

<p><b>1</b></p>	<p><b>Treatment &amp; Condition</b></p> <p>TNF-alpha inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis (nrAS)</p>
<p><b>2</b></p>	<p><b>Associated appraisal body &amp; Summary of ruling</b></p> <p>NICE Technology Appraisal Guidance TA383 (February 2016)</p> <p>Adalimumab, certolizumab pegol, etanercept, golimumab and infliximab are recommended, within their marketing authorisations, as options for treating severe active ankylosing spondylitis in adults whose disease has responded inadequately to, or who cannot tolerate, non-steroidal anti-inflammatory drugs. Infliximab is recommended only if treatment is started with the least expensive infliximab product. People currently receiving infliximab should be able to continue treatment with the same infliximab product until they and their NHS clinician consider it appropriate to stop.</p> <p>Adalimumab, certolizumab pegol and etanercept are recommended, within their marketing authorisations, as options for treating severe non-radiographic axial spondyloarthritis (nrAS) in adults whose disease has responded inadequately to, or who cannot tolerate, non-steroidal anti-inflammatory drugs.</p> <p>The choice of treatment should be made after discussion between the clinician and the patient about the advantages and disadvantages of the treatments available. This may include considering associated conditions such as extra-articular manifestations. If more than 1 treatment is suitable, the least expensive (taking into account administration costs and patient access schemes) should be chosen.</p> <p>The response to adalimumab, certolizumab pegol, etanercept, golimumab or infliximab treatment should be assessed 12 weeks after the start of treatment. Treatment should only be continued if there is clear evidence of response, defined as:</p> <ul style="list-style-type: none"> <li>• a reduction in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score to 50% of the pre-treatment value or by 2 or more units and</li> <li>• a reduction in the spinal pain visual analogue scale (VAS) by 2 cm or more</li> </ul> <p>Treatment with another tumour necrosis factor (TNF) -alpha inhibitor is recommended for people who cannot tolerate, or whose disease has not responded to, treatment with the first TNF-alpha inhibitor, or whose disease has stopped responding after an initial response.</p> <p>When using BASDAI and spinal pain VAS scores, healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect the responses to the questionnaires, and make any adjustments they consider appropriate.</p>

<p><b>3</b></p>	<p><b>Number of people in Northern Ireland expected to take up service/therapy</b> <i>(including new cases per year)</i></p> <p>The Resource Impact Report that accompanies TA383 indicates that no significant costs are expected for the ankylosing spondylitis patient group as a result of implementing the guidance. Significant costs are expected for the nrAS patient group.</p> <p>The table below sets out the population with nrAS in Northern Ireland eligible for treatment with TNF-alpha inhibitors.</p> <table border="1" data-bbox="240 555 1406 1155"> <thead> <tr> <th colspan="3"><b>Number of people with nrAS eligible for treatment in Northern Ireland</b></th> </tr> <tr> <th><b>Population</b></th> <th><b>Proportion</b></th> <th><b>Number of people</b></th> </tr> </thead> <tbody> <tr> <td>Total adult population in Northern Ireland</td> <td></td> <td>1,397,710</td> </tr> <tr> <td>Prevalence of nrAS</td> <td>0.15%</td> <td>2,097</td> </tr> <tr> <td>Of these, people meeting BSR guidelines for TNF-alpha inhibitors treatment</td> <td>38%</td> <td>797</td> </tr> <tr> <td>Those not contraindicated for TNF-alpha inhibitors treatment</td> <td>85%</td> <td>677</td> </tr> <tr> <td>Of these, people who are likely to continue using TNF-alpha inhibitors</td> <td>30%</td> <td>203</td> </tr> <tr> <td>Total number of people estimated to have TNF-alpha inhibitor treatment each year from year 7</td> <td></td> <td>203</td> </tr> </tbody> </table> <p>Using NICE assumptions it is projected that the number of patients on treatment for nrAS will increase from around 46 in year 1 (2016/17) to around 200 from year 7. It is then anticipated that the number of patients on treatment will remain at this level once uptake has reached 30%.</p>	<b>Number of people with nrAS eligible for treatment in Northern Ireland</b>			<b>Population</b>	<b>Proportion</b>	<b>Number of people</b>	Total adult population in Northern Ireland		1,397,710	Prevalence of nrAS	0.15%	2,097	Of these, people meeting BSR guidelines for TNF-alpha inhibitors treatment	38%	797	Those not contraindicated for TNF-alpha inhibitors treatment	85%	677	Of these, people who are likely to continue using TNF-alpha inhibitors	30%	203	Total number of people estimated to have TNF-alpha inhibitor treatment each year from year 7		203
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<p><b>4</b></p>	<p><b>Patient Access Scheme availability</b></p> <p>PAS discounts have been agreed for:</p> <ul style="list-style-type: none"> <li>• certolizumab – first 12 weeks treatment with certolizumab is provided free of charge</li> <li>• golimumab – price of 100mg pen is the same as that of the 50mg pen</li> </ul>																								
<p><b>5</b></p>	<p><b>Costs</b> <i>(before PAS if applicable)</i></p>																								
<p><b>5.1</b></p>	<p><b>Drug cost per patient per annum (for new and prevalent cases)</b></p> <p><u>Adalimumab</u> The licenced dose for these conditions is 40mg every other week. The price of adalimumab is £352.14 for a 40mg pre-filled pen or pre-filled syringe, or a 40mg/0.8ml vial. The annual cost of treatment with adalimumab is estimated at £9,156, assuming the patient has 40mg every other week</p> <p><u>Certolizumab</u> The licenced dose for these conditions is 400mg (given as 2 injections of 200mg each) at weeks 0, 2 and 4. The recommended maintenance dose regimen is</p>																								

200mg every other week or 400mg every 4 weeks. The price of certolizumab pegol is £357.50 for a 200mg pre-filled syringe. The manufacturer (UCB Pharma) has agreed a patient access scheme with the Department of Health. UCB Pharma will provide the first 12 weeks of certolizumab pegol free of charge, which is equivalent to 10 vials. Assuming the recommended dosage is followed, the annual cost for first year of treatment with certolizumab pegol is estimated at £10,368 (or with the patient access scheme, £6,793).

#### Etanercept

The licensed dose for these conditions is 25mg administered by subcutaneous injection twice weekly or 50mg administered once weekly. The price of etanercept is £89.38 for a 25mg pre-filled syringe or a 25mg vial, and £178.75 for a 50mg pre-filled pen or pre-filled syringe. The annual cost of treatment with etanercept, using either twice weekly or once weekly dosage frequency, is estimated at £9,296.

#### Golimumab

The licensed dose for patients with ankylosing spondylitis is 50mg once a month on the same date each month. For patients with a body weight greater than 100kg whose disease does not respond adequately after 4 doses (50mg each), the dosage of golimumab can be increased to 100mg once a month. If there is still no evidence of therapeutic benefit after 3–4 additional doses of 100mg, continued golimumab therapy should be carefully reconsidered. The price of golimumab is £762.97 for a 50mg pre-filled pen or pre-filled syringe and £1,525.94 for a 100mg pre-filled pen. The manufacturer (Merck Sharp & Dohme) has agreed a patient access scheme with the Department of Health. This will make the 100mg dose of golimumab available to the NHS at the same cost as the 50mg dose. Assuming the patient has 50mg every month, the annual cost of treatment with golimumab is estimated at £9,156. Because of the patient access scheme, this cost would remain the same for patients with a body weight greater than 100kg whose disease does not respond adequately to the 50mg per month dosage and who subsequently have monthly doses of 100mg.

#### Infliximab

The licensed dose for patients with ankylosing spondylitis is a 5mg/kg infusion at weeks 0, 2 and 6, then every 6–8 weeks. The NHS list price of the infliximab originator (Remicade<sup>®</sup>) is £419.62 for a 100mg vial. For a patient with a body weight of 73kg, the annual cost for first year of treatment with infliximab therapy (including 3 induction doses) is estimated at between £16,785 and £13,428 (depending on whether the maintenance infusions are repeated every 6 or 8 weeks).

Biosimilar versions of infliximab (Inflectra<sup>®</sup>; Remsima<sup>®</sup>) have a marketing authorisation in the UK for the same indications. The therapeutic indications, dosage and method of administration for Inflectra<sup>®</sup> and Remsima<sup>®</sup> are identical to those for Remicade<sup>®</sup>. The NHS list price of Inflectra<sup>®</sup> and Remsima<sup>®</sup> is £377.66 for a 100mg vial. For a patient with a body weight of 73kg, the annual cost for first year of treatment with Inflectra<sup>®</sup> or Remsima<sup>®</sup> therapy is estimated at between £15,106 and £12,085 (depending on whether the maintenance infusions are repeated every 6 or 8 weeks).

5.2	<p><b>Infrastructure costs per patient per annum</b></p> <p>The HSC Board will work with Trusts to identify any infrastructure requirements.</p>																								
5.3	<p><b>Current in year costs</b></p> <p>The Resource Impact Report that accompanies TA383 indicates that no significant costs are expected for the ankylosing spondylitis patient group as a result of implementing the guidance. Using the NICE assumptions approximately 46 patients in the nrAS patient group would commence treatment in 2016/17. The in-year cost projections for this cohort are £221k. Any in-year costs will be funded on a cost per case basis.</p>																								
5.4	<p><b>Recurrent overall costs per annum (including additional costs)</b></p> <p>NICE has previously appraised TNF-alpha inhibitor treatments for ankylosing spondylitis (TA143 and TA233). Certolizumab pegol and infliximab are additional alternative options for this patient group. There are no significant costs anticipated for this patient group because there are no changes in the anticipated uptake from this group as a result of implementing the guidance.</p> <p>NICE has however indicated that there are likely to be significant costs increasing over a seven year period the nrAS patient group. The annual cost associated with implementing the guidance for the population of Northern Ireland is shown in the table below. The cost from year 7 once steady state reached is equivalent to £1.681m</p> <table border="1" data-bbox="240 1144 1422 1361"> <thead> <tr> <th></th> <th>2016/17</th> <th>2017/18</th> <th>2018/19</th> <th>2019/20</th> <th>2020/21</th> <th>2021/22</th> <th>2022/23</th> </tr> </thead> <tbody> <tr> <td>Population with nrAS having TNF-alpha inhibitor treatment each year</td> <td>46</td> <td>107</td> <td>141</td> <td>173</td> <td>202</td> <td>203</td> <td>203</td> </tr> <tr> <td>Cost impact each year for people with nrAS £(000s)</td> <td>£ 221</td> <td>£ 770</td> <td>£ 1,094</td> <td>£ 1,396</td> <td>£ 1,661</td> <td>£ 1,686</td> <td>£ 1,681</td> </tr> </tbody> </table>		2016/17	2017/18	2018/19	2019/20	2020/21	2021/22	2022/23	Population with nrAS having TNF-alpha inhibitor treatment each year	46	107	141	173	202	203	203	Cost impact each year for people with nrAS £(000s)	£ 221	£ 770	£ 1,094	£ 1,396	£ 1,661	£ 1,686	£ 1,681
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5.5	<p><b>Opportunities for cost savings and how these will be secured</b></p> <p>Cost savings are not anticipated.</p>																								
6	<p><b>Expected implementation period</b></p> <p>There is no impediment to implementation of this guidance.</p>																								
7	<p><b>Commissioning arrangements</b></p> <p>This regime will be formally commissioned by the HSCB/PHA via the Specialist Services Commissioning Team.</p>																								
8	<p><b>Monitoring arrangements</b></p> <p>HSCB currently reviews monthly monitoring information from all Trusts on all biologics used, number of patients treated, and number of patients waiting to commence treatment by banded waiting times.</p>																								

	<p>The Specialist Service Commissioning Team has a long established biologics sub group which meets on a bi-monthly basis. Service monitoring including the review of the monthly data returns is a key function of this group.</p>
<b>9</b>	<p><b>DHSSPS Legislative/Policy Caveats</b> (<i>NICE guidance only</i>)</p> <p>This advice does not override or replace the individual responsibility of health professionals to make appropriate decisions in the circumstances of their individual patients, in consultation with the patient and/or guardian or carer. This would, for example, include situations where individual patients have other conditions or complications that need to be taken into account in determining whether the NICE guidance is fully appropriate in their case.</p>