

1st December 2008

Advagraf and Prograf: Errors in prescribing, dispensing and administration leading to serious adverse drug reactions

Dear Healthcare Professional,

Astellas wishes to draw your attention to a series of cases of prescribing, dispensing and administration errors involving Prograf and Advagraf. Both of these medicines contain the immunosuppressant tacrolimus for use in transplant patients, but are given according to different dosing schedules.

The licensed indications for Advagraf and Prograf are in the Annex overleaf. Prescribers should note that indications are not identical, and that Advagraf is only licensed for use in adults.

The medication errors have resulted in patients being dosed incorrectly. This has caused serious adverse reactions, including biopsy-confirmed acute rejection of transplanted organs and toxicity due to overexposure.

It is important to note the correct use of these medicines:

- **Prograf is an immediate-release formulation that must be taken twice a day, once in the morning and once in the evening.**
- **Advagraf is a prolonged-release formulation that must be taken once a day in the morning.**

Prograf and Advagraf are not interchangeable without careful therapeutic monitoring. Substitution should only be made under the close supervision of a transplant specialist.

Particular care should be taken in prescribing and dispensing the correct brand of tacrolimus, i.e. either Prograf or Advagraf. Prescribers, pharmacists and patients need to be fully aware of the brand being prescribed and the associated dosing regimen.

Changes to product information and labelling to reduce errors

In order to reduce the frequency of medication errors, Astellas is planning to undertake the following corrective actions. These measures have been agreed with the European Medicines Agency (EMA):

- Advagraf will be supplied in an overlabeled outer package, including the words 'once daily' in a larger font. This is an interim measure that will take effect as of 12th December 2008.
- Advagraf will be supplied in a new outer package, including the words 'once daily' and 'prolonged-release hard capsules' in a larger font. This will take effect as of 1st April 2009.
- The summary of product characteristics (SPC) and package leaflet for Advagraf and Prograf will be updated to include special warnings and precautions. The new product information will be made available as of March 2009.

Continued overleaf...

Call for reporting of suspected adverse drug reactions

Suspected adverse drug reactions (including those that arise from medication errors) should be reported. Reporting forms and information can be found at www.yellowcard.gov.uk. Adverse reactions should also be reported to Astellas Pharma Ltd. Please contact 01784 419615.

If you require further information, please contact Astellas Medical Information on 01784 419615 or by email to medinfo@gb.astellas.com

Yours faithfully,



Dr. Willem Jan Atsma
Senior Director
Drug Safety and Pharmacovigilance

Annex

Licensed indications for Prograf:

Prophylaxis of transplant rejection in liver, kidney or heart allograft recipients.

Treatment of allograft rejection resistant to treatment with other immunosuppressive medicinal products

Licensed indications for Advagraf

Prophylaxis of transplant rejection in adult kidney or liver allograft recipients.

Treatment of allograft rejection resistant to treatment with other immunosuppressive medicinal products in adult patients