New oncology reimbursements in Belgium

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OVERVIEW OF BELGIAN REIMBURSEMENT NEWS

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AFINITOR® (EVEROLIMUS)

Afinitor® (everolimus) is now also reimbursed for the treatment of inoperable or metastatic, well differentiated (Grade 1 or 2), non-functional neuroendocrine tumours of gastrointestinal or lung origin showing tumour progression.

The approval and reimbursement for these patients is based on the outcome of **RADIANT-4**, which is a randomised, double-blind, multicentre, phase III study of Afinitor® plus best supportive care (BSC) versus placebo plus BSC in patients with advanced, well-differentiated (Grade 1 or 2) non-functional neuroendocrine tumours of gastrointestinal or lung origin without a history of and no active symptoms related to carcinoid syndrome.[1,2] A total of 302 patients were randomised in a 2:1 ratio to receive either everolimus (10 mg daily) or placebo. The median duration of blinded treatment was 40.4 weeks for patients receiving Afinitor® and 19.6 weeks for those receiving placebo. Patients in the placebo arm did not cross-over to everolimus at the time of progression. Median progression-free survival (PFS) evaluated by Response Evaluation Criteria in Solid Tumours (RECIST), based on independent radiology assessment (primary endpoint) was 11.01 months (95% confidence interval [CI] 9.2, 13.3) with Afinitor® versus 3.91 months (95% CI 3.6, 7.4) with a hazard ratio (HR) of 0.48 (95% CI 0.35, 0.67; p<0.0001).[1] The pre-planned overall survival (OS) interim analysis after 101 deaths (out of 191 required for final analysis) and 33 months of follow-up favoured the everolimus arm although the difference did not reach statistical significance (HR=0.73 [95% CI: 0.48 to 1.11; p=0.071]). No difference in the time to definitive deterioration of WHO PS (≥1 point) and time to definitive deterioration in quality of life (FACT-G total score ≥7 points) was observed between the two arms.[1,2]

KEYTRUDA® (PEMBROLIZUMAB)

Reimbursement for Keytruda® (pembrolizumab) has been extended to all approved indications by the European Medicines Agency (EMA).[3]

Keytruda® was already reimbursed as monotherapy for the treatment of adult patients with advanced (unresectable or metastatic) melanoma.

It is currently also approved as monotherapy:

- for the first-line treatment of metastatic non-small cell lung carcinoma (NSCLC) in adults whose tumours express PD-L1 with a ≥50% tumour proportion score (TPS) with no EGFR or ALK positive tumour mutations and
- for the treatment of locally advanced or metastatic NSCLC in adults whose tumours express PD-L1 with a ≥1% TPS and who have received at least one prior chemotherapy regimen. Patients with EGFR or ALK positive tumour mutations should also have received targeted therapy before receiving Keytruda®.

Approval and reimbursement in first line is based on the outcome of **KEYNOTE-024**.[3,4] Patients in Keynote-024 were treatment naïve and had PD-L1 expression with a ≥50% tumour proportion score (TPS) based on the PD-L1

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IHC 22C3 pharmDx™ Kit. The study excluded patients with:

- EGFR or ALK genomic tumour aberrations;
- autoimmune disease that required systemic therapy within two years of treatment or a medical condition that required immunosuppression;
- who had received more than 30 Gy of thoracic radiation within the prior 26 weeks.

Three hundred and four patients were randomised (1:1) to receive either pembrolizumab at a dose of 200 mg every three weeks or investigator's choice platinum-containing chemotherapy (ICC), including pemetrexed + carboplatin, pemetrexed + cisplatin, gemcitabine + cisplatin, gemcitabine + carboplatin, or paclitaxel + carboplatin. Non-squamous patients could receive pemetrexed maintenance. Patients were treated with pembrolizumab until unacceptable toxicity or disease progression for up to 24 months. Treatment could continue beyond disease progression if the patient was clinically stable and was considered to be deriving clinical benefit by the investigator. Median PFS as assessed by blinded independent central review (BICR) using RECIST 1.1 (primary endpoint) was 10.3 months (95% CI 6.7, not available [NA]) with pembrolizumab versus 6.0 months (95% CI 4.2, 6.2) with ICC with a hazard ratio of 0.50 (95% CI 0.37, 0.68; p<0.001). Overall response rate (ORR) was 45% (95% CI 37, 53) and 28% (95% CI 21, 36), respectively. Hazard ratio for OS was 0.60 (95% CI 0.41, 0.89; p 0.005). Median duration of response (DOR) was not reached with pembrolizumab and was 6.3 months with ICC.[3,4]

Approval and reimbursement in pretreated patients are based on the results of **KEYNOTE-010** in which patients previously treated with platinum-containing therapy and with a PD-L1 expression with a ³1% TPS based on the PDL1 IHC 22C3 pharmDx™ Kit, were randomly assigned to receive pembrolizumab at a dose of 2 (n=344) or 10 mg/kg (n=346) every three weeks or docetaxel at a dose of 75 mg/m² every three weeks (n=343) until disease progression or unacceptable toxicity.[3,5] Co-primary endpoints were OS and PFS as assessed by BICR using RECIST 1.1. Median OS was 10.4 months (95% CI 9.4, 11.9) with pembrolizumab 2 mg/kg every three weeks, 12.7 months (95% CI 10.0, 17.3) with pembrolizumab 10 mg/kg every three weeks and 8.5 months (95% CI 7.5, 9.8) with docetaxel. The HR versus docetaxel was 0.71 (95% CI 0.58, 0.88; p<0.001) for pembrolizumab 2 mg/kg and 0.61 (95% CI 0.49, 0.75; p<0.001) for pembrolizumab 10 mg/kg, respectively. Median PFS was 3.9 months (95% CI 3.1, 4.1) with pembrolizumab 2 mg/kg (HR 0.88 [95% CI 0.73, 1.04]; p 0.068), 4.0 months (95% CI x, x) with pembrolizumab 10 mg/kg (HR 0.79 [95% CI 0.66, 0.94]; p=0.005), and 4.0 months (95% CI 3.1, 4.2) with docetaxel. Overall response rate was 18% for both pembrolizumab arms and 9% with docetaxel.[2] Median DOR was not reached with pembrolizumab and 6.2 months with docetaxel.[3,5]

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