hikma.

Date: 02-Feb-2022

Direct Healthcare Professional Communication

Prograf® (Tacrolimus): Monitoring requirements before switching tacrolimus.

Dear healthcare professional,
Hikma in agreement with the Saudi Food and Drug Authority (SFDA), would like to remind healthcare professionals about important information regarding the monitoring requirements before switching tacrolimus and steps needed to be taken to avoid the risk of graft rejection or increased adverse reactions.

Summary:
- **Patients should not switch their tacrolimus form without the direct supervision of a physician experienced in immunosuppressive therapy and the management of transplant patients.**
- **Physician, before switching patient to a generic product, should monitor tacrolimus blood trough concentrations and serum creatinine levels. The patient should be monitored closely after switching for blood trough concentrations and signs of allograft rejection.**
- **In addition, full blood count, urea levels, liver functions, blood pressure and blood glucose should be monitored.**
- **Unintended, unsupervised, or unintentional switching of tacrolimus is unsafe. It can lead to graft rejection or increased adverse reactions.**

Background on the safety concern:
Tacrolimus is an immunosuppressant drug used in the prophylaxis of transplant rejection in liver, kidney or heart allograft recipients. Tacrolimus is also used in the treatment of allograft rejection resistant to treatment with other immunosuppressive medicinal products.

Tacrolimus is a drug with a narrow therapeutic index. That means differences, even minor ones, in blood levels can lead to transplant rejection or adverse reactions.

Unintended, unsupervised, or unintentional switching of immediate- or prolonged release formulations of tacrolimus is unsafe. This can lead to serious adverse reactions, including graft rejection, which could be a consequence of either under- or overexposure to tacrolimus.

Patients should be kept on a single formulation of tacrolimus with the corresponding daily dose regimen; if changes in formulation or regimen are clinically required, this needs to be done under the close supervision of a physician experienced in immunosuppressive therapy. Following conversion to any alternative formulation, therapeutic drug monitoring must be performed and dose adjustments made to ensure that systemic exposure to tacrolimus is maintained.

Underdosing can result in acute rejection of transplanted organs. Overdosing can lead to toxicity as a result of overexposure to tacrolimus. Numerous cases of accidental overdose have been reported; symptoms have included headache, nausea and vomiting, tremor, lethargy, infections, urticaria, increased blood urea nitrogen and elevated serum creatinine concentrations, and increase in alanine aminotransferase levels.

For any further information, healthcare professionals are encouraged to contact Hikma through the contact details mentioned below.

Call for reporting for adverse reactions

The National Pharmacovigilance and Drug Safety Centre (NPC):
Website https://ade.sfda.gov.sa
Email: npc.drug@sfda.gov.sa
Call center number: 19999
Fax: +966-11-205-7662

Company contact point
Abdulkareem bin Mubarak
Local QPPV
Hikma Pharmaceuticals
Email: SAPV@hikma.com
Tel.: 00966114173731 Ext. 1086
Website: www.hikma.com