ADVICE NOTE FOR INTRAMUSCULAR TRIAMCINOLONE ACETONIDE IN CHILDREN WITH ASTHMA

(For use in a fully assessed and monitored patient as part of a difficult asthma service)

PURPOSE

This document has been drafted to facilitate the safe and effective administration of Triamcinolone Acetonide (TA) (Kenalog®) by intramuscular injection (IM) in the treatment of severe, chronic, difficult to control, asthma. TA is a potent corticosteroid and in the treatment of asthma must only be prescribed and administered under care of the specialist respiratory team.

PHARMACOLOGICAL PROPERTIES

TA is a synthetic glucocorticoid with marked anti-inflammatory and anti-allergic actions.

The intramuscular injection provides an extended duration of therapeutic effect and fewer side effects of the kind associated with oral corticosteroid therapy, particularly gastro-intestinal reactions such as peptic ulceration.

TA is absorbed slowly, though almost completely, following depot administration by deep IM injection. Biologically active levels are achieved systemically for prolonged periods (weeks to months).

Adrenal Suppression

Studies indicate that, following a single IM dose of TA 80mgs, adrenal suppression occurs within 24-48 hours and then gradually returns to normal, usually in around three weeks\(^1\). This finding correlates closely with the extended duration of therapeutic action of TA.

Immune Suppression

The dose and duration of systemic steroid treatment that results in significant immunosuppression is considered to be Prednisolone 2mgs/kg/day for more than one week or 1mg/kg/day for more than one month – or equivalent doses of other steroids\(^2\). In terms of anti-inflammatory equivalence 800mcgs of TA is equivalent to 1 mg of Prednisolone\(^3\).

However, it is not possible to calculate an equivalent daily dose when administered by IM
injection. Immunosuppression is thought to occur with TA when doses exceed normal physiological production, i.e. at more than one 40mg IM injection in a three week period¹.

**PRECAUTIONS / CONTRAINDICATIONS**

Suppression of the inflammatory response and immune function increases susceptibility to infections and their severity. The clinical presentation may be untypical and serious infections such as septicaemia might be masked.

Chickenpox and measles are of particular concern since these normally minor illnesses may be fatal in immunocompromised patients. Unless they have had chickenpox, children receiving parenteral corticosteroids should be regarded as being at risk of severe chickenpox.

Families should be advised to avoid exposure of the child/young person to chickenpox and measles and to make immediate contact with the hospital if it occurs.

Passive protection against chickenpox with varicella zoster immunoglobulin (VZIG) is needed for exposed non-immune patients who are receiving systemic corticosteroids (including TA) or who have used them in the previous 3 months. VZIG must be given within 72 hours of exposure. If exposure occurred longer than the 72 hour period, contact and discuss with the Infectious Diseases (ID) team. VZIG does not prevent infection even if given within 72 hours of exposure, but may attenuate an attack if given within 10 days after exposure¹².

Confirmed chickenpox warrants specialist care and urgent treatment. Manifestations of fulminant illness include pneumonia, hepatitis and disseminated intravascular coagulation, rash is not necessarily a prominent feature. If child develops chickenpox or shingles, admit, treat with IV Aciclovir and discuss with ID team.

During corticosteroid therapy antibody response will be reduced and therefore affect the patients response to vaccines. Live vaccines should NOT be administered.

Patients should carry steroid treatment cards which give clear guidance of the precautions to be taken to minimise risk and which provide details of prescribes, drug, dosage and the duration of treatment.
UNDESIRABLE EFFECTS

Where adverse reactions occur they are usually reversible on cessation of therapy. The incidence of predictable side-effects, including hypothalamic-pituitary-adrenal suppression, correlate with the relative potency of the drug, dosage, timing of administration and duration of treatment.

Severe pain has been reported following intramuscular injection. Sterile abscesses, subcutaneous atrophy, hyper-pigmentation, hypo-pigmentation and Charcot like arthropathy have also occurred.

INTERACTIONS WITH OTHER MEDICINES

If a child/young person is prescribed any of the following discuss with Lead Consultant as TA treatment may be contraindicated:

- TA (Kenalog) may antagonise (decrease) the action of the following drugs:
  Anticholinesterases, Antidiabetics, Antihypertensives, Isoniazid, Human Growth Hormone and Aspirin.
- TA may potentiate (increase) the action of the following drugs: Cyclosporin, Digitalis Glycosides, Oestrogens.
- TA may antagonise or potentiate the action of the following drugs: Anticoagulants, Non-depolarising Muscle Relaxants.
- Hepatic Enzyme Inducers (e.g. barbiturates, phenytoin, carbamazepine, rifampicin) may increase the clearance of Kenalog, reducing the effect of the steroid.
- Ketoconazole may reduce the clearance of Kenalog, resulting in increased effects.
- Clearance of steroids is decreased in hypothyroid patients and increased in hyperthyroid patients.
- Corticosteroids may increase the incidence and/or severity of GI bleeding associated with NSAIDS.
- Amphotericin B and potassium depleting agents e.g., diuretics, increase risk of hypokalaemia.

INDICATIONS FOR USE IN ASTHMA

1. To establish whether a child/young person with severe poorly controlled asthma is steroid responsive
2. To improve asthma control and/or act as a steroid sparing agent in a child/young person with severe, chronic, difficult to control asthma who is not responding to high dose inhaled steroids/oral steroids (step 5 level) characterised by:
   i. Continued repeat hospitalisations despite intensive treatment
   ii. Objective evidence of poorly controlled asthma (E.g. FEV₁<75%, FeNO>50ppb, ACT <20)
   iii. Excessive school absence/evidence of failing educational attainment
3. In a confirmed poor or non compliance situation in a child/young person who is steroid responsive

**PRE-TREATMENT SCREENING**

All children/young people must have additional safety checks as below before commencing TA.

<table>
<thead>
<tr>
<th>Item check</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenal function status</td>
<td></td>
</tr>
<tr>
<td>Child/Young person must</td>
<td></td>
</tr>
<tr>
<td>have had a low dose synacthen test</td>
<td></td>
</tr>
<tr>
<td>within previous 12 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>If abnormal (peak cortisol &lt;500nmol/l) no need to repeat post treatment</td>
</tr>
<tr>
<td></td>
<td>If normal (peak cortisol &gt;500nmol/l) repeat 6-12 months post-treatment</td>
</tr>
<tr>
<td>Chickenpox status</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Has the child/young person had chickenpox?</td>
</tr>
<tr>
<td></td>
<td>If Yes, can this be confirmed by parent or carer ± evidence of scars?</td>
</tr>
<tr>
<td></td>
<td>If yes, no further action is needed and the TA may be given.</td>
</tr>
<tr>
<td></td>
<td>If No, or there is any doubt, check IgG to Varicella Zoster Virus (VZV)</td>
</tr>
<tr>
<td></td>
<td>If negative consider giving VZV vaccination but discuss with ID team if</td>
</tr>
<tr>
<td></td>
<td>concerned that the child may be immunocompromised from current oral</td>
</tr>
<tr>
<td></td>
<td>steroids at an immunosuppressive dose.</td>
</tr>
<tr>
<td></td>
<td>Live vaccines should NOT be given to immunocompromised children</td>
</tr>
<tr>
<td></td>
<td>For more information on immunisation in the immunocompromised child see</td>
</tr>
<tr>
<td></td>
<td>Reference².</td>
</tr>
<tr>
<td>Measles status</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Has the child/young person been vaccinated against Measles?</td>
</tr>
<tr>
<td></td>
<td>If Yes, no further action is needed and the TA may be given.</td>
</tr>
<tr>
<td></td>
<td>If No, or there is any doubt, consider giving MMR vaccination but</td>
</tr>
<tr>
<td></td>
<td>discuss with ID team if concerned that the child may be</td>
</tr>
<tr>
<td></td>
<td>immunocompromised from current oral steroids at an immunosuppressive</td>
</tr>
<tr>
<td></td>
<td>dose as **live vaccines should NOT be given to immunocompromised</td>
</tr>
<tr>
<td></td>
<td>children**.</td>
</tr>
<tr>
<td></td>
<td>For more information on immunisation in the immunocompromised child see</td>
</tr>
<tr>
<td></td>
<td>Reference².</td>
</tr>
</tbody>
</table>
REGIME

Discontinue oral steroids at time of first injection and issue/or update steroid card.

Duration: One IM injection every four to six weeks, depending on response, with a maximum of three injections. Duration of effect is variable, hence subsequent doses should be given when symptoms recur and not at set intervals¹.

Dosage¹:³ TA is not recommended for children under 6 years of age.
Children 6-12 years use 40mgs dose.
Children 12 years+ start at 40mgs. Subsequent dosage depends on the patient's response and period of relief. Consider increasing to 60mgs if poor clinical response.

ADMINISTRATION/PROCEDURE

- Strict aseptic precautions should be observed.
- To avoid the danger of subcutaneous fat atrophy at injection site ensure that deep intramuscular injection is given into the outer quadrant of the gluteal muscle by a nurse experienced in giving deep IM injections.
- Alternate sites should be used for subsequent injections

MONITORING

For the duration of the IM TA treatment the child/young person will be seen every 4-6 weeks by the Lead Consultant for asthma and/or the Clinical Nurse Specialist for asthma at the nurse run asthma clinic or the severe asthma clinic. A structured assessment (See Visit Checklist) will be conducted at every visit.

In patients who have received more than one injection during a three week period, or those receiving daily oral prednisolone prior to commencing IM TA, withdrawal should not be abrupt and additional corticosteroid cover may be required. Discuss with Lead Consultant in Asthma.

Treating Acute Exacerbations

Exacerbations occurring during TA treatment should be dealt with promptly. In the event families will be told to commence high dose bronchodilators and oral steroids, and present to hospital for further assessment. Patients prescribed TA will by definition be children/young people with very difficult to control asthma ± a history of severe acute episodes. At least at the start of TA treatment we would recommend admission for 24-48 hours during exacerbation as decline may have been triggered by recent stoppage of oral steroids.
Discuss with Lead Consultant for asthma. If not available, contact the Respiratory Consultant on call.

Two further interventions will be activated at the start of TA treatment. Firstly, the families will be provided with a letter to present on arrival to hospital. The letter will stress the recommendation to treat the acute asthma with further oral steroids and admit to Ward 6B for further observation. The acute receiving staff may not be familiar with TA and may delay further steroid loading.

Secondly, Philippa Madge will alert all Respiratory Consultants by email 7-10 days in advance of a child/young person commencing TA in case the child is admitted during treatment. The email will specify the intended start and expected end date of the treatment. Copies of the TA protocol will be available on the ward and on the website.

REFERENCES

(1) Electronic Medicines Compendium. Electronic Citation [ 2008  Available from: URL: http://emc.medicines.org.uk


(3) BNF for Children. 2008. Ref Type: Generic

This protocol should be used in conjunction with the package insert and Summary of Product Characteristics. The list of cautions, contraindication and adverse effects is not necessarily complete. For further advice contact Lead Consultant for Asthma and/or the Clinical Nurse Specialist for Asthma.

Prepared by West of Scotland Difficult Asthma Group
Clinical Leads:
Philippa Madge, PhD, Clinical Nurse Specialist in Paediatric Asthma.
Ms Kirsty Graham, Medicines Information Pharmacist.
Dr Conor Doherty, Consultant in Paediatric Infectious Diseases.
Dr James Paton, Reader in Paediatric Respiratory Disease.
June 2013.
Review Date June 2015
### VISIT CHECKLIST

#### BASELINE
- Visit 1
  - Discontinue any concurrent oral steroids
  - Provide steroid card
  - Ask about concurrent medication – Do not proceed if YES for any on the list
  - Ask about concurrent illness – Do not proceed if acutely unwell
  - Explain ‘No vaccines’ during treatment trial
  - Give product patient information leaflet
  - Provide information on acute adrenal suppression illness cover
  - Ask if any other treatment is planned over next 3 months e.g. dental work?
  - Photograph injection sites

#### ASSESSMENT
- **Visit 1**
  - 1st TA
- **Visit 2**
  - 1st TA + 2 weeks
- **Visit 3**
  - 2nd TA
- **Visit 4**
  - 3rd TA
- **Visit 5**
  - 3rd TA + 2/4 weeks

- Any URTI or viral exacerbation?
- Have any new medicines been prescribed?
- Height
- Weight
- FeNO
- FEV₁
- Reversibility
- Asthma Control Test (Short) (25=full control)
- Asthma Control Questionnaire (6=poor control)
- PAQOL (1=extreme to 7=no effect)
- HADS (11-14 mod, 15-21 severe)

#### SIDE-EFFECT SCREENING
- Record BP
- Standard urinalysis
- Injection site (record site used and condition)
- Any facial hair growth?
- Any acne developing?
- Any muscle weakness or fatigue?
- Any other issues raised by the child / parent?