Tacrolimus (Advagraf®) - Immunosuppression in autoimmune conditions

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of Tacrolimus (Advagraf®) can be shared between the specialist and general practitioner or non-medical prescriber in primary care (GP). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In that case, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe drugs for this treatment, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with autoimmune conditions are under regular specialist follow-up. This provides an opportunity to discuss and to monitor drug therapy.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

RESPONSIBILITIES and ROLES

<table>
<thead>
<tr>
<th>Specialist responsibilities</th>
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<tbody>
<tr>
<td>• Ensure FBC, liver and renal function are within normal parameters to allow Tacrolimus (Advagraf®) to commence.</td>
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<td>• If abnormalities found at baseline inform GP as soon as possible.</td>
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<td>• Initiate treatment with Tacrolimus (Advagraf®) or advise GP on initiating treatment.</td>
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<td>• Discuss the benefits and side effects of treatment with the patient and inform GP this has occurred.</td>
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<td>• Ask the GP whether he or she is willing to participate in shared care, and agree with the GP as to who will discuss the shared care arrangement with the patient.</td>
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<td>• Review the patient’s condition and monitor response to treatment regularly where indicated.</td>
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<td>• Advise GP if monitoring is needed, and the frequency.</td>
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<td>• Monitor any other parameters considered necessary, or advise GP on which to monitor.</td>
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<td>• Communicate promptly with the GP when treatment is changed or needs to be changed by the GP, any results of the monitoring undertaken, and assessment of adverse events.</td>
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<td>• Have a mechanism in place to receive rapid referral of a patient from the GP in the event of deteriorating clinical condition.</td>
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<td>• Advise GPs on when to stop treatment (if appropriate).</td>
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<td>• Report adverse events to the MHRA via Yellow Card Scheme.</td>
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<td>• Ensure that clear backup arrangements exist for GPs to obtain advice and support.</td>
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**General Practitioner responsibilities**

- Reply to the request for shared care as soon as practicable.
- Prescribe Tacrolimus (Advagraf ®) at the dose recommended.
- Adjust the dose as advised by the specialist.
- Monitor any parameters considered necessary, if agreed with the specialist to do so.
- Report to and seek advice from the specialist on any aspect of patient care that is of concern and may affect treatment.
- Refer patient to specialist if his or her condition deteriorates.
- Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.
- Report adverse events to the specialist and to the MHRA via the Yellow Card Scheme.

**Patient's role**

1. Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
3. Report any adverse effects to the specialist or GP.

**BACK-UP ADVICE AND SUPPORT**

<table>
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<tr>
<th>Contact details</th>
<th>Telephone No.</th>
<th>Email address:</th>
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</thead>
<tbody>
<tr>
<td>Specialist:</td>
<td>01592 648193</td>
<td><a href="mailto:janegibson@nhs.net">janegibson@nhs.net</a></td>
</tr>
<tr>
<td>Rheumatology Dept</td>
<td>01592 265967 (fax)</td>
<td><a href="mailto:helenharris@nhs.net">helenharris@nhs.net</a></td>
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</tbody>
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Other:

ADTC website - FRDU adverse drug reaction document

**SUPPORTING INFORMATION (taken from the SPC)**

**Licensed indications**

Immunosuppression in autoimmune disease.

Tacrolimus (Advagraf ®) is a licensed medication, but is currently but is currently used ‘off label’ for this indication.

**Dosage and Administration**

(Advagraf ®) 1–3mg once daily.

**Contraindications and precautions for use**

- Live vaccines should not be given to patients taking (Advagraf ®).
- Pregnancy should be avoided in patients taking this drug, due to risk of premature delivery, intra-uterine growth restriction and hyperkalaemia. Breastfeeding should be avoided.
- Hypersensitivity to macrolides.
- Severe renal impairment, uncontrolled hypertension, uncontrolled infections and malignancy.
- Avoid excessive exposure to UV light or sunlight.
Side Effects (also state any specific side-effects which require the consultant to be notified)

- Patients may experience side effects: myalgia, tremor, fatigue, headache, infections, paraesthesia or nausea.
- Rare: pericardial effusion, respiratory distress syndrome, posterior reversible encephalopathy syndrome, dehydration, thrombotic thrombocytopenic purpura, blindness, hirsuitism and Stevens Johnson Syndrome.

For a complete list of side effects see BNF/ Summary of product Characteristics.

Treatment should be withheld and the Rheumatology Department contacted if:

- CREATININE rises by 30% of baseline
- Rise in serum LIPID profile
- POTASSIUM rises above the upper limit of normal range
- ABNORMAL BRUISING – urgent FBC should be performed.
  - PLATELETS < 100 x 10^9
  - Rise in BP outside normal range
- >2 fold increase in ALT (from upper range of normal)

Monitoring (State specific monitoring to be undertaken by the GP / Consultant) see FRDU blood monitoring forms (ADTC website)

Rheumatologist responsibilities:
FBC, liver and renal function are within normal parameters to allow Tacrolimus (Advagraf ®) to commence.
Tacrolimus levels will be checked six monthly in the Rheumatology clinic.

General Practitioner responsibilities:
- While taking Tacrolimus (Advagraf ®) patients will require fortnightly RENAL FUNCTION & BLOOD PRESSURE estimation for 3 months & thereafter monthly.
- F.B.C. & LIVER FUNCTION should be undertaken monthly for 3 months & then every 3 months. SERUM LIPIDS & GLUCOSE should be checked 6 monthly.
- Tacrolimus levels should be checked if renal function deteriorates or drugs with potential for interaction are started (BNF).

Drug Interactions
Tacrolimus (Advagraf ®) has many possible drug interactions

- GRAPEFRUIT JUICE should be avoided
- ST. JOHN’S WORT should not be taken
- ORAL CONTRACEPTIVES are less effective
- IBUPROFEN should not be used.
- NIFEDIPINE and DILTIAZEM should be avoided
- POTASSIUM SPARING DIURETICS should be avoided
- Macrolide antibiotics increase Tacrolimus (Advagraf ®) concentration
- Avoid concomitant use of live vaccines.

For a complete list of drug interactions please see the BNF / Summary of Product Characteristics.

Cost (March 2012)
(Advagraf ®) (modified release) capsules:
50 X 1mg = £71.59
100 X 1mg = £143.17
50 X 3mg = £214.76

Any queries relating to this Shared Care Protocol contact the Clinical Effectiveness Pharmacist (01592) 226915
Document approved by NHS Fife Area Drugs & Therapeutics Committee on behalf of NHS Fife. Date: February 2013
Ishtiaq Mohammed, Clinical Effectiveness Pharmacist