Dear Valued Customer:

We are pleased to announce that ENBREL will now be available via wholesaler distribution. Effective February 4, 2008, ENBREL will transition from the drop-ship order process to standard wholesaler distribution.

This change allows customers to follow the same ordering process used for all items inventoried by their wholesaler.

ENBREL is the only biologic to offer these convenient administration options:

- The 25 mg ENBREL multiple-use vial - NDC 58406-0425-34
- The 25 mg/0.5 mL prefilled syringe - NDC 58406-0455-04
- The 50 mg/mL prefilled syringe - NDC 58406-0435-04
- The 50 mg/mL SureClick™ autoinjector - NDC 58406-0445-04

For more information, or if you have any questions about ENBREL, please call 1-888-4ENBREL (1-888-436-2735).

Please see enclosed Important Treatment Considerations.

Sincerely,

Ned F. Endler
Director, Trade Development
Amgen

AMGEN® Wyeth®

Indications:

Enbrel® (etanercept) is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis. ENBREL can be initiated in combination with methotrexate (MTX) or used alone.

ENBREL is indicated for reducing signs and symptoms of moderately to severely active polyarticular-course juvenile rheumatoid arthritis in patients who have had an inadequate response to one or more DMARDs.

ENBREL is indicated for reducing signs and symptoms, inhibiting the progression of structural damage of active arthritis, and improving physical function in patients with psoriatic arthritis. ENBREL can be used in combination with MTX in patients who do not respond adequately to MTX alone.

ENBREL is indicated for reducing signs and symptoms in patients with active ankylosing spondylitis.

ENBREL is indicated for the treatment of adult patients (18 years or older) with chronic moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

Important Treatment Considerations

IN POSTMARKETING USE, THE FOLLOWING SERIOUS ADVERSE EVENTS HAVE BEEN REPORTED.

- **SERIOUS INFECTIONS AND SEPSIS, INCLUDING FATALITIES**
  - **— MANY OF THESE INFECTIONS OCCURRED IN PATIENTS PREDISPOSED TO INFECTION BECAUSE OF CONCOMITANT IMMUNOSUPPRESSIVE THERAPY AND/OR THEIR UNDERLYING DISEASE**
  - **— RARE CASES OF TUBERCULOSIS HAVE BEEN OBSERVED**
  - **— DISCONTINUE ENBREL IN PATIENTS WITH SERIOUS INFECTIONS OR SEPSIS**
  - **— DO NOT START ENBREL IN THE PRESENCE OF SEPSIS, INFECTION (INCLUDING CHRONIC OR LOCALIZED), OR ALLERGY TO ENBREL OR ITS COMPONENTS**
  - **— USE CAUTION IN PATIENTS PREDISPOSED TO INFECTION, SUCH AS THOSE WITH ADVANCED OR POORLY CONTROLLED DIABETES**
- Cases of CNS demyelinating disorders (some presenting with mental status changes and some associated with permanent disability), transverse myelitis, optic neuritis, multiple sclerosis, and new onset or exacerbation of seizure disorders
  - — The causal relationship to ENBREL therapy is unclear
  - — Exercise caution when considering ENBREL for patients with these disorders
- Rare cases of pancytopenia, including aplastic anemia, some fatal
  - — The causal relationship to ENBREL therapy is unclear
  - — Exercise caution in patients who have a previous history of significant hematologic abnormalities
  - — Advise patients to seek immediate medical attention if they develop signs or symptoms of blood dyscrasias or infection
  - — Consider discontinuing ENBREL if significant hematologic abnormalities are confirmed
- In clinical trials of all TNF inhibitors, a higher rate of lymphoma was seen compared to the general population; however, the risk of lymphoma may be up to several-fold higher in RA and psoriasis patients
  - — The role of TNF inhibitors in the development of lymphoma is unknown
- In clinical trials, the incidence of malignancies other than lymphoma has not increased with exposure to ENBREL and is similar to the projected background rate
- Reactivation of hepatitis B virus (HBV) in chronic carriers
  - — The majority of these reports occurred in patients on concomitant immunosuppressive agents which may also contribute to HBV
  - — Prescribers should exercise caution in prescribing TNF blockers for patients identified as carriers of hepatitis B virus
- In phase 3 psoriasis clinical trials, the most common adverse events in the 50 mg twice weekly and 50 mg weekly (25 mg BIW) arms, respectively, were injection site reaction (16%, 15%), headache (9%, 13%), and upper respiratory infection (10%, 16%)
- In RA clinical trials, the most common adverse events were injection site reaction (37%), infection (64%), and headache (24%)
- Adverse events in the psoriatic arthritis and ankylosing spondylitis trials were similar to those reported in RA clinical trials
- In a JRA study (n = 69), infection (62%), headache (19%), abdominal pain (19%), vomiting (13%), and nausea (9%) occurred more frequently than in adults. The types of infections reported in JRA patients were generally mild and consistent with those commonly seen in outpatient pediatric populations
- Serious adverse reactions reported rarely in a JRA study were varicella (3%), gastroenteritis (3%), depression/personality disorder (1%), cutaneous ulcer (1%), esophagitis/gastritis (1%), group A streptococcal septic shock (1%), type I diabetes mellitus (1%), and soft tissue and postoperative wound infection (1%)

Please see full Prescribing Information on this link: http//www.enbrel.com/pdf/enbrel_pi.pdf

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