IRISH MEDICINES BOARD

Notice Information: Human Medicines - Warning 20 November 2008

Part 1. Product Information

a)	Title:	Medication errors associated with Advagraf prolonged release capsules and Prograf capsules
b)	Product Name/Type:	Prograf 0.5mg, 1mg and 5mg Capsules for immediate release. Advagraf: 0.5mg, 1mg and 5mg Prolonged Release Capsules.
c)	Active Substance:	Active Substance(s): Each Prograf 0.5mg, 1mg and 5mg Capsule contains 0.5mg, 1mg and 5mg of tacrolimus respectively for immediate release. Each Advagraf 0.5mg, 1mg and 5mg Prolonged-Release Capsule contains 0.5mg, 1mg and 5mg of tacrolimus respectively.
d)	Authorisation Number:	PA 1241/14/1 (Prograf 0.5mg Capsules), PA 1241/14/2 (Prograf 1mg Capsules), PA 1241/14/3 (Prograf 5mg Capusles), EU/1/07/387/001 (Advagraf 0.5mg Prolonged-Release Capsules), EU/1/07/387/002 (Advagraf 1mg Prolonged-Release Capsules), EU/1/07/387/009 (Advagraf 5mg Prolonged-Release Capsules)
e)	Authorisation Holder:	Prograf: Astellas Pharma Co. Ltd, 25, The Courtyard, Kikcarbery Business Park, Clondalkin, D22. PA 1241/14/1 (Prograf 0.5mg Capsules), PA 1241/14/2 (Prograf 1mg Capsules), PA 1241/14/3 (Prograf 5mg Capusles). Advagraf: Astellas Pharma Europa B.V., Elisabethhof 19, 2353 EW Leiderdorp, Netherlands. EU/1/07/387/001 (Advagraf 0.5mg Prolonged-Release Capsules), EU/1/07/387/002 (Advagraf 1mg Prolonged-Release Capsules), EU/1/07/387/009 (Advagraf 5mg Prolonged-Release Capsules).

Part 2. Target Audience

a)	Target Audience:	Pharmacists Prescribing Physicians Nurses Healthcare Professionals Patients

Part 3. Problem/Issue

a) Problem/Issue:

The Irish Medicines Board (IMB) wishes to provide information on medication errors that have been reported across Europe associated with the following products: Prograf Capsules and Advagraf Prolonged-Release Capsules. The reported errors have included prescribing, dispensing and administration errors. The errors were due to confusion between the products and their dosage regimen, as well as inappropriate interchanging of the products. It is thought that in some cases, the products were mistakenly considered to be interchangeable. Both products contain the potent immunosuppressive compound, tacrolimus. However, there is a critical difference in the dosing regimen. Prograf is taken in two divided doses (morning and evening), whereas at equivalent doses Advagraf delivers similar drug exposure with once daily dosing . The IMB wishes to emphasise that these two formulations of tacrolimus are not interchangeable without careful blood level monitoring by a transplant specialist and ask that particular case is taken in the prescribing, dispensing and administration of these products to ensure the correct dosage regimen is taken by the patient.

Part 4. Background Information

a) Background Information:

These products have a narrow therapeutic window and careful compliance with the correct dosage regimen is essential to ensure efficacy, while preventing adverse drug reactions. Advagraf Prolonged Release Capsules should be taken once daily, while Prograf Capsules should be taken twice daily. The number of medication errors is small, with only a single case reported in Ireland to date, and the IMB is issuing this warning as a precautionary measure to emphasise the need for care in the prescription, dispensing and administration of these products. The errors have occurred in a number of EU Member States, where there have been cases of misprescription including, for example, where Advagraf prolonged-release has been prescribed for a patient maintained on Prograf. Few cases have led to an adverse reaction because the error has been identified quickly. However, confusion of this type is potentially serious because the products have a narrow therapeutic index and inadequate blood levels of tacrolimus can lead to acute graft rejection, while over-suppression can cause serious adverse drug reactions.

Part 5. Action to be taken

a)	Action to be taken:	Particular care should be taken when prescribing, dispensing or administering these products to ensure the correct dosage regimen. Prograf and Advagraf Prolonged-Release Capsules are not interchangeable without careful blood monitoring and under the supervision of a transplant specialist. Patients should be maintained on the same brand of tacrolimus unless a switch is made by their transplant specialist. Where patients have recently been switched from one product to another by their transplant specialist, special care should be taken to ensure that they fully understand the changed dosing regimen. The likelihood of errors will be reduced if tacrolimus is prescribed by brand, either as Advagraf or Prograf, as is routinely the case for other products with a narrow therapeutic index. Pharmacists should check carefully that they always dispense the correct brand of tacrolimus for each patient If the prescription is unclear (i.e. Advagraf or Prograf prescribed only by generic name or if the prescribed dosing regimen differs from that described in the Summary of Product Characteristics), please confirm the prescribed medication and dosing regimen with the prescribing physician.

Part 6. Keywords

a)	Keywords:	PA 1241/14/1 (Prograf 0.5mg Capsules) PA 1241/14/2 (Prograf 1mg Capsules) PA 1241/14/3 (Prograf 5mg Capusles) EU/1/07/387/001 (Advagraf 0.5mg Prolonged-Release Capsules) EU/1/07/387/002 (Advagraf 1mg Prolonged-Release Capsules) EU/1/07/387/009 (Advagraf 5mg Prolonged-Release Capsules) tacrolimus medication errors