Adalimumab

Instructions for use

Table 1: Instructions for use (Adalimumab)

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, infections, congestive heart failure (CHF) and neurological disease or symptoms
- Recommended measures include:
    - Check for skin cancer
    - Check for lymphadenopathy
    - Laboratory parameters (see **Table 2**)
    - Exclusion of tuberculosis (see tuberculosis chapter)
    - 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 malignancies, risk factors for serious infections, congestive heart failure, and neurological symptoms
- Recommended measures include:
    - Check for skin cancer

- Check for lymphadenopathy
- Laboratory parameters (see **Table 2**)

- Reliable contraception

Post-treatment

- After discontinuation of adalimumab, patients should be followed up with medical history and physical examination
- For information on continued necessity of contraception or management in case of desire to become pregnant immediately after 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 (Adalimumab)

	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:

In placebo-controlled trials, injection-site reactions (erythema, itching, pain, swelling, haemorrhage) were the most frequently reported ADR, occurring in 14 % of patients treated with adalimumab compared to 8 % of patients receiving placebo. The use of adalimumab can be associated with infectious adverse effects. These consisted primarily of upper respiratory tract infections, bronchitis, and urinary tract infections. More serious infections observed included infective endocarditis [1], pneumonia, septic arthritis, prosthetic and post-surgical infections, erysipelas, cellulitis, diverticulitis, and pyelonephritis. Adverse reactions of the haematologic system, including thrombocytopenia and leukopenia, have been infrequently reported with adalimumab. Other rare side effects of adalimumab are severe allergic reactions (rash; hives; itching; difficulty in breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue). Long-term data from global clinical trials are available and reported no new safety signals and a safety profile consistent with known information about the TNFi class [2].

Treatment with adalimumab may result in the formation of autoantibodies and rarely in the development of lupus-like syndrome.

Malignancies, especially lymphoma, associated with the use of adalimumab occur very rarely (see special considerations during treatment) [3-6]. Side effects may be especially likely to occur in elderly patients, who are usually more sensitive than younger adults to the effects of adalimumab.

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 switching to another biological, preferably from a different class [7-9].

Table 3: Overview of important side effects [2]

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 adalimumab 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[10,11]. 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

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

Combination of TNFi and MTX

Treatment with TNFi and methotrexate can be combined. This may reduce the risk of anti-drug antibodies formation [12]. This combination is particularly common for infliximab as the risk for the formation of antidrug antibodies formation is highest. The combination may lead to an increased risk of infection, especially when compared to MTX monotherapy, but data are still scarce [13] (see chapter: “Immunogenicity”).

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/or 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
- 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:

There are no known interactions of adalimumab with the metabolism of other drugs. The combination of adalimumab with immunosuppressive drugs may enhance the risk of infection.

There is insufficient information regarding the concomitant use of adalimumab with other biological therapeutics used to treat the same conditions as adalimumab. The concomitant use of adalimumab with these biologics is not recommended because of the possibility of an increased risk of infection.

Overdose/measures in case of overdose

Dose-limited toxicity has not been studied in clinical trials. The highest examined dose was multiple intravenous infusions at 10 mg/kg[14].

References

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