10447-SIROLIMUS

1. IDENTIFICATION OF THE SUBSTANCE OR PREPARATION.

1.1 Identification of the substance or preparation.

Name: Sirolimus
Bulk code: 10447

1.2 Synonims.

Rapamycin

2. DESCRIPTION

Appearance: Solid poder.
Colour: White.

3. COMPOSITION/INFORMATION ON COMPONENTS.

Formula: $C_{51}H_{79}NO_{13}$
CAS No.: 53123-88-9
Molecular weight: 914.17 g/mol

4. PHYSICO-CHEMICAL DATA.

For more information, see the analysis report.

Solubility: Soluble in acetonitrile and methanol, insoluble in water.
Melting point: 184ºC

5. PROPERTIES/USES.

ACTIVE PHARMACEUTICAL INGREDIENT.

Sirolimus is a macrocyclic lactone originally produced by the S. hygroscopicus bacterium and initially identified as an antifungal agent. Subsequently, it was found to possess a potent immunosuppressive activity, so it began to be used to prevent kidney transplant rejection.

Sirolimus binds to the specific cytosolic protein FKPB-12 to form the complex FKPB 12-sirolimus, which inhibits mTOR activation. As a consequence, lymphocyte activation is inhibited through blocking several specific signal transduction pathways. On the other hand, sirolimus has an inhibitory effect on VEGF and the cell cycle, which explains its usefulness as an antineoplastic agent by inhibiting the angiogenesis and proliferation of tumour cells.

These properties have led to its being used in several neoplasms such as visceral angiomyolipomas, lymphangioleiomyomatosis or facial angiofibromas associated with TSC.

Sirolimus is an immunosuppressive drug with a mechanism of action that is distinct from that of tacrolimus and cyclosporine, with similar efficacy to cyclosporine. In kidney transplants, its ability to decrease the incidence of acute rejection at 6 and 12 months has been demonstrated when combined with cyclosporine and corticosteroids, although no significant changes in graft and patient survival have been observed.

Sirolimus is approved by the FDA for the prevention of acute kidney transplant rejection by co- administering it with cyclosporine and corticosteroids. Due to the interaction between cyclosporine and sirolimus, both should be administered at least 4 hours apart. Food may affect sirolimus absorption by increasing tmax and AUC. It should always be taken alone or with meals to minimise absorption variability.

The latest studies relate it to the treatment of facial angiofibromas in individuals with tuberous sclerosis.

6. DOSAGE.

Orally:

- In capsules for the prophylaxis of organ rejection in adult patients with low-to-moderate immunological risk: dose of 0.5 to 4 mg per capsule.
- Sirolimus oral solution should be mixed with orange juice or water, in a plastic or glass beaker, and shaken for one minute before taking. No other mixing liquids may be used. Grapefruit juice can inhibit cytochrome P450 enzymes in the intestinal wall and increase the variability of sirolimus absorption.

Topical use:

- In the form of ointment for the treatment of angiofibroma, at doses between 0.1 and 0.4%.

7. REMARKS.

STORAGE:
Store at room temperature (25±2ºC), in hermetically sealed containers, in a dry place away from light.

8. BIBLIOGRAPHY.

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