L'utilisation d'un composé de formule (I) où R₁ est H; un alkylation en C₄-C₆ un perfluoroalkyle en C₁-C₃ ou un cycloalkyle en C₃-C₅ R₂ est H; un alkylation en C₁-C₆ facultativement substitué; un perfluoroalkyle en C₁-C₅; ou un cycloalkyle en C₃-C₆ R₃ est un alkylation en C₁-C₆ facultativement substitué; un perfluoroalkyle en C₁-C₆ un cycloalkyle en C₃-C₅ un alkénylation en C₃-C₅ ou un alkylation en C₃-C₆ R₄ est un alkylation en C₁-C₄ facultativement substitué, un alkénylation en C₂-C₄; un alcanoylation en C₂-C₄ un (hydroxy)alkyle en C₂-C₄ ou un

(57) The use of a compound of formula (I) wherein R₁ is H; C₁-C₃ alkyl; C₁-C₃ perfluoroalkyl; or C₃-C₅ cycloalkyl; R₂ is H; optionally substituted C₁-C₆ alkyl; C₁-C₅ perfluoroalkyl; C₁-C₅ cycloalkyl; C₁-C₅ alkyl; or C₃-C₆ alkyl; R₃ is optionally substituted C₁-C₆ alkyl; C₁-C₅ perfluoroalkyl; C₃-C₅ cycloalkyl; C₁-C₅ alkyl; or C₃-C₆ alkyl; R₄ is optionally substituted C₁-C₄ alkyl, C₂-C₄ alkyl; C₂-C₄ alkanoyl; (hydroxy)C₂-C₄ alkyl or (C₂-C₅ alkoxy)C₁-C₂ alkyl; CONR₆₊₋; CO₂R²; halogen; NR₆₊₋; NOSOR₆₊₋; SOR₆₊₋; SO₂NR₆₊₋; or
(aloxy en C₂-C₃) alkyle en C₁-C₂, CONR₅R₆, CO₂R⁷, un halogène, NR₅R₆, NH₂SO₂NR₅R₆, NH₂SO₆R₈, SO₂NR₅R₆R¹₀, ou un groupe phényle, pyridyle, pyrimidinyle, imidazolyle, oxazolyle, thiazolyle.

thiényle ou triazolyle, n'importe quel de ces groupes pouvant être substitué par un méthyle; R⁵ et R⁶ sont, indépendamment l'un de l'autre, un H ou un alkyle en C₁-C₄ ou, combinés à l'atome d'azote auquel ils sont attachés, forment un groupe pyrrolidinyle, piperidino, morpholino. 4-N(R¹¹)-pipérazinyle ou imidazolyle facultativement substitué; R² est H ou un alkyle en C₁-C₄, R⁶ est un alkyle en C₁-C₃ facultativement substitué; R⁷ et R⁸ combinés à l'atome d'azote auquel ils sont attachés forment un groupe pyrrolidinyle, piperidino, morpholino ou 4-N(R¹²)-pipérazinyle facultativement substitué, R¹³ est H; un alkyle en C₁-C₃ facultativement substitué; un (hydroxy)alkyle en C₂-C₃, ou un alcanoyle en C₁-C₄, R¹₂ est H, un alkyle en C₁-C₆ facultativement substitué; CONR¹³R¹⁴, CSN₁R¹⁴, CSN₁R¹₄, ou CN₁DNR¹₃R¹₄, et R² et R⁶ sont, indépendamment l'un de l'autre, H, un alkyle en C₁-C₄ ou un alkyle en C₂-C₄ substitué; un sel pharmaceutiquement acceptable de ce composé; une composition pharmaceutique contenant l'une ou l'autre des deux entités, pour la fabrication d'un médicament pour le traitement ou la prévention des troubles de l'érection chez un animal mâle, dont l'homme; une composition pharmaceutique pour ledit traitement; et une méthode pour ledit traitement dudit animal mâle avec ladite composition pharmaceutique ou avec lesdites entités.
DISCLAIMER WITH RESPECT TO CANADIAN PATENT NO. 2,163,446

1. The patentee of Patent No. 2,163,446, granted on July 7, 1998 for an invention entitled Pyrazolopyrimidinones for the Treatment of Impotence, has, by mistake, accident or inadvertence, and without any wilful intent to defraud or mislead the public,

a) made the specification too broad, claiming more than that of which the patentee or the person through whom the patentee claims was the inventor, or

b) in the specification, claimed that the patentee or the person through whom the patentee claims was the inventor of any material or substantial part of the invention patented of which the patentee was not the inventor, and to which the patentee had no lawful right.

2. The name and complete address of the patentee is Pfizer Research & Development Co. N.V./S.A., La Touche House, International Financial Services Centre, Dublin 1, Ireland.

3. The patentee disclaims the entirety of Claims 14, 15, 16, 17 and 27.

4. The patentee disclaims the entirety of Claim 1 with the exception of the following:

1. The use of a compound of formula (I):

![Chemical Structure](image)

wherein $R^1$ is H; C$_1$-C$_3$ alkyl; C$_1$-C$_3$ perfluoroalkyl; or C$_3$-C$_5$ cycloalkyl;

$R^2$ is H; C$_1$-C$_6$ alkyl optionally substituted with C$_3$-C$_6$ cycloalkyl; C$_1$-C$_3$ perfluoroalkyl; or C$_3$-C$_6$ cycloalkyl;

DISCLAIMER - RENONCIATION
Filed and recorded in Patent Office
Déposé et enregistré au Bureau des Brevets
Hull, this 11 day of November 1998
Hull, ce 11 jour de novembre 1998
$R^3$ is $C_1$-$C_6$ alkyl optionally substituted with $C_3$-$C_6$ cycloalkyl; $C_1$-$C_6$ perfluoroalkyl; $C_3$-$C_6$ cycloalkyl; $C_3$-$C_6$ alkenyl; or $C_3$-$C_6$ alkyne.

$R^4$ is $C_1$-$C_4$ alkyl optionally substituted with OH, NR$_5^5$R$_6^6$, CN, CONR$_5^5$R$_6^6$, or CO$_2$R$_7$; $C_2$-$C_4$ alkenyl optionally substituted with CN, CONR$_5^5$R$_6^6$, or CO$_2$R$_7$; $C_2$-$C_4$ alkanoyl optionally substituted with NR$_5^5$R$_6^6$; (hydroxy) C$_2$-$C_4$ alkyl optionally substituted with NR$_5^5$R$_6^6$; (C$_2$-$C_3$ alkoxy) C$_1$-$C_2$ alkyl optionally substituted with OH or NR$_5^5$R$_6^6$; CONR$_5^5$R$_6^6$; CO$_2$R$_7$; halo; NR$_5^5$R$_6^6$; NH$_2$SO$_2$NR$_5^5$R$_6^6$; NH$_2$SO$_2$R$_8$; SO$_2$NR$_5^5$R$_6^6$; or phenyl, pyridyl, pyrimidinyl, imidazolyl, oxazolyl, thiazolyl, thienyl or triazolyl any of which is optionally substituted with methyl.

$R^5$ and $R^6$ are each independently H or $C_1$-$C_4$ alkyl, or together with the nitrogen atom to which they are attached form a pyrrolidiny1, piperidino, morpholinyl, 4-N(R$_{17}^{17}$)-piperazinyl or imidazolyl group wherein said group is optionally substituted with methyl or OH;

$R^7$ is H or $C_1$-$C_4$ alkyl;

$R^8$ is $C_1$-$C_3$ alkyl optionally substituted with NR$_5^5$R$_6^6$;

$R^9$ and $R^{10}$ together with the nitrogen atom to which they are attached form a pyrrolidiny1, piperidino, morpholinyl or 4-N(R$_{17}^{17}$)-piperazinyl group wherein said group is optionally substituted with $C_1$-$C_4$ alkyl, $C_1$-$C_3$ alkoxy, NR$_{13}^{13}$R$_{14}^{14}$ or CONR$_{13}^{13}$R$_{14}^{14}$;

$R^{11}$ is H; $C_1$-$C_3$ alkyl optionally substituted with phenyl; (hydroxy)C$_2$-$C_3$ alkyl; or $C_1$-$C_4$ alkanoyl;

$R^{12}$ is H; $C_1$-$C_6$ alkyl; (C$_1$-$C_3$ alkoxy)C$_2$-$C_6$ alkyl; (hydroxy)C$_2$-$C_6$ alkyl; (R$_{13}^{13}$R$_{14}^{14}$N)C$_2$-$C_6$ alkyl; (R$_{13}^{13}$R$_{14}^{14}$NOC)C$_1$C$_6$ alkyl; CONR$_{13}^{13}$R$_{14}^{14}$; C$_{10}$NR$_{13}^{13}$R$_{14}^{14}$; or C(NH)NR$_{13}^{13}$R$_{14}^{14}$; and

$R^{13}$ and $R^{14}$ are each independently H; $C_1$-$C_4$ alkyl; (C$_1$-$C_3$ alkoxy)C$_2$-$C_4$ alkyl; or (hydroxy)C$_2$-$C_4$ alkyl;

or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity, for the manufacture of a medicament for the curative or prophylactic treatment of an erectile dysfunction in man or sexual dysfunction in woman.
5. The patentee disclaims the entirety of Claim 8 with the exception of the following:

8. The use according to any one of claims 1 to 7 for the manufacture of a medicament for the curative or prophylactic treatment of erectile dysfunction in man.

6. The patentee disclaims the entirety of Claim 9 with the exception of the following:

9. The use according to any one of claims 1 to 7 for the manufacture of a medicament for the curative or prophylactic treatment of sexual dysfunction in woman.

7. The patentee disclaims the entirety of Claim 10 with the exception of the following:

10. A pharmaceutical composition for the curative or prophylactic treatment of erectile dysfunction in man, comprising a compound of formula (I) according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable diluent or carrier.

8. The patentee disclaims the entirety of Claim 11 with the exception of the following:

11. A pharmaceutical composition for the curative or prophylactic treatment of sexual dysfunction in woman comprising a compound of formula (I) according to any one of claims 1-7, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable diluent or carrier.

9. The patentee disclaims the entirety of Claim 12 with the exception of the following:

12. A process for the preparation of a pharmaceutical composition for the curative or prophylactic treatment of erectile dysfunction in man comprising formulating a compound of formula (I) according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, with a pharmaceutically acceptable diluent or carrier.
10. The patentee disclaims the entirety of Claim 13 with the exception of the following:

13. A process for the preparation of a pharmaceutical composition for the curative or prophylactic treatment of sexual dysfunction in woman comprising formulating a compound of formula (I) according to any one of claims 1-7, or a pharmaceutically acceptable salt thereof, with a pharmaceutically acceptable diluent or carrier.

11. The patentee disclaims the entirety of Claim 20 with the exception of the following:

20. A commercial package containing, as active pharmaceutical ingredient, a compound of formula (I) according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, together with instructions for its use for the curative or prophylactic treatment of erectile dysfunction in man.

12. The patentee disclaims the entirety of Claim 21 with the exception of the following:

21. A commercial package containing, as active pharmaceutical ingredient, a compound of formula (I) according to any one of claims 1-7, or a pharmaceutically acceptable salt thereof, together with instructions for its use for the curative or prophylactic treatment of sexual dysfunction in woman.

13. The patentee disclaims the entirety of Claim 25 with the exception of the following:

25. The use of an effective amount of a cGMP PDE inhibitor, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity, for the oral treatment of erectile dysfunction in man, wherein the cGMP PDE inhibitor is a selective inhibitor of cGMP-specific PDE5.
14. The patentee disclaims the entirety of Claim 26 with the exception of the following:

26. The use of an effective amount of a cGMP PDE inhibitor, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity, for the manufacture of a medicament for the curative or prophylactic oral treatment of erectile dysfunction in man, wherein the cGMP PDE inhibitor is a selective inhibitor of cGMP-specific PDE$_V$.

Date: November 8, 2002

Witness:

Pfizer Research and Development
Company N.V. / S.A.

By: Susan Webb
Name: Susan Webb
Title: Director
1. The patentee of Patent No. 2,163,446, granted on July 7, 1998, for an invention entitled Pyrazolopyrimidinones for the Treatment of Impotence, has, by mistake, accident or inadvertence, and without any willful intent to defraud or mislead the public,

   a) made the specification too broad, claiming more than that of which the patentee or the person through whom the patentee claims was the inventor, or

   b) in the specification, claimed that the patentee or the person through whom the patentee claims was the inventor of any material or substantial part of the invention patented of which the patentee was not the inventor, and to which the patentee had no lawful right.

2. The name and complete address of the patentee is Pfizer Ireland Pharmaceuticals, Pottery Road, Dun Laoghaire County, Dublin, Republic of Ireland.

3. The patentee disclaims the entirety of Claims 9, 11, 13, 19 and 21.

4. The patentee disclaims the entirety of Claim 1 with the exception of the following:

   1. The use of a compound of formula (I):

      ![Chemical Structure](image)

      wherein $R^1$ is H; C$_1$-C$_3$ alkyl; C$_1$-C$_3$ perfluoroalkyl; or C$_3$-C$_5$ cycloalkyl;

      $R^2$ is H; C$_1$-C$_6$ alkyl optionally substituted with C$_3$-C$_6$ cycloalkyl; C$_1$-C$_3$ perfluoroalkyl; or C$_3$-C$_6$ cycloalkyl;
R³ is C₁-C₈ alkyl optionally substituted with C₃-C₈ cycloalkyl; C₁-C₆ perfluoroalkyl; C₃-C₅ cycloalkyl; C₃-C₆ alkenyl; or C₃-C₆ alkynyl;

R⁴ is C₁-C₄ alkyl optionally substituted with OH, NR⁵R⁶, CN, CONR⁵R⁶ or CO₂R⁷; C₂-C₄ alkenyl optionally substituted with CN, CONR⁵R⁶ or CO₂R⁷; C₂-C₄ alkanoyl optionally substituted with NR⁵R⁶; (hydroxy) C₂-C₄ alkyl optionally substituted with NR⁵R⁶; (C₂-C₃ alkoxy) C₁-C₂ alkyl optionally substituted with OH or NR⁵R⁶; CONR⁵R⁶; CO₂R⁷; halo; NR⁵R⁶; NH₂SO₂NR⁵R⁶; NH₂SO₂R⁸; SO₂NR⁶R¹⁰; or phenyl, pyridyl, pyrimidinyl, imidazolyl, oxazolyl, thiazolyl, thienyl or triazolyl any of which is optionally substituted with methyl;

R⁵ and R⁶ are each independently H or C₁-C₄ alkyl, or together with the nitrogen atom to which they are attached form a pyrrolidinyl, piperidino, morpholino, 4-N(R¹¹)piperazinyl or imidazolyl group wherein said group is optionally substituted with methyl or OH;

R⁷ is H or C₁-C₄ alkyl;

R⁸ is C₁-C₃ alkyl optionally substituted with NR⁵R⁶;

R⁹ and R¹⁰ together with the nitrogen atom to which they are attached form a pyrrolidinyl, piperidino, morpholino or 4-N(R¹²)piperazinyl group wherein said group is optionally substituted with C₁-C₄ alkyl, C₁-C₃ alkoxy, NR¹²R¹⁴ or CONR¹³R¹⁴;

R¹¹ is H; C₁-C₃ alkyl optionally substituted with phenyl; (hydroxy)C₂-C₃ alkyl; or C₁-C₄ alkanoyl;

R¹² is H; C₁-C₆ alkyl; (C₁-C₃ alkoxy)C₂-C₆ alkyl; (hydroxy)C₂-C₆ alkyl; (R¹³R¹⁴N)C₂-C₆ alkyl; (R¹³R¹⁴NO)C₁-C₆ alkyl; CONR¹³R¹⁴; CSNR¹³R¹⁴; or C(NH)NR¹³R¹⁴; and

R¹³ and R¹⁴ are each independently H; C₁-C₄ alkyl; (C₁-C₃ alkoxy)C₂-C₄ alkyl; or (hydroxy)C₂-C₄ alkyl;

or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity, for the manufacture of a medicament for the curative or prophylactic treatment of an erectile dysfunction in man.

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5. The patentee disclaims the entirety of Claim 22 with the exception of the following:

   22. The use according to any one of claims 1 to 8 wherein the medicament is adapted for oral treatment.

6. The patentee disclaims the entirety of Claim 23 with the exception of the following:

   23. A pharmaceutical composition according to claim 10 which is adapted for oral treatment.

7. The patentee disclaims the entirety of Claim 24 with the exception of the following:

   24. A commercial package according to claim 20 wherein the active pharmaceutical ingredient is adapted for oral treatment.

Date: March 11, 2004.

Witness
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Commission Expires 12/11/2008

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Title:
PYRAZOLOPYRIMIDINONES FOR THE TREATMENT OF IMPOTENCE

Abstract

The use of a compound of formula (I) wherein
R1 is H; C1-C3 alkyl; C1-C3 perfluoroalkyl; or C2-C5 cycloalkyl; R2 is H; optionally substituted C1-C5 alkyl; C1-C3 perfluoroalkyl; or C2-C5 cycloalkyl; R3 is optionally substituted C1-C6 alkyl; R1-C6 perfluoroalkyl; C2-C5 cycloalkyl; C1-C4 alkyl; or C3-C6 alkynyl; R4 is optionally substituted C1-C4 alkyl; C2-C4 alkenyl, C2-C4 alkynyl, (hydroxy)C2-C4 alkyl or (C2-C3 alkoxy)C1-C2 alkyl; CONR2R4; CO2R7; halo; NR1R2R4; NSO2NR2R4; NOSR2R4; SO2NR2R4, or phenyl, pyridyl, pyrimidinyl, imidazolyl, oxazolyl, thiazolyl, thiophenyl or triazolyl any of which is optionally substituted with methyl; R5 and R6 are each independently H or C1-C4 alkyl, or together with the nitrogen atom to which they are attached form an optionally substituted pyridinyl, piperidino, morpholino, 4-N(R11)-piperazinyl or imidazolyl group; R7 is H or C1-C4 alkyl; R8 is optionally substituted C1-C4 alkyl; R9 and R10 together with the nitrogen atom to which they are attached form an optionally substituted pyridinyl, piperidino, morpholino or 4-N(R12)-piperazinyl group; R11 is H; optionally substituted C1-C4 alkyl; (hydroxy)C2-C3 alkyl; or C1-C4 alkenyl; R12 is H; optionally substituted C1-C4 alkyl; CONR13R14; CSNR13R14; or C(NH)NR13R14 and R13 and R14 are each independently H, C1-C4 alkyl; or substituted C2-C4 alkyl; or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity, for the manufacture of a medicament for the curative or prophylactic treatment of erectile dysfunction in a male animal, including man; a pharmaceutical composition for said treatment; and a method of said treatment of said male animal with said pharmaceutical composition or with said entity.
PYRAZOLOPYRIMIDINONES FOR THE TREATMENT OF IMPOTENCE

This invention relates to the use of a series of pyrazolo[4,3-d]pyrimidin-7-ones for the treatment of impotence.

Impotence can be defined literally as a lack of power, in the male, to copulate and may involve an inability to achieve penile erection or ejaculation, or both. More specifically, erectile impotence or dysfunction may be defined as an inability to obtain or sustain an erection adequate for intercourse. Its prevalence is claimed to be between 2 and 7% of the human male population, increasing with age, up to 50 years, and between 18 and 75% between 55 and 80 years of age. In the USA alone, for example, it has been estimated that there are up to 10 million impotent males, with the majority suffering from problems of organic rather than of psychogenic origin.

Reports of well-controlled clinical trials in man are few and the efficacy of orally administered drugs is low. Although many different drugs have been shown to induce penile erection, they are only effective after direct injection into the penis, e.g. intraurethrally or intracavernosally (i.c.), and are not approved for erectile dysfunction. Current medical treatment is based on the i.c injection of vasoactive substances and good results have been claimed with phenoxybenzamine, phentolamine, papaverine and prostaglandin E1, either alone or in combination; however, pain, priapism and fibrosis of the penis are associated with the i.c. administration of some of these agents. Potassium channel openers (KCO) and vasoactive intestinal polypeptide (VIP) have also been shown to be active i.c., but cost and stability issues could limit development of the latter. An alternative to the i.c. route is the use of glyceryl trinitrate (GTN) patches applied to the penis, which has been
shown to be effective but produces side-effects in both patient and partner.

As a general alternative to pharmacological intervention, a variety of penile prostheses has been used to assist achievement of an erection. The short term success rate is good, but problems with infection and ischaemia, especially in diabetic men, make this type of treatment a final option rather than first-line therapy.

The compounds of the invention are potent inhibitors of cyclic guanosine 3',5'-monophosphate phosphodiesterases (cGMP PDEs) in contrast to their inhibition of cyclic adenosine 3',5'-monophosphate phosphodiesterases (cAMP PDEs). This selective enzyme inhibition leads to elevated cGMP levels which, in turn, provides the basis for the utilities already disclosed for the said compounds in EP-A-0463756 and EP-A-0526004, namely in the treatment of stable, unstable and variant (Prinzmetal) angina, hypertension, pulmonary hypertension, congestive heart failure, atherosclerosis, conditions of reduced blood vessel patency e.g. post-percutaneous transluminal coronary angioplasty (post-PTCA), peripheral vascular disease, stroke, bronchitis, allergic asthma, chronic asthma, allergic rhinitis, glaucoma, and diseases characterised by disorders of gut motility, e.g. irritable bowel syndrome (IBS).

Unexpectedly, it has now been found that these disclosed compounds are useful in the treatment of erectile dysfunction. Furthermore the compounds may be administered orally, thereby obviating the disadvantages associated with i.c. administration. Thus the present invention concerns the use of a compound of formula (I):
wherein $R^1$ is H; C$_1$--C$_3$ alkyl; C$_1$--C$_3$ perfluoroalkyl; or C$_2$--C$_3$ cycloalkyl;
$R^2$ is H; C$_1$--C$_6$ alkyl optionally substituted with C$_1$--C$_4$ cycloalkyl; C$_1$--C$_3$ perfluoroalkyl; or C$_2$--C$_6$ cycloalkyl;
$R^3$ is C$_1$--C$_6$ alkyl optionally substituted with C$_1$--C$_4$ cycloalkyl; C$_1$--C$_6$ perfluoroalkyl; C$_3$--C$_5$ cycloalkyl; C$_3$--C$_6$ alkenyl; or C$_1$--C$_6$ alkynyl;
$R^4$ is C$_1$--C$_4$ alkyl optionally substituted with OH, NR$^5$R$^6$, CN, CONR$^5$R$^6$ or CO$_2$R$^7$; C$_2$--C$_4$ alkenyl optionally substituted with CN, CONR$^5$R$^6$ or CO$_2$R$^7$; C$_2$--C$_4$ alkanoyl optionally substituted with NR$^5$R$^6$; (hydroxy)C$_2$--C$_4$ alkyl optionally substituted with NR$^5$R$^6$; (C$_2$--C$_3$ alkoxy)C$_1$--C$_2$ alkyl optionally substituted with OH or NR$^5$R$^6$; CONR$^5$R$^6$; CO$_2$R$^7$; halo; NR$^5$R$^6$; NHSO$_2$NR$^5$R$^6$; NHSO$_2$R$^8$; SO$_2$NR$^5$R$^{10}$; or phenyl, pyridyl, pyrimidinyl, imidazolyl, oxazolyl, thiazolyl, thiienyl or triazolyl any of which is optionally substituted with methyl;
$R^5$ and $R^6$ are each independently H or C$_1$--C$_4$ alkyl, or together with the nitrogen atom to which they are attached form a pyrrolidinyl, piperidino, morpholino, 4-N(R$^{11}$)-piperazinyl or imidazolyl group wherein said group is optionally substituted with methyl or OH;
R' is H or C₁₋₄ alkyl;
R₈ is C₁₋₃ alkyl optionally substituted with NR₉R'⁰;
R² and R¹⁰ together with the nitrogen atom to which they are attached form a pyrrolidinyl, piperidino, morpholino or 4-N(R¹²) piperazinyl group wherein said group is optionally substituted with C₁₋₄ alkyl, C₁₋₃ alkoxy, NR¹³R¹⁴ or CONR¹³R¹⁴;
R¹¹ is H; C₁₋₃ alkyl optionally substituted with phenyl; (hydroxy)C₂₋₃ alkyl; or C₁₋₄ alkanoyl;
R¹² is H; C₁₋₄ alkyl; (C₁₋₃ alkoxy)C₂₋₃ alkyl; (hydroxy)C₂₋₃ alkyl; (R¹³R¹⁴N)C₁₋₄ alkyl; (R¹³R¹⁴NOC)C₁₋₄ alkyl; CONR¹³R¹⁴; CSNR¹³R¹⁴; or C(NH)NR¹³R¹⁴;
and R¹³ and R¹⁴ are each independently H; C₁₋₄ alkyl; (C₁₋₃ alkoxy)C₂₋₄ alkyl; or (hydroxy)C₂₋₄ alkyl;
or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity, for the manufacture of a medicament for the curative or prophylactic treatment of erectile dysfunction in a male animal, including man.

In the above definition, unless otherwise indicated, alkyl groups having three or more carbon atoms, alkenyl and alkynyl groups having four or more carbon atoms, alkoxy groups having three carbon atoms and alkanoyl groups having four carbon atoms may be straight chain or branched chain. Halo means fluoro, chloro, bromo or iodo.

The compounds of formula (I) may contain one or more asymmetric centres and thus they can exist as enantiomers or diastereoisomers. Furthermore, certain compounds of formula (I) which contain alkenyl groups
may exist as cis-isomers or trans-isomers. In each instance, the invention includes both mixtures and separate individual isomers.

The compounds of formula (I) may also exist in tautomeric forms and the invention includes both mixtures and separate individual tautomers.

The pharmaceutically acceptable salts of the compounds of formula (I) which contain a basic centre are, for example, non-toxic acid addition salts formed with inorganic acids such as hydrochloric, hydrobromic, sulphuric and phosphoric acid, with organo-carboxylic acids, or with organo-sulphonic acids. Compounds of formula (I) can also provide pharmaceutically acceptable metal salts, in particular non-toxic alkali metal salts, with bases. Examples include the sodium and potassium salts.

A preferred group of compounds of formula (I) is that wherein \( R^1 \) is H, methyl or ethyl; \( R^2 \) is \( C_1 - C_3 \) alkyl; \( R^3 \) is \( C_2 - C_5 \) alkyl or allyl; \( R^4 \) is \( C_1 - C_2 \) alkyl optionally substituted with \( \text{OH} \), \( \text{NR}^5 \text{R}^6 \), \( \text{CN} \), \( \text{CONR}^5 \text{R}^6 \) or \( \text{CO}_2 \text{R}^7 \); acetyl optionally substituted with \( \text{NR}^5 \text{R}^6 \); hydroxyethyl optionally substituted with \( \text{NR}^2 \text{R}^6 \); ethoxymethyl optionally substituted with \( \text{OH} \) or \( \text{NR}^5 \text{R}^6 \); \( \text{CH} = \text{CHCN} \); \( \text{CH} = \text{CHN} \text{R}^5 \text{R}^6 \); \( \text{CH} = \text{CHCO}_2 \text{R}^7 \); \( \text{CONR}^5 \text{R}^6 \); \( \text{CO}_2 \text{H} \); Br; \( \text{NR}^5 \text{R}^6 \); \( \text{NHSO}_2 \text{NR}^5 \text{R}^6 \); \( \text{NHSO}_2 \text{R}^6 \); \( \text{SO}_2 \text{NR}^5 \text{R}^6 \); or pyridyl or imidazolyl either of which is optionally substituted with methyl; \( R^5 \) and \( R^6 \) are each independently H, methyl or ethyl, or together with the nitrogen atom to which they are attached form a piperidino, morpholino, 4-\( \text{N} (\text{R}^{11}) \)-piperazinyl or imidazolyl group wherein said group is optionally substituted with methyl or \( \text{OH} \); \( R^7 \) is H or t-butyl; \( R^8 \) is methyl or \( \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{NR}^5 \text{R}^6 \); \( R^9 \) and \( R^{10} \) together with the nitrogen atom to which they are attached form a piperidino or 4-\( \text{N} (\text{R}^{12}) \)-piperazinyl group wherein said group is optionally substituted with \( \text{NR}^{13} \text{R}^{14} \) or \( \text{CONR}^{13} \text{R}^{14} \); \( R^{11} \) is H, methyl, benzyl, 2-
hydroxyethyl or acetyl; \( R^{12} \) is \( H, \ C_1-\ C_3, \) alkyl, (hydroxy)\( C_2-\ C_3, \) alkyl, CSNR\(^{13}\)R\(^{14} \) or C(NH)NR\(^{13}\)R\(^{14} \); and \( R^{13} \) and \( R^{14} \) are each independently \( H \) or methyl.

A more preferred group of compounds of formula (I) is that wherein \( R^{1} \) is methyl or ethyl; \( R^{2} \) is \( C_1-\ C_3, \) alkyl; \( R^{3} \) is ethyl, n-propyl or allyl; \( R^{4} \) is \( CH_2NR^{5}R^{6}, \) COCH\(_2\)NR\(^{5}\)R\(^{6}, \) CH(\( OH\))CH\(_2\)NR\(^{5}\)R\(^{6}, \) CH\(_2\)OCH\(_2\)CH\(_3, \) CH\(_2\)OCH\(_2\)CH\(_2\)OH, CH\(_2\)OCH\(_2\)CH\(_3\)NR\(^{5}\)R\(^{6}, \) CH=CHCON(\( CH\))\(_2, \) CH=CHCO\(_2\)R\(^{7}, \) CONR\(^{5}\)R\(^{6}, \) CO\(_2\)H, Br, NHSO\(_2\)NR\(^{5}\)R\(^{6}, \) NHSO\(_2\)CH\(_2\)CH\(_2\)CH\(_3\)NR\(^{5}\)R\(^{6}, \) SO\(_2\)NR\(^{5}\)R\(^{10}, \) 2-pyridyl, 1-imidazolyl or 1-methyl-2-imidazolyl; \( R^{5} \) and \( R^{6} \) together with the nitrogen atom to which they are attached form a piperidino, 4-hydroxypiperidino, morpholino, 4-N(\( R^{11} \))-piperazinyl or 2-methyl-1-imidazolyl group; \( R^{7} \) is \( H \) or t-butyl; \( R^{9} \) and \( R^{10} \) together with the nitrogen atom to which they are attached form a 4-carbamoylpiperidino or 4-N(\( R^{12} \))-piperazinyl group; \( R^{11} \) is \( H, \) methyl, benzyl, 2-hydroxyethyl or acetyl; and \( R^{12} \) is \( H, \ C_1-\ C_3, \) alkyl, 2-hydroxyethyl or CSNH\(_2\).

A particularly preferred group of compounds of formula (I) is that wherein \( R^{1} \) is methyl or ethyl; \( R^{2} \) is n-propyl; \( R^{3} \) is ethyl, n-propyl or allyl; \( R^{4} \) is COCH\(_2\)NR\(^{5}\)R\(^{6}, \) CONR\(^{5}\)R\(^{6}, \) SO\(_2\)NR\(^{5}\)R\(^{10}, \) or 1-methyl-2-imidazolyl; \( R^{5} \) and \( R^{6} \) together with the nitrogen atom to which they are attached form a morpholino or 4-N(\( R^{11} \))-piperazinyl group; \( R^{9} \) and \( R^{10} \) together with the nitrogen atom to which they are attached form a 4-N(\( R^{12} \))-piperazinyl group; \( R^{11} \) is methyl or acetyl; and \( R^{12} \) is \( H, \) methyl, 2-propyl or 2-hydroxyethyl.

Especially preferred individual compounds of the invention include:

5-(2-ethoxy-5-morpholinoacetylphenyl)-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-(5-morpholinoacetyl-2-n-propoxyphenyl)-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

A preliminary investigation was carried out with a view to isolating and characterising the cyclic nucleotide PDEs of human corpus cavernosum, relaxation of which leads to penile erection. Studies of substrate specificity, response to activators and inhibitor sensitivity, have demonstrated that human corpus cavernosum contains three distinct PDE enzymes.
Methods

Fresh frozen human penis was obtained from IIAM (Pennsylvania). Tissue was thawed at room temperature, the corpus cavernosum was dissected from the penis to yield approximately 2-4 g of tissue and the following isolation protocol was followed. Tissue was coarsely chopped in ice-cold isotonic buffer (35 ml) containing 250 mM sucrose, 1 mM EDTA, 0.5 mM PMSF and 20 mM HEPES, pH 7.2, and the mixture subjected to brief (1 min.) treatment with a Silversen mixer/emulsifier.

Homogenates were prepared using homogeniser tubes with teflon pestles and soluble fraction was prepared by centrifugation at 100,000 x g for 60 min. at 4°C. 10 ml of high speed supernatant was applied to a Pharmacia Mono Q anion exchange column (1 ml bed volume) equilibrated with buffer containing 1 mM EDTA, 0.5 mM PMSF and 20 mM HEPES, pH 7.2 (chromatography buffer). The column was then washed with 5 bed volumes of chromatography buffer, after which PDEs were eluted using a continuous gradient of 0-500 mM NaCl (total volume 35 ml) and 1 ml fractions collected.

Column fractions were assayed for PDE activity using 500 nM cGMP or 500 nM cAMP as substrate. cAMP PDE activity was also determined in the presence of 1 μM unlabelled cGMP and the PDE activity of selected fractions was determined in the presence of 10 mM CaCl₂ and 10 units/ml bovine brain calmodulin. Appropriate fractions were pooled and stored at 4°C during the course of the study.

Inhibition studies were performed using a substrate concentration of 500 nM throughout. All inhibitors were dissolved in DMSO and concentration-response curves were constructed over the range 3 x 10⁻¹⁰ to 1 x 10⁻⁴ M in half log increments. IC₅₀ values were calculated using the sigmoidal curve fitting algorithm of biostat.
Results

Human corpus cavernosum soluble PDEs were separated into three distinct fractions of activity. The first, fraction I, (designated by order of elution) represents the major PDE present and is highly selective for cGMP as substrate. This fraction was found to be insensitive to stimulation by calcium/calmodulin and was classified as PDE_v.

Fraction II hydrolyses cGMP and cAMP, with the latter activity being stimulated in the presence of cGMP, and is classified as PDE_{II}, whilst fraction III is cAMP selective and this activity is inhibited in the presence of cGMP, consistent with PDE_{III} activity.

In order to further characterise the PDE isoenzymes present in the tissue, studies were performed using a variety of inhibitors. Inhibitor studies with fractions I and II were performed using cGMP as substrate, whilst fraction III studies utilised cAMP. These studies confirmed that fraction I corresponds to PDE_v, whilst fraction III was clearly identified as PDE_{III}; fraction II (PDE_{II}) was relatively insensitive to all the inhibitors tested.

In summary, the above investigation identified three PDE isoenzymes in human corpus cavernosum tissue. The predominant PDE is the cGMP-specific PDE_v, whilst cGMP-stimulated cAMP PDE_{II} and cGMP-inhibited cAMP PDE_{III} are also present.

The compounds of the invention have been tested in vitro and found to be potent and selective inhibitors of the cGMP-specific PDE_v. For example, one of the especially preferred compounds of the invention has an IC_{50} = 6.8 nM v. the PDE_v enzyme, but demonstrates only weak inhibitory activity against the PDE_{II} and PDE_{III} enzymes with IC_{50} = >100 μM and 34 μM respectively. Thus relaxation of the corpus cavernosum tissue and
consequent penile erection is presumably mediated by elevation of cGMP levels in the said tissue, by virtue of the PDE inhibitory profile of the compounds of the invention.

Furthermore, none of the compounds of the invention tested in rat and dog, both intravenously (i.v.) and orally (p.o.) at up to 3 mg/Kg, has shown any overt sign of adverse acute toxicity. In mouse, no deaths occurred after doses of up to 100 mg/Kg i.v.. Certain especially preferred compounds showed no toxic effects on chronic p.o. administration to rat at up to 10 mg/Kg and to dog at up to 20 mg/Kg.

In man, certain especially preferred compounds have been tested orally in both single dose and multiple dose volunteer studies. Moreover, patient studies conducted thus far have confirmed that one of the especially preferred compounds induces penile erection in impotent males.

Although the compounds of the invention are envisaged primarily for the treatment of erectile dysfunction or male sexual dysfunction, they may also be useful for the treatment of female sexual dysfunction including orgasmic dysfunction related to clitoral disturbances.

Generally, in man, oral administration of the compounds of the invention is the preferred route, being the most convenient and avoiding the disadvantages associated with i.c. administration. A preferred dosing regimen for a typical man is 5 to 75 mg of compound three times daily. In circumstances where the recipient suffers from a swallowing disorder or from impairment of drug absorption after oral administration, the drug may be administered parenterally, e.g. sublingually or buccally.

For veterinary use, a compound of formula (I) or a non-toxic salt thereof is administered as a suitably acceptable formulation in accordance with
normal veterinary practice and the veterinary surgeon will determine the dosing regimen and route of administration which will be most appropriate for a particular male animal.

Thus the invention includes a pharmaceutical composition for the curative or prophylactic treatment of erectile dysfunction in a male animal, including man, comprising a compound of formula (I), or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable diluent or carrier.

There is further provided a process for the preparation of a pharmaceutical composition for the curative or prophylactic treatment of erectile dysfunction in a male animal, including man, comprising formulating a compound of formula (I), or a pharmaceutically acceptable salt thereof, with a pharmaceutically acceptable diluent or carrier.

The invention also provides a method of treating a male animal, including man, to cure or prevent erectile dysfunction which comprises treating said male animal with an effective amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity.

In a further aspect, the invention includes the use of a cGMP PDE inhibitor, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity, for the oral treatment of erectile dysfunction in man.

The invention also includes a method of orally treating man to cure or prevent erectile dysfunction, which comprises treatment with an orally effective amount of a cGMP PDE inhibitor, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity.
The invention also extends to a commercial package containing, as active pharmaceutical ingredient, a compound of the formula I or a pharmaceutically acceptable salt thereof, together with instructions for its use for the curative or prophylactic treatment of erectile dysfunction in a male animal.

Moreover, the invention includes the use of a cGMP PDE inhibitor, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity, for the manufacture of a medicament for the curative or prophylactic oral treatment of erectile dysfunction in man.
THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. The use of a compound of formula (I):

\[
\text{\begin{align*}
&\text{R}^1 \text{ is } H, \ C_1-\ C_3 \text{ alkyl, } C_1-\ C_3 \text{ perfluoroalkyl, or } \\
&\text{C}_3-\ C_5 \text{ cycloalkyl;}
\end{align*}}
\]
\[
\text{R}^2 \text{ is } H, \ C_1-\ C_6 \text{ alkyl optionally substituted with } \\
\text{C}_3-\ C_6 \text{ cycloalkyl, } C_1-\ C_3 \text{ perfluoroalkyl, or } C_3-\ C_6 \\
\text{cycloalkyl;}
\]
\[
\text{R}^3 \text{ is } C_1-\ C_6 \text{ alkyl optionally substituted with } C_3-\ C_6 \\
\text{cycloalkyl, } C_1-\ C_6 \text{ perfluoroalkyl, } C_3-\ C_5 \text{ cycloalkyl, } \\
\text{C}_3-\ C_6 \text{ alkenyl, or } C_3-\ C_6 \text{ alkynyl; } \text{R}^4 \text{ is } C_1-\ C_4 \text{ alkyl } \\
\text{optionally substituted with OH, } \text{NR}^5\text{R}^6, \text{CN, CONR}^5\text{R}^6 \\
\text{or } \text{CO}_2\text{R}^7; \ C_2-\ C_4 \text{ alkenyl optionally substituted with } \text{CN, CONR}^5\text{R}^6 \\
\text{or } \text{CO}_2\text{R}^7; \ C_2-\ C_4 \text{ alkanoyl optionally substituted with } \\
\text{NR}^5\text{R}^6; \ (\text{hydroxy})\text{C}_2-\text{C}_4 \text{ alkyl } \\
\text{optionally substituted with } \text{NR}^5\text{R}^6; \ (\text{C}_2-\text{C}_3 \text{ alkoxy}) \\
\text{C}_1-\text{C}_2 \text{ alkyl optionally substituted with OH or } \\
\text{NR}^5\text{R}^6, \text{CONR}^5\text{R}^6, \text{CO}_2\text{R}^7, \text{halo, } \text{NR}^5\text{R}^6, \text{NHSO}_2\text{NR}^5\text{R}^6, \\
\text{NHSO}_2\text{R}^8, \text{SO}_2\text{NR}^9\text{R}^{10}, \text{or phenyl, pyridyl.}
\end{align*}}
\]
pyrimidinyl, imidazolyl, oxazolyl, thiazolyl, thienyl or triazolyl any of which is optionally substituted with methyl; R⁵ and R⁶ are each independently H or C₁-C₄ alkyl, or together with the nitrogen atom to which they are attached form a pyrrolidinyl, piperidino, morpholino, 4-N(R¹¹)-piperazinyl or imidazolyl group wherein said group is optionally substituted with methyl or OH;
R⁷ is H or C₁-C₄ alkyl;
R⁸ is C₁-C₃ alkyl optionally substituted with NR⁵R⁶;
R⁹ and R¹⁰ together with the nitrogen atom to which they are attached form a pyrrolidinyl, piperidino, morpholino or 4-N(R¹²)-piperazinyl group wherein said group is optionally substituted with C₁-C₄ alkyl, C₁-C₃ alkoxy, NR¹³R¹⁴ or CONR¹³R¹⁴;
R¹¹ is H, C₁-C₃ alkyl optionally substituted with phenyl, (hydroxy)C₂-C₃ alkyl, or C₁-C₄ alkanoyl;
R¹² is H, C₁-C₆ alkyl; (C₁-C₃ alkoxy)C₂-C₆ alkyl, (hydroxy)C₂-C₆ alkyl; (R¹³R¹⁴N)C₂-C₆ alkyl; (R¹³R¹⁴NOC)C₁-C₆ alkyl; CONR¹³R¹⁴, CSNR¹³R¹⁴; or C(NH)NR¹³R¹⁴;
and R¹³ and R¹⁴ are each independently H, C₁-C₄ alkyl;
(C₁-C₃ alkoxy)C₂-C₄ alkyl, or (hydroxy)C₂-C₄ alkyl, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity, for the manufacture of a medicament for the curative or prophylactic
treatment of an erectile dysfunction in a male animal or sexual dysfunction in a female animal.

2. The use according to claim 1 wherein in the compound of formula (I) \( R^1 \) is H, methyl or ethyl; \( R^2 \) is C\(_1\)C\(_3\) alkyl; \( R^3 \) is C\(_2\)-C\(_3\) alkyl or allyl; \( R^4 \) is C\(_1\)-C\(_2\) alkyl optionally substituted with OH, NR\(^5\)R\(^6\), CN, CONR\(^5\)R\(^6\) or CO\(_2\)R\(^7\); acetyl optionally substituted with NR\(^5\)R\(^6\); hydroxyethyl optionally substituted with NR\(^5\)R\(^6\); ethoxymethyl optionally substituted with OH or NR\(^5\)R\(^6\); CH-CHCN, CH-CHCONR\(^5\)R\(^6\); CH=CHCO\(_2\)R\(^7\), CONR\(^5\)R\(^6\), CO\(_2\)H, Br, NR\(^5\)R\(^6\), NHSO\(_2\)NR\(^5\)R\(^6\), NHSO\(_2\)R\(^8\), SO\(_2\)NR\(^9\)R\(^{10}\); or pyridyl or imidazolyl either of which is optionally substituted with methyl; \( R^5 \) and \( R^6 \) are each independently H, methyl or ethyl, or together with the nitrogen atom to which they are attached form a piperidino, morpholino, 4-N(R\(^{11}\))-piperazinyl or imidazolyl group wherein said group is optionally substituted with methyl or OH; \( R^7 \) is H or t-butyl; \( R^8 \) is methyl or CH\(_2\)CH\(_2\)CH\(_2\)NR\(^5\)R\(^6\), \( R^9 \) and \( R^{10} \) together with the nitrogen atom to which they are attached form a piperidino or 4-N(R\(^{12}\))-piperazinyl group wherein said group is optionally substituted with NR\(^{13}\)R\(^{14}\) or CONR\(^{13}\)R\(^{14}\); \( R^{11} \) is H, methyl, benzyl, 2-hydroxyethyl or acetyl, \( R^{12} \) is H, C\(_1\)-C\(_3\) alkyl, (hydroxy)C\(_2\)-C\(_3\) alkyl, CSNR\(^{13}\)R\(^{14}\) or C(NH)NR\(^{13}\)R\(^{14}\); and \( R^{13} \) and \( R^{14} \) are each independently H or methyl.

3. The use according to claim 2 wherein in the compound of formula (I) \( R^1 \) is methyl or ethyl; \( R^2 \) is C\(_1\)-C\(_3\) alkyl; \( R^3 \) is ethyl, n-propyl or allyl; \( R^4 \) is CH\(_2\)NR\(^5\)R\(^6\),
COCH₂NR⁵R⁶, CH(OH)CH₂NR⁵R⁶, CH₂OCH₂CH₃, CH₂OCH₂CH₂OH, CH₂OCH₂CH₂NR⁵R⁶, CH-CHCON(CH₃)₂, CH-CHCO₂R⁷, CONR⁵R⁶, CO₂H, Br, NH₂SO₄ NR⁹R¹₀, NH₂SO₂CH₂CH₂CH₂NR⁵R⁶, SO₂NR⁹R¹₀, 2-pyridyl, 1-imidazolyl or 1-methyl-2-imidazolyl, R⁵ and R⁶ together with the nitrogen atom to which they are attached form a piperidino, 4-hydroxypiperidino, morpholino, 4-N(R¹¹)piperazinyl or 2-methyl-1-imidazolyl group; R⁷ is H or t-butyl; R⁹ and R¹₀ together with the nitrogen atom to which they are attached form a 4-carbamoylpiperidino or 4-N(R¹²)piperazinyl group; R¹¹ is H, methyl, benzyl, 2-hydroxyethyl or acetyl; and R¹² is H, C₁-C₃ alkyl, 2-hydroxyethyl or CSNH₂.

4. The use according to claim 3 wherein in the compound of formula (I) R¹ is methyl or ethyl; R² is n-propyl; R³ is ethyl, n-propyl or allyl; R⁴ is COCH₂NR⁵R⁶, CONR⁵R⁶, SO₂NR⁹R¹₀ or 1-methyl-2-imidazolyl; R⁵ and R⁶ together with the nitrogen atom to which they are attached form a morpholino or 4-N(R¹¹)piperazinyl group; R⁹ and R¹₀ together with the nitrogen atom to which they are attached form a 4-N(R¹²)-piperazinyl group; R¹¹ is methyl or acetyl; and R¹² is H, methyl, 2-propyl or 2-hydroxyethyl.

5. The use according to claim 4 wherein the compound of formula (I) is selected from:

5-(2-ethoxy-5-morpholinoacetylphenyl)-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

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5-(5-morpholinoacetyl-2-n-propoxyphenyl)-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-[2-ethoxy-5-(4-methyl-1-piperazinylsulphonyl)-phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-[2-allyloxy-5-(4-methyl-1-piperazinylsulphonyl)-phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-[2-ethoxy-5-[(4-(2-propyl)-1-piperazinylsulphonyl)-phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-[2-ethoxy-5-[(4-(2-hydroxyethyl)-1-piperazinylsulphonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-{5-[4-(2-hydroxyethyl)-1-piperazinylsulphonyl]-2-n-propoxyphenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-[2-ethoxy-5-(4-methyl-1-piperazinylcarbonyl)-phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one; and

5-[2-ethoxy-5-(1-methyl-2-imidazolyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one, or a pharmaceutically acceptable salt thereof.

6. The use according to claim 4 wherein the compound of formula (I) is 5-(2-ethoxy-5-morpholinoacetylphenyl)-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one or a pharmaceutically acceptable salt thereof.

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7. The use according to claim 4 wherein the compound of
formula (I) is 5-[2-ethoxy-5-(4-methyl-1-piperazinyl-
sulphonyl)-phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-
pyrazolo[4,3-d]pyrimidin-7-one or a pharmaceutically
acceptable salt thereof.

8. The use according to any one of claims 1 to 7
wherein the said male animal is man.

9. The use according to any one of claims 1 to 7
wherein the said female animal is woman.

10. A pharmaceutical composition for the curative or
prophylactic treatment of erectile dysfunction in a male
animal, including man, comprising a compound of formula (I)
according to any one of claims 1 to 7, or a pharmaceutically
acceptable salt thereof, together with a pharmaceutically
acceptable diluent or carrier.

11. A pharmaceutical composition for the curative or
prophylactic treatment of sexual dysfunction in a female
animal, including woman, comprising a compound of formula (I)
according to any one of claims 1 to 7, or a pharmaceutically
acceptable salt thereof, together with a pharmaceutically
acceptable diluent or carrier.

12. A process for the preparation of a pharmaceutical
composition for the curative or prophylactic treatment of

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erectile dysfunction in a male animal comprising formulating a compound of formula (I) according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, with a pharmaceutically acceptable diluent or carrier.

13. A process for the preparation of a pharmaceutical composition for the curative or prophylactic treatment of sexual dysfunction in a female animal comprising formulating a compound of formula (I) according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, with a pharmaceutically acceptable diluent or carrier.

14. A process according to claim 12 wherein the said male animal is man.

15. A process according to claim 13 wherein the said female animal is woman.

16. The use of a compound of formula (I) according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, for the curative or prophylactic treatment of erectile dysfunction in a male animal.

17. The use of a compound of formula (I) according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, for the curative or prophylactic treatment of sexual dysfunction in a female animal.
18. The use of a compound of formula (I) according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, for the curative or prophylactic treatment of erectile dysfunction in man.

19. The use of a compound of formula (I) according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, for the curative or prophylactic treatment of sexual dysfunction in woman.

20. A commercial package containing, as active pharmaceutical ingredient, a compound of formula (I) according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, together with instructions for its use for the curative or prophylactic treatment of erectile dysfunction in a male animal.

21. A commercial package containing, as active pharmaceutical ingredient, a compound of formula (I) according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, together with instructions for its use for the curative or prophylactic treatment of sexual dysfunction in a female animal.

22. The use according to any one of claims 1 to 9 wherein the medicament is adapted for oral treatment.

23. A pharmaceutical composition according to claim 10
or 11 which is adapted for oral treatment.

24. A commercial package according to claim 20 or 21 wherein the active pharmaceutical ingredient is adapted for oral treatment.

25. The use of a cGMP PDE inhibitor, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity, for the oral treatment of erectile dysfunction in man.

26. The use of a cGMP PDE inhibitor, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity, for the manufacture of a medicament for the curative or prophylactic oral treatment of erectile dysfunction in man.

27. The use according to claim 25 or 26 wherein the inhibitor is a cGMP PDEγ inhibitor.

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