Astagraf XL® (tacrolimus) – Expanded indication

- On November 29, 2018, the FDA approved Astagraf XL (tacrolimus) extended-release capsules, for the prophylaxis of organ rejection in kidney transplant patients in combination with other immunosuppressants in adult and pediatric patients.
    - Previously, Astagraf XL was approved for the same indication in adults.
- Tacrolimus is also available generically as a capsule and ointment, and as brand extended-release tablets (Envarsus XR®), and brand injection and granules for suspension (Prograf®).
    - Tacrolimus capsules and Prograf are indicated for the prophylaxis of organ rejection, in patients receiving allogeneic kidney transplant, liver transplants and heart transplant, in combination with other immunosuppressants.
    - Tacrolimus ointment is indicated as second-line therapy for the short-term and non-continuous chronic treatment of moderate to severe atopic dermatitis.
    - Envarsus XR is indicated for the prophylaxis of organ rejection in kidney transplant patients converted from tacrolimus immediate-release formulations, in combination with other immunosuppressants.
- The safety and effectiveness of Astagraf XL in *de novo* pediatric kidney transplant patients have been established. Use of Astagraf XL in pediatric kidney transplant patients is based on adequate and well controlled studies of Astagraf XL in adult kidney transplant patients and supported by pharmacokinetic and safety data of Astagraf XL in pediatric transplant patients 4 years of age and older who are able to swallow capsules intact and Prograf capsules in adult and pediatric transplant patients.
    - A pharmacokinetic and safety study included 25 *de novo* pediatric kidney transplant patients, 4 to 15 years of age, randomized to Prograf or Astagraf XL. Tacrolimus exposures for the two drug products were comparable on days 7 and 28. Among the 13 pediatric kidney transplant patients who completed 52 weeks on Astagraf XL, there were no graft loss, deaths or episodes of biopsy-proven acute rejection.
    - Another pharmacokinetic and safety study included 48 stable pediatric kidney transplant patients, 5 to 16 years of age, who were converted from a Prograf-based regimen to Astagraf XL. Tacrolimus systemic exposures for the two drug products were comparable. Acute rejections were reported in 2 of the 48 kidney pediatric patients that responded to subsequent treatment. There were no graft failures or deaths following use of Astagraf XL during the 54-week follow up.
- Astagraf XL carries a boxed warning for malignancies and serious infections in transplant patients; and increased mortality in female liver transplant patients.
- The recommended starting dose of Astagraf XL in pediatric patients is 0.3 mg/kg orally once daily, in combination with Simulect® (basiliximab), mycophenolate mofetil, and steroids, administered within 24 hours following reperfusion.
    - Astagraf XL blood concentrations should be 10 to 20 ng/mL during the first month and 5 to 15 ng/mL after the first month.

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- Astagraf XL is not substitutable for tacrolimus extended-release tablets, tacrolimus immediate-release capsules or tacrolimus for oral suspension. Under or overexposure to tacrolimus may result in graft rejection or other serious adverse reactions.
- Consult the Astagraf XL drug label for adult dosing.

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