Application and Case for Introduction of New Medicine
Service Developments

Anti-TNF for Inflammatory eye disease (uveitis resistant/sight threatening, scleritis resistant/sight threatening)

Purpose of this form: for providers to apply to commissioners for in-year funding of any new drug or extended use of an existing drug (e.g. new indication, new patient group) that will impact on prescribing costs in primary care. This includes where the prescribing will be passed on to primary care prescribers or where the drug is prescribed in hospital but generates additional PBR costs or is excluded from the Payment by Results Tariff and costs are passed on to commissioners. For simple new medicine service developments with no major funding implications please just complete the clinical section 1. and conflict of interest section 3.

Process:

Medicines Management Subgroup – assesses application, establishes evidence base and costs, consults with stakeholders, discusses with other centres, to form a preliminary recommendation on adoption

Area Meds Management Committee – assesses recommendation. Formal representation from providers, commissioners. Formulates recommendation to commissioners

Commissioners – make formal decision on whether new medicine service development is to be funded

Please complete this form as fully as possible. Please complete all relevant sections legibly. Any missing or illegible information will delay the application. You must discuss this application with the relevant Pharmacy Dept. / Medicines Management team. Applications completed by pharmaceutical companies are not acceptable.
**Section 1 Clinical information**

| Name of medicine (generic and brand name): | TNF blockers-  
| | Infliximab (Remicade)  
| | Adalimumab (Humira) |
| Strength(s) and form(s) of preparation: | Infliximab 5mg/kg monthly (initial dose)  
| Dose & schedule of administration: | Adalimumab 40mg every other week |
| Licensed indication(s): | RA, Psoriatic arthritis, AS, Crohn’s disease |
| Proposed Indication (if different from or in addition to the above): | Inflammatory eye disease  
| | Uveitis resistant/sight threatening  
| | Scleritis resistant/sight threatening |
| Is this treatment instead of or in addition to any current treatment? Please give details: | In addition |
| Reason for proposed change  
If replacing current treatment please state how it compares regarding efficacy and safety / tolerability | • Uveitis and scleritis with sight threatening features are relatively rare diseases. About 30% are associated with systemic disease, particularly JIA, rheumatoid arthritis, granulomatosis with polyangiitis (Wegener’s granulomatosis) and Behcets disease (BD) however a significant number are isolated/idiopathic.  
• Many individuals need systemic therapy with corticosteroid and combination immunosuppressants but a significant minority are resistant to standard therapies.  
• Commonly used standard therapies are corticosteroid (CS), methotrexate, tacrolimus, ciclosporin A, MMF and azathioprine.  
• Untreated these individuals have a high risk of suffering persistent visual loss.  
• Majority of sufferers are of working age and consequences of visual loss in this group are likely to be significant  
• Rescue treatment with steroids has a number of ocular complications and in itself can cause visual loss.  
• The major causes of visual loss in uveitis are-  
  o cystoid macular oedema (CMO) (fluid within the retina) which leads to permanent visual loss if persists >6weeks  
  o Vaso-occlusive disease (retinal blood vessel occlusion) |
- Persistent active vitritis (inflammation with white cells in the vitreous jelly)
  - Cataract (due to inflammation and also steroid–related)
  - Glaucoma (due to inflammation and also steroid–related)

- Scleritis affects the surface of the eye and can be very painful and debilitating.
- Visual loss usually results from:
  - scleral thinning and perforation
  - corneal ulceration
  - cataract and glaucoma (treatment–associated)
  - corneal grafting may be required
  - globe rupture and endophthalmitis

- Treatment with infliximab has been shown to have a major impact on acute flares of disease (vitritis and vaso-occlusion) as well as CMO which is the commonest cause of visual loss.
- It is effective for uveitis associated with BD as well as idiopathic forms.
- Data for adalimumab are more limited but this agent is worth considering because of its lower cost and home administration, and as an alternative if AE.
- TNF blockers have been shown to be safe and well tolerated in a number of other conditions, and are considered less toxic than high dose corticosteroid (particularly bearing in mind the ocular toxicity of CS) and some of the more potent immunosuppressants used for eye disease such as tacrolimus or ciclosporin A.

### Proposed place in therapy relative to other therapies (include protocol for use if available)

- Usual treatment for uveitis or scleritis is:
  - induction therapy with CS either topical, systemic (oral or IV) or peri- or intra-ocular injection
  - a systemic agent is usually commenced concomitantly often MMF or tacrolimus
  - flares of disease are treated with CS rescue and addition of a second agent, or change in therapy if intolerant/AE
  - CS are tapered to minimal dose if disease is controlled

- We propose to use TNF blockers in the following circumstances:
  - Persistent active vitritis with visual loss or CMO resistant to maintenance CS + 2 previous immunosuppressants alone or in combination
  - Acute sight-threatening disease (vaso-occlusive disease or fulminant vitritis) resistant to CS where delay in treatment to allow standard immunosuppressants to take effect is likely to lead to permanent sequelae
  - When disease is controlled, TNF blockers would be continued for 2 years and then an attempt made to step down/cease treatment and continue/substitute a standard maintenance drug regime, but resume TNF
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<th>Predicted clinical impact on Primary Care</th>
<th>Hospital only</th>
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<td>e.g. will it be initiated in hospital only but then prescribed in primary care, or may it be initiated in primary care? Will it require shared care? Please describe:</td>
<td>Monitoring for efficacy will be by ophthalmology assessment including detailed imaging, fluorescein angiography etc. All patients are already managed in our joint monthly rheumatology/ophthalmology clinic. Infusions will be administered by the rheumatology unit at Broadgreen Hospital and patients will have full medical support and helpline access as would any patient being treated with TNF blockers.</td>
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<td>Monitoring requirements (e.g. for efficacy, side-effects) – if any? Do these differ from current situation?</td>
<td>Uveitis and Scleritis are rare conditions and there are no RCTs, no meta analyses or consensus statements. Numerous well designed observational studies demonstrate the efficacy of infliximab in idiopathic posterior uveitis, including for reducing disease flares/vitritis, resolution of CMO, and for steroid-sparing effect. (1,2,3,4) There is one well performed prospective trial for uveitis. In this study patients received infliximab in addition to standard therapy and outcomes were described after 2 years with 2 year efficacy in 75% of patients (5) Infliximab is strongly recommended for treatment of uveitis in Behcets disease in European guidelines (6). The newly established National Centre for BD are due to publish recommendations for managing BD in the near future, and Infliximab for uveitis is supported by these (personal communication, Prof RJ Moots). Several case series and a recent large cohort study support the use of adalimumab for refractory uveitis (7). Several case reports and small case series demonstrate the efficacy of infliximab and adalimumab in the treatment of Scleritis associated with RA, WG as well as idiopathic disease (7,8,9,10) Our own experience at a large tertiary centre. We currently have 18 patients being treated with TNF blockers for uveitis, 16 of whom are receiving Infliximab and 2 adalimumab. 4 patients are currently being treated with TNF blockers for Scleritis (2 RA, 1 WG, 1 idiopathic). 10/22 patients are under the age of 40 and 16/22 in full time employment. The indication for biologic treatment was persistent CMO in 12, active vitritis and visual loss in 6 and fulminant disease in 2. Underlying diagnoses were BD (10), intermediate uveitis with CMO (4) and others (4). All our patients have been funded via ECT panel requests to local PCTs or North Wales Health Board, and all requests were approved. The number of patients commencing treatment by year are-</td>
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<td>Brief summary of evidence in support of requested medicine / additional use</td>
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<td>Meta-analyses, systematic reviews, double-blind randomised controlled trials in peer-reviewed journals. Ensure that evidence to support advantages / benefits of the new medicine over existing treatments is included where appropriate. Include any relevant morbidity, mortality, health economic and quality of life benefits.</td>
<td>2009 2</td>
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Of 22 patients, 21 have had what we would judge a good or excellent response with improvement of vision, resolution of CMO and steroid sparing, and discontinuation of at least 1 concomitant medication. One individual with a poor response had persistent CMO for many months prior to treatment and underscores the importance of early treatment of this complication.

References

Please list and include copies or internet links with the application

12.

Section 2 Financial information

Costs: (excluding VAT)
Cost per patient per year of medicine:

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<th>Adalimumab</th>
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<td>5mg/kg x 80kg = £1678.48 per dose</td>
<td>approx cost = £10,000 per annum</td>
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X 12 doses = 20141.76 per year

New pts per annum
| Year to be treated for the whole organisation: | Aintree 0.5  
| RLBUHT 6  
| St Helens 0.25  
| Warrington 0.5  
| Southport 0.25 | **Total 7.5**  
This does not include Behcets patients who are funded centrally via specialist commissioning.  
| Additional costs e.g. day case tariff, tests per patient per year: | Ward attender tariff 12 x £107 = £1284 per year  
| Any impact on PBR activity? Please give details: | Attendance for infusion once a month – costed above  
| Overall financial impact: | Assume 50/50 split between Adalimumab and Infliximab cost £15,712 x 7.5 = £118,000 per annum. Costs assuming 2 years of therapy= £236,000 annually. Please note these figures reflect pan Mersey area.  
| Current treatment(s) usually used (if any): | Corticosteroids  
| Mycophenolate £846 per annum assuming 1g BD dosage  
| Tacrolimus | None PbR excluded therapy  
| Cost per patient per year currently treated (excluding VAT): |  
| Number of patients per year currently treated: |  
| Current additional costs e.g. day case tariff, tests per patient per year: |  
| Predicted financial impact on Primary Care e.g. Is the medicine hospital only but PbR excluded, will it be initiated in hospital only but then prescribed in primary care, or may it be initiated in primary care? Please describe: |  

Section 3 Conflicts of Interest

Please state any potential conflicts of interest e.g. funding of research, equipment, consulting or speaking fees etc. in relation to this request:

| None |

Name of Applicant: **D Mewar**

Role: **Consultant Rheumatologist**

Organisation name: **Royal Liverpool and Broadgreen University Hospitals NHS Trust**

I confirm I have sent a copy of this form to my organisation’s Drug & Therapeutics Committee / Medicines Management Committee or equivalent, and it has been approved following the appropriate procedure within my organisation.

Signature of Applicant: …………………………………………………………………………….

Name of Clinical Director / CCG Prescribing Lead: … **K Nelson**……

Signature Clinical Director / Prescribing Lead: …………………………………

Name of Chief Pharmacist / Head of Medicines Management: **Paul Mooney**…………

Signature of Chief Pharmacist / Head of Medicines Management: ……………………

Please note that the application will not be considered unless the Chief Pharmacist / Clinical Director / Prescribing Lead / Head of Medicines Management in your organisation have signed this form.