HAUTE AUTORITÉ DE SANTÉ

GASTROENTEROLOGY
ONCOLOGY
New medicinal product
March 2017

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

AKYNZEO (palonosetron + netupitant), combination setron

No clinical benefit demonstrated in prevention of nausea and vomiting after highly emetogenic chemotherapy compared with the standard treatment (setron + aprepitant + corticosteroid)
Insufficient clinical benefit after moderately emetogenic chemotherapy, in the absence of clinical data

Main points

- AKYNZEO has marketing authorisation in the prevention of acute and delayed nausea and vomiting associated with highly emetogenic cisplatin-based chemotherapy and moderately emetogenic chemotherapy.
- In the context of a highly emetogenic chemotherapy or anthracycline/cyclophosphamide, the available data do not make it possible to assess the benefit of AKYNZEO compared with the standard treatment (setron + corticosteroid + aprepitant) in the prevention of nausea and vomiting. The transferability and the impact on morbidity and mortality and on quality of life have not been demonstrated to date.
- Its clinical benefit after a moderately emetogenic chemotherapy has not been established.

Therapeutic strategy

In adults, to prevent chemo-induced nausea and vomiting, antiemetics are generally used in combination. The consensus protocols are as follows:

- After a highly emetogenic or anthracycline- and cyclophosphamide-based chemotherapy:
  - in the acute phase (0-24 hours after the chemotherapy): 5-HT3 (setron) + corticosteroid (dexamethasone) + aprepitant
  - in the delayed phase (up to the 4th day after the chemotherapy): aprepitant (D2, D3) + dexamethasone corticosteroid (D2, D3 and D4 if highly emetogenic chemotherapy).
- After a moderately emetogenic chemotherapy;
  - in the acute phase (0-24 hours after the chemotherapy): 5-HT3 (including palonosetron via IV) + corticosteroid (dexamethasone) +/- aprepitant
  - in the delayed phase (up to the 3rd day after the chemotherapy): corticosteroid (dexamethasone) or 5-HT3 or aprepitant (D2, D3).

Role of the proprietary medicinal product in the therapeutic strategy

After a highly emetogenic cisplatin-based chemotherapy, the role of AKYNZEO cannot be specified.
After a moderately emetogenic chemotherapy, the clinical benefit of this medicinal product has not been established.

Clinical data

- **In the prevention of nausea and vomiting induced by** a **cisplatin- or anthracycline/cyclophosphamide-based chemotherapy**, the available data do not make it possible to clearly assess the benefit of AKYNZEO compared with the standard treatment (setron + corticosteroid + NK1 receptor antagonists):
- **After a cycle of highly emetogenic cisplatin-based chemotherapy**, a phase II study established the superiority (complete response defined by the absence of vomiting or use of rescue antiemetic treatment up to 120 hours) of the fixed-dose combination of netupitant 300 mg + palonosetron 0.5 mg compared with oral palonosetron 0.5 mg (13.2% reduction, 95% CI [4.4; 21.9], p = 0.004). The width of the confidence interval makes the effect size difficult to evaluate, and these data do not make it possible to clearly assess the therapeutic benefit of AKYNZEO

compared with the standard antiemetic treatment that combines aprepitant + anti-HT3 + corticosteroid. A second study, not published and not available at the time of granting of the marketing authorisation, established the non-inferiority of the fixed-dose combination netupitant 300 mg + palonosetron (0.5 mg) compared with a standard antiemetic treatment combining aprepitant + granisetron + dexamethasone. It is uncertain whether the results observed in Asian patients can be extrapolated to the French population.

- **After a anthracycline/cyclophosphamide-based chemotherapy**, the available data establish that AKYNZEO is more effective than oral palonosetron administered at a dose of 0.5 mg to prevent nausea and vomiting during the delayed phase. These data do not make it possible to assess the therapeutic benefit of AKYNZEO compared with the standard treatment (oral aprepitant + injectable palonosetron + dexamethasone).
- **After moderately emetogenic chemotherapy**, the therapeutic benefit of AKYNZEO has not been established compared with the standard antiemetic treatment.
- The safety profile of AKYNZEO is comparable with that of the combination of aprepitant + palonosetron + dexamethasone. However, constipation occurred more often on netupitant/palonosetron (3.6%) than on aprepitant + palonosetron (1.0%) in a comparative safety study.

Benefit of the medicinal product

Prevention of acute and delayed nausea and vomiting associated with **highly** emetogenic cisplatin-based cancer chemotherapies:

- The actual clinical benefit* of AKYNZEO is substantial.
- AKYNZEO does not provide any clinical added value** (CAV V, none) compared with the standard treatment combining a setron, aprepitant and a corticosteroid.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

Prevention of acute and delayed nausea and vomiting associated with **moderately** emetogenic cancer chemotherapies:

- The actual clinical benefit* of AKYNZEO is insufficient to justify reimbursement by National Health Insurance.
- Does not recommend inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 22 March 2017 (CT-14838) and is available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the ACB, which can be substantial, moderate, low or insufficient for reimbursement of the medicinal product for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV (equivalent to “no CAV”) means “no clinical added value”.