Tacrolimus Conversion - FAQ for Clinicians

1. **Why is BC Transplant transitioning patients from Prograf to Sandoz immediate release tacrolimus?**
   The decision to switch brands of tacrolimus was extensively reviewed and approved by the medical/clinical transplant experts in BC to ensure optimal health outcomes for all patients. Patient health and safety is always our top priority and as such, BC Transplant is working closely with transplant clinics and care teams across the province to support all our patients through this transition. Switching brands of tacrolimus will provide an opportunity to maximize resources, expand coverage for new treatments, and improve patient access to more medications, without compromising patient safety and drug efficacy.

2. **What clinical evidence supports switching to Sandoz tacrolimus?**
   Sandoz immediate release tacrolimus is approved by Health Canada and has been evaluated through numerous clinical studies that collectively confirm safety, efficacy and similar pharmacokinetic profiles for the majority of transplant patients who switched between Prograf and alternate brands of immediate release tacrolimus.

   For renal and liver transplant recipients, one study (Alloway et al. (2017)) compared Prograf with alternate tacrolimus products (Sandoz, Dr. Reddy) using pharmacokinetic parameters to successfully demonstrate bioequivalence. Another study (Bloom et al. (2013)) on renal subpopulations (ie. female, African American, diabetes, steroid use) also confirmed similar outcomes regardless of patient characteristics. De novo renal populations were studied in a large multicentre, randomized study (Arns et al. (2017)). The outcomes showed no relevant difference in pharmacokinetic parameters between Prograf and the alternate brand. Comparable trough levels between Prograf and alternate brand were demonstrated in renal, liver and heart transplant recipients in a study by Spence et al. (2012). For pediatric renal transplant recipients, negligible change in pharmacokinetic parameters or allograft function were noted in a conversion study (Naicker et al. (2017)). A British Columbia conversion study of Glomerulonephritis patients (Barbour et al. (2018)) demonstrated no difference in mean tacrolimus levels and favourable outcomes.

   For a full list of clinical studies, please visit BC Transplant's webpage, under 'Resources for Health Professionals'.

3. **Are Prograf and Sandoz tacrolimus interchangeable?**
   Although there is strong clinical evidence that support bioequivalence between Sandoz and Prograf tacrolimus, the transition from Prograf to Sandoz tacrolimus should be completed by transplant clinical care teams.

4. **What are potential side effects of the Sandoz tacrolimus?**
   Patients are not expected to have any new side effects after switching to Sandoz tacrolimus. Post-transplant clinicians will engage and educate their patients about the change and monitor for additional or persistent adverse effects and monitor tacrolimus blood levels after the brand switch. In the event that a patient experiences unexpected side effects after switching, they are advised to contact their transplant clinic immediately.

5. **What about patients on long-acting tacrolimus (Advagraf?)**
   This medication conversion will **not** impact patients on Advagraf. Only patients on Prograf immediate release tacrolimus are impacted.

6. **When will I need to begin prescribing or dispensing Sandoz tacrolimus?**
   The implementation dates for the conversion vary based on the location of your clinic. The implementation roll-out dates are as follows:
   - Initiation for de novo transplant patients to Sandoz tacrolimus at **BC Children's Hospital** and **Vancouver General Hospital** on **November 4, 2019.**
   - Conversion of current transplant patients from Prograf to Sandoz tacrolimus at the clinics in **Kamloops, Kelowna, Penticton, Trail** and **Prince George** on **November 18, 2019.**
   - Initiation for de novo transplant patients to Sandoz tacrolimus at **St. Paul's Hospital** on **January 6, 2020.**
   - Conversion of current transplant patients from Prograf to Sandoz at all remaining clinics at **Vancouver General Hospital, BC Children's Hospital, St. Paul's Hospital, Surrey, Victoria** and **Nanaimo** on **January 6, 2020.**

7. **How will the conversion process work?**
   When patients visit the post-transplant clinics, the transplant clinicians will have a consultation with the patient regarding the conversion to Sandoz tacrolimus. The transplant clinicians will need to document the conversion date for each patient based on the patient's existing supply of Prograf tacrolimus. Patients will be advised to use up their existing supply of Prograf tacrolimus before transitioning to Sandoz tacrolimus. Patients will also be advised to have tacrolimus pre-dose level drawn five to seven days after they switch. A second tacrolimus blood level is recommended a week later. The therapeutic drug level results will be reviewed and dose may be adjusted according to the required therapeutic range for that patient's clinical status post-transplant.

8. **What support will be provided to clinicians during the tacrolimus conversion?**
   Clinical support resources have been developed by BC Transplant to support transplant clinics and pharmacies through the conversion. Please see the 'Resources for Health Professionals' section on our webpage to view or download these resources. Transplant clinics and pharmacies are encouraged to share these resources with their team and front-line staff who will be involved in the conversion process.

   Prior to the conversion implementation, funding will be allocated for additional clinical personnel to be on-site at the transplant clinics during the implementation to provide support and education for patients. In addition, there will be ongoing communication between clinics and BC Transplant throughout the conversion period to support clinicians and patients through the change.

9. **Is there any change in process for prescriptions?**
   During the tacrolimus conversion period, transplant partner pharmacies will maintain a supply of both Prograf and Sandoz tacrolimus to allow time for patients to convert to Sandoz. The transplant pharmacies will be waiting for the "Pharmacy Alert" notice from the transplant clinic to let them know it is okay to dispense Sandoz tacrolimus.

10. **How should I approach patient discussions?**
    As healthcare professionals, transplant clinicians and pharmacists are trusted as a source of information, expertise, and experience. Highlight the following educational points with your patients:
    - Is safe and effective.
    - Works similarly to their current medication (Prograf tacrolimus).
    - Adds no increased risk of adverse reactions.
    - Doesn't involve major changes to their routines or dosing.
    - Is available at the same pharmacy that they currently attend.
    - Is well studied and that the conversion from Prograf to alternate brands of tacrolimus have been successful around the world.

    Prior to implementation, BC Transplant will distribute patient support materials to transplant clinics and pharmacies that summarize the tacrolimus conversion. These materials are intended to support patients through the change and can be a useful reference when explaining the conversion process to patients.