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

HEALTH TECHNOLOGY ASSESSMENT

Cimzia

200 mg solution for injection x 2 pre-filled syringes + 2 alcohol wipes

Certolizumab pegol

Therapeutic indications	Cimzia is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.
Start - end date of procedure	27.02.2020 – 30.09.2020
Final decision	Addition of therapeutic indication for the medicinal product in Annex № 1 of the Positive Drug List (PDL) for home treatment of diseases paid by the National Health Insurance Fund (NHIF).

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

Health problem

Psoriasis is a chronic recurrent disease primarily involving the skin and joints, with a possible association with endocrine and cardiovascular diseases. The disease affects patients' quality of life to a degree comparable to that of other socially significant diseases, such as diabetes, chronic respiratory diseases and neoplasms. In some patients psoriasis also affects the ability to develop social contacts, leading to psychological stigma.

The clinical picture of psoriasis is typical, with skin lesions mainly affecting the scalp (Corona psoriatica), elbows, knees and extensor surfaces. The disease has a chronic recurrent course with some of the cases having a tendency to progress to a larger skin area, development of arthritis and comorbidities of the endocrine and cardiovascular systems.

Disease complications can be related to the skin (dissemination of skin lesions to erythroderma or generalized pustular psoriasis - von Zumbusch), joints (psoriatic arthritis, spondyloarthritis, dactylitis, ankylosis), as well as resulting from associated endocrine diseases (metabolic syndrome, diabetes mellitus) and cardiovascular diseases. The appearance of complications negatively impacts disease prognosis.

The treatment of disease is conducted with topical, systemic and phototherapy following accepted international and national therapeutic guidelines and standards.

Cimzia (certolizumab pegol) is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

Cimzia is an alternative to systemic therapy with methotrexate (MTX), retinoids, cyclosporine, as well as infliximab, adalimumab, etanercept, ustekinumab, secukinumab, ixekizumab, guselkumab, risankizumab in patients with no benefit from the standard treatment or in those who developed serious adverse reactions during the systemic treatment or phototherapy. Cimzia is an alternative therapy for women with psoriasis during the period of breastfeeding.

Epidemiological data

Psoriasis affects from 1% to 5% of the population in different parts of the world. In Bulgaria, the incidence of psoriasis is 1.8% of the population. Over 50% of patients have the mild form of disease and the majority of them do not receive treatment. Moderate to severe form of frequency (affecting more than 3% of the body surface) is observed in 17% of patients and requires continuous treatment.

Efficacy data

The principal trials for the treatment of psoriasis with Cimzia (certolizumab pegol) 200 mg and 400 mg are CIMPASI-1 and CIMPASI-2 and CIMPACT.

CIMPASI-1 and CIMPASI-2 are randomized, double-blind, placebo-controlled phase 3 studies in patients with moderate to severe plaque psoriasis. Both studies are placebo-controlled and double-blinded until week 16. Patients who by that week had reached a Psoriasis Area Severity Index (PASI) 50 response would switch to the maintenance phase of treatment until 48th week, then would switch to an open-label period until 144th week.

The CIMPACT study is a multicenter, randomized, double-blind, parallel-group phase 3 study. The aim of the study was to evaluate the efficacy and safety of two dosage regimens of certolizumab (CZP) - 200 mg and 400 mg versus placebo and etanercept (ETN) 50 mg once every 2 weeks for 12 weeks in patients with moderate to severe plaque psoriasis.

The results of the three studies and two certolizumab dosage regimens demonstrated a clinically and statistically significant improvement in disease severity in patients, as assessed by PASI 75 and PASI 90 reduction after 16 weeks of treatment versus placebo. Similar results were achieved with respect to PASI 50 and PASI 100 reduction. Response levels to therapy show a stable increase over time, with differences versus placebo first appearing at week 4 and the result remaining in effect until week 16.

Etanercept 50 mg is employed as alternative in one of the groups during the first 12 weeks of the CIMPACT study. Certolizumab pegol 400 mg outperformed etanercept in the number of psoriasis patients achieving a PASI 75 reduction at week 12 (66.70% vs 53.30%), while certolizumab pegol 200 mg did not yield a statistically significant difference despite higher absolute values (61.3% and 53.3%).

As regards the body surface area affected by psoriasis (BSA), the results indicate that both CZP dosage regimens show an improvement in that index at week 16 compared to placebo - 6.4%, 8.1% and 22.1%.

The results of the individual studies show that both CZP dosage regimens resulted in a clinically and statistically significant improvement in PGA (Physician's Global Assessment) score.

Health-related quality of life (HRQoL) in psoriasis patients treated with certolizumab pegol was assessed using the DLQI (Dermatology Life Quality Index). The change in DLQI score represents a secondary endpoint in the CIMPASI-1 and CIMPASI-2 studies, as well as an endpoint in CIMPACT. The results of the individual studies and two doses of certolizumab pegol show a clinically and statistically significant improvement in the DLQI score at week 16 compared to placebo group. The percentage of patients who achieved a DLQI score ≤1,

corresponding to no impact on quality of life increased from baseline to 31.3% at week 8 and 47.1% at week 16.

Both dosage regimens of certolizumab pegol show statistically significant improvements in depression and anxiety at weeks 12 and 16, while deterioration of symptoms is observed in placebo-treated patients.

Safety data

Certolizumab pegol at a dose of 400 mg every 2 weeks and 200 mg every 2 weeks have similar safety profile. By week 16, the proportion of patients with serious adverse events was 3.5% with certolizumab pegol and 3.7% with placebo. The proportion of patients who discontinued treatment due to adverse events in controlled clinical trials was 1.5% in patients treated with certolizumab pegol and 1.4% in patients treated with placebo.

The most common side effects are bacterial infections, viral infections, headache, urticaria, hypertension, hepatitis, pyrexia, pain, fatigue, pruritus, application site reaction.

Comparators data

Drugs of choice in patients with moderate to severe psoriasis are biological medicinal products, represented by blocking antibodies or fusion proteins directed against key structures in disease pathogenesis. Certolizumab pegol is the only biological agent that can be used relatively safely during pregnancy and lactation.

Pharmacoeconomic indicators

Published health technology assessments, performed by state institutions serving other national health care systems

Health technology assessments from NICE, SMC (Scotland) and HAS (France) have been presented, all of them being positive and recommending reimbursement.

A pharmacoeconomic cost-benefit analysis has been applied from the perspective of the National Health Insurance Fund (NHIF) for a one year time horizon. All biological agents for the treatment of plaque psoriasis in Bulgaria, included in the Positive Drug List (PDL) and paid by the NHIF have been selected for comparison, namely adalimumab, etanercept, infliximab, ixekizumab, secukinumab, ustekinumab. An adapted Markov model has been applied.

Only direct costs of drug therapy have been included. Costs of treating adverse drug reactions (ADRs) or costs related to other medical services have not been included as they are similar to the alternatives being compared.

Analysis results show that infliximab is the dominant alternative. Next in order cost-effective alternatives are ustekinumab, secukinumab and certolizumab.

Budget impact analysis

The performed budget impact analysis indicates that influence on the budget will be negative, assuming redistribution of market share of higher cost alternatives, and will lead to savings for NHIF, without taking into account risk sharing agreements and patient access schemes.

Conclusion

Cimzia (certolizumab pegol) is an alternative treatment for moderate to severe psoriasis in women of childbearing potential for whom other therapeutic alternatives are deemed risky or impossible. The medicinal product is the only biological agent that can be used relatively safely during pregnancy and lactation.

Efficacy of certolizumab pegol at both therapeutic doses in patients with psoriasis after 16 weeks of treatment was statistically significantly higher than placebo. Patients receiving certolizumab pegol reported an improvement in quality of life. Cost-benefit analysis indicates that cetrolizumab is the fourth cost-effective alternative after infliximab, ustekinumab and secukinumab. The budget impact analysis indicates that inclusion of Cimzia in PDL for the treatment of plaque psoriasis will lead to savings for the NHIF.