Tezacaftor/ivacaftor (Symkevi®) with ivacaftor monopreparation (Kalydeco®) for the treatment of cystic fibrosis

Summary of recommendations by *Zorginstituut Nederland* (National Health Care Institute, the Netherlands) dated 24 April 2019

Zorginstituut Nederland carried out an assessment in relation to extending the specific conditions for the medicinal product Tezacaftor/ivacaftor (Symkevi®) with ivacaftor monopreparation (Kalydeco®), and concluded as follows.

In a letter dated 21 January 2019 (CIBG-19-07506), the Minister of Health, Welfare and Sport (VWS) asked *Zorginstituut Nederland* to assess whether Symkevi® in combination with Kalydeco® is interchangeable with a drug currently included in the reimbursed package. The *Zorginstituut* has completed its assessment.

The manufacturer has asked for inclusion on List 1B of the Health Insurance Decree.

Symkevi® is a combination tablet. Each film-coated tablet contains 100 mg tezacaftor and 150 mg ivacaftor. The registered indication reads as follows: "Tezacaftor/ivacaftor (Symkevi®) is indicated in a combination regimen with ivacaftor (Kalydeco®) 150 mg tablets for the treatment of patients with cystic fibrosis (CF) aged 12 years and older who are *homozygous* for the *F508del* mutation
or
for those who are *heterozygous* for the *F508del* mutation and have one of the following mutations in the CFTR gene: *P67L, R117C, L206W, R352Q, A455E, D579G, 711+3A→G, S945L, S977F, R1070W, D1152H, 2789+5G→A, 3272-26A→G* and *3849+10kbC→T*."

The manufacturer has only requested reimbursement for the first part of the indication, i.e. tezacaftor/ivacaftor with ivacaftor for patients with a homozygotic *F508del* mutation.

Therapeutic value
Tezacaftor/ivacaftor in combination with ivacaftor monopreparation was compared with lumacaftor/ivacaftor (Orkambi®) in this pharmacotherapeutic report. The *Zorginstituut* was advised by the Scientific Advisory Committee (WAR).

Zorginstituut Nederland concluded that, for the treatment of cystic fibrosis in patients aged 12 years and older with a homozygous *F508del* mutation in the CFTR gene, the therapeutic value of tezacaftor/ivacaftor in combination with ivacaftor monopreparation is equal to that of lumacaftor/ivacaftor as a supplement to standard symptomatic therapy.

Budget impact analysis
The list price of Symkevi®/Kalydeco® exceeds that of Orkambi® by €15,740.60. If Orkambi® and Symkevi®/Kalydeco® gain an equal share of the market (both about 250 patients), the total additional costs could amount to approximately €3.9 million.
The manufacturer was exempt from carrying out a pharmacoeconomic analysis.

Advice
The therapeutic value of the combination product Symkevi® (in combination with Kalydeco®) is equal to that of the combination product Orkambi® for the indication assessed. Orkambi® has been included on List 1B. For technical reasons, we advise the Minister to place Symkevi® on List 1B of the Medicines Reimbursement System (GVS) and to stipulate the following condition for both Symkevi® and Kalydeco®.
Price agreements have already been made for Orkambi®. In view of its identical therapeutic value, Symkevi® will only be eligible for inclusion in the GVS if the price of Symkevi® in combination with Kalydeco® does not exceed that of Orkambi®.

Conditions for Symkevi®
Only for use in combination with Kalydeco® for the treatment of cystic fibrosis (CF) patients aged 12 years and older who are homozygous for the *F508del* mutation in the CFTR gene.

Conditions for Kalydeco®
Only for use in combination with Symkevi® for the treatment of cystic fibrosis (CF) patients aged 12 years and older who are homozygous for the *F508del* mutation in the CFTR gene.

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The original text of this excerpt from advice of Zorginstituut Nederland was in Dutch. Although great care was taken in translating the text from Dutch to English, the translation may nevertheless have resulted in discrepancies. Rights may only be derived on the basis of the Dutch version of Zorginstituut Nederland's advice.
Furthermore, Zorginstituut Nederland points out that only the summary of this report was translated. A proper understanding of all relevant considerations and facts would require familiarity with the Dutch version of this report, including all appendices.