SUMMARY

ivacaftor

KALYDECO 13.4 mg, 25 mg, 50 mg, 75 mg

granules in sachet

Inclusion on list, modification of the listing conditions

Adopted by the Transparency Committee on 18 December 2024

Summary of opinion

Favourable opinion for reimbursement only in "the treatment of infants aged at least 1 month to less than 4 months, weighing 3 kg to less than 25 kg **with cystic fibrosis who have one of the following gating (class III) mutations in the *CFTR* gene: *G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N* or *S549R.*"**

Unfavourable opinion for reimbursement in the other situations covered by the MA indication.

Transparency Committee's conclusions

Clinical Benefit

- Cystic fibrosis is a serious disease that is life-limiting for patients. The impact of this chronic disease on quality of life is particularly high.
- This is a curative medicinal product.
- The efficacy/adverse effects ratio is high in gating (class III) mutations in the CFTR gene. In the absence of data supplied, it has not been adequately established in the *R117H* mutation of the CFTR gene.
- This is a first-line treatment in the absence of available therapies for patients who have gating (class III) mutations in the CFTR gene.

Public health benefit

Considering:

- the seriousness of the disease and its prevalence/incidence,
- the unmet medical need,
- the partial response to the identified need given:
  - the absence of evidence of an impact on morbidity and mortality but an expected impact in the same way as that observed for children in the higher age group (absence of mortality data but impact on morbidity based on the results of secondary and tertiary endpoints from

a non-comparative 24-week study on a small number of patients with gating (class III) mutations in the CFTR gene),

- the lack of evidence of an impact on quality of life,
- an expected impact on the care and/or life pathway of patients and their families as well as on the organisation of care related to the possibility of starting treatment early from the age of 1 month,

KALYDECO (ivacaftor) is likely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of KALYDECO (ivacaftor) 13.4 mg, 25 mg, 50 mg, 75 mg granules in sachet is:

- **substantial only in the indication "the treatment of infants aged at least 1 month to less than 4 months, weighing 3 kg to less than 25 kg with cystic fibrosis who have one of the following gating (class III) mutations in the CFTR gene: *G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N* or *S549R*",**
- **insufficient to justify public funding in the other MA situations.**

The Committee issues the following opinions:

- **a favourable opinion for inclusion of KALYDECO (ivacaftor) 13.4 mg, 25 mg, 50 mg, 75 mg granules in sachet in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use only within the scope retained and at the MA dosages.**
- **an unfavourable opinion for inclusion of KALYDECO (ivacaftor) 13.4 mg, 25 mg, 50 mg, 75 mg granules in sachet in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use in the other situations covered by the MA indication.**

➔ **Recommended reimbursement rate for inclusion in the list of covered drugs for outpatients: 65%**

Clinical Added Value

Considering:

- an efficacy and safety of ivacaftor in infants aged at least 1 month to less than 4 months similar to those observed in older children, based on the results of the same non-comparative phase 3 study,
- the safety profile of ivacaftor, which appears to be acceptable in this age group,
- the substantial medical need in the treatment of cystic fibrosis in patients who have one of the gating (class III) mutations in the CFTR gene mentioned in the MA, in the absence of any other treatment targeting the causes of the disease,

and despite:

- the follow-up limited to 24 weeks of treatment not enabling evaluation of the long-term efficacy and safety of ivacaftor,
- the small size of the cohort concerned by the 1 to 4-months age category, missing data and the absence of comparative data versus a historical cohort, for example,

the Committee considers that, as in children aged over 4 months, KALYDECO (ivacaftor) 13.4 mg, 25 mg, 50 mg, 75 mg granules in sachet provides a substantial clinical added value (CAV

II) in the treatment of cystic fibrosis in infants aged at least 1 month to less than 4 months and weighing 3 kg to less than 25 kg who have one of the following gating (class III) mutations in the CFTR gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N or S549R.