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BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

CIMZIA (certolizumab pegol), anti-TNFα

Substantial actual benefit in the treatment of active psoriatic arthritis when the response to disease-modifying antirheumatic drugs is inadequate.

Main points

- CIMZIA, in combination with methotrexate, has Marketing Authorisation in the treatment of active psoriatic arthritis in adults when the response to disease-modifying antirheumatic drugs (DMARDs) is inadequate. It can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate
- The level of evidence of the initial demonstration of the structural effect of CIMZIA (slowing of radiographic progression of joint damage) had been considered low by the Committee.
- The new follow-up data (after 96 weeks of treatment) indicate that maintenance of the absence of radiological progression and the benefit of the medicinal product can be reappraised on the basis of these results. This trend will need to be confirmed when the final data become available.

Pre-existing indications

- CIMZIA already has Marketing Authorisation in the treatment of rheumatoid arthritis and ankylosing spondylitis. (This summary does not cover these indications.)

Therapeutic use

- The treatment of psoriatic arthritis combines symptomatic treatment (NSAID with or without analgesics) with DMARDs. Its aim should be to achieve clinical remission or, failing that, a low level of disease activity.
- In the absence of contraindications, NSAIDs are the first-line symptomatic treatment. Local corticosteroid injections at the symptom sites (especially in arthritis and enthesitis) may be considered. In the majority of cases, systemic corticosteroid therapy is not justified for treating axial manifestations, but may be considered in certain special situations.
- Standard DMARDs – methotrexate, leflunomide and sulfasalazine (off-label use) – may be considered when peripheral arthritis is refractory to symptomatic treatment. However, these treatments are not currently indicated in isolated axial or enthesitis-related manifestations.
- TNF inhibitors (adalimumab, etanercept, infliximab, golimumab and certolizumab pegol) must be offered to patients in whom disease activity persists despite standard treatment.
  The choice of treatment must take account of the degree and severity of the cutaneous lesions, which may be independent of the severity of the psoriatic arthritis. CIMZIA is not indicated in cutaneous psoriasis.
  If a first TNF inhibitor is ineffective, a switch to a different one may be beneficial. Another antibody, STELARA (ustekinumab), which is not a TNF inhibitor but an inhibitor of IL-12 and IL-23, has been granted Marketing Authorisation in this indication in patients showing inadequate response to non-biologic DMARD therapy.

- **Role of the medicinal product in the therapeutic strategy**
  When considering treatment with a TNF inhibitor, e.g. in active forms of psoriatic arthritis refractory to standard DMARDs including methotrexate, CIMZIA as a subcutaneous injection every 2 weeks is an alternative to other available TNF inhibitors. In the absence of any direct comparison, its role in relation to the other available biological therapies cannot be defined.

Clinical data

- Review of initial data
  The efficacy of certolizumab in the treatment of psoriatic arthritis has been evaluated in a placebo-controlled study with two co-primary endpoints: ACR20 response at week 12 and change versus baseline in modified total Sharp score (mTSS) at week 24.
  The proportion of patients achieving an ACR20 response at week 12 was statistically higher with certolizumab than with placebo, i.e. an absolute difference of 33.7%; 95% CI [22.8; 44.6], $p < 0.001$ at a dosage of 200 mg/2 weeks and of 27.6% [16.5; 38.7], $p < 0.001$ at a dosage of 400 mg/4 weeks.
  The radiological endpoint showed no difference between certolizumab and placebo. At 48 weeks, no statistically significant difference in mTSS was observed between certolizumab 200 mg and 400 mg and placebo.
- New follow-up data at week 96
  The follow-up data showed maintenance of efficacy in terms of clinical signs and indicate the absence of progression of structural damage, with a mean change in mTSS score of -0.08 (95% CI [-0.42; 0.27]), 0.04 (95% CI [-0.30; 0.38]) or 0.14 (95% CI [-0.04; 0.33]) depending on the group. This trend will need to be confirmed when the final data from study PsA001 become available.
- Although no new safety signals have been identified, there are only limited long-term data. The adverse events most frequently associated with certolizumab pegol were infections.

Special prescribing conditions

- Medicine requiring initial annual hospital prescription.
- Initial and repeat prescription restricted to specialists in rheumatology and internal medicine.
- Exception drug status.

Benefit of the medicinal product

- The actual benefit* of CIMZIA is now substantial given that:
  - the initial data had demonstrated the efficacy of CIMZIA versus placebo in terms of clinical signs and structural damage, although the level of evidence demonstrating the structural damage was considered low,
  - the open follow-up data at week 96 indicate maintenance of the absence of radiological progression.
- Recommends continued inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

* The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

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