Specialised Services Circular

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NICE Technology Appraisal 321: Dabrafenib for treating unresectable or metastatic BRAF V600 mutation-positive melanoma

Circulation

For action	**For information**
Area Team Directors Area Team Directors of Commissioning Area Team Heads of Specialised Area Team IFR Leads Area Team Finance Leads Area Team Pharmacists Area Teams to circulate to: Acute Trust Chief Executives; Acute Trust Medical Directors Acute Trust Chief Pharmacists Clinical Reference Group Chairs: onward circulation relevant CRG members	Regional Directors of Commissioning Regional Heads of Specialised Commissioning Regional Finance Leads

Background

Melanoma is a type of skin cancer which in its early stages is normally asymptomatic and, if detected early, before it has spread, can be curable by resection. However, at presentation, around 10% of melanomas will have metastasised. Melanoma can spread to nearby lymph nodes (stage III, of which stage IIIc disease includes tumours of varying size with extensive lymph node involvement but no metastases) or to other parts of the body (stage IV). It occurs more commonly in fair-skinned people and there is strong evidence that ultra violet exposure is causal. People with an above-average mole count, sun-sensitive skin, or a strong family history of melanoma are at greatly increased risk.

The incidence of melanoma is increasing in England with rates doubling approximately every 10-20 years. There were 10,656 new diagnoses of melanoma in 2010 and 1871 deaths registered in the England in 2010. In the UK, melanoma is diagnosed at a mean age of around 50 years but approximately 20% of cases occur in young adults aged between 15 and 39 years old. Five-year survival rates are approximately 20-30% for stage IIIc disease and approximately 7-20% for stage IV disease.

BRAF is part of the RAS/MAPK signalling pathway, which helps to control cell proliferation, differentiation and death. Companion diagnostic tests can be used to detect the BRAF mutation, including the cobas test, generic PCR sequencing tests and other validated BRAF mutation tests. The mutated form BRAFV600 is found in approximately 50% of melanomas.

Early recognition of melanoma and accurate diagnosis presents the best opportunity for cure by surgical resection of the tumour. A very small minority of people with advanced disease can still have their tumour removed. First line treatment for people with a BRAFV600 mutation is normally vemurafenib, but dacarbazine and ipilimumab are also treatment options. Radiotherapy, immunotherapy and combination chemotherapy have also been studied in randomised clinical trials.

NICE technology appraisal No. 269 recommends vemurafenib as an option for treating BRAFV600 mutation-positive unresectable or metastatic melanoma. NICE technology appraisal No. 268 recommends ipilimumab as an option for treating advanced (unresectable or metastatic) melanoma in people who have received prior therapy and TA319 recommends ipilimumab as a first line option within the same indication.

Dabrafenib (Tafinlar, GlaxoSmithKline) is an inhibitor of the BRAF V600 protein kinase. When the activity of protein kinase is blocked, the cancer cells stop growing and die. Dabrafenib has a marketing authorisation in the UK in monotherapy for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation.

Summary

NICE in their Technology Appraisal published 22 October 2014 have stated that:

> Dabrafenib is recommended, within its marketing authorisation, as an option for treating unresectable or metastatic BRAF V600 mutation-positive melanoma only if the company provides dabrafenib with the discount agreed in the patient access scheme.

The list price of dabrafenib is £1400 for a pack of 75-mg capsules (28 capsules per pack) and £933.33 for a pack of 50-mg capsules (28 capsules per pack) (excluding VAT; 'British national formulary' [BNF] edition 67). It is taken orally at a recommended dose of 150 mg twice daily. GlaxoSmithKline has agreed a patient access scheme with the Department of Health that makes dabrafenib available with a discount applied at the point of purchase or invoice. The size of the discount is commercial in confidence.

It should be noted that dabrafenib in the above indication is not routinely commissioned in England in patients who have received prior vemurafenib therapy and have progressed. An exception will be where there has been severe intolerance to vemurafenib within 2 months of initiating treatment which has necessitated discontinuation. In addition, vemurafenib is also not routinely commissioned in patients who have received and progressed on dabrafenib.

Dabrafenib is recommended by NICE "*within its marketing authorisation*" which is as monotherapy. Dabrafenib is therefore only routinely commissioned when it is given as monotherapy.

At the agreed PAS price, NICE does not expect the guidance to have a significant impact on NHS resources. This is because most people who are eligible for treatment with dabrafenib are already eligible for treatment with vemurafenib which has a similar cost.

NHS England will commission dabrafenib according to the criteria contained within this circular from 20th January 2015.

There have been 68 requests (up to the end of September) to the Cancer Drug Fund for dabrafenib in patients who have been intolerant to vemurafenib. Assuming similar numbers apply up to the point of transfer to routine commissioning, this equates to circa £900k transferring to the NHS England baseline taking into account the PAS scheme and patients who will have progressed on treatment. New patients will be cost neutral as they would have received vemurafenib.

Action

Area Teams are asked to note this position and to work with providers to ensure that dabrafenib in its NICE approved indication is not administered to patients who have received prior vemurafenib except where the exception above is met.

Area Teams should ensure that Trusts are purchasing dabrafenib at the agreed PAS price. Any enquiries from NHS organisations about the patient access scheme should be directed to the GlaxoSmithKline customer contact centre on 0800 221

441.

The test costs circa £120. However, area teams should also note that the company manufacturing vemurafenib (Roche) is currently making BRAF V600 mutation testing free of charge by funding 3 BRAF reference testing centres in the UK. However, the company has informed NICE that it will withdraw funding for BRAF V600 mutation testing from 1st January 2015. Roche have already provided 12 months' notice to Trusts regarding the withdrawal of the free service. The expenditure implications of this should already be reflected Trusts' financial plans. As the test is not excluded or unbundled from Tariff there will be no impact for commissioner expenditure plans.

Further Information

NICE Technology Appraisal 321: Dabrafenib for treating unresectable or metastatic BRAF V600 mutation-positive melanoma can be found at http://guidance.nice.org.uk/TA321

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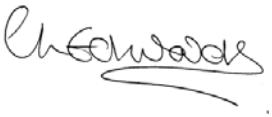

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