Certolizumab – pegol

Instructions for use

Table 1: Instructions for use (Certolizumab – pegol)

Pre-treatment

100 % Agreement [1]

- Physicians are encouraged to enrol their patients in a registry (if available)
- Objective assessment of the disease (such as PASI/BSA/PGA; arthritis)
- HRQoL (such as DLQI/Skindex-29 or -17)
- History and clinical examination should focus on prior exposure to treatments, malignancies, infection, congestive heart failure, and neurological symptoms
- Recommended measures include:
    - Check for malignancy, mainly skin cancer, and premalignant lesions
    - Check for lymphadenopathy
    - Laboratory parameters (see **Table 2**)
    - Exclusion of tuberculosis (see chapter: “tuberculosis”)
    - Check for evidence of active infections
    - Check need for vaccinations
- Discuss contraception (see chapter: “wish for child/pregnancy“)

During treatment

- Objective assessment of the disease (such as PASI/BSA/PGA; arthritis)
- HRQoL such as (DLQI/Skindex-29 or -17)
- Clinical examination should focus on lymphadenopathy, malignancies, especially skin cancer, premalignant lesions, risk factors for serious infections, congestive heart failure, and neurological symptoms
- Recommended measures include:
    - Laboratory parameters (see **Table 2**)

- Discuss contraception (see chapter: “wish for child/ pregnancy”)

Post-treatment

- After discontinuation of certolizumab – pegol, patients should be followed up with medical history and physical examination.
- For information regarding the ongoing need for contraception immediately following biologic treatment cessation, please see chapter: “wish for child / pregnancy”

[1] due to personal-financial conflict of interest 3 abstentions

Recommendations for lab controls

Table 2: Recommended laboratory controls (Certolizumab – pegol)

	Period in weeks			
Parameter	**Pre-treatment**	**4**	**12**	**Thereafter, every 3-6 months**
Full blood count	x	x	x	x
Liver enzymes	x	x	x	x
Serum creatinine	x			
Urine status	x			
Pregnancy test (urine or blood)	x*			
CRP	x			
HBV/HCV	x			
HIV	x			
Interferon gamma release assay (TB exclusion)	x			

Not all tests may be necessary for all patients. Patient history, risk exposure and patient characteristics have to be taken into account. Further specific testing may be required according to clinical signs, risk, and exposure.

** Pregnancy test is recommended as it is important to know if a patient is pregnant when starting a systemic treatment. Certolizumab is the suggested biologic treatment option, for women who are planning conception or are pregnant and require a systemic therapy.*

The recommendations are based on clinical experience. No evidence is available.

Adverse drug reactions

Please see SmPC and other sources for complete listing. The guideline subcommittee decided to comment on the following aspects:

Most evidence for adverse drug reactions to certolizumab-pegol are derived from studies on rheumatoid arthritis. Specific studies on psoriasis [1,2] show a safety profile comparable to etanercept (12 weeks) and a safety profile that was consistent with the therapeutic class of TNFi for psoriasis up to 48 weeks. These data are derived from 234 (CIMPASI-1 [1]), 227 (CIMPASI-2[1]) and 559 patients (CIMPACT [2]). Most common adverse drug reactions consisted of nasopharyngitis, upper respiratory tract infections, and headache. No opportunistic infections were reported. Serious infections were rare.

In line with the other TNFi and the SmPC the following adverse events can be expected:

Common are viral infections, bacterial infections. Uncommon infections are serious bacterial infections (sepsis), tuberculosis or fungal infections.

Special attention is needed for non-melanoma skin cancer (NMSC) as psoriasis patients are more at risk for NMSC [3]. However, in this SR adjustment for highly relevant confounding factors such as prior phototherapy were lacking [3]. For more detailed information see chapter malignancies. Other malignancies, especially lymphoma, associated with the use of certolizumab-pegol are uncommon. Other rare side effects of certolizumab-pegol are severe allergic reactions and lupus-like syndrome.

Other

As a class, TNFi may be associated with the development or worsening of demyelinating diseases and MS (see respective chapters).

Worsening of pre-existing heart failure, and accordingly TNFi are contraindicated in patients with severe heart failure (NYHA class III or IV), and patients with less severe disease should be monitored carefully and undergo regular monitoring by a cardiologist (see respective chapters).

TNFi induced paradoxical psoriasis

TNFi are effectively used in the field of inflammatory musculoskeletal, skin and bowel diseases. However, TNFi induced cutaneous side effects are possible. Paradoxical reactions include the development of psoriasis, pustular psoriasis and psoriasiform lesions, reflecting an immunological paradox, as TNFi are used in the treatment of psoriasis. Psoriasis can be triggered in 1,5 – 5 % under the use of TNFi. In 52% of the cases the appearance is a palmoplantar pustulosis, in 49% a plaque type and in 15% a guttata-type. A potential mechanism could be the increase of the interferon alpha

production. These psoriasiform lesions can be managed by topical or systemic anti-psoriatic-therapies and/or switch to another biological, preferably from a different class. [4-6]

Table 3: Overview of important side effects

Very frequent	Injection-site reaction
Frequent	Infections
Occasional	Tuberculosis, reactivation of latent tuberculosis, heart failure
Rare	Allergic reactions, adverse reactions of the haematologic system, demyelinating diseases
Very rare	Autoantibodies, drug-induced lupus, malignancies

Special consideration during treatment

Please see SmPC and other sources for complete listing. The guideline subcommittee decided to comment on the following aspects:

Surgery

There is little evidence on the effects of certolizumab in patients with psoriasis undergoing surgery. For the group of TNFi in general, studies in rheumatoid arthritis patients suggest a small increase in postoperative wound infections to even a reduction in case of continued treatment[7,8]. For elective surgery it is conceivable to interrupt treatment prior to the procedure three to five half-lives, especially in patients with diabetes or other increased risk of infections.

Infections

Corresponding monitoring measures during treatment should take into account that symptoms such as fever can be suppressed during TNFi therapy.

Combination of TNFi and MTX

A treatment with TNFi and methotrexate can be combined. This may reduce the risk of formation of anti-drug antibodies[9]. This combination is particularly common for infliximab as the risk for the formation of antidrug antibodies is highest. The combination may lead to an increased risk of infection, especially when compared to MTX monotherapy, but data is still scarce[10].

Important contraindications

Please see SmPC and other sources for complete listing. The guideline subcommittee decided to comment on the following aspects:

Absolute contraindications

- Active tuberculosis or other severe infections such as sepsis, and opportunistic infections
- Congestive heart failure (NYHA class III/IV)

Relative contraindications

- Latent tuberculosis
- History of recurrent or severe infections, localized infections, conditions predisposing to infections
- Patients living in geographical areas where tuberculosis and histoplasmosis are widespread
- Psoriasis patients with concomitant systemic lupus erythematosus or multiple sclerosis (MS)
- PUVA > 200 treatments (especially if followed by CsA use) – see chapter: "cancer"
- Malignancies and lymphoproliferative disorders (see chapter: "malignancies")

Drug interactions

Please see SmPC and other sources for complete listing. The guideline subcommittee decided to comment on the following aspects:

The combination of cetolizumab-pegol with immunosuppressive drugs may enhance the risk of infection. There is insufficient information regarding the concomitant use of certolizumab-pegol with other biological therapeutics used to treat the same conditions. The concomitant use of certolizumab-pegol with these biologics is not recommended because of the possibility of an increased risk of infection.

Overdose/measures in case of overdose

No dose-limited toxicity was observed in clinical trials. Repeated subcutaneous study injections of 800 mg have been given.

References

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