, irbesartan, olmesartan, telmisartan, eprosartan, and losartan.

9. The use according to claim 1, wherein the nephrotoxin is a nephrotoxic drug substance, wherein the nephrotoxic drug substance is a HIV protease inhibitor selected from the group consisting of indinavir and ritonavir.

10. The use according to claim 1, wherein the nephrotoxin is a nephrotoxic drug substance, wherein the nephrotoxic drug substance is a peptic ulcer medicine

selected from the group consisting of cimetidine, esomeprazole, lansoprazole, omeprazole, pantoprazole, and rabeprazole.

11. The use according to claim 1, wherein the nephrotoxin is a nephrotoxic drug substance, wherein the nephrotoxic drug substance is a non-steroidal anti-inflammatory drug selected from the group consisting of ibuprofen, ketoprofen, diclofenac, and aspirin.

12. The use according to claim 1, wherein the nephrotoxin is a nephrotoxic drug substance, wherein the nephrotoxic drug substance is a laxative selected from sodium phosphate.

13. The use according to claim 1, wherein the nephrotoxin is a nephrotoxic drug substance, wherein the nephrotoxic drug substance is a contrast agent, optionally an iodinated contrast agent (e.g. iothalamate, or iodixanol, or iohexol).

14. The use according to claim 1, wherein the nephrotoxin is an endogenous nephrotoxin and wherein the endogenous nephrotoxin is myoglobin.

15. The use according to claim 14, wherein the subject has a creatine phosphokinase serum level of at least 5 times greater than baseline.

16. The use according to any one of claims 14 or 16, wherein the subject has experienced or is suffering from physical trauma or crush injury, exposure to electrical current, extreme physical exertion or activity, and temperature extremes.

17. The use according to any one of claims 1, or claims 14 to 16, wherein the medicament is to be administered to the subject prior to exposure to, or engagement with activities (e.g. extreme physical activity) associated with or at risk for onset of rhabdomyolysis.

18. The use according to claims 1 to 13, wherein the subject's exposure to the nephrotoxic drug substance is more than once, or at regular intervals over a treatment period.

19. The use according to claim 18, wherein the subject's exposure to the nephrotoxic drug substance is at least twice, optionally at least once daily over a period of at least 3 days, or 7 days.

20. The use according to any one of the preceding claims, wherein the kidney condition or disease is nephrotoxin-induced acute kidney injury or kidney failure.

21. The use according to any one of claims 1 to 20, wherein the kidney condition or disease is selected from rhabdomyolysis, hemolysis, myoglobinuria, or optionally tumour lysis or myeloma-induced acute kidney injury.

22. The use according to any one of the preceding claims, wherein the subject has a pre-existing condition or disease that increases the subject's risk of developing a kidney condition or disease when exposed to the nephrotoxin.

23. The use according to claim 22, wherein the subject has a pre-existing kidney condition or disease, optionally wherein said pre-existing kidney condition is chronic kidney disease; optionally wherein the subject has a history of renal impairment or requires dialysis.

24. The use according to claim 22 or 23, wherein the subject has reduced renal function, optionally wherein the subject has blood urea nitrogen levels of at least 1.5 to 3 times higher than baseline, and/or serum creatinine levels at least 1.5 to 3 times higher than baseline, and/or oliguria.

25. The use according to any one of claims 1 to 13, or 18 to 24, wherein the medicament is to be administered to the subject prior to the subject's exposure to the nephrotoxic drug substance.

26. The use according to claim any one of claims 1 to 13, or 18 to 25, wherein a dose of the medicament is to be administered to the subject within 24 hours or less before a dose of the nephrotoxic drug substance is administered to the subject.

27. The use according to claim 26, wherein a dose of the medicament is to be administered to the subject within 6 hours or less, and optionally within 2 hours

or less, before the nephrotoxic drug substance is to be administered to the subject.

28. The use according to any one of the preceding claims, wherein the medicament is to be administered to the subject after the onset of reduced renal functions as characterized by any one or combination of: blood urea nitrogen levels of at least 1.5 to 3 times higher than baseline, serum creatinine levels of at least 1.5 to 3 times higher than baseline, and oliguria.

29. The use according to claim 28, wherein a dose of the medicament is to be administered to the subject 1 to 24 hours; optionally 1 to 6 hours, after the onset of reduced renal function.

30. The use according to any one of claims 1 to 13, or claims 18 to 29 , wherein the medicament is to be administered repeatedly to a subject during a first period of time which commences before and overlaps with a second period of time wherein the subject is exposed to repeatedly to the nephrotoxic drug substance.

31. The use according to any one of the preceding claims, wherein the medicament is to be administered to the subject at a dose of 0.001 to 10 mg/kg, and optionally 0.1 to 10 mg/kg.

32. The use according to any one of the preceding claims, wherein the subject is a human subject.

33. The use according to any one of the preceding claims, wherein the medicament is formulated for administration by infusion or by injection, preferably subcutaneous, intramuscular or intravenous injection or intravenous or subcutaneous infusion.

34. Use of Compound I or a pharmaceutically acceptable salt thereof as defined in claim 1 in the manufacture of a medicament for the prevention and/or reduction of blood urea nitrogen levels of at least 1.5 to 3 times higher than baseline and/or serum creatinine levels of at least 1.5 to 3 times higher than baseline in a subject exposed to a nephrotoxin.

35. The use according to claim 34, wherein the nephrotoxin is as defined in any one of claims 1 to 2, 4 to 6, or claims 8 to 14.

36. The use according to claim 34 or 35, wherein the subject is defined as in any one of claims 1, 3, 7, 15 to 16, 22 to 24 or 32.

37. The use according to claims 34 to 36, wherein the use is as defined in any one of claims 17 to 19, or claims 25 to 31.

38. The use according to claims 34 to 37, wherein the medicament is formulated for administration by injection or infusion, preferably intravenous injection or infusion.