

PRIME EUROPEAN THERAPEUTICALS SpA - Sole Shareholder

Registered Office: Viale Bance Maria, 25 - 20122 Milatin - Administrative Office: Viale It Maria, 86 - 26900 Lcdi
for Construction and General International Construction of the Construction of the Construction of the Cons

CERTIFICATE OF ANALYSIS

Product:

SIROLIMUS

| | SINOMINO | | | | | |
|---|--|-------------|--|---------------|------------------|--|
| _ | MANUFACTURING SITE: EUTICALS SpA – Via Volturno 41/43 – 20089 Rozzano (MI) | | | | | |
| | | E1400162A | | Code: | 30124 | |
| | | ebruary 201 | | Re-test date: | February 2019 | |
| | TEST | | SPECIFICATIONS | | ANALYSIS VALUE | |
| | Characters: | | | | 1 | |
| | - Appearance | | White to almost-white powder. | | complies | |
| | - Solubility | | Soluble in ether, acetone, methanol; slightly soluble in practically insoluble in water | n-hexane; | complies | |
| | Identification: | 1 | | | | |
| | - HPLC | | the RT of the main peak of the product under analysis neconcordant with that of the standard | nust be | complies | |
| | - IR spectrum | | comply with the standard material | | complies | |
| | Loss on Drying (TGA): | | not more than 1.0 % | | not detectable | |
| | Sulfated ash | | not more than 0.1 % | | 0.0 % | |
| | Specific optical rotation | | - 140 to -160° (on anhydrous and solvent free basis, 10 methanol) | mg/mL in | - 149° | |
| | Heavy metals | Į. | not more than 20 ppm | | less than 20 ppm | |
| | Water (K.F.) | b | not more than 0.5 % | 1 | 0.2 % | |
| | Sirolimus isomer (rrt 1.1) | 1 | report the found value | | 2.5 % | |
| | Assay (HPLC) | | between 96.5 % and 102.0 % (on anhydrous basis, expressed as sum of Sirolimus and | Sirolimus | 100.4 % | |
| | Related substances (HPLC): | 1 | somer) | | | |
| | - 27-O-demethyl-rapamycin | 1 | not more than 0.5 % | İ | 0.2 % | |
| | - 16-O-demethyl-rapamycin | 1 | not more than 0.5 % | 1 | 0.1 % | |
| | - Prolylrapamycin | 1 | not more than 0.5 % | 1 | 0.2 % | |
| | - 27-demethoxyrapamycin | r | not more than 0.2 % | 1 | not detectable | |
| | - 40-oxorapamycin | l r | not more than 0.2 % | | 0.1 % | |
| | - 11-ethyl- & 23-ethy-rapam. | | not more than 0.5 % | 1 | 0.2 % | |
| | - Any other | | not more than 0.2 % each | | 0.1 % | |
| - | - Total (specified+unspecified) | n n | of more than 1.5 % | | 0.8 % | |
| | Residual solvents: | | | | -10 | |
| | - Acetone | n | ot more than 500 ppm | | 3 ppm | |
| | - Ethyl ether | n | ot more than 500 ppm | 1 | not detectable | |
| | TAMC | n | ot more than 100 ufc/g | | < 10 ufc/g | |
| | TYMC | n | ot more than 10 ufc/g | | < 10 ufc/g | |
| | | 1 | | | - To didg | |

Milan - September 5, 2016

This is to certify that the batch was manufactured according to c-GMP

DR/SSA MICHELA RAMP

Qualified

Q.C. Manager

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