Healthcare Improvement Scotland

NICE Health Technology Appraisal - Assessment Report **Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for the treatment of rheumatoid arthritis not previously treated with disease-modifying anti-rheumatic drugs and after the failure of conventional disease-modifying anti-rheumatic drugs only (review of technology appraisal guidance 130, 186, 224, 234 and a part review of technology appraisal guidance 225 and 247)**	
TO: NICE **12 September 2013**	**FROM: Healthcare Improvement Scotland**

Comment provided to Healthcare Improvement Scotland by:
[redacted], [redacted], [redacted]

1. The report is likely to be applicable to Scotland; there are minor differences in SIGN and NICE guidelines regarding the management of early RA but these are not likely to influence the major conclusions (for instance NICE recommends [incorrectly in my view] the use of combination cDMARD therapy at diagnosis whereas SIGN recognises that step-up strategies of care [initial mono therapy, stepping up aggressively in patients with persistent disease activity] are as effective)
2. The BSRBR data should be used with extreme caution where they are used to assess efficacy rather than toxicity. The registry was set up to capture serious adverse events and not efficacy – the timing of measures of disease activity and HAQ score in relation to the start of therapy is critical to interpretation, whereas it is of minimal importance in relation to long term toxicity. e.g. a DAS28 and/or HAQ measured after 4 weeks of bDMARD therapy will result in a false baseline reading, reducing the measured 'response' between the initial and subsequent scores.
3. Population 1: the conclusion that bDMARD therapy is highly unlikely to be cost effective in patients who are cDMARD naïve is almost certainly correct. The conclusion that infliximab + MTX is likely to be the most efficacious bDMARD in these patients is not secure, based as it is on small patient numbers and in the absence of direct comparisons
4. In general, the strategy of care in RA is to 'treat-to-target' - frequent review, formal assessment of disease activity and escalation of treatment in patients with persistent disease activity. The report has really not captured this, and as a result misses a key problem in clinical care – patients starting on MTX mono therapy have concomitant steroid (oral or parenteral), dose escalation, and addition of other DMARDs (typically 'triple therapy' with MTX/SSZ/HCQ)

if/when their disease is poorly controlled – usually defined in practice as having DAS28>3.2. The problem then arises – what should be done if a patient still has active disease despite triple therapy+steroid? At the moment the answer is to use bDMARD if DAS28>5.1, but to do nothing if DAS28>3.2 but <5.1. The pursuit of good disease control hits a higher hurdle at this point in the pathway than had previously been present. Paradoxically, therefore, the best option for the patient can be withdrawal of therapy to allow the DAS28 score to drift upwards (>5.1) to render the patient eligible for biologic therapy … which makes no sense.