| Biogen | TYSABRI® (natalizumab) | Oncology | Relapsing-remitting multiple sclerosis (RRMS) | New evidence examination:  
• SMR – unspecified  
HAS/Transparency Commission (Official notice: 21 June 2017) (Notice published: 18 July 2017) | The Transparency Commission concluded that the data from this study did not change the conclusions of its previous opinion of 29 February 2012, subject to a re-evaluation of the therapeutic strategy. Given the serious adverse events during the development of the product with an important residual and potential of its medium-term administration risks, alemtuzumab treatment is reserved for severe forms of RRMS. Given the potentially serious side effects of the product and the absence of data comparative forms in highly active RRMS and forms secondarily progressive, it is difficult to determine the place of the recently reported daclizumab in MS with breakouts. (Click here for the source) |
| BMS | OPDIVO® (nivolumab) | Oncology | Treatment of advanced melanoma in combination with YERVOY® (ipilimumab) | Extension of indication:  
• SMR – important  
• SMR – insufficient  
• ASMR V (No improvement)  
HAS/Transparency Commission (Official notice: 03 May 2017) (Notice published: 07 July 2017) | The Transparency Commission concluded that the SMR was important in combination treatment of nivolumab and ipilimumab as the 1st line treatment of patient who are without the B-RAF mutation and metastasis and to be administered only in specialist centres. The SMR score was considered insufficient in any other cases of combination treatment of nivolumab and ipilimumab. The ASMR score was V (absence) to treat patients with advanced melanoma due to: a) efficacy demonstrated compared to monotherapy by ipilimumab was not considered a standard of care and b) an increase in toxicity and discontinuation of treatment due to adverse events in approximately one in two patients. (Click here for the source) |
| BMS | YERVOY® (ipilimumab) | Oncology | 1st and 2nd line treatment of advanced melanoma | Technology re-evaluation:  
• SMR – important  
• SMR – insufficient  
• ASMR V (No improvement)  
HAS/Transparency Commission (Official notice: 07 June 2017) (Notice published: 07 July 2017) | The Transparency Commission concluded that the SMR was important as a monotherapy in the treatment of advanced melanoma in the 2nd line in the absence of B-RAF mutation, and in the 3rd line in the presence of the B-RAF mutation. SMR was insufficient to justify reimbursement in treatment-naive patients regardless of the B-RAF mutation status. SMR was insufficient to justify reimbursement as a monotherapy in the treatment of advanced melanoma in the 2nd line in the presence of the B-RAF mutation. (Click here for the source) |
<table>
<thead>
<tr>
<th>Company</th>
<th>Product</th>
<th>Therapy Area</th>
<th>Indication</th>
<th>Reason for Rejection/Registration</th>
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<tbody>
<tr>
<td>Celgene</td>
<td>VIDAZA® (azacitidine)</td>
<td>Oncology</td>
<td>Acute myeloid leukaemia (AML) with more than 30% bone marrow blasts</td>
<td>Extension of indication: • SMR – insufficient&lt;br&gt;Has/Transparency Commission (Official notice: 21 June 2017) (Notice published: 05 July 2017)&lt;br&gt;The Transparency Commission rejected the extension of indication for azacitidine for treating of acute myeloid leukaemia with more than 30% bone marrow blasts. The manufacturer: a) did not provide comparative data among adults under 65 or in those with AML relapsed or refractory; b) did not demonstrate superiority data in overall survival for 65+ y.o. when compared to the SoC (induction chemotherapy or cytarabine in SC or best supportive care) and non-inferiority evidence compared to other alternatives, especially eligible patient for initial chemotherapy).&lt;br&gt;(Click here for the source)</td>
</tr>
<tr>
<td>CTRS</td>
<td>NEOFORDEX® (dexamethasone)</td>
<td>Oncology</td>
<td>Multiple myeloma</td>
<td>New technology registration: • SMR – important&lt;br&gt;ASMR IV – minor improvement&lt;br&gt;Has/Transparency Commission (Official notice: 19 October 2017) (Notice published: 05 July 2017)&lt;br&gt;The minor therapeutic improvement for this drug is based on dexamethasone 40 mg comparison with DECTANCYL (dexamethasone 0.5 mg) as a part of the therapeutic protocols for symptomatic multiple myeloma. The presentation of dexamethasone NEOFORDEX 40 mg is more suitable than the 0.5 mg presentation. The ASMR score was V (minor improvements) due to reduction in number of utilisation (drug uptake) when compared to DECTANCYL (dexamethasone 0.5 mg), although reduction in uptake did not demonstrate any clinical benefit.&lt;br&gt;(Click here for the source)</td>
</tr>
<tr>
<td>Gilead</td>
<td>DESCOVY® (emtricitabine, tenofovir alafenamide)</td>
<td>Infections</td>
<td>HIV-1 infection</td>
<td>New technology registration: • SMR – important&lt;br&gt;ASMR V – no improvement&lt;br&gt;Has/Transparency Commission (Official notice: 07 June 2017) (Notice published: 12 July 2017)&lt;br&gt;There was no clinical benefit demonstrated for the second-line treatment of patients with HIV infection. The SMR was considered important for reimbursement of DESCOVY. There was no improvement in clinical benefit based on: a) efficacy was demonstrated only in virologically controlled patients versus TRUVADA (tenofovir disoproxil / emtricitabine); b) tolerability data for kidney function was different compared to TRUVADA; c) there are other alternative treatment options without the risk of renal function; d) the absence of comparative data in treatment naïve patient with detectable viral load.&lt;br&gt;(Click here for the source)</td>
</tr>
<tr>
<td>Company</td>
<td>Product</td>
<td>Therapy Area</td>
<td>Indication</td>
<td>Technology Re-evaluation</td>
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| Janssen-Cilag | IMBRUVICA® (ibrutinib) | Oncology | Relapsed or refractory mantle cell lymphoma | Technology re-evaluation:  
- SMR – unspecified  
- ASMR III – moderate improvement | The Transparency Commission considered the evidence submitted and concluded that: a) the result in terms of progression-free survival was observed in favour of IMBRUVICA compared with temsirolimus, which is a clinically relevant comparator; b) there was no difference in overall survival between the IMBRUVICA and temsirolimus groups; c) better tolerability profile of IMBRUVICA compared to temsirolimus in terms of grade-3 adverse events with a rate of 67.6% versus 87.1%, respectively. (Click here for the source) |
| Eli Lilly | OLMIANT® (baricitinib) | Immunology | Moderate to severe rheumatoid arthritis | New technology registration:  
- SMR – important  
- ASMR V – no improvement | The Transparency Commission considered the evidence submitted and concluded that SMR was important for reimbursement, whereas ASMR was V (no improvement in clinical benefits) due to a) the demonstration superiority of OLMIANT (baricitinib) in combination with methotrexate (MTX) when compared with adalimumab (HUMIRA) in combination with MTX in 2nd line after failure of MTX; b) there was a lack of comparison with alternatives available in 3rd line treatment (including tocilizumab, abatacept, rituximab); c) there were concerns about long-term tolerance, particularly with regard to risk of infectious and potential cardiovascular and carcinogenic risks. (Click here for the source) |
| MSD | KEYTRUDA® (pembrolizumab) | Oncology | Melanoma, non-small cell lung cancer (NSCLC) and classical Hodgkin lymphoma | New technology registration:  
- SMR – important  
- ASMR V – no improvement | The Transparency Commission opinion was based on the provision of a 1-bottle, 4 ml to 25 mg / ml solution in dilution solution for infusion in addition to the 1-bottle powder for concentrate for solution for infusion containing 50 mg of pembrolizumab. The SMR for KEYTRUDA 25 mg / ml concentrate for solution for infusion was important for reimbursement in three indications within the marketing authorization. The ASMR does not improve the actual clinical benefit of ASMR V compared to KEYTRUDA 50 mg powder for concentrate for solution for infusion. (Click here for the source) |
France

Novartis

ODOMZO®
(sonidegib),
Hedgehog
inhibitor

Oncology

Treatment of locally advanced basal cell carcinoma (BCC) that is not eligible for curative surgery or radiation therapy

New technology registration:
• SMR – important
• ASMR IV – minor improvement

HAS/Transparency Commission
(Official notice: 8 June 2017)
(Notice published: 12 July 2017)

Pfizer

XALKORI®
(crizotinib)

Oncology

Indicated for adult patients with Non-small cell lung cancer (NSCLC) ROS1 (Proto- Oncogene 1, Receptor Tyrosine Kinase) positive and advanced

Extension of indication:
• SMR – Low (first line)
• SMR – Moderate (second line)
• ASMR V (No improvement)

HAS/Transparency Commission
(Official notice: 5 July 2017)
(Notice published: 07 July 2017)

Sanofi-Aventis

DETCENE®
(dacarbazine)

Oncology

Advanced metastatic melanoma

Technology re-evaluation:
• SMR – insufficient

HAS/Transparency Commission
(Official notice: 3 May 2017)
(Notice published: 19 July 2017)

Takeda

NINLARO®
(ixazomib citrate)

Oncology

Treatment of multiple myeloma

New technology registration:
• SMR – important
• ASMR V – no improvement

HAS/Transparency Commission
(Official notice: 5 July 2017)
(Notice published: 18 July 2017)

The Transparency Committee concluded that concluded that the only available data the opinion was based on was from a subgroup of a non-comparative Phase II study that included two patient profiles: locally advanced BCC and metastatic BCC. Efficacy results are based on the overall response rate (complete or partial response). ODOMZO is an alternative to ERIVEDGE in this indication. There was no comparative study. ODOMZO provided a minor improvement in actual benefit in locally advanced basal cell carcinoma treatment for those patients who are not eligible for curative surgery or radiation therapy. (Click here for the source)

The Transparency Commission considered the current evidence submitted and concluded that XALKORI® did not demonstrate the Improvement of Medical Benefit and provided assessment of ASMR V. Furthermore, the TC stated that: a) there is limited evidence (two cohorts one of a phase I and the other of a phase II clinical trials) with a suboptimal level of demonstration and in an intermediate evaluation criteria; b) no comparison to chemotherapy usually is used in this context; c) there is a lack of solid data on the prognostic value of positive ROS1 receptor tyrosine kinase factor. (Click here for the source)

No clinical benefit was demonstrated in the treatment of advanced metastatic melanoma after rescue immunotherapies and/or targeted therapies on B-RAF mutations. There is insufficient clinical data, particularly in the 1st line, due to the use of immunotherapy and therapies targeting mutations of B-RAF. (Click here for the source)

The Transparency Committee concluded that: a) there was a difference in progression-free survival in favour of NINLARO in combination with lenalidomide and dexamethasone in relation to the same combination administered alone, as observed by the independent review panel; b) the lack of robustness of this progression-free survival (no difference between the two groups to support the primary endpoint, which was noted in the second analysis and was not provided in the clinical protocol. (Click here for the source)