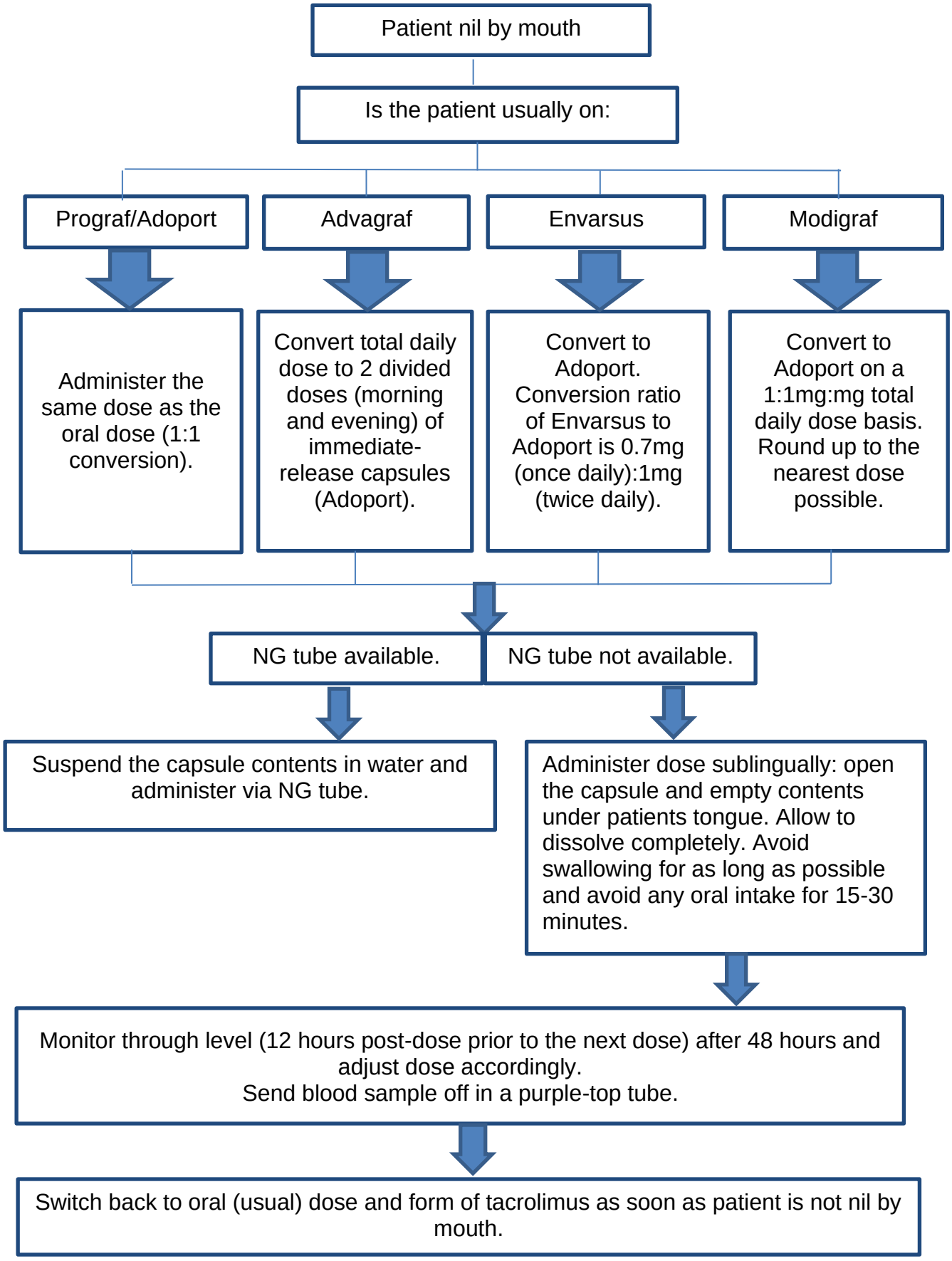
Royal Cornwall Hospitals
NHS Trust

# Administration of Sublingual Tacrolimus in Renal Transplant Patients who are Nil By Mouth Clinical Guideline

## V2.0

## September 2023

## Summary


Patient nil by mouth
Is the patient usually on:
Prograf/Adoport
Advagraf
Envarsus
Modigraf
Administer the same dose as the oral dose (1:1 conversion).
Convert total daily dose to 2 divided doses (morning and evening) of immediate-release capsules (Adoport).
Convert to Adoport. Conversion ratio of Envarsus to Adoport is 0.7mg (once daily):1mg (twice daily).
Convert to Adoport on a 1:1mg:mg total daily dose basis. Round up to the nearest dose possible.
NG tube available.
NG tube not available.
Suspend the capsule contents in water and administer via NG tube.
Administer dose sublingually: open the capsule and empty contents under patients tongue. Allow to dissolve completely. Avoid swallowing for as long as possible and avoid any oral intake for 15-30 minutes.
Monitor through level (12 hours post-dose prior to the next dose) after 48 hours and adjust dose accordingly.
Send blood sample off in a purple-top tube.
Switch back to oral (usual) dose and form of tacrolimus as soon as patient is not nil by mouth.

# 1. Aim/Purpose of this Guideline

This guideline applies to medical, nursing and pharmacy staff involved in the care of renal transplant patients who are taking tacrolimus and unable to take it orally. Although intravenous preparation of tacrolimus is available, it has to be administered via a continuous infusion over 24 hours and doses have been missed due to the unavailability of the right equipment i.e. PVC-free giving sets.

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Royal Cornwall Hospital Trust rch-tr.infogov@nhs.net

# 2. The Guidance

## 2.1. Introduction

2.1.1. Tacrolimus is indicated in the prophylaxis of transplant rejection in kidney allograft recipients.

2.1.2. It should only be initiated and modified by the renal consultants or under the instructions of a renal consultant.

2.1.3. Tacrolimus should be prescribed and dispensed by brand name. Inadvertent switching between formulations of tacrolimus can lead to graft rejection or increased adverse effects, including under- or over immunosuppression, due to clinically relevant differences in systemic exposure to tacrolimus.

2.1.4. Transplant notes are available under ‘patient notes’ in JAC and lists the transplant medications that the patient is currently taking. Information about transplant medications is also available under ‘medications’ in VitalData.

2.1.5. It should never be used in combination with ciclosporin.

## 2.2. Dose and conversions

2.2.1. Tacrolimus is available in 4 different formulations:

2.2.1.1. Adoport and Prograf

- Adoport and Prograf are immediate-release capsules taken twice a day (e.g. morning and evening).
- Prograf, the branded version of tacrolimus, came off patent in 2008. The generic formulation, Adoport, is now prescribed in preference to Prograf in renal transplant patients as a cost-saving measure. However, patients who are admitted with Prograf should be kept on the same brand unless advised by a Renal consultant.
- No dose conversion is needed if Adoport or Prograf is given sublingually.

2.2.1.2. Advagraf

- Advagraf is a prolonged-release capsule taken once a day.
- The total daily dose of Advagraf needs to be converted to twice daily Adoport on a 1:1 (mg:mg) total daily dose basis.

Example:

Advagraf 2mg once a day = Adoport 1mg twice daily

2.2.1.3. Envarsus

- Envarsus is a prolonged-release tablet taken once a day.
- Envarsus needs to converted to a twice daily Adoport dose for it to be given sublingually, based on a conversion ratio of 0.7:1 (mg:mg) (see Table 1).
- Black patients may need higher tacrolimus doses to achieve similar trough levels. The recommended conversion ratio of Envarsus to Adoport is 0.85:1 (mg:mg).

| Dose of Envarsus (once daily) | Dose of Adoport (twice daily) |
|---|---|
| 0.75mg | 0.5mg |
| 1mg | 0.75mg |
| 1.5mg | 1mg |
| 1.75mg | 1.25mg |
| 2mg | 1.5mg |

Table 1: Conversion of Envarsus (once daily) to Adoport (twice daily) on a 0.75:1 (mg:mg) total daily dose basis.

2.2.1.4. Modigraf

- Modigraf is a granular formulation of tacrolimus taken twice a day.
- Patients requiring conversion to Adoport capsules for sublingual administration, should be converted on a 1:1mg:mg total daily dose basis. If equal doses are not possible, the total dose of Adoport should be rounded up to the nearest dose possible, with the higher dose given in the morning and the lower dose in the evening.

2.3. Administration

2.3.1. Adoport is available in four strengths: 0.5mg, 0.75mg, 1mg and 5mg.

2.3.2. It should be administered immediately following removal from the blister.

2.3.3. It should be administered on an empty stomach or at least 1 hour before or 2-3 hours after a meal, to achieve maximal absorption.

2.3.4. If a nasogastric (NG) tube is available, the contents of the Adoport/Prograf capsules can be administered via the NG tube.

2.4. Interactions

2.4.1. Tacrolimus is metabolized by the enzyme CYP3A4.

2.4.2. Drugs that may increase tacrolimus blood level include erythromycin, clarithromycin, diltiazem, nicardipine, verapamil, felodipine, fluconazole, itraconazole and ketoconazole.

2.4.3. Drugs that may decrease tacrolimus blood level include carbamazepine, phenobarbital, phenytoin, rifampicin, orlistat and St John's wort.

2.4.4. Nephrotoxic drugs e.g. NSAIDs, aminoglycosides and aciclovir should be used with caution.

2.4.5. Tacrolimus may cause hyperkalaemia therefore potassium-sparing diuretics should only be initiated with regular monitoring of U&Es.

2.4.6. Grapefruit juice should be avoided. It has been reported to increase the blood level of tacrolimus.

2.4.7. Tacrolimus may increase levels of dabigatran. The manufacturer of dabigatran does not recommend concomitant use of both drugs.

2.4.8. Tacrolimus may reduce the clearance of steroid-based contraceptives leading to increased hormone exposure.

2.4.9. Avoid live vaccines.

## 2.5. Monitoring

2.5.1. Blood trough levels should be monitored 12 hours post-dose, just prior to

the next dose. Patients should be instructed not to take their tacrolimus prior to the blood test so that the blood levels taken represent the trough concentration and to take it immediately after the blood test.

2.5.2. The frequency of blood level monitoring should be discussed with the renal consultants.

2.5.3. Blood samples should be sent off in a purple top tube.

2.5.4. The renal consultants should be notified of the tacrolimus level when it has been reported so that dose adjustments can be made if necessary to achieve the desired tacrolimus level.

# 3. Monitoring compliance and effectiveness

| Information Category | Detail of process and methodology for monitoring compliance |
|---|---|
| **Element to be monitored** | Conversion of doses if the patient is taking a different brand of tacrolimus i.e. not Adoport/Prograf.<br>Tacrolimus level when administered sublingually – whether the bioavailability is similar as oral administration. |
| **Lead** | Renal pharmacists. |
| **Tool** | Clinical audit using EPMA report and Maxims for tacrolimus levels. |
| **Frequency** | Monitoring done every time a patient is switched to sublingual tacrolimus for the first year to allow dose titration according to tacrolimus level if required. A 3-monthly monitoring can then be implemented after determining if the proposed conversion ratio is suitable/needs amending.<br>Report completed and shared every 3 months. |
| **Reporting arrangements** | MPC, Renal Governance via meeting minutes |
| **Acting on recommendations and Lead(s)** | Renal Governance and MPC via specialist Renal pharmacist |
| **Change in practice and lessons to be shared** | Auditing use via JAC system for patients prescribed Tacrolimus Sublingual against tacrolimus levels and ensuring good practice (every 3 years) Learning will be shared via specialist medicine learning group |

# 4. Equality and Diversity

4.1. This document complies with the Royal Cornwall Hospitals NHS Trust service Equality and Diversity statement which can be found in the Equality Diversity And Inclusion Policy or the Equality and Diversity website.

4.2. Equality Impact Assessment

The Initial Equality Impact Assessment Screening Form is at Appendix 2.

# Appendix 1. Governance Information

| Information Category | Detailed Information |
|---|---|
| **Document Title:** | Administration of Sublingual Tacrolimus in Renal Transplant Patients who are Nil By Mouth Clinical Guideline V2.0 |
| **This document replaces (exact title of previous version):** | Administration of Sublingual Tacrolimus in Renal Transplant Patients who are Nil By Mouth Clinical Guideline V1.0 |
| **Date Issued/Approved:** | August 2023 |
| **Date Valid From:** | September 2023 |
| **Date Valid To:** | September 2026 |
| **Directorate / Department responsible (author/owner):** | Pollyanna Bastian, Lead Pharmacist for General Medicine |
| **Contact details:** | 01872 252598 |
| **Brief summary of contents:** | Administration of Sublingual Tacrolimus and the conversion ratio of different brands of tacrolimus to Adoport. |
| **Suggested Keywords:** | Tacrolimus, sublingual, transplant, nil by mouth, immunosuppression |
| **Target Audience:** | **RCHT:** Yes<br>**CFT:** No<br>**CIOS ICB:** No |
| **Executive Director responsible for Policy:** | Chief Medical Officer |
| **Approval route for consultation and ratification:** | Renal Governance and Renal Consultants. |
| **Manager confirming approval processes:** | Racheal Pearce |
| **Name of Governance Lead confirming consultation and ratification:** | Siobhan Hunter |
| **Links to key external standards:** | None |
| **Related Documents:** | https://www.medicines.org.uk/emc/product/585/smpc |

| Information Category | Detailed Information |
|---|---|
| | https://www.medicines.org.uk/emc/product/4703/smpc<br>https://www.medicines.org.uk/emc/product/7804/smpc<br>https://www.medicines.org.uk/emc/product/7526/smpc<br>https://www.medicines.org.uk/emc/product/461/smpc<br>https://pubmed.ncbi.nlm.nih.gov/25631834/<br>https://accpjournals.onlinelibrary.wiley.com/doi/full/10.1002/phar.1149 |
| **Training Need Identified?** | No |
| **Publication Location (refer to Policy on Policies – Approvals and Ratification):** | Internet and Intranet |
| **Document Library Folder/Sub Folder:** | Clinical / Renal |

**Version Control Table**

| Date | Version Number | Summary of Changes | Changes Made by |
|---|---|---|---|
| 21.05.2020 | V1.0 | Initial issue | Rachel Tan, Specialist Renal Pharmacist |
| September 2023 | V2.0 | Full up date and transposed to new template. | Pollyanna Bastian, Lead Pharmacist for General Medicine |

**All or part of this document can be released under the Freedom of Information Act 2000**

**All Policies, Strategies and Operating Procedures, including Business Plans, are to be kept for the lifetime of the organisation plus 6 years.**

**This document is only valid on the day of printing.**

**Controlled Document**

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# Appendix 2. Equality Impact Assessment

## Section 1: Equality Impact Assessment (EIA) Form

The EIA process allows the Trust to identify where a policy or service may have a negative impact on an individual or particular group of people.

For guidance please refer to the Equality Impact Assessment Policy (available from the document library) or contact the Equality, Diversity, and Inclusion Team rcht.inclusion@nhs.net

| Information Category | Detailed Information |
|---|---|
| **Name of the strategy / policy / proposal / service function to be assessed:** | Administration of Sublingual Tacrolimus in Renal Transplant Patients who are Nil By Mouth Clinical Guideline V2.0. |
| **Directorate and service area:** | Pharmacy |
| **Is this a new or existing Policy?** | Existing |
| **Name of individual completing EIA** (Should be completed by an individual with a good understanding of the Service/Policy): | Pollyanna Bastian, Lead Pharmacist for General Medicine |
| **Contact details:** | 01872 252598 |

| Information Category | Detailed Information |
|---|---|
| **1. Policy Aim - Who is the Policy aimed at?** (The Policy is the Strategy, Policy, Proposal or Service Change to be assessed) | Clinical staff within RCHT managing renal transplant patients. |
| **2. Policy Objectives** | To allow the administration of tacrolimus sublingually when patients are nil by mouth. |
| **3. Policy Intended Outcomes** | To prevent missed doses of transplant medications. |
| **4. How will you measure each outcome?** | Clinical audit |
| **5. Who is intended to benefit from the policy?** | RCHT clinical staff and patients |

| Information Category | Detailed Information |
|---|---|
| **6a. Who did you consult with?**<br>(Please select Yes or No for each category) | • Workforce: Yes<br>• Patients/ visitors: No<br>• Local groups/ system partners: No<br>• External organisations: Yes<br>• Other: No |
| **6b. Please list the individuals/groups who have been consulted about this policy.** | Renal pharmacists at Salford Royal NHS FT and Newcastle upon Tyne Hospitals. |
| **6c. What was the outcome of the consultation?** | There is a lack of evidence in the conversion of oral to sublingual tacrolimus so a 1:1 conversion ratio will be used and levels will be monitored.<br><br>Approved |
| **6d. Have you used any of the following to assist your assessment?** | **National or local statistics, audits, activity reports, process maps, complaints, staff or patient surveys:**<br>No |

**7. The Impact**

Following consultation with key groups, has a negative impact been identified for any protected characteristic? Please note that a rationale is required for each one.

Where a negative impact is identified without rationale, the key groups will need to be consulted again.

| Protected Characteristic | (Yes or No) | Rationale |
|---|---|---|
| **Age** | No | |
| **Sex** (male or female) | No | |
| **Gender reassignment** (Transgender, non-binary, gender fluid etc.) | No | |
| **Race** | No | |
| **Disability** (e.g. physical or cognitive impairment, mental health, long term conditions etc.) | No | |
| **Religion or belief** | No | |

| Protected Characteristic | (Yes or No) | Rationale |
|---|---|---|
| **Marriage and civil partnership** | No | |
| **Pregnancy and maternity** | No | |
| **Sexual orientation** (e.g. gay, straight, bisexual, lesbian etc.) | No | |

**A robust rationale must be in place for all protected characteristics. If a negative impact has been identified, please complete section 2. If no negative impact has been identified and if this is not a major service change, you can end the assessment here.**

I am confident that section 2 of this EIA does not need completing as there are no highlighted risks of negative impact occurring because of this policy.

Name of person confirming result of initial impact assessment: Pollyanna Bastian, Lead Pharmacist for General Medicine.

**If a negative impact has been identified above OR this is a major service change, you will need to complete section 2 of the EIA form available here:**
Section 2. Full Equality Analysis