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| **Emory Hospitals****Emory Transplant Center Policies & Procedures** | **Activated:** 07/17/2018 |
| **Section:** Kidney and Pancreas Transplant Programs | **Last Review Date:**07/17/2018 |

**Policy: Kidney/Pancreas Post Transplant: Tacrolimus Formulation Conversion**

**Statement: Activation Date: 06.27.2018**

**Affected Departments:** Emory University Hospital’s Kidney (Pancreas) Transplant Programs

**Vision Strategy:** Patient Care

**Protocol Statement:** This protocol provides guidelines on the conversion between available tacrolimus formulations that are prescribed to kidney and/or kidney/pancreas transplant recipients.

**Scope/Procedure:**

**Policy Statement:** The Emory Transplant Center and all the solid organ transplant programs will comply with all applicable federal, state, and local laws, regulations, policies and protocols regarding the management of transplant patients.

**Admin Responsibility:** All transplant program physicians, practitioners and clinical staff members are responsible for compliance with this clinical protocol.

**Protocol/Procedure:**

I. Background

In recent years, new formulations of tacrolimus have become available on the market. The available formulations include tacrolimus IR (Prograf®), tacrolimus XL (Astagraf XL®), and tacrolimus XR (Envarsus XR®). Based on patient factors, such as medication cost, tolerability, and the inpatient formulary, patients may require conversion between the available formulations. However, the dosing of each formulation is not equivalent and tacrolimus has a narrow therapeutic index. Therefore, careful conversion and close therapeutic drug monitoring is recommended.

II. Criteria for Conversion

1. Any transplant recipient receiving tacrolimus with the following criteria may benefit from formulation conversion:
	1. Inability to afford medication copay requiring enrollment in a Patient Assistance Program.
	2. Poor tolerability with tacrolimus peak-related side effects (tremor, headaches).
	3. Patient who is on tacrolimus XR or XL formulation who are admitted to the hospital will require conversion to tacrolimus IR due to inpatient formulary.

III. Conversion Recommendations

1. The recommended conversion between preparations is

Tacrolimus IR:Tacrolimus XL:Tacrolimus XR (Prograf:Astagraf:Envarsus)

1:1:0.75, rounding to the nearest tablet size. Note that none of the available tablets or capsules can be cut or crushed.

1. Available tablet/capsule sizes:
	1. Tacrolimus IR (Prograf®): 0.5mg, 1mg, and 5mg capsules
	2. Tacrolimus XL (Astagraf®): 0.5mg, 1mg, and 5mg capsules
	3. Tacrolimus XR (Envarsus®): 0.75mg, 1mg, and 4mg tablets
2. Refer to the table below for dosing conversion, capsule strengths, and quantity to order for new prescriptions.

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| Tacrolimus IR (Prograf®) RegimenConversion ratio 100% | Capsule Strength & Quantity\* | Tacrolimus XL (Astagraf®) RegimenConversion ratio 100% | Capsule Strength & Quantity\* | Tacrolimus XR (Envarsus®) RegimenConversion ratio 75% | Tablet Strength & Quantity\* |
| 0.5mg daily | 0.5mg (30) | 0.5mg qAM | 0.5mg (30) | 0.75mg qAM | 0.75mg (30) |
| 0.5mg q12h | 0.5mg (60) | 1mg qAM | 1mg (30) | 0.75mg qAM | 0.75mg (30) |
| 1mg q12h | 1mg (60) | 2mg qAM | 1mg (60) | 1.5mg qAM | 0.75mg (60) |
| 1.5mg q12h | 0.5mg (180) | 3mg qAM | 1mg (90) | 2.25mg qAM | 0.75mg (90) |
| 2mg q12h | 1mg (120) | 4mg qAM | 1mg (120) | 3mg qAM | 1mg (90) |
| 2.5mg q12h | 0.5mg (60) & 1mg (120) | 5mg qAM | 5mg (30) | 4mg qAM | 4mg (30) |
| 3mg q12h | 1mg (180) | 6mg qAM | 1mg (30) & 5mg (30) | 5mg qAM | 4mg (30) & 1mg (30) |
| 4mg q12h | 1mg (240) | 8mg qAM | 1mg (90) & 5mg (30) | 6mg qAM | 4mg (30) & 1mg (60) |
| 5mg q12h | 5mg (60) | 10mg qAM | 5mg (60) | 8mg qAM | 4mg (60)  |
| 6mg q12h | 1mg (60) & 5mg (60) | 12mg qAM | 1mg (60) & 5mg (60) | 9mg qAM | 4mg (60) & 1mg (30) |
| 7mg q12h | 1mg (120) & 5mg (60) | 14mg qAM | 1mg (120) & 5mg (60) | 11mg qAM | 4mg (60) & 1mg (90) |
| 8mg q12h | 1mg (180) & 5mg (60) | 16mg qAM | 1mg (30) & 5mg (90) | 12mg qAM | 4mg (90) |
| 9mg q12h | 1mg (240) & 5mg (60) | 18mg qAM | 1mg (90) & 5mg (90) | 14mg qAM | 4mg (90) & 1mg (60) |
| 10mg q12h | 5mg (120) | 20mg qAM | 5mg (120) | 15mg qAM | 4mg (90) & 1mg (90) |
| 11mg q12h | 1mg (60) & 5mg (120) | 22mg qAM | 1mg (60) & 5mg (120) | 17mg qAM | 4mg (120) & 1mg (30) |
| 12mg q12h | 1mg (120) & 5mg (120) | 24mg qAM | 1mg (120) & 5mg (120) | 18mg qAM | 4mg (120) & 1mg (60) |

\*Based on 30-day supply

 V. Tacrolimus level monitoring and follow-up

1. If converting from tacrolimus IR to tacrolimus XR or XL, obtain tacrolimus trough level within 1-2 weeks.
2. If converting from tacrolimus XR or XL to tacrolimus IR, obtain tacrolimus trough level within 5-7 days.
3. Dose adjustments based on levels:
	1. Typically, tacrolimus IR doses are adjusted in 1-2mg increments based on the patient’s level and goal range. Remember that with XL and XR formulations, the dose is given only once per day. Therefore, doses should generally be adjusted in 2-4mg increments.

**References:**

1. Tremblay S, Nigro V, Weinberg J, Woodle ES, Alloway RR. A steady-state head-to-head pharmacokinetic comparison of all FK-506 (tacrolimus) formulations (ASTCOFF): An open-label, prospective, randomized, two-arm, three-period crossover study. *Am J Transplant.* 2017;17:432-442.
2. Prograf [package insert]. Killorglin, County Kerry, Ireland: Astellas Ireland Co., Ltd.; 1994.
3. Astagraf XL [package insert]. Killorglin, County Kerry, Ireland: Astellas Ireland Co., Ltd.; 1994.
4. Envarsus XR [package insert]. North Rhine-Westphalia, Germany: Rottendorf Pharma GmbH; 1994.

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| **Regulatory References:** | http://euhnotes.eushc.org/icons/ecblank.gif |

**Related Policies/Procedures:**

**Policy: Kidney/Pancreas Post Transplant Medication Management Protocol**

**Approved By**
**Transplant Leadership Group**

**Key Words For Search:** Tacrolimus, Astagraf, Envarsus, Conversion