



June 2019

Captain Krista Pedley
Director, Office of Pharmacy Affairs (OPA)
Health Resources and Services Administration (HRSA)
Department of Health and Human Services (HHS)
5600 Fishers Lane, Parklawn Building, Mail Stop 10C-03
Rockville, Maryland 20857

Re: Limited Distribution System for PROGRAF® (tacrolimus) and ASTAGRAF XL® (tacrolimus extended-release capsules)

Dear Captain Pedley:

Astellas Pharma US, Inc. (“Astellas”) markets PROGRAF® (tacrolimus) 5 mg/mL (National Drug Code (NDC): 0469-3016-01) for injection; 0.5 mg (NDC: 0469-0607-73), 1 mg (NDC: 0469-0617-73), and 5 mg (NDC: 0469-0657-73) capsules; and 0.2 mg (NDC: 0469-1230-50) and 1 mg (NDC: 0469-1330-50) granules (tacrolimus for oral suspension) (collectively “Prograf”), a calcineurin-inhibitor immunosuppressant indicated for the prophylaxis of organ rejection in patients receiving allogeneic liver, kidney, or heart transplants, in combination with other immunosuppressants (collectively “organ transplant(s)”). Astellas also markets ASTAGRAF XL® (tacrolimus extended-release capsules) 0.5 mg (NDC: 0469-0647-73), 1 mg (NDC: 0469-0677-73), and 5 mg (NDC: 0469-0687-73) capsules (collectively “Astagraf”), a calcineurin-inhibitor immunosuppressant indicated for the prophylaxis of organ rejection in kidney transplant patients in combination with other immunosuppressants in adult and pediatric patients (collectively “kidney transplant(s)").

Due to another manufacturer’s shortage of its generic tacrolimus products, we anticipate that we will be unable to meet the demand for Prograf and Astagraf. The risks imposed by anticipated unpredictability in demand are heightened by the critical role these drugs play in the lives of many patients with organ transplants and kidney transplants, respectively.

In an effort to ensure that all of our customers have an equal opportunity to access Prograf and Astagraf, effective immediately, we are instituting a limited distribution system. We anticipate that this limited distribution system will remain in place for the foreseeable future and will best ensure that all organ transplant patients

Astellas

1 Astellas Way, Northbrook, IL 60062



and kidney transplant patients of all providers have equal access to Prograf and Astagraf, respectively.

The limited distribution system will impact all customers in a fair and consistent fashion. As detailed below, based on our review of the guidance received from OPA, this limited distribution system complies with the relevant 340B program guidance.

Please feel free to share this information with 340B covered entities and other interested parties as you think appropriate. If there other questions, please call 1-800-727-7003.

Limited Distribution System

Effective immediately, Astellas is implementing a limited distribution system, which will limit the number of Prograf ampules, capsules, and granules and Astagraf capsules available per month to each U.S. customer (both 340B and non-340B) based on each customer's historical total milligram purchases per product and dosage form (ampules, capsules, and granules). Specifically, for Prograf capsules, a monthly allocation percentage for each direct customer will be calculated based on the customer's total Prograf capsule milligram purchases (*i.e.*, 0.5 mg, 1 mg, and 5 mg) made between May 1, 2018 and April 30, 2019 (the "Allocation Calculation Period") divided by the total Prograf capsule milligram sales (*i.e.*, 0.5 mg, 1 mg, and 5 mg) during the Allocation Calculation Period. Then, to determine each customer's allocation amount for the month, each customer's pre-determined allocation percentage will be applied to the current monthly available supply of Prograf 0.5 mg capsules, 1 mg capsules, and 5 mg capsules.

This same monthly allocation methodology will be undertaken for Astagraf capsules.

For Prograf ampules, a similar total milligram allocation calculation will be undertaken for the single stock keeping unit (SKU) that Astellas sells for this formulation (*i.e.*, 5 mg/mL ampules).

For Prograf granules, a comparable total milligram allocation methodology will be used for both the 0.2 mg and 1 mg formulations that Astellas sells. However, because the granules formulation was first made available to the U.S. market in March 2019, the granules allocation calculation period only runs between March 13, 2019 through April 30, 2019 ("Granules Allocation Calculation Period").



Each customer's monthly allocation amounts will start on the first day of each calendar month and apply until the last day of that same calendar month (e.g., June 1, 2019 through June 30, 2019). Then on the first day of the next calendar month (e.g., July 1, 2019), new allocation amounts for each customer will be determined using each customer's pre-determined allocation percentage applied to our available Prograf and Astagraf supply for that month. Any customer that reaches its monthly allocation limit may place additional orders for Prograf or Astagraf at the beginning of the next month (subject, of course, to that subsequent month's allocation amount). Any Prograf or Astagraf that was not sold during the prior month will be rolled over and available for sale in the following month.

This monthly percentage-based allocation will provide Astellas the necessary means to adjust customers' maximum allotment in response to changes in Prograf and Astagraf availability, as they may occur, while maintaining equity among all customers.

For new direct customers with no purchases of Prograf or Astagraf capsules during the Allocation Calculation Period, a maximum monthly allocation of 10 bottles (100 capsules) per new customer order will be established. For Prograf ampules, a maximum monthly allocation of one (1) box (10 ampules) per new customer order will be instituted. For Prograf granules, a maximum monthly allocation of one (1) carton (50 packets) per new customer¹ order will be allowed.

Under this limited distribution system, customer orders for Prograf and Astagraf will be filled on a first-in, first-out (FIFO) basis, until a customer reaches its predetermined allocation amount for the month. A customer's 340B participation status and the price a customer pays for Prograf and Astagraf will not affect its allotment. Customers may continue to order Prograf and Astagraf through their normal distribution pathway (either direct from Astellas or through a wholesaler or distributor) under the limited distribution system.

We will advise wholesalers of their allocations and will ask wholesalers to accordingly limit Prograf and Astagraf sales to all of their customers using the same methodology, Allocation Calculation Period, Granules Allocation Calculation Period, and other requirements that Astellas is employing with respect to its direct customers.

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¹ For Prograf granules, a new direct customer is defined as a customer with no purchases of Prograf granules during the Granules Allocation Calculation Period.



Without immediate implementation of this limited distribution system, Astellas will not be able to ensure equitable customer access to Prograf and Astagraf, due to another manufacturer's shortage of its generic tacrolimus, which threatens to affect the ability individuals with organ transplants and kidney transplants may have in obtaining Prograf and Astagraf, respectively, from their customary healthcare provider. We believe this limited distribution system will help ensure that we are able to meet the existing needs of all our current and future customers, including 340B covered entities, as well as the Medicaid program, the Department of Veteran Affairs and Federal Supply Schedule entities, which otherwise could be precluded from being able to purchase Prograf and Astagraf. Thus, Astellas is implementing this limited distribution system in order to best ensure that all organ transplant patients and kidney transplant patients of all providers have equal access to Prograf and Astagraf, respectively.

Sincerely,

Astellas Pharma US, Inc.]