2 ELEMENTS FOR A PUBLIC SUMMARY

2.1 Overview of disease occurrence and distribution (epidemiology)

2.1.1 Rheumatoid arthritis (RA) disease occurrence and distribution

There are 25 to 50 cases of RA for every 100,000 people. Geographically, only small differences in the number of RA cases exist, with some populations in Asia and Africa showing the lowest risk. The cases of RA range from 8 for every 100,000 people in Japan to 1,000 for every 100,000 people in the United Kingdom. In Europe and North America, the rate of RA is estimated between 0.5 and 1.0% for the time period from 1999 to 2006.

Rheumatoid arthritis is seen in all races and ethnic groups, and affects all age groups; however, the rate of RA increases with age. Differences in gender have been reported for RA with a higher rate of new and existing cases in women, specifically aged 50 and over. Women are 2 to 3 times more likely to be affected than men are, and the rate of new and existing cases of RA is even more different between elderly women and elderly men. The rate of RA in women is 1.37% compared to 0.74% in men.

Smoking is the most convincing behavior that is a risk factor for RA, therefore an increased risk of cardiovascular events ranging from a relative risk of 1.6 to 2.14 was also seen in patients with RA.

2.1.2 Psoriatic Arthritis (PsA) disease occurrence and distribution

The cases of PsA ranged from 3 to 8 per 100,000 people per year. Most studies have been done in Europe; Greece had the lowest PsA rate and Nordic countries had the highest rates. Most studies do not show a difference in PsA rate between men and women except for two studies.

The estimated rate of PsA ranged from 0.17% to 0.56%. Many risk factors for PsA in the group of psoriasis patients have been identified and include a special measure of weight and height called body mass index (BMI) at the age of 18 (but current BMI did not help to predict risk),
effect on nails, similar wounds at site of injury seen by patient, being female, and younger age at start of psoriasis.

2.1.3 Axial Spondyloarthritis (AxSpA) disease occurrence and distribution

Axial spondyloarthritis (axSpA) encompasses the full disease spectrum, including patients with and without definitive evidence of inflammation of the sacroiliac joints on x-ray. The subpopulation with an evidence of the inflammation on the sacroiliac joints on x-ray is called ankylosing spondylitis (AS) while the subpopulation without an evidence on x-ray is called non- radiographic axial spondyloarthritis (nr-axSpA).

Since nr-axSpA is a recent concept, there is very little information on occurrence and distribution of nr-axSpA.

The occurrence of AS varies by country. The highest occurrence of AS was 7.3 per 100,000 people per year in the USA and Norway and the lowest occurrence of AS was in Greece with a rate of 1.5 per 100,000 people per year. In general, AS occurs more frequently in men than in women with a start of disease between the age of 35 to 44 years for women and between the age of 45 to 54 years for men.

2.2 Summary of treatment benefits

The tumor necrosis factor alpha (TNFα) blocker Cimzia® has been approved for the treatment of moderate to severe active RA in adult patients.

The effectiveness and safety of Cimzia® have been evaluated in controlled clinical studies compared with a non-active substance (placebo) in the approved indication of RA as well as for PsA and axSpA:

- C87027 included 982 patients with RA. The primary endpoints were the 20% clinical improvement after 24 weeks of treatment (ACR20* response at Week 24) and change in joint damage progression after 52 weeks of treatment (change in x-ray radiographic measurement mTSS* at Week 52). Clinical improvement was achieved in 59% of patients receiving
Cimzia® 200mg (228/388) and 14% of patients receiving placebo (27/198). No change in
radiographic damage progression (mTSS*≤0) was achieved in 69% of patients receiving

Cimzia® 200mg (251/364) and 52% of patients receiving placebo (94/181).

- C87050 included 619 patients with RA. The primary endpoint was 20% clinical improvement after 24 weeks of treatment (ACR20* response at Week 24). This was achieved in 57% of patients receiving Cimzia® 200mg (141/246) and 9% of patients receiving placebo (11/127).

- PsA001 included 409 patients with PsA. The primary endpoint was the 20% improvement after 12 weeks of treatment on the ACR criteria (ACR20* response at Week 12). This was achieved by 55% of patients receiving Cimzia® (150/273) and 24% of patients receiving placebo (33/136).

- AS001 included 325 patients with axSpA. The primary endpoint was the 20% improvement after 12 weeks of treatment on the ASAS criteria (ASAS20* response at Week 12). This was achieved by 61% of patients receiving Cimzia® (132/218) and 38% of patients receiving placebo (41/107).

*ACR20=20% improvement of American College of Rheumatology response criteria; ASAS20=Assessment in Axial Spondyloarthritis International Society 20% response criteria; mTSS=modified Total Sharp Score.

2.3 Unknowns relating to treatment benefits

The product label in the EU (European Union) does not recommend the use of Cimzia® (also known as certolizumab pegol [CZP]) during pregnancy. The use of CZP in children and adolescents is not approved. The product risks that are associated with elderly (65 years and above) are less clear because less data are available. In the clinical studies, there was an apparently higher incidence of infections among patients ≥65 years of age, compared to younger patients, although experience is limited. Caution should be exercised when treating the elderly, and particular attention paid with respect to occurrence of infections. Heart disease and infections are more common in this group. The product label contains a contraindication for moderate to severe heart failure and warning information on both heart disease and infection. The safety of Cimzia® on patients with underlying damage to main organs like kidney and liver is unknown. Good clinical practice will suggest carefulness when treating patients who have organ problems. No recommendations on dose adjustment can be made based on available information.