SHARED CARE ARRANGEMENT AND PRESCRIBING INFORMATION FOR ORAL TACROLIMUS (ADULTS ONLY - NON-RENAL PATIENTS)

Note: This document should be read in conjunction with the current Summary of Product Characteristics (SmPC).

Patient safety is paramount. The prescriber who prescribes the medicine legally assumes clinical responsibility for the drug and the consequences of its use.

GENERIC AND BRAND NAME (formulations and strength)

Name: Tacrolimus (Adoport® (twice daily), Prograf® (twice daily), Advagraf® (once daily)

Formulation: Capsule

Strength: Adoport® 500microgram, 750 microgram,1mg, 2mg and 5mg; Prograf® 500microgram,1mg and 5mg; Advagraf® 500microgram,1mg, 3mg and 5mg

Note: Within NHS Grampian the formulations in use are Adoport®, Prograf® and Advagraf®. Tacrolimus is a drug with a narrow therapeutic index, it is vital that patients are not switched between formulations unless advised and managed by the specialist service.

Therefore, care must be taken to prescribe Tacrolimus by **brand name** to avoid potential toxicity or potential graft-rejection as per MHRA Drug Safety Update June 2012.

STATUS OF MEDICINE

Licence status: Licensed (prophylaxis of transplant rejection in transplant recipients)

Formulary status: Formulary

Black triangle medicine: NO

Risk minimisation materials: NO

CONDITION(S) TO BE TREATED

Prophylaxis of transplant rejection, treatment of steroid resistant rejection. It may also be used in patients with intolerable side effects to ciclosporin.

TYPICAL DOSAGE REGIME	
Licensed dose	See Specialist service/SmPC for advice – variable according to condition being treated
Route of administration	Oral
Recommended starting dose	See Specialist service for advice – variable according to condition being treated
Titration dose/increment	See Specialist service for advice
Maximum dose	See Specialist service for advice
Situations requiring dose adjustment	See Specialist service for advice and Monitoring Schedule for DMARDs
Duration of treatment	See Specialist service for advice

RESPONSIBILITY OF ACUTE CARE/SPECIALIST SERVICE

- Baseline:
  - Full Blood Count (FBC); liver function tests.
  - LFTs; urea, U&Es; lipids, urinalysis and blood pressure (BP).
- Copy of baseline results to be shared with primary care.
- Exclude pregnancy before starting therapy:
  - If contraception needed non-hormonal methods should be used
  - Advise patient to contact their physician immediately should pregnancy occur.
- Initiation of therapy and recommendations for dose increments. This should remain under the control of the specialist service.
- Decision on final dose required for patient.
- A single dose of pneumococcal polysaccharide vaccine and annual influenza vaccine should be given; patients should be referred to receive these vaccines in accordance with local protocol.

RESPONSIBILITY OF PRIMARY CARE

A Practice agreeing to prescribe Tacrolimus should:

- Prescribe medication (by brand name) under the guidance of the Consultant from the relevant specialist service.
- The General Practitioner (GP) has primary responsibility for monitoring according to the Monitoring Schedule for DMARDs
- Ensure the GP is aware that the drug can cause:
  - Nephrotoxicity
  - Increase in blood pressure
  - Infection and increased risk of malignancy – benign, malignant neoplasms and skin malignancies
  - Changes to visual status and gastrointestinal upset
  - Be aware of potential drug interactions.

- Patients should be asked about the presence of sore throat, abnormal bruising or bleeding at each visit.
- Ensure that the relevant monitoring requirements have been undertaken at the correct frequency.
- Ensure when the patient has an intercurrent illness FBC, U+E and LFTs are done and abnormal results are acted upon promptly.
- Only continue to prescribe medication if it is being satisfactorily monitored.
- Contact the relevant specialist service in the event of a drug reaction, monitoring abnormality, or if you are concerned in any way regarding the current treatment regime.
- Be alert for any of the known adverse reactions.
- The patient should be encouraged to ensure blood tests are undertaken at the correct intervals.
- It is responsibility of primary care to ensure that the medication is recorded on the patient's clinical medication record. This will facilitate central searches for annual vaccinations in order to ensure patients receiving DMARDs are called yearly by the HSCP teams for required vaccinations.

CARE WHICH IS THE RESPONSIBILITY OF THE PRESCRIBING CLINICIAN

- Prescribe medication (**by brand name**) under guidance of the relevant specialist service.
- Check before prescribing each instalment of medication that the monitoring is up to date and that results are within the normal range.
- Ensure no interacting medications are prescribed in primary care.
- Monitor for concordance with therapy.
- Report any adverse events to consultant and the MHRA using the Yellow Card System.
- If an intercurrent illness occurs, when writing laboratory request forms always include details of the patient's medication.
- If bloods are taken due to intercurrent illness, ensure they are monitored and contact hospital consultant to advise if results are out with range.
- A single dose of pneumococcal polysaccharide vaccine and annual influenza vaccine should be given; patients should be referred to receive these vaccines in accordance with local protocol.

Note: In addition to absolute values for haematological or biochemical indices a rapid change or a consistent upward/downward trend in any value should prompt caution and extra vigilance.

Note: If something unexpected occurs contact on call registrar or Consultant for the appropriate specialty. Notify the consultant if the drug is stopped.

MONITORING

Refer to the NHSG Guidelines For The Monitoring of Disease Modifying Anti-Rheumatic Drugs (DMARDs) For Healthcare Professionals. Results should be reviewed and action taken as per monitoring guidance.

RESPONSIBILITY OF OTHER HEALTHCARE PROFESSIONALS

N/A

RESPONSIBILITY OF THE PATIENT

- Take medication regularly as directed by the specialist/doctor.
- Attend hospital and GP clinic appointments as requested by specialist/GP practice. Failure to attend appointments may result in medication being reviewed/stopped.
- Report any adverse effects/illness to the specialist/GP and present rapidly to specialist/GP should their condition significantly worsen.
- To minimise the risk of skin cancer, exposure to sunlight and Ultra Violet light should be limited by wearing protective clothing and using sunscreen with a high protection factor.
- The patient should ensure all blood tests are undertaken at the correct intervals.

PRESCRIBING INFORMATION

For specific product information consult the current summary of product characteristics (http://emc.medicines.org.uk/), the BNF/BNF for Children (https://www.medicinescomplete.com/mc/index.htm)

CONTRAINDICATIONS

- Hypersensitivity to tacrolimus or other macrolides.
- Hypersensitivity to any of the excipients (see SmPC).

PREGNANCY

Tacrolimus should not be used during pregnancy unless there is no suitable alternative treatment to prevent transplant rejection. Discuss with relevant specialist service.

BREAST-FEEDING

Further discussion is required with the relevant specialist service.

COMMON SIDE EFFECTS AND THEIR MANAGEMENT

Blood and lymphatic system disorders	Leucopenia, anemia, thrombocytopenia, leukocytosis and red blood cell abnormalities
Metabolism and nutrition disorders	Hyperglycaemia, diabetes mellitus and hyperkalaemia, hypomagnesaemia, hypophosphataemia, hypokalaemia, hypocalcaemia, hyponatraemia, fluid overload, hyperuricaemia, appetite decreased, metabolic acidosis, hyperlipidaemia, hypercholesterolaemia, hypertriglyceridaemia and other electrolyte abnormalities

Vascular disorders	Hypertension, haemorrhage, thromboembolic and ischaemic events, peripheral vascular disorders and vascular hypotensive disorders
Gastrointestinal disorders	Diarrhoea, nausea, gastrointestinal inflammatory conditions, gastrointestinal ulceration and perforation, gastrointestinal haemorrhages, stomatitis and ulceration, ascites, vomiting, gastrointestinal and abdominal pains, dyspeptic signs and symptoms, constipation, flatulence, bloating and distension and loose stools
Skin and subcutaneous tissue disorders	Alopecia, acne, rash, pruritus and increased sweating
Musculoskeletal and connective tissue disorders	Arthralgia, muscle spasms, back and limb pain
Neoplasms benign, malignant and unspecified (including cysts and polyps)	Benign neoplasm and neoplasm
Psychiatric disorders	Insomnia, anxiety symptoms, confusion and disorientation, depression, depressed mood, mood disorders and disturbances, nightmare, hallucination and mental disorders
Nervous system disorders	Tremor, headache, seizures, disturbances in consciousness, paraesthesias and dysaesthesias, peripheral neuropathies, dizziness, writing impaired and nervous system disorders
Respiratory, thoracic and mediastinal disorders	Dyspnoea, parenchymal lung disorders, pleural effusion, pharyngitis, cough and nasal congestion and inflammation
Hepatobiliary disorders	Cholestasis and jaundice, hepatocellular damage and hepatitis and cholangitis
Other very common or common side effects	Ischaemic coronary artery disorders, tachycardia, tinnitus, vision blurred, photophobia, eye disorders, asthenic conditions, febrile disorders, oedema, pain and discomfort, body temperature perception disturbed, hepatic enzymes and function abnormalities, blood alkaline phosphatase increased and weight increase

Action abnormal monitoring results are per NHSG Disease Modifying Anti-Rheumatic Drugs (DMARDs) Monitoring Guidance.

The specialist service should be contacted if there are any patient specific issues or concerns regarding side effects or abnormal results.

COMMON DRUG INTERACTIONS (for a full list see SmPC)

For a full list of the numerous drug interactions with tacrolimus, please refer to the current Summary of Product Characteristics (SmPC) 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. Advice can be obtained from the specialist service if required.

- Live vaccines should be avoided in patients taking mycophenolate mofetil.
- Some important interactions to consider include the following:
  - Grapefruit and grapefruit juice contain a compound which may potentially inhibit tacrolimus metabolism.
  - Caution 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 SmPC or seek advice from the Gastroenterology Department.
- To minimise the risk of skin cancer, exposure to sunlight and ultra violet light should be limited by wearing protective clothing and using sunscreen with a high protection factor.

ADVERSE DRUG REPORTING

If an adverse reaction should occur, inform relevant medical practitioner as soon as possible.

Report to the MHRA using the Yellow Card System https://yellowcard.mhra.gov.uk/

REFERENCES

Adoport 0.5 mg Hard Capsules - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)

ACUTE CARE/SPECIALIST SERVICE CONTACT INFORMATION

In the event of a concern being raised, the primary care practitioner should contact the referring consultant for the appropriate specialist service via the hospital switchboard, via their secretary, by email or letter, whichever is more appropriate. If the concern is urgent, and out of hours advice is required, the on call Registrar for the speciality may be contacted via the switchboard.

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