Cayman Pharma s.r.o.
ul. Práce 657, 277 11 NERATOVICE
CZECH REPUBLIC
Tel. +420 315 665 360

# CERTIFICATE OF QUALITY

No.:1106D181 

**CUSTOMER:** A.C.E.F. SPA / METALPHARMACEUTICAL IND. SL.

**PRODUCT:** **ALPROSTADIL**
7-{(1R,2R,3R*)-3-Hydroxy-2-[€-(3S)-3-hydroxy-1-octenyl]-5-oxocyclo-pentyl}-heptanoic acid
$C_{20}H_{34}O_5$ = 354.5
CAS – 745-65-3

**BATCH No.:** 1012S02

**PRODUCTION DATE:** 12/2010

**ATEST No.:** A100269

**QUANTITY:** 1.0 g

**RE-TEST DATE:** 12/2013

| TEST METHOD: | SPECIFICATION: | RESULT: |
|---|---|---|
| 1. Identification | | |
| a) by IR spectrum | IR spectrum of CRS EPh | IR spectrum conforms |
| b) by RT WS HPLC | RT of WS HPLC | RT conforms |
| 2. Description | | |
| a) visual | a white or off white powder | a white powder |
| b) by absorbance | the sum of absorbance NMT 0.150 | 0.016 |
| 3. Assay (HPLC, calculated with reference to anhydrous substance, abs. %): | 96.0 - 102.5 % * | 100.0 % |
| 4. HPLC purity (EPh HPLC method, norm. %): | | |
| a) $PGA_1$ | NMT 1.3 % | < 0.1 % |
| b) $PGB_1$ | NMT 0.1 % | not detected |
| other impurities | | |
| c) 15-keto-$PGE_1$ | NMT 0.1 % | not detected |
| d) 15(R)-$PGE_1$ | NMT 0.1 % | not detected |
| e) 11(β)-$PGE_1$ | NMT 0.5 % | not detected |
| f) 8-iso-$PGE_1$ | NMT 0.1 % | not detected |
| g) $PGE_2$ | NMT 0.5 % | not detected |
| h) 5-trans-$PGE_2$ | NMT 0.5 % | not detected |
| i) $PGE_1$ ethylester | NMT 0.3 % | not detected |

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|---|---|---|
| j) $PGE_1$ isopropylester | NMT 0.3 % | not detected |
| k) TPPO | NMT 0.5 % | not detected |
| l) other impurities single | NMT 0.1 % | not detected |
| m) other impurities total | NMT 1.5 % | not detected |
| 5. HPLC purity (in-house HPLC method, mol. %): | | |
| a) 14-methyl-$PGE_1$ | NMT 0.5 % | not detected |
| b) $PGD_1$ | NMT 0.1 % | < 0.1 % |
| c) 4-trans-$PGE_2$ | NMT 0.5 % | not detected |
| d) 6-trans-$PGE_2$ | NMT 0.5 % | < 0.1 % |
| e) 13,14-dihydro-$PGE_1$ | NMT 0.5 % | not detected |
| f) Dimer | NMT 0.1 % | not detected |
| 6. Water content | NMT 0.5 % | < 0.1 % |
| 7. Residue on ignition | NMT 0.5 % | 0.1 % |
| 8. Spec. optic rotation (c=1, ethanol) $[\alpha]_D^{20}$ | -70.0° to -60.0° | - 67.4° |
| 9. Content of solvents (USP GC method): | | |
| a) Acetone | NMT 0.5 % | < 0.5 % |
| b) Chloroform | NMT 10 ppm | not detected |
| c) Tetrahydrofurane | NMT 10 ppm | not detected |
| d) *n*-Hexane | NMT 290 ppm | not detected |
| e) Ethyl acetate | NMT 300 ppm | not detected |
| f) *tert.* Butyl methyl ether | NMT 300 ppm | not detected |
| g) Methyl alcohol | NMT 300 ppm | not detected |
| h) *tert.* Butyl alcohol | NMT 300 ppm | not detected |
| i) Isopropyl alcohol | NMT 300 ppm | not detected |
| j) *n*-Heptane | NMT 300 ppm | not detected |
| k) *n*-Pentane | NMT 300 ppm | < 300 ppm |
| *l)* Dichloromethane | NMT 5 ppm | not detected |
| *m)* Toluene | NMT 20 ppm | not detected |

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| TEST METHOD: | SPECIFICATION: | RESULT: |
|---|---|---|
| 11. Heavy metals: | | |
| a) rhodium content | NMT 20 ppm | 11 ppm |
| b) chromium content | NMT 20 ppm | < 5 ppm |
| 12. Microbial testing (CFU/g): | | |
| Total aerobic microbial count | NMT $10^3$ ($2x10^3$)/1 g | 10 |
| Total yeasts & moulds count | NMT $10^2$ ($2x10^2$)/1 g | < 5 |
| Specific microorganisms: | | |
| - Bile-tolerant $G^-$ bacteria | 0/1 g | not found |
| - Salmonella sp. | 0/1 g | not found |
| - Escherichia coli | 0/1 g | not found |
| - Staphylococcus aureus | 0/1 g | not found |
| - Pseudomonas aeruginosa | 0/1 g | not found |

* 95.0 - 102.5 % at re-testing

**RESULT: Product has been manufactured in accordance with principles of GMP as detailed in ICH Guideline Q7A**
**Product conforms to the specification in SBR380K/03, App. No. 2**
**Note: Product conforms to the specification in Ph. Eur. 7., harmonised method.**

AUTHORIZED PERSON * OPRÁVNĚNÁ OSOBA
Cayman Pharma s.r.o.
QA
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Ing. Jana Hartmanová
Authorized Person
(pursuant to EudraLex 4/II, §2.14 & §2.22.1)

Date: Jun. 27, 2011