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Summary of Investigation Results

Infliximab (genetical recombination) [including biosimilars] Etanercept (genetical recombination) [including biosimilars]

April 21, 2026

Non-proprietary name

- a. Infliximab (genetical recombination) and biosimilars
- b. Etanercept (genetical recombination) and biosimilars

Brand name (marketing authorization holder)

- a. Remicade for I.V. Infusion 100 (Tanabe Pharma Corporation) and biosimilars
- b. Enbrel 10 mg for S.C. Injection, 25 mg for S.C. Injection, Enbrel 25 mg PEN 0.5 mL for S.C. Injection, 50 mg PEN 1.0 mL for S.C. Injection, Enbrel 25 mg Syringe 0.5 mL for S.C. Injection, 50 mg Syringe 1.0 mL for S.C. Injection, Enbrel 25 mg Syringe 0.5 mL for S.C. CLICWISE use, 50 mg Syringe 1.0 mL for S.C. CLICWISE use (Pfizer Japan Inc.), and biosimilars

Japanese market launch

- a. May 2002
- b. 10 mg for S.C. Injection: December 2009; 25 mg for S.C. Injection: March 2005; 25 mg PEN 0.5 mL: June 2018; 50 mg PEN 1.0 mL: June 2013; 25 mg Syringe 0.5 mL: June 2008; 50 mg Syringe 1.0 mL: October 2010; CLICWISE use: February 2022

Indications

a.

Treatment of the following diseases in patients who have had an inadequate response to conventional treatments:

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Rheumatoid arthritis (including prevention of structural joint damage)

Refractory Behcet's uveoretinitis

Psoriasis vulgaris, psoriatic arthritis, pustular psoriasis, erythrodermic psoriasis

Ankylosing spondylitis

Intestinal Behcet's disease, neuro-Behcet's disease, and vasculo-Behcet's disease

Acute-phase Kawasaki's disease

Treatment and maintenance therapy for Crohn's disease in patients with either of the following conditions (only in patients who have had an inadequate response to conventional treatments)

Patients with an active phase of moderate to severe Crohn's disease

Patients with external fistulas

Treatment of moderate to severe ulcerative colitis (only in patients who have had an inadequate response to conventional treatments)

b.

< Enbrel 10 mg for S.C. Injection and 25 mg for S.C. Injection >

Treatment of the following diseases in patients who have had an inadequate response to conventional treatments:

Rheumatoid arthritis (including prevention of structural joint damage)

Polyarticular juvenile idiopathic arthritis

< Other than the above >

Rheumatoid arthritis in patients who have had an inadequate response to conventional treatments (including prevention of structural joint damage)

Summary of revisions

a. b.

"Autoimmune hepatitis" should be added to the 11.1 Clinically Significant Adverse Reactions section in 11. ADVERSE REACTIONS.

Investigation results and background of the revision

Cases involving autoimmune hepatitis were evaluated. Cases in which a causal relationship between infliximab (genetical recombination) or etanercept (genetical recombination) and autoimmune hepatitis was reasonably possible have been reported. As a result of



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consultation with expert advisors regarding the causality assessment of the cases and the necessity of revision of PRECAUTIONS, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary.

Reference: Number of cases*¹ and patient mortalities involving autoimmune hepatitis reported in Japan and overseas*²

a.

A total of 9 cases have been reported in Japan to date. (A causal relationship between the drug and the event was reasonably possible for 2 cases, including 1 case in which the drug was administered outside the indications approved in Japan.)

No patient mortalities have been reported in Japan to date.

A total of 4 cases have been reported overseas to date. (A causal relationship between the drug and the event was reasonably possible for these cases.)

No patient mortalities have been reported overseas to date.

b.

A total of 4 cases have been reported in Japan to date (including 2 cases in which a causal relationship between the drug and the event was reasonably possible).

No patient mortalities have been reported in Japan to date.

A total of 6 cases have been reported overseas to date. (A causal relationship between the drug and the event was reasonably possible for these cases.)

No patient mortalities have been reported overseas to date.

*1: Cases corresponding to MedDRA v28.0 PT "Autoimmune hepatitis" among those collected in the PMDA's safety database for drugs

*2: Cases corresponding to all of the following criteria among cases extracted by the marketing authorization holder as suspected cases of autoimmune hepatitis due to drug administration



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- A positive result for autoantibodies such as antinuclear antibody (ANA) was described in the case report form
- Information on liver enzyme test values was included in the case report form and the event was assessed as Grade 3 or higher by Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0
- Cases considered to satisfy a condition of “other causes of liver disorders have been excluded,” which is one of the diagnostic criteria of autoimmune hepatitis in “Clinical practice guidelines for autoimmune hepatitis (AIH) (2021)” for which other causes such as hepatitis virus and alcohol are not clearly described in the case report form

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their conflict of interest declarations concerning the relevant products, pursuant to the “Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency” (PMDA Administrative Rule No. 20-8, dated December 25, 2008).

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