Ixekizumab

Instructions for use

Table 1: Instructions for use (Ixekizumab)

Pre-treatment

100 % Agreement [1]

- Physicians are encouraged to enrol their patients in a registry (if available)
- Objective assessment of disease (such as PASI/BSA/PGA; arthritis)
- HRQoL (such as DLQI/Skindex-29 or -17)
- Medical history and physical examination including prior exposure to treatments, malignancies, infection, inflammatory bowel disease
- Recommended measures include:
  - Check for skin cancer
  - Check for lymphadenopathy
  - Laboratory parameters (see **Table 2**)
  - Exclusion of tuberculosis (see chapter tuberculosis)
  - Check for evidence of active infection
  - Check need for vaccines
- Reliable contraception

During treatment

- Objective assessment of the disease (such as PASI/BSA/PGA; arthritis)
- HRQoL (such as DLQI, Skindex-29 or 17)
- Laboratory parameters (see **Table 2**)
- Medical history and physical examination focusing on infections (in particular upper respiratory tract infections, candida, tuberculosis), contraception, signs or symptoms of inflammatory bowel disease

Post-treatment

- After discontinuation of ixekizumab, 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 (Ixekizumab)

	Period in weeks/months	
Parameter	**Pre-treatment**	**After 3-6 months**
Full blood count	X	X
Liver enzymes	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:

Common adverse events (occurring in ≥10% of patients) include injection site reactions, upper airway infections. Adverse events (occurring in 1-10% of patients) include oropharyngeal pain, nausea, tinea infections, mucocutaneous herpes simplex.

Injection site reactions

The most frequent injection site reactions observed were erythema and pain. These reactions were predominantly mild to moderate in severity and did not lead to discontinuation of ixekizumab. [1] The SmPC also notes that a single-blind randomized cross-over study [2] compared the original formulation with a citrate-free formulation in 45 healthy patients. During injection and 10 minutes after, VAS pain score was significantly lower in patients who received the citrate-free formulation (difference in LS Mean VAS score -21.69 and -4.47, respectively). [1,2]

Infections

In the placebo-controlled period of the phase III clinical studies in plaque psoriasis, infections were reported in 27.2 % of patients treated with ixekizumab for up to 12 weeks compared with 22.9 % of patients treated with placebo.

The majority of infections were non-serious and mild to moderate in severity, most of which did not necessitate treatment discontinuation. Serious infections occurred in 13 (0.6 %) of patients treated with ixekizumab and in three (0.4 %) of patients treated with placebo. Over the entire treatment period, infections were reported in 52.8 % of patients treated with ixekizumab (46.9 per 100 patient years). Serious infections were reported in 1.6 % of patients treated with ixekizumab (1.5 per 100 patient years).

Laboratory assessment of neutropenia and thrombocytopenia

In plaque psoriasis studies, 9% of patients receiving ixekizumab developed neutropenia. In most cases, the blood neutrophil count was ≥1,000 cells/mm^3. Such levels of neutropenia may persist, fluctuate or be transient. 0.1% of patients receiving ixekizumab developed a neutrophil count <1000 cells/mm^3. In general, neutropenia did not require discontinuation of ixekizumab. 3% of patients exposed to ixekizumab had a shift from a normal baseline platelet value to <150,000 platelet cells/mm^3 to ≥75,000 cells/mm ^{3}. Thrombocytopenia may persist, fluctuate or be transient.

Inflammatory Bowel Disease

Cases of new or exacerbations of Crohn's disease and ulcerative colitis have been reported. Caution should be exercised when prescribing ixekizumab to patients with inflammatory bowel disease, including Crohn's disease and ulcerative colitis, and patients should be monitored closely.

Candidiasis

Related to the mechanism of action of ixekizumab higher rates of fungal infections, primarily non-serious skin and mucosal candida infections are observed. Early treatment of candida infections, either

with topical or systemic treatment is recommended. For further information on treatment of candidiasis, see SmPC of antifungal drugs or international guidelines. [3,4]

Treatment with IL-17 inhibitors is associated with increased risk of infection[5], particularly by mucocutaneous and cutaneous candidiasis. Cases are usually described as mild-to-moderate, respond to standard treatment and do not require treatment discontinuation. In case of recurrent infections, consider changing the antipsoriatic drug. Note that clinically significant, severe infections are always a contraindication for all biologics.

Recently, two new large studies have been published regarding the safety of ixekizumab. In data from 17 clinical trials involving more than 18,000 patient-years of exposure in almost 7000 patients, the long-term safety profile was consistent with that previously reported in patients with psoriasis. No new or unexpected safety events were detected. [6]

Another study on the safety of ixekizumab in patients with psoriatic arthritis (PsA) in 1401 patients with 2247.7 patient-years showed that the overall safety profile and tolerability of ixekizumab were consistent with the known safety profile in patients with PsA. No new or unexpected safety events were detected [7].

Special consideration during treatment

Please see SmPC and other sources for complete listing [8]. The guideline subcommittee decided to comment on the following aspects based on references [8-12]:

Surgery

There is no data on the management of surgery in patients treated with ixekizumab. The decision to discontinue ixekizumab prior to surgery must be based on individual factors, such as type and risk of surgical procedure, patient characteristics, severity of psoriasis in case of treatment discontinuation etc. Counselling with the surgeon is advised.

Important contraindications

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

Absolute contraindications:

- Clinically important active infections

Relative contraindications:

- Pregnancy or breastfeeding
- Inflammatory bowel disease

Drug interactions

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

In plaque psoriasis studies, the safety of ixekizumab in combination with other immunomodulatory agents or phototherapy has not been evaluated.

No interaction was seen when ixekizumab was administered concomitantly with methotrexate (MTX) and/or corticosteroids in patients with psoriatic arthritis.

Overdose/ measures in case of overdose

Doses up to 180 mg have been administered subcutaneously in clinical trials without dose-limiting toxicity . Overdoses up to 240 mg, subcutaneously, as a single administration in clinical trials, have been reported without any serious adverse events. In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

References

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