ETANERCEPT

ETVEZA 25

℞

25mg Powder for Solution for Injection (SC)
Tumor Necrosis Factor alpha Inhibitor

Formulation-
Each vial contains:
Etanercept 25mg

Drug Description-
Etanercept the INN for Recombinant Human Tumor Necrosis Factor-α Receptor II: IgG Fc (rhTNFR: Fc) Fusion Protein for Injection is a dimeric fusion protein consisting of the extracellular ligand-binding portion of the human 75 kilodalton (p75) tumor necrosis factor receptor (TNFR) linked to the Fc portion of human IgG1. The Fc component of etanercept contains the CH2 domain, the CH3 domain and hinge region, but not the CH1 domain of IgG1. Etanercept is produced by recombinant DNA technology in a Chinese hamster ovary (CHO) mammalian cell expression system.

The Molecular Weight of the monomer is 63-77kDa and Dimer is 450kDa

The Sequence of 15 Amino Acids at N-terminal is Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly

Available Form- Etanercept (Etveza 25) is available as a white lyophilized powder and is a colorless or slightly yellow and transparent liquid when dissolved in water.

Inactive Ingredients- Mannitol, Sucrose, Tromethamine

Pharmacodynamics:
Pharmacotherapeutic group: Immunosuppressants, Tumor Necrosis Factor alpha (TNF-α) inhibitors.
Tumor necrosis factor (TNF) is a dominant cytokine in the inflammatory process of rheumatoid arthritis. Elevated levels of TNF are also found in the synovium and psoriatic plaques of patients with psoriatic arthritis and in serum and synovial tissue of patients with ankylosing spondylitis. In plaque psoriasis, infiltration by inflammatory cells, including T-cells, leads to increased TNF levels in psoriatic lesions compared with levels in uninvolved skin. Etanercept is a competitive inhibitor of TNF binding to its cell surface receptors, and thereby inhibits the biological activity of TNF. TNF and lymphotoxin are pro-inflammatory cytokines that bind to two distinct cell surface receptors: the 55-kilodalton (p55) and 75-kilodalton (p75) tumour necrosis factor receptors (TNFRs). Both TNFRs exist naturally in membrane-bound and soluble forms. Soluble TNFRs are thought to regulate TNF biological activity.
TNF and lymphotoxin exist predominantly as homotrimers, with their biological activity dependent on cross-linking of cell surface TNFRs. Dimeric soluble receptors, such as etanercept, possess a higher affinity for TNF than monomeric receptors and are considerably more potent competitive inhibitors of TNF binding to its cellular receptors. In addition, use of an immunoglobulin Fc region as a fusion element in the construction of a dimeric receptor imparts a longer serum half-life.

Mechanism of action
Much of the joint pathology in rheumatoid arthritis and ankylosing spondylitis and skin pathology in plaque psoriasis is mediated by pro-inflammatory molecules that are linked in a network controlled by TNF. The mechanism of action of etanercept is thought to be its competitive inhibition of TNF binding to cell surface TNFR, preventing TNF-mediated cellular responses by rendering TNF biologically inactive. Etanercept may also modulate biologic responses controlled by additional downstream molecules (e.g., cytokines, adhesion molecules, or proteinases) that are induced or regulated by TNF.

Pharmacokinetics
The clinical study results indicated rh TNFR: Fc was absorbed slowly at injection site after subcutaneous injection. The peak blood concentration achieved at 48 hours after single administration, the absolute bioavailability was 76%. After administered twice weekly, the blood concentration at steady state was two times of the peak concentration of single dose.
11 active RA patients were injected with Yisaipu 25mg subcutaneously twice a week for consecutive 6 weeks, the time to steady state for rhTNFR:Fc was 480±20h, Cmax(ss) was 3.0±0.2μg/ml, Cmin(ss) was 2.6±0.2μg/ml, the mean Css was 2.8±0.3μg/ml, the fluctuation index (FI) was 12.8±3.3%. After the last administration of rhTNFR:Fc, T1/2was 74±4h, Tmax was 53±6h and CL was 102.8 ± 10.4ml/h.
No significant difference in blood concentration was observed among healthy persons, patients with acute renal failure and patients with abnormal liver functions, therefore, the dose does not need to be adjusted for the patients with renal function impairment. The influence of MTX on the pharmacokinetics of rhTNFR:Fc was not observed in the above studies.

INDICATION
Rheumatoid arthritis
Etanercept in combination with methotrexate is indicated for the treatment of moderate to severe active rheumatoid arthritis in adults when the response to disease-modifying antirheumatic drugs, including methotrexate (unless contraindicated), has been inadequate.
Etanercept can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate.
Etanercept is also indicated in the treatment of severe, active and progressive rheumatoid arthritis in adults not previously treated with methotrexate.
Etanercept, alone or in combination with methotrexate, has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function.

Axial spondyloarthritis
Ankylosing spondylitis (AS)
Treatment of adults with severe active ankylosing spondylitis who have had an inadequate response to conventional therapy.

Plaque psoriasis
Treatment of adults with moderate to severe plaque psoriasis who failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapy, including ciclosporin, methotrexate or psoralen and ultraviolet-A light (PUVA).

DOSAGE AND ADMINISTRATION
Posology and method of administration
Etanercept treatment should be initiated and supervised by specialist physicians experienced in the diagnosis and treatment of rheumatoid arthritis, ankylosing spondylitis, plaque psoriasis. Patients treated with Etanercept should be given the Patient Alert Card.

Posology
Rheumatoid arthritis
25 mg Etanercept administered twice weekly is the recommended dose. Alternatively, 50 mg administered once weekly has been shown to be safe and effective.

Ankylosing spondylitis
The recommended dose is 25 mg Etanercept administered twice weekly, or 50 mg administered once weekly.
Available data suggest that a clinical response is usually achieved within 12 weeks of treatment. Continued therapy should be carefully reconsidered in a patient not responding within this time period.

Plaque psoriasis
The recommended dose of Etanercept is 25 mg administered twice weekly or 50 mg administered once weekly. Alternatively, 50 mg given twice weekly may be used for up to 12 weeks followed, if necessary, by a dose of 25 mg twice weekly or 50 mg once weekly. Treatment with Etanercept should continue until remission is achieved, for up to 24 weeks. Continuous therapy beyond 24 weeks may be appropriate for some adult patients. Treatment should be discontinued in patients who show no response after 12 weeks. If re-treatment with Etanercept is indicated, the same guidance on treatment duration should be followed. The dose should be 25 mg twice weekly or 50 mg once weekly.

SPECIAL POPULATIONS
Renal and hepatic impairment
No dose adjustment is required.

Elderly
No dose adjustment is required. Posology and administration are the same as for adults 18-64 years of age.

METHOD OF ADMINISTRATION
Etanercept is administered by subcutaneous injection. The injection sites could be thighs, abdomen and upper arms.
Etanercept is reconstituted with 1ml WFI before use. The solution should be colorless or light yellow, clear and transparent. The reconstituted solution could be stored at 2-8°C in confined environment for 72 hours.

CONTRAINDICATION
- Hypersensitivity to the active substance or to any of the excipients listed
- Sepsis or risk of sepsis.
- Treatment with Etanercept should not be initiated in patients with active infections, including chronic or localised infections

WARNING AND PRECAUTION
Infections
Patients should be evaluated for infections before, during, and after treatment with etanercept, taking into consideration that the mean elimination half-life of etanercept is approximately 70 hours (range 7 to 300 hours).
Serious infections, sepsis, tuberculosis, and opportunistic infections, including invasive fungal infections, listeriosis and legionellosis, have been reported with the use of etanercept. These infections were due to bacteria, mycobacteria, fungi, viruses and parasites (including protozoa). In some cases, particular fungal and other opportunistic infections have not been recognised, resulting in delay of appropriate treatment and sometimes death. In evaluating patients for infections, the patient's risk for relevant opportunistic infections (e.g., exposure to endemic mycoses) should be considered.
Patients who develop a new infection while undergoing treatment with etanercept should be monitored closely. Administration of etanercept should be discontinued if a patient develops a serious infection. The safety and efficacy of etanercept in patients with chronic infections have not been evaluated. Physicians should exercise caution when considering the use of etanercept in patients with a history of recurring or chronic infections or with underlying conditions that may predispose patients to infections, such as advanced or poorly controlled diabetes.

Tuberculosis
Cases of active tuberculosis, including miliary tuberculosis and tuberculosis with extra-pulmonary location, have been reported in patients treated with etanercept.
Before starting treatment with etanercept, all patients must be evaluated for both active and inactive ('latent') tuberculosis. This evaluation should include a detailed medical history with personal history of tuberculosis or possible previous contact with tuberculosis and previous and/or current immunosuppressive therapy. Appropriate screening tests, i.e., tuberculin skin test and chest X-ray, should be performed in all patients (local recommendations may apply). It is recommended that the conduct of these tests should be recorded in the patient's alert card. Prescribers are reminded of the risk of false negative tuberculin skin test results, especially in patients who are severely ill or immunocompromised.
If active tuberculosis is diagnosed, etanercept therapy must not be initiated. If inactive ('latent') tuberculosis is diagnosed, treatment for latent tuberculosis must be started with anti-tuberculosis therapy before the initiation of etanercept, and in accordance with local recommendations. In this situation, the benefit/risk balance of etanercept therapy should be very carefully considered.
All patients should be informed to seek medical advice if signs/symptoms suggestive of tuberculosis (e.g., persistent cough, wasting/weight loss, low-grade fever) appear during or after etanercept treatment.

Hepatitis B reactivation
Reactivation of hepatitis B in patients who were previously infected with the hepatitis B virus (HBV) and had received concomitant TNF-antagonists, including Etanercept, has been reported. This includes reports of reactivation of hepatitis B in patients who were anti-HBc positive but HBsAg negative. Patients should be tested for HBV infection before initiating treatment with etanercept. For patients who test positive for HBV infection, consultation with a physician with expertise in the treatment of hepatitis B is recommended. Caution should be exercised when administering etanercept in patients previously infected with HBV. These patients should be monitored for signs and symptoms of active HBV infection throughout therapy and for several weeks following termination of therapy. Adequate data from treating patients infected with HBV with anti-viral therapy in conjunction with TNF-antagonist therapy are not available. In patients who develop HBV infection, etanercept should be stopped and effective anti-viral therapy with appropriate supportive treatment should be initiated.

Worsening of hepatitis C
There have been reports of worsening of hepatitis C in patients receiving etanercept. Etanercept should be used with caution in patients with a history of hepatitis C.

Concurrent treatment with anakinra
Concurrent administration of etanercept and anakinra has been associated with an increased risk of serious infections and neutropenia compared to etanercept alone. This combination has not demonstrated increased clinical benefit. Thus, the combined use of etanercept and anakinra is not recommended.

Concurrent treatment with abatacept
In clinical studies, concurrent administration of abatacept and etanercept resulted in increased incidences of serious adverse events. This combination has not demonstrated increased clinical benefit; such use is not recommended.

Allergic reactions
Allergic reactions associated with etanercept administration have been reported commonly. Allergic reactions have included angioedema and urticaria; serious reactions have occurred. If any serious allergic or anaphylactic reaction occurs, etanercept therapy should be discontinued immediately and appropriate therapy initiated.

Immunosuppression
The possibility exists for TNF-antagonists, including etanercept, to affect host defences against infections and malignancies since TNF mediates inflammation and modulates cellular immune responses.
Two juvenile idiopathic arthritis patients developed varicella infection and signs and symptoms of aseptic meningitis, which resolved without sequelae. Patients with a significant exposure to varicella virus should temporarily discontinue etanercept therapy and be considered for prophylactic treatment with Varicella Zoster Immune Globulin.
The safety and efficacy of etanercept in patients with immunosuppression have not been evaluated.

Malignancies and lymphoproliferative disorders
Solid and haematopoietic malignancies (excluding skin cancers)
Reports of various malignancies (including breast and lung carcinoma and lymphoma) have been received in the postmarketing period.
In the controlled portions of clinical trials of TNF-antagonists, more cases of lymphoma have been observed among patients receiving a TNF-antagonist compared with control patients. However, the occurrence was rare, and the follow-up period of placebo patients was shorter than for patients receiving TNF-antagonist therapy. In the postmarketing setting, cases of leukaemia have been reported in patients treated with TNF-antagonists. There is an increased background risk for lymphoma and leukaemia in rheumatoid arthritis patients with long-standing, highly active, inflammatory disease, which complicates risk estimation.
Based on current knowledge, a possible risk for the development of lymphomas, leukaemia or other haematopoietic or solid malignancies in patients treated with a TNF-antagonist cannot be excluded. Caution should be exercised when considering TNF-antagonist therapy for patients with a history of malignancy or when considering continuing treatment in patients who develop a malignancy.
Malignancies, some fatal, have been reported among children, adolescents and young adults (up to 22 years of age) treated with TNF-antagonists (initiation of therapy ≤18 years of age), including etanercept in the postmarketing setting. Approximately half the cases were lymphomas. The other cases represented a variety of different malignancies and included rare malignancies typically associated with immunosuppression. A risk for the development of malignancies in children and adolescents treated with TNF-antagonists cannot be excluded.

Skin cancers
Melanoma and non-melanoma skin cancer (NMSC) have been reported in patients treated with TNF-antagonists, including etanercept. Postmarketing cases of Merkel cell carcinoma have been reported very infrequently in patients treated with Etanercept. Periodic skin examination is recommended for all patients, particularly those with risk factors for skin cancer.
Combining the results of controlled clinical trials, more cases of NMSC were observed in patients receiving etanercept compared with control patients, particularly in patients with psoriasis.

Vaccinations
Live vaccines should not be given concurrently with etanercept.

Autoantibody formation
Treatment with etanercept may result in the formation of autoimmune antibodies.

Haematologic reactions
Rare cases of pancytopenia and very rare cases of aplastic anaemia, some with fatal outcome, have been reported in patients treated with etanercept. Caution should be exercised in patients being treated with Etanercept who have a previous history of blood dyscrasias. All patients and parents/caregivers should be advised that if the patient develops signs and symptoms suggestive of blood dyscrasias or infections (e.g., persistent fever, sore throat, bruising, bleeding, paleness) whilst on etanercept, they should seek immediate medical advice. Such patients should be investigated urgently, including full blood count; if blood dyscrasias are confirmed, etanercept should be discontinued.

Neurological disorders
There have been rare reports of CNS demyelinating disorders in patients treated with etanercept. Additionally, there have been very rare reports of peripheral demyelinating polyneuropathies (including Guillain-Barré syndrome, chronic inflammatory demyelinating polyneuropathy, demyelinating polyneuropathy, and multifocal motor neuropathy). Although no clinical trials have been performed evaluating etanercept therapy in patients with multiple sclerosis, clinical trials of other TNF antagonists in patients with multiple sclerosis have shown increases in disease activity. A careful risk/benefit evaluation, including a neurologic assessment, is recommended when prescribing etanercept to patients with pre-existing or recent onset of demyelinating disease, or to those who are considered to have an increased risk of developing demyelinating disease.

Combination therapy
In a controlled clinical trial of two years duration in rheumatoid arthritis patients, the combination of Etanercept and methotrexate did not result in unexpected safety findings, and the safety profile of etanercept when given in combination with methotrexate was similar to the profiles reported in studies of etanercept and methotrexate alone. Long-term studies to assess the safety of the combination are ongoing. The long-term safety of etanercept in combination with other disease-modifying antirheumatic drugs (DMARD) has not been established.
The use of etanercept in combination with other systemic therapies or phototherapy for the treatment of psoriasis has not been studied.

Renal and hepatic impairment
Based on pharmacokinetic data, no dose adjustment is needed in patients with renal or hepatic impairment; clinical experience in such patients is limited.

Congestive heart failure
Physicians should use caution when using etanercept in patients who have congestive heart failure (CHF). There have been postmarketing reports of worsening of CHF, with and without identifiable precipitating factors, in patients taking etanercept. There have also been rare (< 0.1%) reports of new onset CHF, including CHF in patients without known pre-existing cardiovascular disease. Some of these patients have been under 50 years of age.

Alcoholic hepatitis
In a phase II randomised placebo-controlled study of 48 hospitalised patients treated with etanercept or placebo for moderate to severe alcoholic hepatitis, Etanercept was not efficacious, and the mortality rate in patients treated with Etanercept was significantly higher after 6 months. Consequently, etanercept should not be used in patients for the treatment of alcoholic hepatitis. Physicians should use caution when using etanercept in patients who also have moderate to severe alcoholic hepatitis.

Wegener's granulomatosis
Etanercept is not recommended for the treatment of Wegener's granulomatosis.

Hypoglycaemia in patients treated for diabetes
There have been reports of hypoglycemia following initiation of etanercept in patients receiving medication for diabetes, necessitating a reduction in anti-diabetic medication in some of these patients.

Special populations
Elderly
In the Phase 3 studies in rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis, no overall differences in adverse events, serious adverse events, and serious infections in patients age 65 or older who received etanercept were observed compared with younger patients. However, caution should be exercised when treating the elderly and particular attention paid with respect to occurrence of infections.

Pediatric population
Vaccinations
It is recommended that pediatric patients, if possible, be brought up to date with all immunisations in agreement with current immunisation guidelines prior to initiating etanercept therapy .
Inflammatory bowel disease (IBD) and uveitis in patients with juvenile idiopathic arthritis (JIA). There have been reports of IBD and uveitis in JIA patients being treated with etanercept

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION
Concurrent treatment with anakinra
Adult patients treated with etanercept and anakinra were observed to have a higher rate of serious infection when compared with patients treated with either etanercept or anakinra alone (historical data).
In addition, in a double-blind, placebo-controlled trial in adult patients receiving background methotrexate, patients treated with Etanercept and anakinra were observed to have a higher rate of serious infections (7%) and neutropenia than patients treated with etanercept. The combination etanercept and anakinra has not demonstrated increased clinical benefit, and is therefore not recommended.

Concurrent treatment with abatacept
In clinical studies, concurrent administration of abatacept and etanercept resulted in increased incidences of serious adverse events. This combination has not demonstrated increased clinical benefit; such use is not recommended.

Concurrent treatment with sulfasalazine
In a clinical study of adult patients who were receiving established doses of sulfasalazine, to which etanercept was added, patients in the combination group experienced a statistically significant decrease in mean white blood cell counts in comparison to groups treated with etanercept or sulfasalazine alone. The clinical significance of this interaction is unknown. Physicians should use caution when considering combination therapy with sulfasalazine.

Non-interactions
In clinical trials, no interactions have been observed when etanercept was administered with glucocorticoids, salicylates (except sulfasalazine), nonsteroidal anti-inflammatory drugs (NSAIDs), analgesics, or methotrexate.
No clinically significant pharmacokinetic drug-drug interactions were observed in studies with methotrexate, digoxin or warfarin.

Fertility, pregnancy and lactation
Women of childbearing potential
Women of childbearing potential should be advised to use appropriate contraception to avoid becoming pregnant during etanercept therapy and for three weeks after discontinuation of therapy.

Pregnancy
Developmental toxicity studies performed in rats and rabbits have revealed no evidence of harm to the foetus or neonatal rat due to etanercept. A higher rate of major birth defects was observed in an observational study comparing pregnancies exposed to etanercept during the first trimester, with pregnancies not exposed to etanercept or other TNF-antagonists (adjusted odds ratio 2.4, 95% CI: 1.0 - 5.5). The types of major birth defects were consistent with those most commonly reported in the general population and no particular pattern of abnormalities was identified. No change in the rate of spontaneous abortion, stillbirth, or minor malformations was observed. Etanercept is not recommended during pregnancy.
Etanercept crosses the placenta and has been detected in the serum of infants born to female patients treated with etanercept during pregnancy. The clinical impact of this is unknown, however, infants may be at increased risk of infection. Administration of live vaccines to infants for 16 weeks after the mother's last dose of etanercept is generally not recommended.

Breast-feeding
Etanercept has been reported to be excreted in human milk following subcutaneous administration. In lactating rats following subcutaneous administration, etanercept was excreted in the milk and detected in the serum of pups. Because immunoglobulins, in common with many medicinal products, can be excreted in human milk, a decision must be made whether to discontinue breast-feeding or to discontinue etanercept therapy, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility
Preclinical data about peri- and postnatal toxicity of etanercept and of effects of etanercept on fertility and general reproductive performance are not available.

Effects on ability to drive and use machines
No studies on the effects on the ability to drive and use machines have been performed.

Undesirable effects
Summary of the safety profile
The most commonly reported adverse reactions are injection site reactions (such as pain, swelling, itching, reddening and bleeding at the puncture site), infections (such as upper respiratory infections, bronchitis, bladder infections and skin infections), allergic reactions, development of autoantibodies, itching, and fever.
Serious adverse reactions have also been reported for Etanercept. TNF-antagonists, such as Etanercept, affect the immune system and their use may affect the body's defences against infection and cancer. Serious infections affect fewer than 1 in 100 patients treated with Etanercept. Reports have included fatal and life-threatening infections and sepsis. Various malignancies have also been reported with use of Etanercept, including cancers of the breast, lung, skin and lymph glands (lymphoma).
Serious haematological, neurological and autoimmune reactions have also been reported. These include rare reports of pancytopenia and very rare reports of aplastic anaemia. Central and peripheral demyelinating events have been seen rarely and very rarely, respectively, with Etanercept use. There have been rare reports of lupus, lupus-related conditions, and vasculitis.

Tabulated list of adverse reactions
The following list of adverse reactions is based on experience from clinical trials in adults and on postmarketing experience.
Within the organ system classes, adverse reactions are listed under headings of frequency (number of patients expected to experience the reaction), using the following categories: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data).

INFECTIONS AND INFESTATIONS:
Very common: Infections (including upper respiratory tract infections, bronchitis, cystitis, skin infections)
Uncommon: Serious infections (including pneumonia, cellulitis, septic arthritis, sepsis and parasitic infection)
Rare: Tuberculosis, opportunistic infections (including invasive fungal, protozoal, bacterial, atypical mycobacterial, viral infections, and Legionella)
Not known: Listeria, hepatitis B reactivation

Neoplasms benign, malignant and unspecified (including cysts and polyps):
Uncommon: Non-melanoma skin cancers
Rare: Lymphoma, melanoma
Not known: Leukaemia, Merkel cell carcinoma

Blood and lymphatic system disorders:
Uncommon: Thrombocytopenia
Rare: Anaemia, leukopenia, neutropenia, pancytopenia
Very rare: Aplastic anaemia

Immune system disorders:
Common: Allergic reactions (see Skin and subcutaneous tissue disorders), autoantibody formation*
Uncommon: Systemic vasculitis (including anti-neutrophilic cytoplasmic antibody positive vasculitis)
Rare: Serious allergic/anaphylactic reactions (including angioedema, bronchospasm), sarcoidosis
Not known: Macrophage activation syndrome, worsening of symptoms of dermatomyositis

Nervous system disorders:
Rare: Seizures
CNS demyelinating events suggestive of multiple sclerosis or localised demyelinating conditions, such as optic neuritis and transverse myelitis
Very rare: Peripheral demyelinating events, including Guillain-Barré syndrome, chronic inflammatory demyelinating polyneuropathy, demyelinating polyneuropathy, and multifocal motor neuropathy

Eye disorders:
Uncommon: Uveitis, scleritis

Cardiac disorders:
Rare: Congestive heart failure

Respiratory, thoracic and mediastinal disorders:
Uncommon: Interstitial lung disease (including pneumonitis and pulmonary fibrosis)

Hepatobiliary disorders:
Rare: Elevated liver enzymes, autoimmune hepatitis

Skin and subcutaneous tissue disorders:
Common: Pruritus
Uncommon: Angioedema, urticaria, rash, psoriasiform rash, psoriasis (including new onset or worsening and pustular, primarily palms and soles)
Rare: Cutaneous vasculitis (including leukocytoclastic vasculitis), Stevens-Johnson syndrome, erythema multiforme
Very rare: Toxic epidermal necrolysis

Musculoskeletal and connective tissue disorders:
Rare: Subacute cutaneous lupus erythematosus, discoid lupus erythematosus, lupus-like syndrome

General disorders and administration site conditions:
Very common: Injection site reactions (including bleeding, bruising, erythema, itching, pain, swelling)
Common: Fever

Overdose
No dose-limiting toxicities were observed during clinical trials of rheumatoid arthritis patients. The highest dose level evaluated has been an intravenous loading dose of 32 mg/m2 followed by subcutaneous doses of 16 mg/m2 administered twice weekly. One rheumatoid arthritis patient mistakenly self-administered 62 mg Etanercept subcutaneously twice weekly for 3 weeks without experiencing undesirable effects. There is no known antidote to Etanercept.

Storage : Keep out of reach of children. Protect from light and moisture. Store between 2°-8°C. Do not freeze.
Single use only; Discard any remaining portion

Availability :
USP Type 1 Clear Glass Vial with colored flip-off seal x 2mL (Box of 1's)

Caution :
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reaction, report to the FDA: **www.fda.gov.ph**

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