REPUBLIC OF BULGARIA
NATIONAL COUNCIL ON PRICES AND REIMBURSEMENT OF MEDICINAL PRODUCTS

HEALTH TECHNOLOGY ASSESSMENT

Kengrexal

50 mg powder for concentrate for solution for injection/infusion x 10 vial

INN Cangrelor

Therapeutic indication	Co-administered with acetylsalicylic acid (ASA), is indicated for the reduction of thrombotic cardiovascular events in adult patients with ischemic heart disease undergoing percutaneous coronary intervention (PCI) who have not received an oral P2Y12 inhibitor prior to the PCI procedure and in whom oral therapy with P2Y12 inhibitors is not feasible or desirable.
Start - end of the procedure	29.12.2022 – 10.11.2023
Final decision	Inclusion in Annex 2 of the Positive Drug List (PDL) for purchase by the healthcare facilities with state and/or municipality ownership and under Article 5 of the Medical Establishments Act.

Summary of the report on the clinical and pharmacoeconomic assessment of the health technology of the medicinal product Kengrexal

Health problem

Percutaneous coronary intervention (PCI) with coronary stent implantation is a widely used method to reduce the risk of death or occurrence of fatal/nonfatal acute myocardial infarction (AMI) or sudden cardiac death (SCD) in patients with acute coronary syndromes (ACS), as well as to reduce ischemic burden and improve quality of life in patients with stable angina pectoris. Despite advances in the use of simultaneous pharmacotherapy, thrombotic complications during PCI remain a major problem.

The clinical picture is expressed in ischemic chest pain (angina). The classification of angina in patients with coronary artery disease (CAD) defines it as: chronic stable angina, unstable angina and angina in ACS. Electrocardiographic examination divides patients with ACS into two groups: ACS without ST-segment elevation and AMI with ST-segment elevation. ACS require urgent coronary angiography to clarify the anatomy of the coronary vessels, and the indications for coronary angiography in cases of stable chronic angina pectoris are defined in the recommendations of the European Society of Cardiology.

The need for percutaneous coronary intervention is determined depending on the clinical course of CAD. The available evidence outlines the need for the earliest possible administration of antiplatelet and anticoagulant drugs before or during PCI to achieve efficacy related to suppression of platelet aggregation and activation, as well as in cases of unknown coronary anatomy. Oral P2Y12 receptor antagonists and acetylsalicylic acid are the most widely used for prevention of coronary and stent thrombosis.

Kengrexal (cangrelor) is the second parenteral antiplatelet agent to be studied for use during PCI (periprocedural) in patients with stable coronary artery disease and ACS. Kengrexal is a direct platelet P2Y12-receptor inhibitor that blocks adenosine diphosphate (ADP) - induced platelet activation and aggregation. The drug binds selectively and reversibly to the P2Y12 receptor to prevent further signaling and platelet activation. It is characterized by rapid action in patients with urgent PCI due to coronary artery disease, manifested against the background of simultaneous treatment with acetylsalicylic acid, without, however, a reduction in mortality; the cangrelor/clopidogrel/acetylsalicylic acid strategy showed an advantage over the acetylsalicylic acid/clopidogrel strategy in reducing the risk of ischemic events at the 48th hour. Reduces thrombotic cardiovascular events in patients with PKI to whom oral therapy with P2Y12-receptor inhibitors is not applicable.

Efficacy data

The therapeutic efficacy and safety profile of cangrelor were analyzed in three clinical trials - **CHAMPION PCI, CHAMPION PLATFORM** and **CHAMPIONPHOENIX**.

The **CHAMPION PCI** and **CHAMPION PLATFORM** clinical trials randomize patients for treatment with cangrelor, administered as a bolus injection, followed by intravenous infusion or clopidogrel) loading dose of 600 mg (either before or after PCI). The results show a primary efficacy rate of 4.7% for the group of cangrelor treatment and 5.9% for the clopidogrel group. The primary safety endpoint was 0.16% for the cangrelor treatment group and 0.11% for the clopidogrel treatment group. Stent thrombosis was recorded in 0 .8% of patients in the cangrelor group and 1.4% for the clopidogrel treatment group. The incidence of adverse effects was low for both patient groups, although transient dyspnea was observed statistically significantly in the cangrelor-treated group. The benefit of cangrelor administration on the primary endpoint was unidirectional throughout the observation period.

The results of a clinical trial **CHAMPION PHOENIX** was on 13,418 target lesions in randomized patients. The outcome was analyzed according to the number of angiographically targeted for PCI lesions with high-risk characteristics (bifurcations, trunk stenosis, presence of thrombus, coiled vessels, eccentric and calcified lesions, multi-vessel treatment). At the 48th hour, the frequency of events increased progressively in the group of patients treated with clopidogrel with the complexity of the lesions. The use of Kengrexal reduced this incidence at the 48th hour by 21% (statistically significant difference with clopidogrel).

Safety data

The most common adverse drug reactions are dyspnoea, ecchymosis, and decreased hematocrit and hemoglobin. Kengrexal is associated with a higher incidence of minor bleeding than clopidogrel. The majority of cases with mild bleeding are ecchymosis, lacrimation, and hematoma smaller than 5 cm.

Data on comparators

The main comparative alternatives are oral P2Y12-receptor inhibitors and GP IIb/IIIa receptor inhibitors.

Pharmacoeconomic indicators

Published health technology assessments performed by governmental institutions intended for the health care systems of other countries

One assessment has been published by other government institutions - Haute Autorité de santé - HAS (France). HAS recommends inclusion of the technology in reimbursable products for hospital use.

Applied analysis
The cost effectiveness pharmacoeconomic analysis (CEA) was applied, in which the final result in terms of health benefits is presented in the form of a life year gained (LYG). Clopidogrel was chosen as a comparative alternative. The perspective of the analysis is that of the paying institution. The selected time horizon is one treatment episode. Costs and outcomes are discounted at an annual discount rate of 3.5%. Decision Tree modeling is applied. The results of the analysis show that Kengrexal is a cost-effective alternative.

Costs for the assessed health technology
Kengrexal therapy costs, administration costs and implied costs are included in the model.

Subgroup analysis
Not attached.

Budget impact analysis
The analysis of the budget impact was carried out from the perspective of the paying institution - NHIF, which reimburses medical facilities. The time horizon is 5 years. The estimated number of patients to be treated with Kengrexal in the first year is 80 and in the fifth year – 392. The budget impact analysis was carried out, developing 2 scenarios "World with Kengrexal" and "World without Kengrexal". The analysis forecasted an increase in costs over a five-year period for the NHIF, excluding risk-sharing agreements and patient access schemes.

Conclusion

Kengrexal (Cangrelor) is the only medicinal product that is administered intravenously for a short period of time (up to 4 hours maximum) without more critical events compared to GP IIb/IIIa receptor inhibitors, and it also has a short half-life. Its use is restricted to patients with known coronary anatomy or patients who have to undergo emergency angioplasty and who have not previously received P2Y12-receptor antagonists. The budget impact analysis predicts an increase in expenditure.