NICE Multiple Technology Appraisal

Comments on ACD for

TNF alpha inhibitors for AS and non radiographic axial spondyloarthritis

TO: NICE

FROM: Healthcare Improvement Scotland

DEADLINE: 19 JUNE 2015

Comment provided to Healthcare Improvement Scotland [redacted], Senior Lecturer in Rheumatology, University of Glasgow

Comments on the NICE ACD

We welcome this ACD, which is overall very thorough and consistent with clinical practice in Scotland. The only significant discrepancy and clinical issue is the specific recommendation against **sequential use or switching to another TNF inhibitor** in those who have failed to respond or lost efficacy with their first TNFi (Section 1.6 in the ACD).

There is currently no SIGN guidance for AS/axSpA, while the SMC advice for the specific agents either does not comment on switching or includes the line “"Switching to a second TNF blocker might be beneficial especially in patients with loss of response”. In clinical practice, most rheumatology centers in Scotland have been switching appropriately selected patients with AS to subsequent TNFi with good effect and response. These decisions are made on an individual-by-individual basis with efforts made to exclude other causes of pain or failure to first TNFi (eg fibromyalgia, mechanical back pain) and include repeat imaging to confirm objective evidence of “inflammation”. This has been in line with the ASAS and EULAR guidelines.

We are also aware if the anxiety the inability to switch in England has caused patients and clinicians (also commented on in ACD 4.24 & 4.54), and that this has often resulted in patients remaining on an ineffective/partially effective first TNFi rather than switching to a more effective subsequent TNFi.
We acknowledge that the published evidence for switching is limited, and that RCTs for this are unlikely to ever be performed; however, the data from observational studies (eg DANBIO commented on in section 4.12) and clinical experience supports switching and is reflected in the comments in the ACD in sections 4.12 (*The Assessment Group concluded that, despite a decrease in response rates, sequential treatment with TNF-alpha inhibitors can be beneficial for people with ankylosing spondylitis*) and 4.59 (*The Committee concluded that sequential treatment with TNF-alpha inhibitors is likely to be beneficial, but that clinical data are limited)*. The decision to specifically not recommend sequential use is therefore based on *insufficient cost-effectiveness evidence to allow it to recommend sequential use of TNF-alpha inhibitors as a cost-effective use of NHS resources (4.69)* although *the Assessment Group had not modelled sequential use (4.49).*

This specific recommendation against switching would therefore be a retrograde and negative step for patients in Scotland. If the committee feels unable to recommend sequential use due to lack of evidence, then there should not be any specific recommendation relating to this, rather than specifically recommending *against* switching.

Comments using the specific headings:

1. Do you consider that all the relevant evidence has been taken into account?

   Overall very thorough, but it does not appear that all data about sequential use of TNFi has been taken into account (see also above). Specifically, there is more data supporting the effectiveness of switching between TNF inhibitors in ankylosing spondylitis in the NOR-DMARD register (Lie et al Ann Rheum Dis 2011;70:157-63) and the ATTRA register (Pavelka et al Rheumatologica 2012;50:294-306).

2. Do you consider that the analysis of clinical and cost effectiveness has used an appropriate comparator which reflects Scottish practice?

   Yes

3. Do you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence?

   Yes

4. Are the provisional recommendations of the Appraisal Committee sound and do they constitute a suitable basis for the preparation of guidance to the NHS?

   See above comments about switching

5. Are the patient pathways and treatment options described in the assessment applicable to NHSScotland?

   Generally yes, apart from the above comments about switching/sequential use.

6. Would the provisional recommendations change the patient pathways and/or patient numbers in NHSScotland?

   Overall unlikely to be significant change in numbers. Most specialist units are already treating non-radiographic axSpA in line with the licensing, SMC and ASAS guidelines (mentioned in the SMC advice). There would however be a negative impact on selected patients if switching were no longer allowed (see above)

7. Do you think there is any reason why this provisional guidance would not be as valid in Scotland as it is in England and Wales?

   Yes. While most recommendations are consistent with current practice, the recommendation not to switch patients (section 1.6) would have negative implications on patients with ongoing active and severe disease.