New haematology reimbursements in Belgium

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OVERVIEW OF BELGIAN REIMBURSEMENT NEWS

CHAPTER VIII FOR “PERSONALISED DRUGS”

From July 1st 2019, a new chapter will be introduced in the reimbursement of drugs: “chapter VIII”. This chapter collects drugs for which reimbursement is conditioned by the presence/absence of a molecular biomarker. Chapter VIII very much resembles chapter IV: the reimbursement conditions of the drugs are listed in different paragraphs and a priori authorisation by the Insurance Agency is required. Next to a list of these drugs, chapter VIII also holds a list of the coupled predictive biomarkers. This makes it possible to link the reimbursement of both drug and biomarker, so both can be assessed in the same reimbursement procedure and reimbursement can start simultaneously after a uniform decision.

For the moment, chapter VIII only holds drugs with a companion molecular biology test. Drugs that are merely linked to an immunohistochemistry or hereditary test are not in this scope and stay in chapter IV. Some drugs have an indication linked to a molecular biomarker and another indication without a link. These drugs will have a paragraph in chapter VIII but also a paragraph in chapter IV. More information on the new chapter and the linked reimbursement can be found on the RIZIV/INAMI website.

Drugs that are reimbursed via chapter VIII as of July 1st are: tretinoin, trastuzumab, imatinib, arsenic trioxide, erlotinib, cetuximab, panitumumab, lapatinib, gefitinib, nilotinib, vemurafenib, crizotinib, bosutinib, dabrafenib, pertuzumab, afatinib, trastuzumab emtansine, ibrutinib, dasatinib, idelalisib, ponatinib, ceritinib, osimertinib, trametinib, venetoclax, cobimetinib, ucleicinib, and midostaurin. Reimbursement demand forms for these drugs can be found at the same locations as the demand forms for the drugs in chapter IV.

As a transitional measure, authorisations for the drugs in chapter IV that were delivered before the entry into force of chapter VIII can retain their validity in accordance with the provisions stated on these authorisations.

JAKAVI

Reimbursement criteria of ruxolitinib (Jakavi®) have been modified. Jakavi is reimbursed:

- for the treatment of disease-related symptomatic splenomegaly and symptoms in adult patients with primary myelofibrosis, myelofibrosis post polycythemia vera and myelofibrosis post essential thrombocytopenia with an IPSS score of >2, with symptomatic palpable splenomegaly >5 cm under the ribs and confirmed by ultrasonography or MRI, and with <10% blasts in peripheral blood, and platelets >50 x 10^9/L, and life expectancy >6 months, and not eligible for bone marrow transplant (€6820000);

- and for the treatment of adult patients with polycythaemia vera who are resistant to hydroxycarbamide or do not tolerate hydroxycarbamide provided at least one of the following criteria is applicable:

  - need of phlebotomy in order to maintain a haematocrit <45% despite treatment with hydroxycarbamide for >3 months at the maximum tolerated dose or a dose of >2 grams/day, or
  - platelets >400 x 10^9/L and leucocytes >10 x 10^9/L despite treatment with hydroxycarbamide for >3 months at the maximum tolerated dose or a dose of >2 grams/day, or
  - failure to reduce spleen volume by >50% or persistent splenomegaly-related symptoms despite treatment with hydroxycarbamide for >3 months at the maximum tolerated dose or a dose of >2 grams/day, or
tolerated dose or a dose of >2 gram/day, or
• absolute neutrophils <1.0 x 10⁹/L x or platelets
  <100 x 10⁹/L or haemoglobin <10 g/dL at the minimal
dose required in order to obtain at least a partial
response, or at least one mucus or any other non
hematological toxicity related to hydroxycarbamide
(i.e. mucocutaneous symptoms, severe gastrointestinal
symptoms, fever, or intolerable pruritus) (€8660000).
Reimbursement should be claimed by a haematologist (via
the eHealth platform for €8660000).

Two randomised phase III studies were conducted in patients
with myelofibrosis.
COMFORT-I was a double-blind, randomised, placebo-con-
trolled study in 309 patients who were refractory to or were
not candidates for available therapy. The primary efficacy
endpoint was proportion of subjects achieving ≥35% reduc-
tion from baseline in spleen volume at week 24 as measured
by Magnetic Resonance Imaging (MRI) or Computed Tomo-
graphy (CT).
COMFORT-II was an open-label, randomised study in 219
patients. Patients were randomised 2:1 to ruxolitinib versus
best available therapy. In the best available therapy (BAT) arm,
47% of patients received hydroxyurea and 16% of patients
received glucocorticoids. The primary efficacy endpoint was
proportion of patients achieving ≥35% reduction from baseline
in spleen volume at week 48 as measured by MRI or CT.

A randomised, open-label, active-controlled phase III study
(RESPONSE) was conducted in 222 polycythæmia vera
patients who were resistant to or intolerant of hydroxyurea
defined according to the European LeukemiaNet (ELN)
international working group published criteria. Patients
were randomised 1:1 to receive ruxolitinib or BAT (hydrox-
yurea [59.5%], interferon/pegylated interferon [11.7%], ana-
grelide [7.2%], pipobroman [1.8%], or observation [15.3%])
The primary composite endpoint was the proportion of
patients achieving both an absence of phlebotomy eligibility
(haematocrit control) and a >35% reduction from baseline
in spleen volume at week 32. Phlebotomy eligibility was defined as a
confirmed haematocrit of >45% i.e. at least three percentage
points higher than the haematocrit at baseline or a confirmed
haematocrit of >48%, depending on which was lower.
The results of these trials are summarised in the Table 1.

| TABLE 1. The results of the COMFORT-I, COMFORT-II and RESPONSE trials. |
|-----------------|-----------------|-----------------|-----------------|
|                 | COMFORT-I       | COMFORT-II      | RESPONSE        |
|                 | Jakavi/Placebo | Jakavi/BAT      | Jakavi/BAT      |
| N               | 155/153        | 144/72          | 110/112         |
| Time points     | Week 24        | Week 48         | Week 32         |
| % of patients   | 41.9%/0.7%     | 28.5%/0         | 20.9%/0.9%      |
| with spleen     | 34.1-50.1      | 21.3-36.6       | 20.9*0.9*       |
| volume reduced  | <0.0001        | <0.0001         | <0.001          |
| by >35%         | 95% CI         |                  |                 |

N: number of patients, CI: confidence interval, BAT: best available therapy.
*composite primary endpoint (see text).