NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Melanoma (stage III or IV) - ipilimumab

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name: Dr. Paul Nathan

Name of your organisation [redacted]

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology? **yes**
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)? **yes**
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)? **no**
- other? (please specify)

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

What is the expected place of the technology in current practice?

Unresectable metastatic melanoma has an extremely poor prognosis. Until recently no systemic treatment had been proven to improve overall survival which unfortunately is less than a year.

Standard palliative treatment is with the chemotherapy agent dacarbazine (DTIC). Although being well tolerated it has minimal activity in advanced melanoma. Response rates are quoted as being 5-15%. Duration of response is generally 3-4 months and there is no proven survival benefit with the agent.

Ipilimumab is the first systemic agent proven to improve overall survival in advanced melanoma and represents a major step forward in the treatment of this disease.

Ipilimumab would be appropriate under the current EU licence for the treatment of unresectable metastatic melanoma for the second and subsequent lines of treatment.

No predictive biomarker exists that can identify the sub-group of patients who derive significant benefit from the drug.

The drug should be prescribed and managed by oncologists with a special interest in melanoma working from a cancer centre that can provide appropriate support for patients on treatment.

The most recent UK clinical guidelines for the management of melanoma pre-date the availability of ipilimumab and therefore do not provide guidance on its use.

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

The advantages and disadvantages of the technology

There are no standard alternatives for the second and subsequent lines of treatment for metastatic melanoma. Ipilimumab therefore represents a new standard of care in this setting.

The advantages of the technology are that this is the first available agent to extend overall life expectancy for this disease. Accumulating evidence is that there are a sub-group of patients who have durable responses measured in many years. It is unknown whether some of these patients are cured.

Disadvantages are that a) there is no predictive biomarker to identify the population of patients who benefit and b) the side – effect profile of drug induced auto-immune phenomena is unfamiliar to many oncologists. However, highly effective supportive information is in place and this is not a major issue.

The evidence base for the drug comes from high quality international multi-centre randomised phase III studies in the 2nd and 1st line setting. A number of previous phase II studies also revealed the significant clinical activity of the agent. The studies were able to prove an overall survival advantage – the most relevant clinical endpoint.

The phase III studies are entirely applicable to UK practice.

The side effect profile of drug-induced autoimmune disease is manageable with steroid intervention under most circumstances. The clinical algorithms provided for the management of these phenomena are robust and easy to follow. From an oncologists perspective, the severity of these side effects compares favourably with many of the significant side effects caused by conventional chemotherapeutics. As the spectrum and treatment of side effects differs from conventional chemotherapeutics, treating oncologists need to be made aware of side effect management.

In my view the overall benefit from ipilimumab in the metastatic setting far outweighs concerns regarding toxicity.

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Any additional sources of evidence

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Implementation issues
No significant implantation issues that I can see.