SHARED CARE AGREEMENT

Name of medicine Tacrolimus (Adoport®, Prograf® & Advagraf®)

Indication Solid organ transplant adult patients

Version: **4.0** Approval date: **December 2023** Review date: **December 2026**

The Shared Care Agreement (SCA) is intended to facilitate the accessibility and safe prescribing of complex treatments across the secondary/primary care interface. It does not contain all of the relevant product information, which should be sought using the current British National Formulary and manufacturer's Summary of Product Characteristics. The SCA must be used in conjunction with the NHS Lothian Procedure for the Shared Care of Medicines, available here.

Roles and Responsibilities

Listed below are specific responsibilities that are additional to those included in the NHS Lothian Policy and Procedures for Shared Care. Please refer to the policy for core roles and responsibilities that apply to all Shared Care Agreements.

Consultant

- Monitoring blood pressure, liver function tests and renal function with communication of those results to GP.
- Blood level monitoring and adjustment of tacrolimus dosage
- If a dose change is necessary, then this is communicated to the patient immediately by telephone with additional written confirmation. The letter informing of the dose change is also sent to the GP
- Frequency of follow up will depend on transplant type and time from transplant
- Patient education is the responsibility of the specialist team. The patient information leaflets for specific tacrolimus brands can be found at www.medicines.org.uk

General Practitioner and primary care non-medical prescribers

- Prescribing maintenance tacrolimus therapy (but not dosage adjustment)
- Adverse drug reaction/interaction monitoring and liaison with the hospital consultant regarding any complications of treatment
- Although blood level monitoring is routinely carried out by the specialist team during clinic visits, in exceptional circumstances the team may request that the GP arranges for blood tests to be taken locally for patient convenience – see Monitoring section below
- Patient should be prescribed and maintained on the same brand of tacrolimus (either Adoport®, Prograf® or Advagraf®). NB occasionally due to patient religious beliefs other brands of tacrolimus might be used like Envarsus or Modigraf.

Patient, Relatives, Carers

- Importance of maintaining treatment with the same brand of tacrolimus.
- Patients are advised to purchase and use sunscreens [SPF 50 or above] and protective clothing to reduce sunlight exposure.

Support and Advice for the GP and primary care non-medical prescribers

For patient-related queries, contact the relevant consultant, as detailed on any correspondence or discharge letter, directly either via phone or e-mail. E-mail requests should copy in the practice's clinical e-mail address and ask that the reply is sent to all, so that the reply is picked up even if the sender is not available.

Specialist Team Numbers

Transplant Unit Ward: 0131 242 2068
Renal Transplant Pharmacist: 0131 536 1000 Bleep 2294
Liver Transplant Pharmacist: 0131 536 1000 Bleep 5132

The names and contact details of the patient`s consultant and their secretary are given on the discharge letter.

Please phone directly if there is an urgent enquiry.

Key information on the medicine

Please refer to the current edition of the British National Formulary (BNF), available at www.bnf.org, and Summary of Product Characteristics (SPC), available at www.medicines.org.uk for detailed product and prescribing information and specific guidance.

Background to disease and use of drug for the given indication

Tacrolimus is a macrolide immunosuppressant which suppresses T-cell activation, T-helper-cell-dependent B-cell proliferation, and the production of lymphokines such as interleukins –2 and –3. This mode of action is similar to that of ciclosporin but tacrolimus is more potent. Tacrolimus is used in combination with other immunosuppressant's following solid organ transplantation.

Indication

Tacrolimus is licensed for immunosuppression in kidney and liver transplantation and for the treatment of steroid resistant rejection. It may also be used in patients with intolerable side effects to ciclosporin.

All transplant recipients will commence therapy post-operatively with an immediate release preparation of tacrolimus, either Adoport® or Prograf®. The initial dose will be stabilised according to target trough levels as per protocols and dose changes will be advised to GPs and patients directly. In the post-transplant setting, some patients may be changed to Advagraf®, a once-daily modified release preparation of tacrolimus. Any changes made will be communicated with GP and patient.

Dosage and Administration

The initial immediate release tacrolimus dosage (with Adoport® or Prograf®) is 0.1 to 0.2 mg/kg/day, given in two divided doses at 10am and 10pm. The daily modified release tacrolimus dosage (Advagraf®) is equivalent to the total daily dose of the immediate release Adoport® and Prograf® preparations, although careful monitoring is required when switching between formulations.

Tacrolimus trough blood concentrations require to be monitored with a target range of 5-12 nanograms/mL. However, the target blood level for an individual patient will depend on the time since transplant, the history of rejection and side effects and will be advised by a transplant specialist.

Oral tacrolimus products must be prescribed by brand name.
There are three main oral formulations of tacrolimus used by the transplant teams in NHS Lothian:

- Immediate release capsule, Adoport® and Prograf®, taken twice daily
- Prolonged release capsule, Advagraf®, taken once daily

Within NHS Lothian the formulations in use are Adoport®, Prograf® and Advagraf®. As tacrolimus is a drug with a narrow therapeutic index it is vital that patients are not switched between formulations. Therefore care must be taken to prescribe tacrolimus by BRAND name to avoid potential toxicity or potential graft rejection.

Please note that other branded generic preparations of tacrolimus are available but not routinely used in NHS Lothian. However on rare occasions for example due to patient religious beliefs Envarsus or Modigraf may need to be used. Do not hesitate to contact the specialist teams using the contact information above if you have any concerns regarding tacrolimus prescribing by brand.

Switching between formulations (including generic immediate release brands) requires careful therapeutic monitoring and should only be carried out under the close supervision of a transplant specialist.
See MHRA safety alert for further information http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON155756

Communication with GP regarding dose changes will be by letter predominantly and occasionally via telephone or email. Patients will be informed of immediate dose changes in clinic as face to face conversations or phoned out with clinic.

The transplant pharmacists extensively counsel the patients on their medications prior to discharge. At this point they receive supply of their new medications and a Green Book which is specifically outlining their regimen (Transplant Unit Medications Reminder - The Green Book (nhslothian.scot)). Patients are therefore well rehearsed at managing immediate dose changes.

Adoport®, Prograf® and Advagraf® should be taken on an empty stomach, either one hour before or two hours after a meal. Advagraf® should be taken in the morning.

Monitoring

The following blood tests are performed by the transplant specialist team at clinic:

Test	Frequency	Action if Abnormal Result
Urea + electrolytes Renal function Trough level	Monthly for first 6 months, thereafter according to clinic follow-up frequency	To be determined and reviewed by transplant consultant

In exceptional circumstances the team may request that the GP arranges for repeat blood tests to be taken at the GP practice for patient convenience. If the GP agrees to this, the specialist will give advice on the management of abnormal results.

To obtain a trough level – take a morning blood sample (5mL in an EDTA pink tube) when the patient has omitted the morning dose. Send the sample to the clinical chemistry laboratory, locally (if available) or Royal Infirmary of Edinburgh. No special transport arrangements are needed.

Cautions, contraindications

For a full list of cautions and contraindications please refer to the current Summary of Product Characteristics (SPC) available on www.medicines.org.uk

Pregnancy and Fertility

Any patients planning pregnancy should discuss this with transplant consultant.

Patients wishing to breastfeed should discuss this with the consultant. Tacrolimus can be considered in pregnant woman due to the need for continued treatment, when there is no safer alternative and when the perceived benefit justifies the potential risk to the fetus.

Adverse effects

For a full list of drug adverse effects please refer to the current Summary of Product Characteristics (SPC) available on www.medicines.org.uk

As with other immunosuppressive agents, exposure to UV light and sunlight should be limited by wearing protective clothing and using sunscreen with a high protection factor. This is because of the potential for malignant skin changes.

Drug interactions

For a full list of drug interactions please refer to the current Summary of Product Characteristics (SPC) available on www.medicines.org.uk

Tacrolimus is extensively metabolised in the liver via the cytochrome P-450 enzyme system and may have an inducing or inhibitory effect on these enzymes. Therefore care should be taken when co-administering other drugs known to be metabolised by this system.

- Grapefruit and grapefruit juice contain a compound which may potentially inhibit tacrolimus metabolism.
- Great care should be taken when prescribing other nephrotoxic drugs e.g. NSAIDs. When tacrolimus is used concomitantly with potentially neurotoxic drugs, e.g. aciclovir, the neurotoxicity of these drugs may be increased.
- ACE inhibitors, potassium sparing diuretics and salt substitutes may increase the risk of hyperkalaemia.

Great care should be taken when prescribing any new medicines. Refer to the current SPC or seek advice from the transplant unit.

The presence of this SCA does not compel a primary care prescriber to prescribe if they feel that it is out with the scope of their competencies (as per GMC guidance on safe prescribing) or resources, as ultimate responsibility lies with the prescribing, not the recommending, clinician.

For office use only:

Approved by the General Practice Prescribing Committee (GPPC) on 5th December 2023