**Table 11. Components of Disease Activity in Psoriatic Arthritis**

| | Placebo N=104 | | Etanercept[a] N=101 | |
|---|---|---|---|---|
| Parameter (median) | Baseline | 6 Months | Baseline | 6 Months |
| Number of tender joints[b] | 17.0 | 13.0 | 18.0 | 5.0 |
| Number of swollen joints[c] | 12.5 | 9.5 | 13.0 | 5.0 |
| Physician global assessment[d] | 3.0 | 3.0 | 3.0 | 1.0 |
| Patient global assessment[d] | 3.0 | 3.0 | 3.0 | 1.0 |
| Morning stiffness (minutes) | 60 | 60 | 60 | 15 |
| Pain[d] | 3.0 | 3.0 | 3.0 | 1.0 |
| Disability index[e] | 1.0 | 0.9 | 1.1 | 0.3 |
| CRP (mg/dL)[f] | 1.1 | 1.1 | 1.6 | 0.2 |

[a] $p < 0.001$ for all comparisons between etanercept and placebo at 6 months.
[b] Scale 0-78.
[c] Scale 0-76.
[d] Likert scale: 0=best; 5=worst.
[e] Health Assessment Questionnaire: 0=best; 3=worst; includes eight categories: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and activities.
[f] Normal range: 0-0.79 mg/dL.

Among patients with PsA who received etanercept, the clinical responses were apparent at the time of the first visit (4 weeks) and were maintained through 6 months of therapy. Responses were similar in patients who were or were not receiving concomitant MTX therapy at baseline. At 6 months, the ACR 20/50/70 responses were achieved by 50%, 37%, and 9%, respectively, of patients receiving etanercept, compared to 13%, 4%, and 1%, respectively, of patients receiving placebo. Similar responses were seen in patients with each of the subtypes of PsA, although few patients were enrolled with the arthritis mutilans and ankylosing spondylitis-like subtypes. The results of this study were similar to those seen in an earlier single-center, randomized, placebo-controlled study of 60 patients with PsA.

The skin lesions of psoriasis were also improved with etanercept, relative to placebo, as measured by percentages of patients achieving improvements in the Psoriasis Area and Severity Index (PASI). Responses increased over time, and at 6 months, the proportions of patients achieving a 50% or 75% improvement in the PASI were 47% and 23%, respectively, in the etanercept group (N=66), compared to 18% and 3%, respectively, in the placebo group (N=62). Responses were similar in patients who were or were not receiving concomitant MTX therapy at baseline.

Radiographic Response

Radiographic changes were also assessed in the PsA study. Radiographs of hands and wrists were obtained at baseline and months 6, 12, and 24. A modified Total Sharp Score (TSS), which included distal interphalangeal joints (ie, not identical to the modified TSS used for RA) was used by readers blinded to treatment group to assess the radiographs. Some radiographic features specific to PsA (eg, pencil-and-cup deformity, joint space widening, gross osteolysis, and ankylosis) were included in the scoring system, but others (eg, phalangeal tuft resorption, juxta-articular and shaft periostitis) were not.

Most patients showed little or no change in the modified TSS during this 24-month study (median change of 0 in both patients who initially received etanercept or placebo). More placebo-treated patients experienced larger magnitudes of radiographic worsening (increased TSS) compared to etanercept treatment during the controlled period of the study. At 12 months, in an exploratory analysis, 12% (12 of 104) of placebo patients compared to none of the 101 etanercept-treated patients had increases of 3 points or more in TSS. Inhibition of radiographic progression was maintained in patients who continued on etanercept during the second year. Of the patients with 1-year and 2-year x-rays, 3% (2 of 71) had increases of 3 points or more in TSS at 1 and 2 years.

Physical Function Response

In the PsA study, physical function and disability were assessed using the HAQ Disability Index (HAQ-DI) and the SF-36 Health Survey. Patients treated with 25 mg etanercept twice weekly showed greater improvement from baseline in the HAQ-DI score (mean decreases of 54% at both months 3 and 6) in comparison to placebo (mean decreases of 6% at both months 3 and 6) ($p < 0.001$). At months 3 and 6, patients treated with etanercept showed greater

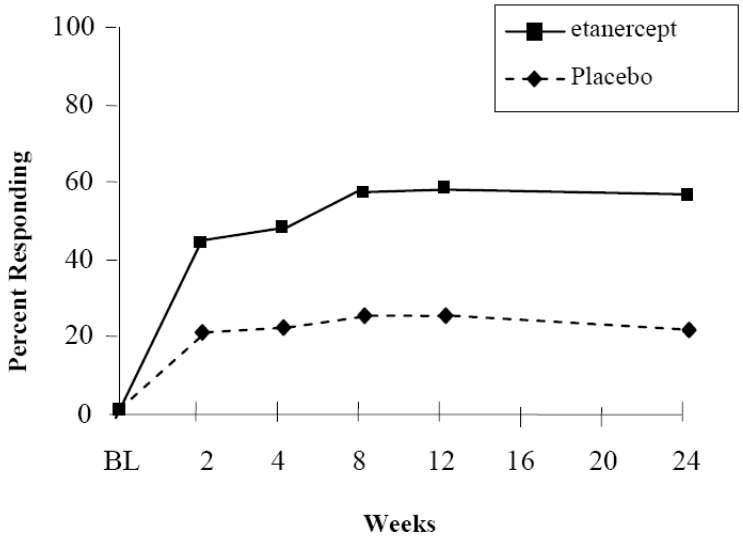
improvement from baseline in the SF-36 physical component summary score compared to patients treated with placebo, and no worsening in the SF-36 mental component summary score. Improvements in physical function and disability measures were maintained for up to 2 years through the open-label portion of the study.

### 14.4 Ankylosing Spondylitis

The safety and efficacy of etanercept were assessed in a randomized, double-blind, placebo-controlled study in 277 patients with active AS. Patients were between 18 and 70 years of age and had AS as defined by the modified New York Criteria for Ankylosing Spondylitis. Patients were to have evidence of active disease based on values of ≥ 30 on a 0-100 unit Visual Analog Scale (VAS) for the average of morning stiffness duration and intensity, and two of the following three other parameters: a) patient global assessment, b) average of nocturnal and total back pain, and c) the average score on the Bath Ankylosing Spondylitis Functional Index (BASFI). Patients with complete ankylosis of the spine were excluded from study participation. Patients taking hydroxychloroquine, sulfasalazine, methotrexate, or prednisone (≤ 10 mg/day) could continue these drugs at stable doses for the duration of the study. Doses of 25 mg etanercept or placebo were administered SC twice a week for 6 months.

The primary measure of efficacy was a 20% improvement in the Assessment in Ankylosing Spondylitis (ASAS) response criteria. Compared to placebo, treatment with etanercept resulted in improvements in the ASAS and other measures of disease activity (Figure 2 and Table 12).

**Figure 2. ASAS 20 Responses in Ankylosing Spondylitis**




At 12 weeks, the ASAS 20/50/70 responses were achieved by 60%, 45%, and 29%, respectively, of patients receiving etanercept, compared to 27%, 13%, and 7%, respectively, of patients receiving placebo ($p \leq 0.0001$, etanercept vs placebo). Similar responses were seen at Week 24. Responses were similar between those patients receiving concomitant therapies at baseline and those who were not. The results of this study were similar to those seen in a single-center, randomized, placebo-controlled study of 40 patients and a multicenter, randomized, placebo-controlled study of 84 patients with AS.

**Table 12. Components of Ankylosing Spondylitis Disease Activity**

| | Placebo N=139 | | Etanercept[a] N=138 | |
|---|---|---|---|---|
| Median values at time points | Baseline | 6 Months | Baseline | 6 Months |
| ASAS response criteria | | | | |
| Patient global assessment[b] | 63 | 56 | 63 | 36 |
| Back pain[c] | 62 | 56 | 60 | 34 |
| BASFI[d] | 56 | 55 | 52 | 36 |
| Inflammation[e] | 64 | 57 | 61 | 33 |
| Acute phase reactants | | | | |
| CRP (mg/dL)[f] | 2.0 | 1.9 | 1.9 | 0.6 |
| Spinal mobility (cm): | | | | |
| Modified Schober's test | 3.0 | 2.9 | 3.1 | 3.3 |
| Chest expansion | 3.2 | 3.0 | 3.3 | 3.9 |
| Occiput-to-wall measurement | 5.3 | 6.0 | 5.6 | 4.5 |

[a] $p < 0.0015$ for all comparisons between etanercept and placebo at 6 months. P values for continuous endpoints were based on percent change from baseline.
[b] Measured on a Visual Analog Scale (VAS) with 0="none" and 100="severe."
[c] Average of total nocturnal and back pain scores, measured on a VAS with 0="no pain" and 100="most severe pain."
[d] Bath Ankylosing Spondylitis Functional Index (BASFI), average of 10 questions.
[e] Inflammation represented by the average of the last 2 questions on the 6-question Bath Ankylosing Spondylitis Disease Activity Index (BASDAI).
[f] C-reactive protein (CRP) normal range: 0-1.0 mg/dL.

### 14.5 Adult Plaque Psoriasis

The safety and efficacy of etanercept were assessed in two randomized, double-blind, placebo-controlled studies in adults with chronic stable PsO involving ≥ 10% of the body surface area, a minimum Psoriasis Area and Severity Index (PASI) score of 10 and who had received or were candidates for systemic antipsoriatic therapy or phototherapy. Patients with guttate, erythrodermic, or pustular psoriasis and patients with severe infections within 4 weeks of screening were excluded from study. No concomitant major antipsoriatic therapies were allowed during the study.

Study I evaluated 672 subjects who received placebo or etanercept SC at doses of 25 mg once a week, 25 mg twice a week, or 50 mg twice a week for 3 months. After 3 months, subjects continued on blinded treatments for an additional 3 months during which time subjects originally randomized to placebo began treatment with blinded etanercept at 25 mg twice weekly (designated as placebo/etanercept in Table 13); subjects originally randomized to etanercept continued on the originally randomized dose (designated as etanercept/etanercept groups in Table 13).

Study II evaluated 611 subjects who received placebo or etanercept SC at doses of 25 mg or 50 mg twice a week for 3 months. After 3 months of randomized, blinded treatment, subjects in all three arms began receiving open-label etanercept at 25 mg twice weekly for 9 additional months.

Response to treatment in both studies was assessed after 3 months of therapy and was defined as the proportion of subjects who achieved a reduction in PASI score of at least 75% from baseline. The PASI is a composite score that takes into consideration both the fraction of body surface area affected and the nature and severity of psoriatic changes within the affected regions (induration, erythema and scaling).

Other evaluated outcomes included the proportion of subjects who achieved a score of "clear" or "minimal" by the Static Physician Global Assessment (sPGA) and the proportion of subjects with a reduction of PASI of at least 50% from baseline. The sPGA is a 6-category scale ranging from "5=severe" to "0=none" indicating the physician's overall assessment of the PsO severity focusing on induration, erythema and scaling. Treatment success of "clear" or "minimal" consisted of none or minimal elevation in plaque, up to faint red coloration in erythema and none or minimal fine scale over < 5% of the plaque.

Subjects in all treatment groups and in both studies had a median baseline PASI score ranging from 15 to 17, and

the percentage of subjects with baseline sPGA classifications ranged from 54% to 66% for moderate, 17% to 26% for marked and 1% to 5% for severe. Across all treatment groups, the percentage of subjects who previously received systemic therapy for PsO ranged from 61% to 65% in Study I and 71% to 75% in Study II, and those who previously received phototherapy ranged from 44% to 50% in Study I and 72% to 73% in Study II.

More subjects randomized to etanercept than placebo achieved at least a 75% reduction from baseline PASI score (PASI 75) with a dose response relationship across doses of 25 mg once a week, 25 mg twice a week and 50 mg twice a week (Tables 13 and 14). The individual components of the PASI (induration, erythema and scaling) contributed comparably to the overall treatment-associated improvement in PASI.

**Table 13. Study I Outcomes at 3 and 6 Months**

| | Placebo/Etanercept 25 mg BIW (N=168) | Etanercept/Etanercept | | |
|---|---|---|---|---|
| | | 25 mg QW (N=169) | 25 mg BIW (N=167) | 50 mg BIW (N=168) |
| **3 Months** | | | | |
| PASI 75 n (%) | 6 (4%) | 23 (14%)[a] | 53 (32%)[b] | 79 (47%)[b] |
| Difference (95% CI) | | 10% (4, 16) | 28% (21, 36) | 43% (35, 52) |
| sPGA, "clear" or "minimal" n (%) | 8 (5%) | 36 (21%)[b] | 53 (32%)[b] | 79 (47%)[b] |
| Difference (95% CI) | | 17% (10, 24) | 27% (19, 35) | 42% (34, 50) |
| PASI 50 n (%) | 24 (14%) | 62 (37%)[b] | 90 (54%)[b] | 119 (71%)[b] |
| Difference (95% CI) | | 22% (13, 31) | 40% (30, 49) | 57% (48, 65) |
| **6 Months** | | | | |
| PASI 75 n (%) | 55 (33%) | 36 (21%) | 68 (41%) | 90 (54%) |

[a] p=0.001 compared with placebo.
[b] p < 0.0001 compared with placebo.

**Table 14. Study II Outcomes at 3 Months**

| | Placebo (N=204) | Etanercept | |
|---|---|---|---|
| | | 25 mg BIW (N=204) | 50 mg BIW (N=203) |
| PASI 75 n (%) | 6 (3%) | 66 (32%)[a] | 94 (46%)[a] |
| Difference (95% CI) | | 29% (23, 36) | 43% (36, 51) |
| sPGA, "clear" or "minimal" n (%) | 7 (3%) | 75 (37%)[a] | 109 (54%)[a] |
| Difference (95% CI) | | 34% (26, 41) | 50% (43, 58) |
| PASI 50 n (%) | 18 (9%) | 124 (61%)[a] | 147 (72%)[a] |
| Difference (95% CI) | | 52% (44, 60) | 64% (56, 71) |

[a] p < 0.0001 compared with placebo.

Among PASI 75 achievers in both studies, the median time to PASI 50 and PASI 75 was approximately 1 month and approximately 2 months, respectively, after the start of therapy with either 25 or 50 mg twice a week.

In Study I, subjects who achieved PASI 75 at month 6 were entered into a study drug withdrawal and retreatment period. Following withdrawal of study drug, these subjects had a median duration of PASI 75 of between 1 and 2 months.
In Study I, among subjects who were PASI 75 responders at 3 months, retreatment with their original blinded etanercept dose after discontinuation of up to 5 months resulted in a similar proportion of responders as in the initial

double-blind portion of the study.

In Study II, most subjects initially randomized to 50 mg twice a week continued in the study after month 3 and had their etanercept dose decreased to 25 mg twice a week. Of the 91 subjects who were PASI 75 responders at month 3, 70 (77%) maintained their PASI 75 response at month 6.

### 14.6 Pediatric Plaque Psoriasis

A 48-week, randomized, double-blind, placebo-controlled study enrolled 211 pediatric subjects 4 to 17 years of age, with moderate to severe plaque psoriasis (PsO) (as defined by a sPGA score ≥ 3 [moderate, marked, or severe], involving ≥ 10% of the body surface area, and a PASI score ≥ 12) who were candidates for phototherapy or systemic therapy, or were inadequately controlled on topical therapy. Subjects in all treatment groups had a median baseline PASI score of 16.4, and the percentage of subjects with baseline sPGA classifications was 65% for moderate, 31% for marked, and 3% for severe. Across all treatment groups, the percentage of subjects who previously received systemic or phototherapy for PsO was 57%.

Subjects received etanercept 0.8 mg/kg (up to a maximum of 50 mg per dose) or placebo once weekly for the first 12 weeks. After 12 weeks, subjects entered a 24-week open-label treatment period, in which all subjects received etanercept at the same dose. This was followed by a 12-week withdrawal-retreatment period.

Response to treatment was assessed after 12 weeks of therapy and was defined as the proportion of subjects who achieved a reduction in PASI score of at least 75% from baseline. The PASI is a composite score that takes into consideration both the fraction of body surface area affected and the nature and severity of psoriatic changes within the affected regions (induration, erythema and scaling).

Other evaluated outcomes included the proportion of subjects who achieved a score of "clear" or "almost clear" by the sPGA and the proportion of subjects with a reduction in PASI score of at least 90% from baseline. The sPGA is a 6-category scale ranging from "5 = severe" to "0 = none" indicating the physician's overall assessment of the PsO severity focusing on induration, erythema and scaling. Treatment success of "clear" or "almost clear" consisted of none or minimal elevation in plaque, up to faint red coloration in erythema and none or minimal fine scale over < 5% of the plaque.

Efficacy results are summarized in Table 15.

**Table 15. Pediatric Plaque Psoriasis Outcomes at 12 Weeks**

| | Placebo (N = 105) | Etanercept 0.8 mg/kg Once Weekly (N = 106) |
|---|---|---|
| PASI 75, n (%) | 12 (11%) | 60 (57%) |
| PASI 90, n (%) | 7 (7%) | 29 (27%) |
| sPGA "clear" or "almost clear" n (%) | 14 (13%) | 55 (52%) |

Maintenance of Response

To evaluate maintenance of response, subjects who achieved PASI75 response at Week 36 were re-randomized to either etanercept or placebo during a 12-week randomized withdrawal period. The maintenance of PASI 75 response was evaluated at Week 48. The proportion of subjects who maintained PASI75 response at Week 48 was higher for subjects treated with etanercept (65%) compared to those treated with placebo (49%).

## 15 REFERENCES

1. National Cancer Institute. Surveillance, Epidemiology, and End Results Database (SEER) Program. SEER Incidence Crude Rates, 13 Registries, 1992-2002.
2. Bröms G, Granath F, Ekbom A, et al. Low Risk of Birth Defects for Infants Whose Mothers Are Treated With Anti-Tumor Necrosis Factor Agents During Pregnancy. *Clin Gastroenterol Hepatol*. 2016;14:234-241.e5

## 16 HOW SUPPLIED/STORAGE AND HANDLING

Administration of one 50 mg Eticovo single-dose prefilled syringe provides a dose equivalent to two 25 mg Eticovo single-dose prefilled syringes.

**Eticovo Single-Dose Prefilled Syringe**

Each Eticovo (etanercept-ykro) injection is supplied as a clear to opalescent, colorless to pale yellow, sterile, and preservative-free solution for subcutaneous administration in single-dose prefilled syringes with a 27-gauge, ½-inch needle.

| | | |
|---|---|---|
| **50 mg/mL** single-dose prefilled syringe | Carton of 4 | NDC 71202-003-04 |
| **25 mg/0.5 mL** single-dose prefilled syringe | Carton of 4 | NDC 71202-004-04 |

Eticovo should be refrigerated at 36°F to 46°F (2°C to 8°C). Do not use Eticovo beyond the expiration date stamped on the carton or barrel label. DO NOT SHAKE. Store Eticovo in the original carton to protect from light or physical damage.

For convenience, storage of individual single-dose prefilled syringes at room temperature between 73°F to 81°F (23°C to 27°C) for a maximum single period of 14 days is permissible, with protection from light and sources of heat. Once a single-dose prefilled syringe has been stored at room temperature, it should not be placed back into the refrigerator. If not used within 14 days at room temperature, the single-dose prefilled syringe should be discarded. Do not store Eticovo in extreme heat or cold. DO NOT FREEZE. Keep out of the reach of children.

## 17 PATIENT COUNSELING INFORMATION

Advise the patient and/or caregiver to read the FDA-approved patient labeling *(Medication Guide and Instructions for Use)* before the patient starts using Eticovo, and each time the prescription is renewed, as there may be new information they need to know.

Patients or their caregivers should be provided the Eticovo "Medication Guide" and provided an opportunity to read it and ask questions prior to initiation of therapy. The healthcare provider should ask the patient questions to determine any risk factors for treatment. Patients developing signs and symptoms of infection should seek medical evaluation immediately.

**Patient Counseling**

Patients should be advised of the potential benefits and risks of Eticovo. Physicians should instruct their patients to read the Medication Guide before starting Eticovo therapy and to reread each time the prescription is renewed.

Infections
Inform patients that Eticovo may lower the ability of their immune system to fight infections. Advise patients of the importance of contacting their doctor if they develop any symptoms of infection, tuberculosis or reactivation of hepatitis B virus infections.

Other Medical Conditions
Advise patients to report any signs of new or worsening medical conditions, such as central nervous system demyelinating disorders, heart failure or autoimmune disorders, such as lupus-like syndrome or autoimmune hepatitis. Counsel about the risk of lymphoma and other malignancies while receiving Eticovo. Advise patients to report any symptoms suggestive of a pancytopenia, such as bruising, bleeding, persistent fever or pallor.

Allergic Reactions
Advise patients to seek immediate medical attention if they experience any symptoms of severe allergic reactions.

**Administration of Eticovo**

If a patient or caregiver is to administer Eticovo, the patient or caregiver should be instructed in injection techniques and how to measure and administer the correct dose [see the Eticovo (etanercept-ykro) “Instructions for Use” insert].

The first injection should be performed under the supervision of a qualified healthcare professional. The patient’s or caregiver’s ability to inject subcutaneously should be assessed. Patients and caregivers should be instructed in the technique, as well as proper syringe and needle disposal, and be cautioned against reuse of needles and syringes.

A puncture-resistant container for disposal of needles, and syringes should be used.

SAMSUNG
BIOEPIS

**Eticovo (etanercept-ykro)**

**Manufactured by:**
Samsung Bioepis Co., Ltd.
107, Cheomdan-daero, Yeonsu-gu, Incheon, 21987, Republic of Korea
U.S. License Number 2046

Product of Denmark

**Medication Guide**
**Eticovo (E-Ti-Ko-Vo)**
**(etanercept-ykro)**
**injection, for subcutaneous use**

Read the Medication Guide that comes with Eticovo before you start using it and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking with your healthcare provider about your medical condition or treatment. It is important to remain under your healthcare provider's care while using Eticovo. Eticovo is a prescription medicine called a Tumor Necrosis Factor (TNF) blocker that affects your immune system.

**What is the most important information I should know about Eticovo?**

Eticovo may cause serious side effects, including:

1. Risk of Infection
2. Risk of Cancer

**1. Risk of infection**

Eticovo can lower the ability of your immune system to fight infections. Some people have serious infections while taking Eticovo. These infections include tuberculosis (TB), and infections caused by viruses, fungi, or bacteria that spread throughout their body. Some people have died from these infections.

- Your healthcare provider should test you for TB before starting Eticovo.
- Your healthcare provider should monitor you closely for symptoms of TB during treatment with Eticovo even if you tested negative for TB.
- Your healthcare provider should check you for symptoms of any type of infection before, during, and after your treatment with Eticovo.

You should not start taking Eticovo if you have any kind of infection unless your healthcare provider says it is okay.

**2. Risk of cancer**

- There have been cases of unusual cancers, some resulting in death, in children and teenage patients who started using TNF-blocking agents at less than 18 years of age.
- For children, teenagers, and adults taking TNF-blocker medicines, including etanercept products, the chances of getting lymphoma or other cancers may increase.
- People with rheumatoid arthritis, especially those with very active disease, may be more likely to get lymphoma.

**Before starting Eticovo, be sure to talk to your healthcare provider:**

Eticovo may not be right for you. Before starting Eticovo, tell your healthcare provider about all of your medical conditions, including:

**Infections. Tell your healthcare provider if you:**

- have an infection. See **"What is the most important information I should know about Eticovo?"**
- are being treated for an infection.
- think you have an infection.
- have symptoms of an infection such as fever, sweats or chills, cough or flu-like symptoms, shortness of breath, blood in your phlegm, weight loss, muscle aches, warm, red or painful areas on your skin, sores on your body, diarrhea or stomach pain, burning when you urinate or urinating more often than normal, and feel very tired.
- have any open cuts on your body.
- get a lot of infections or have infections that keep coming back.
- have diabetes, HIV, or a weak immune system. People with these conditions have a higher chance for infections.
- have TB, or have been in close contact with someone with TB.
- were born in, lived in, or traveled to countries where there is a risk for getting TB. Ask your healthcare provider if you are not sure.
- live, have lived in, or traveled to certain parts of the country (such as the Ohio and Mississippi River valleys, or the Southwest) where there is a greater risk for getting certain kinds of fungal infections (histoplasmosis, coccidioidomycosis, blastomycosis). These infections may happen or become more severe if you use Eticovo. Ask your healthcare provider if you do not know if you live or have lived in an area where these infections are common.
- have or have had hepatitis B.

**Also, before starting Eticovo, tell your healthcare provider:**

- **About all the medicines you take including prescription and over-the-counter medicines, vitamins and herbal supplements including:**
  - **Orencia (abatacept) or Kineret (anakinra).** You have a higher chance for serious infections when taking Eticovo with Orencia or Kineret.
  - **Cyclophosphamide (Cytoxan).** You may have a higher chance for getting certain cancers when taking Eticovo with cyclophosphamide.
  - **Anti-diabetic medicines.** If you have diabetes and are taking medication to control your diabetes, your healthcare provider may decide you need less anti-diabetic medicine while taking Eticovo.

Keep a list of all your medications with you to show your healthcare provider and pharmacist each time you get a new medicine. Ask your healthcare provider if you are not sure if your medicine is one listed above.

**Other important medical information you should tell your healthcare provider before starting Eticovo, includes if you:**

- have or had a nervous system problem such as multiple sclerosis or Guillain-Barré syndrome.
- have or had heart failure.
- are scheduled to have surgery.
- have recently received or are scheduled to receive a vaccine.
  - All vaccines should be brought up-to-date before starting Eticovo.
  - People taking Eticovo should not receive live vaccines.
  - Ask your healthcare provider if you are not sure if you received a live vaccine.
- have been around someone with varicella zoster (chicken pox).
- are pregnant or plan to become pregnant. It is not known if Eticovo will harm your unborn baby. If you took Eticovo during pregnancy, talk to your healthcare provider prior to administration of live vaccines to your infant.
- are breastfeeding or plan to breastfeed. Eticovo can pass into breast milk. Talk to your healthcare provider about the best way to feed your baby while taking Eticovo

See the section **"What are the possible side effects of Eticovo?"** below for more information**.**

**What is Eticovo?**

Eticovo is a prescription medicine called a Tumor Necrosis Factor (TNF) blocker.

Eticovo is used to treat:

- **moderately to severely active rheumatoid arthritis (RA).** Eticovo can be used alone or with a medicine called methotrexate.
- **moderately to severely active polyarticular juvenile idiopathic arthritis (JIA) in children ages 2 years and older.**
- **psoriatic arthritis (PsA).** Eticovo can be used alone or with methotrexate.
- **ankylosing spondylitis (AS).**
- **chronic moderate to severe plaque psoriasis (PsO) in children 4 years and older and adults** who may benefit from taking injections or pills (systemic therapy) or phototherapy (ultraviolet light).

You may continue to use other medicines that help treat your condition while taking Eticovo, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and prescription steroids, as recommended by your healthcare provider.

Eticovo can help reduce joint damage and the signs and symptoms of the above-mentioned diseases. People with these diseases have too much of a protein called tumor necrosis factor (TNF), which is made by your immune system. Eticovo can reduce the effect of TNF in the body and block the damage that too much TNF can cause, but it can also lower the ability of your immune system to fight infections. See **"What is the most important information I should know about Eticovo?"** and **"What are the possible side effects of Eticovo?"**

**Who should not use Eticovo?**

**Do not use Eticovo if you:**

- have an infection that has spread through your body (sepsis).

**How should I use Eticovo?**

- Eticovo is given as an injection under the skin (subcutaneous or SC).

- If your healthcare provider decides that you or a caregiver can give the injections of Eticovo at home, you or your caregiver should receive training on the right way to prepare and inject Eticovo. Do not try to inject Eticovo until you have been shown the right way by your healthcare provider or nurse.
- Eticovo is available as a single-dose prefilled syringe.
- See the detailed "Instructions for Use" with this Medication Guide for instructions about the right way to store, prepare, and give your Eticovo injections at home.
- Your healthcare provider will tell you how often you should use Eticovo. Do not miss any doses of Eticovo. If you forget to use Eticovo, inject your dose as soon as you remember. Then, take your next dose at your regular(ly) scheduled time. In case you are not sure when to inject Eticovo, call your healthcare provider or pharmacist. **Do not use Eticovo more often than as directed by your healthcare provider.**
- Your child's dose of Eticovo depends on his or her weight. Your child's healthcare provider will tell you which form of Eticovo to use and how much to give your child.

**What are the possible side effects of Eticovo?**

**Eticovo can cause serious side effects, including:**

- **See "What is the most important information I should know about Eticovo?"**
- **Infections.** Eticovo can make you more likely to get infections or make any infection that you have worse. Call your healthcare provider right away if you have any symptoms of an infection. See **"Before starting Eticovo, be sure to talk to your healthcare provider"** for a list of symptoms of infection.
- **Previous Hepatitis B infection.** If you have been previously infected with the hepatitis B virus (a virus that affects the liver), the virus can become active while you use Eticovo. Your healthcare provider may do a blood test before you start treatment with Eticovo and while you use Eticovo.
- **Nervous system problems.** Rarely, people who use TNF-blocker medicines have developed nervous system problems such as multiple sclerosis, seizures, or inflammation of the nerves of the eyes. Tell your healthcare provider right away if you get any of these symptoms: numbness or tingling in any part of your body, vision changes, weakness in your arms and legs, and dizziness.
- **Blood problems.** Low blood counts have been seen with other TNF-blocker medicines. Your body may not make enough of the blood cells that help fight infections or help stop bleeding. Symptoms include fever, bruising or bleeding very easily, or looking pale.
- **Heart failure including new heart failure or worsening of heart failure you already have.** New or worse heart failure can happen in people who use TNF-blocker medicines like Eticovo. If you have heart failure your condition should be watched closely while you take Eticovo. Call your healthcare provider right away if you get new or worsening symptoms of heart failure while taking Eticovo, such as shortness of breath or swelling of your lower legs or feet.
- **Psoriasis.** Some people using Eticovo developed new psoriasis or worsening of psoriasis they already had. Tell your healthcare provider if you develop red scaly patches or raised bumps that may be filled with pus. Your healthcare provider may decide to stop your treatment with Eticovo.
- **Allergic reactions.** Allergic reactions can happen to people who use TNF-blocker medicines. Call your healthcare provider right away if you have any symptoms of an allergic reaction. Symptoms of an allergic reaction include a severe rash, a swollen face, or trouble breathing.
- **Autoimmune reactions, including:**
  - **Lupus-like syndrome.** Symptoms include a rash on your face and arms that gets worse in the sun. Tell your healthcare provider if you have this symptom. Symptoms may go away when you stop using Eticovo.
  - **Autoimmune hepatitis.** Liver problems can happen in people who use TNF-blocker medicines, including Eticovo. These problems can lead to liver failure and death. Call your healthcare provider right away if you have any of these symptoms: feel very tired, skin or eyes look yellow, poor appetite or vomiting, pain on the right side of your stomach (abdomen).

**Common side effects of Eticovo include:**

- **Injection site reactions** such as redness, swelling, itching, or pain. These symptoms usually go away within 3 to 5 days. If you have pain, redness, or swelling around the injection site that does not go away or gets worse, call your healthcare provider.
- **Upper respiratory infections** (sinus infections).

These are not all the side effects with Eticovo. Tell your healthcare provider about any side effect that bothers you or does not go away.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**How should I store Eticovo?**

- Store Eticovo in the refrigerator between 36°F to 46°F (2°C to 8°C).
- Store Eticovo in the original carton to protect from light or physical damage.
- If needed, you may store the Eticovo prefilled syringe at room temperature between 73°F to 81°F (23°C to 27°C), 1 time, for up to 2 weeks (14 days).
  - Once Eticovo has reached room temperature, do not put it back in the refrigerator.
- Throw away Eticovo that has been stored at room temperature after 2 weeks (14 days).
- **Do not** store Eticovo in extreme heat or cold such as in your vehicle's glove box or trunk.
- **Do not freeze.**
- **Do not shake.**
- **Keep Eticovo and all medicines out of the reach of children.**

**General information about the safe and effective use of Eticovo.**

Medicines are sometimes prescribed for purposes not mentioned in a Medication Guide. Do not use Eticovo for a condition for which it was not prescribed. Do not give Eticovo to other people, even if they have the same condition. It may harm them.

This Medication Guide summarizes the most important information about Eticovo. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about Eticovo that was written for healthcare professionals.

**What are the ingredients in Eticovo?**

**Single-dose Prefilled Syringe**

**Active Ingredient:** etanercept-ykro

**Inactive Ingredients:** sodium chloride, sodium phosphate dibasic heptahydrate, sodium phosphate monobasic monohydrate, sucrose, and Water for Injection, USP

SAMSUNG
BIOEPIS

Manufactured by: Samsung Bioepis Co., Ltd.
107, Cheomdan-daero, Yeonsu-gu, Incheon, 21987, Republic of Korea, U.S. License Number 2046
Product of Denmark
For more information, call 1-877-888-4231.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Issued: 04/2019

**Instructions for Use**
**Eticovo (E-Ti-Ko-Vo)**
**(etanercept-ykro)**
**injection, for subcutaneous use**
**Single-dose Prefilled Syringe**

**Read this Instructions for Use before you start using Eticovo and each time you get a refill of your prescription. There may be new information.**

- **Do not** try to give yourself the injection unless your healthcare provider or nurse has shown you how to give the injection

**How do I prepare and give an injection with Eticovo Single-dose Prefilled Syringe?**

There are 2 types of Eticovo single-dose prefilled syringes:

- The 50 mg/mL single-dose prefilled syringe that contains one 50 mg dose of Eticovo.
- The 25 mg/0.5 mL single-dose prefilled syringe that contains one 25 mg dose of Eticovo.

Your healthcare provider will tell you which one to use. **Before you start, check the prefilled syringe label to make sure that it is the right dose.**

A 50 mg dose can be given as one injection using a 50 mg/mL single-dose prefilled syringe or as two injections using 25 mg/0.5 mL single-dose prefilled syringes. Your healthcare provider will tell you whether the two injections with 25 mg/0.5 mL single-dose prefilled syringes should be given on the same day once a week or on two different days (3 or 4 days apart) in the same week.

**Children must weigh at least 138 pounds (63 kg) to use Eticovo.**

**Storage of Eticovo prefilled syringe**

- Store Eticovo prefilled syringe in the refrigerator between 36°F to 46°F (2°C to 8°C).
- Store Eticovo prefilled syringe in the original carton to protect from light or physical damage.
- If needed, you may store your Eticovo prefilled syringe at room temperature between 73°F to 81°F (23°C to 27°C), 1 time, for up to 2 weeks (14 days).
  - Once Eticovo prefilled syringe has reached room temperature, do not put it back in the refrigerator.
- Throw away Eticovo prefilled syringe that has been stored at room temperature after 2 weeks (14 days).
- **Do not** store Eticovo prefilled syringe in extreme heat or cold. For example, avoid storing Eticovo prefilled syringe in your vehicle's glove box or trunk.
- **Do not freeze.**
- **Do not shake.**
- **Keep Eticovo prefilled syringe and all medicines out of the reach of children.**

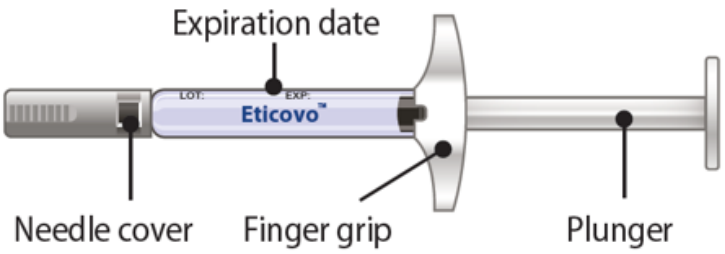
If you have any questions about storage, contact your healthcare provider or call 1-877-888-4231 for further instructions.

**What you will need for each injection.**

**Included in the carton:**

- **1 Eticovo single-dose prefilled syringe (see Figure A).**
  **Each carton contains 4 Eticovo single-dose prefilled syringes.**

**Figure A**



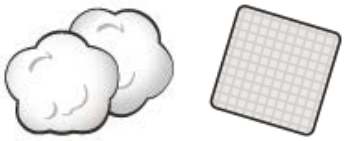

**Not included in the carton (see Figure B):**

**Figure B**

- **1 alcohol swab**


- **Sharps disposal container**

- **1 cotton ball or gauze**



- **1 adhesive bandage**

See **Step 4: "Disposing of Supplies"** at the end of this Instructions for Use.

**Step 1: Setting up for an Injection**

1. Select a clean, well-lit, flat work surface, such as a table.

2. Take the Eticovo carton containing the prefilled syringes out of the refrigerator and place it on your flat work surface. Remove one prefilled syringe and place it on your work surface. Carefully lift the prefilled syringe straight up out of the box. **Do not shake** the prefilled syringe of Eticovo. Place the carton containing any remaining prefilled syringes back into the refrigerator between 36°F to 46°F (2°C to 8°C).

3. Check the expiration date (EXP:) on the prefilled syringe. **Do not** use the prefilled syringe if the expiration date has passed. **Do not** use the prefilled syringe if it has been dropped onto a hard surface. Parts of the prefilled syringe may be broken. **Do not** use the prefilled syringe if the needle cover is missing or not securely attached. Contact your pharmacist for assistance if the expiration date has passed, if the prefilled syringe has been dropped on a hard surface, or if the needle cover is missing or not securely attached.

4. **Leave Eticovo prefilled syringe at room temperature for at least 30 minutes before injecting.** This is important to make the medicine easier and more comfortable to inject. **Do not** remove the needle cover while allowing it to reach room temperature. **Do not warm Eticovo in any other way** (for example, **do not** warm it in a microwave or in hot water.)

5. Gather all the additional supplies you will need for your injection. These include an alcohol swab, a cotton ball or gauze, and a sharps disposal container (see **Step 4: "Disposing of Supplies"**).

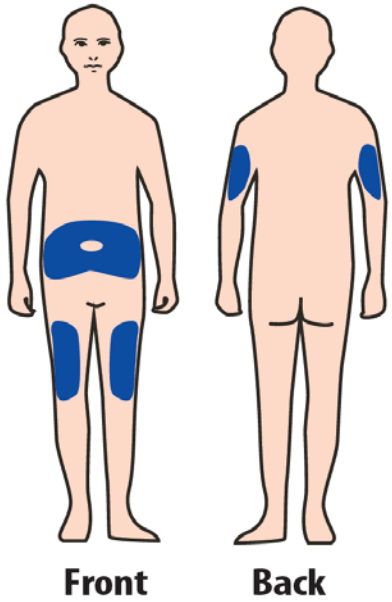
6. Wash your hand with soap and warm water.

7. **Look at the medicine in the prefilled syringe.** The medicine should be clear or almost clear, colorless to pale yellow, and may contain small white or almost clear particles. **Do not** use the solution if it is discolored, cloudy, or if it contains particles that are not small, white or almost clear.

**Step 2: Choosing and Preparing an Injection Site**

1. The recommended injection sites for Eticovo are **(see Figure C):**
    - front of the middle thigh
    - stomach-area (abdomen). If you are injecting into the abdomen, choose a site that is at least 2 inches (5 cm) away from the belly button.
    - back of the upper arm. Use the back of the upper arm only if someone else is giving you the injection.

**Figure C**




2. **Rotate the site for each injection. Do not** inject into areas that are red, hard, bruised, or tender. **Do not** inject into scars or stretch marks.

3. If you have psoriasis, do not inject into any raised, thick, red, or scaly skin patches, or lesions.

4. To prepare the area of skin where Eticovo is to be injected, wipe the skin at the injection site with an alcohol swab. **Do not touch this area again before giving the injection.**

**Step 3: Injecting Eticovo Using Prefilled Syringe**

**Do not** remove the needle cover from the prefilled syringe until you are ready to inject.

1. Pick up the prefilled syringe from your flat work surface. Pull the needle cover straight off (see **Figure D**) and throw it away (dispose of) in a sharps disposal container.
   **Do not** touch the plunger while removing the needle cover and **do not** twist or bend the needle cover while removing it, as this may damage the needle.

   When you remove the needle cover, there may be a drop of liquid at the end of the needle. This is normal.
   **Do not** touch the needle or allow it to touch any surface.
   **Never recap the needle.**
   **Do not** touch or bump the plunger. Doing so could cause the liquid to leak out.

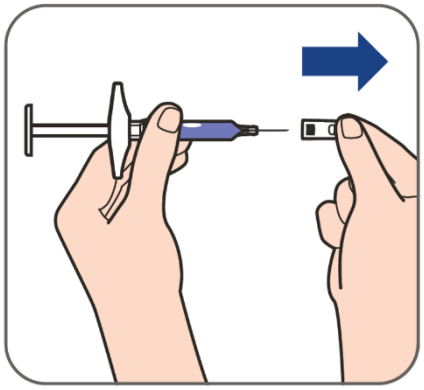


**Figure D**

2. Hold the prefilled syringe at a 45 degree angle to the skin (see **Figure E**).
   With your other hand, gently pinch a fold of skin at the cleaned injection site. **With a quick, dart-like motion, insert the needle fully into the skin.**

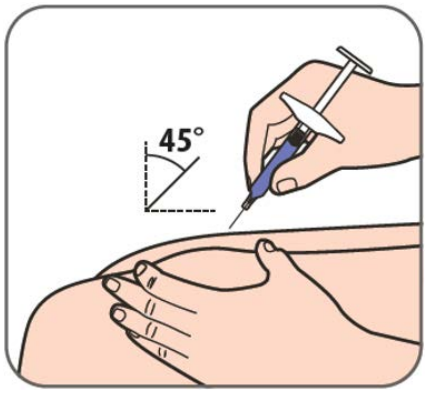



**Figure E**

3. Let go of the skin that you are pinching after the needle is completely inserted. With your free hand, hold the syringe near its base to stabilize it. Slowly **push down the plunger to inject all of the Eticovo solution.**
   (see **Figure F**).

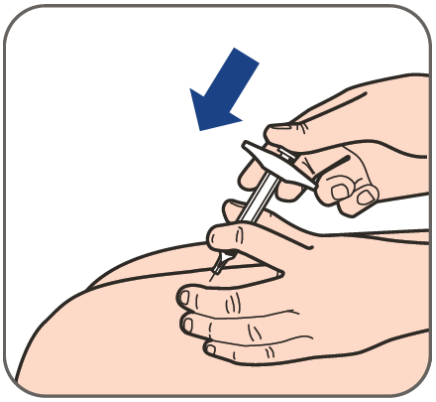


**Figure F**

4. **When the syringe is empty, pull the needle out of the skin, being careful to keep it at the same angle as inserted** (see **Figure G**)**.** If there is bleeding at the injection site, press a gauze pad or cotton ball over the injection site for 10 seconds. **Do not** rub the injection site. If needed, cover the injection site with an adhesive bandage.

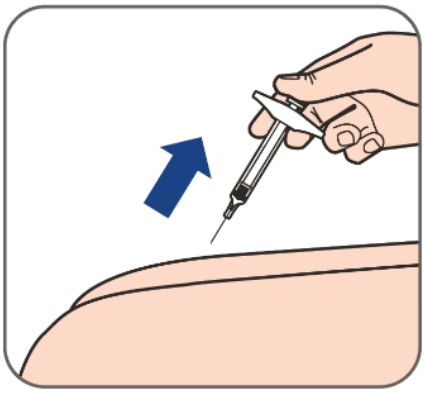
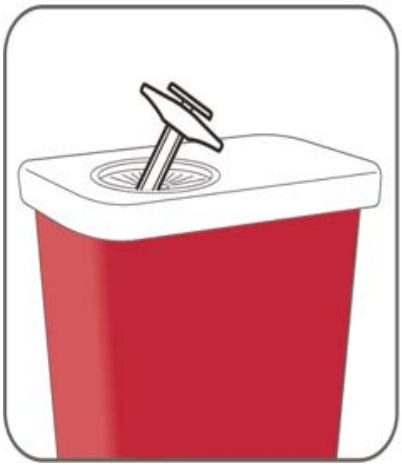


**Figure G**

**Step 4: Disposing of Supplies**

The syringe should **never** be reused. **Never** recap the needle. Recapping could lead to a needle stick injury.

- Put the used prefilled syringe in a FDA-cleared sharps disposal container right away after use. **Do not** throw away (dispose of) prefilled syringe in your household trash.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  - upright and stable during use,
  - leak-resistant, and
  - properly labeled to warn of hazardous waste inside the container.



- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used syringes and needles. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go the FDA's website at: http://www.fda.gov/safesharpsdisposal
- **Do not** reuse the Eticovo prefilled syringe.
- **Do not** recycle the syringe or sharps disposal container or throw them into household trash.

**Important: Always keep the sharps disposal container out of the reach of children.**

This Instructions for Use has been approved by the U.S Food and Administration.

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