Etanercept

Instructions for use

Table 1: Instructions for use (Etanercept)

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 infection
    - Check need for vaccinations
- Reliable contraception

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**)

- Reliable contraception

Post-treatment

- After discontinuation of etanercept, 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 4 abstentions

Recommendations for lab controls

Table 2: Recommended laboratory controls (Etanercept)

	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.

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:

Analysis of results from two major North-American studies that followed up 506 patients up to four years showed no increase in the incidence of malignancies or infections among psoriasis patients treated with etanercept compared to patients receiving placebo and/or to the general population [1], and a low risk of serious infection of 0.9 per 100 patient-years [2]. Of note, no case of lymphoma or of tuberculosis was reported, and major cardiovascular events were very rare.

As a class, TNFi may be associated with the development or worsening of demyelinating diseases and MS. Infliximab and etanercept have been associated with 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.

Although antinuclear antibodies (ANA) and, to a lesser extent, anti-double strand (ds) DNA antibodies may develop during the use of TNFi (between 10 and 70 % for etanercept in patients with RA and 18 % in psoriasis patients [1]), they are often of IgM isotype and disappear after discontinuation of therapy, while clinical autoimmune manifestations, notably drug-induced lupus, remain very rare.

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. [3-5]

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 etanercept in patients with psoriasis undergoing surgery. Studies in patients with rheumatoid arthritis (RA) suggest a small increase in postoperative wound infections to even a reduction in case of continued treatment. 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.

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

- Pregnancy/breastfeeding
- Latent tuberculosis
- History of recurrent or severe infections, localized infections, conditions predisposing to infections
- PUVA > 200 treatments (especially if followed by CsA use) – see also chapter: “Cancer”
- Demyelinating disease
- Malignancies or 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:

There are no known interactions of etanercept with the metabolism of other drugs. The combination of etanercept with immunosuppressive drugs may enhance the risk of infection. The combination of etanercept and anakinra has been associated with an increased risk of serious infections and neutropenia, and has not demonstrated increased clinical benefit. The concurrent administration of etanercept and abatacept did not demonstrate an increased clinical benefit. On the contrary, there was an increased incidence of SAE. The concomitant use of etanercept 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 with patients suffering from RA. Intravenous administration of 32 mg/m² was the highest examined dose, followed by subcutaneous injections of 16 mg/m² twice weekly (BIW). There is no known antidote for etanercept [6].

References

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