astellas
Leading Light for Life

IMPORTANT DRUG WARNING

Subject: Important Information Regarding Risk of Medication and Dispensing Errors with ASTAGRAF XL (tacrolimus extended-release capsules)

Dear Healthcare Provider,

ASTAGRAF XL™ (tacrolimus extended-release capsules) has been approved by the U.S. Food and Drug Administration (FDA) for the prophylaxis of organ rejection in patients receiving a kidney transplant. It is recommended that ASTAGRAF XL be used concomitantly with mycophenolate mofetil (MMF) and corticosteroids, with or without basiliximab induction. Therapeutic drug monitoring is recommended for all patients receiving ASTAGRAF XL. ASTAGRAFXL extended-release capsules are not interchangeable or substitutable with tacrolimus immediate-release capsules and should not be used simultaneously with cyclosporine.

Astellas would like to inform you of important risk information regarding medication and dispensing errors, including inadvertent or unintentional substitution, between twice-daily immediate-release and ASTAGRAF XL (once-daily extended-release) tacrolimus formulations. These errors have led to serious adverse events, including graft rejection, or other adverse reactions, which could be a consequence of either under- or over-exposure to tacrolimus.

The *Warnings and Precautions*section (5.5) of the enclosed ASTAGRAF XL Package Insert describes the risk of medication and dispensing errors:

> ASTAGRAF XL extended release capsules are not interchangeable or substitutable with tacrolimus immediate release capsules. Medication and dispensing errors, including inadvertent or unintentional substitution between twice-daily immediate-release and ASTAGRAF XL (once-daily extended-release) tacrolimus formulations have been observed in postmarketing surveillance of ASTAGRAF XL in countries where it is approved and marketed. This has led to serious adverse events, including graft rejection, or other adverse reactions, which could be a consequence of either under- or over-exposure to tacrolimus.
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> Note that ASTAGRAF XL is supplied in short, square bottles and contains the statement “ONCE DAILY” on its label. ASTAGRAF XL will not be initially marketed in blister packaging.

Medication errors can be minimized by health care professionals by specifying tacrolimus immediate- or extended- release in the written prescriptions. Similarly the medication errors

in the pharmacy can be minimized by clearly marking the shelves where ASTAGRAF XL, Prograf, and other generic tacrolimus formulations are stored; avoiding or decreasing computer selection errors by highlighting or flagging the different tacrolimus formulation products in computer menus so each tacrolimus formulation has a different appearance; educating pharmacy staff on the various approved tacrolimus formulation product differences so knowledge deficits will not contribute to ASTAGRAFXL medication errors.

As stated in the *Patient Counseling Information* section (17) of the enclosed ASTAGRAF XL Package Insert, advise patients to:

- Inspect your ASTAGRAF XL medicine when you receive a new prescription and before taking it. If the appearance of the capsule is not the same as usual, or if dosage instructions have changed, speak to your doctor or pharmacist as soon as possible to make sure that you have the right medicine.

Encourage patients prescribed ASTAGRAF XL to review the enclosed ASTAGRAF XL Medication Guide in which the risk of medication errors is described as follows:

> People who take ASTAGRAF XL have sometimes been given the wrong medicine because some medicines have the same ingredient (medicine) as ASTAGRAF XL. **You should check your ASTAGRAF XL when you get a new prescription to make sure you have received the right medicine.**
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> - Call your doctor right away if you think you were given the wrong medicine.
> - Ask your doctor or pharmacist if you are not sure what ASTAGRAF XL should look like.

ASTAGRAF XL will be available as 0.5 mg, 1 mg, and 5 mg strength extended-release hard gelatin capsules. See Table 1 at the end of this letter for pictures of the ASTAGRAF XL capsules and bottles. For additional copies of the Medication Guide or to see pictures of the ASTAGRAF XL capsules and bottles, please visit www.ASTAGRAFXL.com.

To report medication errors and/or adverse events potentially associated with ASTAGRAF XL, please call Astellas at 1-800-727-7003 or report them to FDA's MedWatch Reporting System by:

- Phone at 1-800-FDA-1088 (1-800-332-1088)
- Facsimile at 1-800-FDA-0178 (1-800-332-0178)
- Mail using FDA Form 3500 located at http://www.fda.gov/medwatch

Please read the enclosed ASTAGRAF XL Package Insert for full prescribing information, including Boxed Warnings and Warnings and Precautions, for a description of this important risk information that is summarized above.

Please contact Astellas at 1-800-727-7003 or www.ASTAGRAFXL.comif you have any questions about ASTAGRAF XL or the information in this letter.

Sincerely,

Jeffrey Bloss, MD
Vice President, Astellas Scientific and Medical Affairs

Table 1 Pictures of ASTAGRAF XL Capsules and Bottles

ASTAGRAF XL	0.5 mg	1 mg	5 mg
Capsule appearance (actual size)			
Bottle appearance