

1	<p><b>Treatment &amp; Condition</b></p> <p>Nivolumab in combination with ipilimumab for treating advanced melanoma</p>
2	<p><b>Associated appraisal body &amp; Summary of ruling</b></p> <p>NICE Technology Appraisal guidance TA400 (July 2016)</p> <p>Nivolumab in combination with ipilimumab is recommended, within its marketing authorisation, as an option for treating advanced (unresectable or metastatic) melanoma in adults, only when the company provides ipilimumab with the discount agreed in the patient access scheme.</p>
3	<p><b>Number of people in Northern Ireland expected to take up service/therapy (including new cases per year)</b></p> <p>Following positive NICE guidance (TA366 and TA384), pembrolizumab and nivolumab monotherapy are now the most commonly used first-line treatment options for advanced (unresectable or metastatic) melanoma regardless of BRAF-V600 mutation status. These treatments have a higher response rate and better toxicity profile than ipilimumab, which has now been largely superseded for first-line use.</p> <p>Previously, an assessment of patient numbers likely to be treated pembrolizumab or nivolumab concluded that 39 patients are likely to be treated with either of these treatments as a single agent. These estimates are based on first or second-line use.</p> <p>Nivolumab with ipilimumab will now be an option for the same patient population who have previously been offered single agent pembrolizumab or nivolumab.</p> <p>The opinion of local oncologists is that patients will be selected carefully due to the potential for high toxicity, and it is estimated that approximately a third of those who would have been offered single agent pembrolizumab or nivolumab will now be considered suitable for Nivolumab with ipilimumab. This equates to about 13 patients per year.</p>
4	<p><b>Patient Access Scheme availability</b></p> <p>The company has agreed a patient access scheme for ipilimumab with the Department of Health. This scheme provides a simple discount to the list price of ipilimumab with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence.</p>
5	<p><b>Costs (before PAS if applicable)</b></p>
5.1	<p><b>Drug cost per patient per annum (for new and prevalent cases)</b></p> <p>Nivolumab is available at a list price of £439 per 4ml (40mg) vial (excluding VAT).</p>

	<p>Ipilimumab is available at a list price of £3,750 per 10ml (50mg) vial and £15,000 per 40ml (200mg) vial (excluding VAT).</p> <p>The recommended starting dose of the combined regimen is nivolumab 1mg per kilogram of body weight and ipilimumab 3mg per kilogram of body weight, administered intravenously over a 90minute period every 3 weeks for a total of 4 doses. This is followed by maintenance treatment with nivolumab alone at a dose of 3mg per kilogram body weight, administered intravenously over a 60minute period every 2 weeks.</p> <p><u>Nivolumab</u> The cost per person of nivolumab is as follows (based on an average body weight of 77.2kg):</p> <ul style="list-style-type: none"> <li>• Initial doses of nivolumab (given with ipilimumab) = 77.2mg per dose = £878 per dose = £3,512 per initial course of nivolumab (4 doses)</li> <li>• Maintenance dosing (nivolumab alone) = 231.6mg per dose = £2,634 per dose = £52,680 for the remainder of the year</li> <li>• Total = £3,512 + £52,680 = £56,192 per patient per year of nivolumab</li> </ul> <p><u>Ipilimumab</u> The cost per person of ipilimumab is as follows (based on an average body weight of 77.2kg):</p> <ul style="list-style-type: none"> <li>• 231.6mg per dose = £18,750 per dose = £75,000 per course (4 doses) [before application of any PAS discount]</li> </ul>
<p><b>5.2</b></p>	<p><b>Infrastructure costs per patient per annum</b></p> <p>Any additional infrastructure costs associated with the introduction of new cancer therapies will be managed as part of the routine commissioning process.</p>
<p><b>5.3</b></p>	<p><b>Current in year costs</b></p> <p>Costs will depend on the number of patients receiving the treatment. Local oncologists have estimated that 13 patients will be eligible for treatment in the current year at a cost of approximately £95k.</p>
<p><b>5.4</b></p>	<p><b>Recurrent overall costs per annum (including additional costs)</b></p> <p>The NICE guidance for TA400 advises that ‘no resource impact is anticipated because there are cost savings from reduced administration costs and dosage when the 2 existing technologies are combined, but these savings are not expected to be significant.’</p> <p>However, local oncologists estimate that 13 patients are now eligible to receive a further dose of ipilimumab.</p> <p>The gross cost associated with TA400 is expected to be £975,000 (before the PAS is applied). However, the assessment of TA366 (pembrolizumab for advanced melanoma not previously treated with ipilimumab) included savings of £593,000 (before PAS). Therefore, the net cost associated with TA400 is expected to be £382,000 (before PAS).</p>

	There will be ongoing monitoring of use of ipilimumab via the cost per case arrangement.
<b>5.5</b>	<b>Opportunities for cost savings and how these will be secured</b> It's not expected that there will be opportunities for savings.
<b>6</b>	<b>Expected implementation period</b> There is no impediment to immediate implementation for new patients.
<b>7</b>	<b>Commissioning arrangements</b> This regimen will be formally commissioned by the HSCB/PHA via the Specialist Services Commissioning Team initially on a cost-per-case (CPC) basis for a period of 12 months.
<b>8</b>	<b>Monitoring arrangements</b> The HSCB cost per case process will generate quarterly reports on the number of applications.  HSCB currently routinely reviews quarterly monitoring information in relation to the usage of all recurrently funded specialist cancer drugs across both the Cancer Centre and other Units.  The monitoring pro forma will be adapted to capture information in respect of this regimen and this group of patients. This monitoring report is submitted to the Specialist Services Commissioning Team for formal review and comment by the Team.
<b>9</b>	<b>DHSSPS Legislative/Policy Caveats</b> 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.