MORE THAN
WHAT YOU SEE

The experience keeps getting better.

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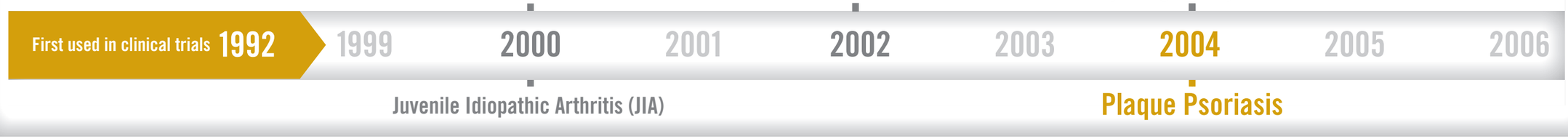
SEE A WORLD OF DIFFERENCE

From clinical trials to the real world—14 years of continuous clinical experience



FIRST CHOICE FOR EXPERIENCE

- ENBREL is the #1 biologic prescribed worldwide[2]
- Over 63,000 psoriatic patients treated globally[2]
- More than 440,000 patients treated with ENBREL worldwide[2]
- The British Association of Dermatologists identified ENBREL as the first-choice TNF therapy for the treatment of **psoriasis** and **psoriatic arthritis**[3]

FIRST CHOICE FOR ESTABLISHED SAFETY PROFILE

Established in years of clinical study

- In psoriasis trials of up to 2.5 years, adverse events were similar to placebo[4,5]
- During **96 weeks** of high-dose ENBREL 50 mg twice weekly and **no new safety signals** were observed[1,6]
- Patients have received ENBREL for up to **8 years** in rheumatoid arthritis trials[7]
- Safety and tolerability established in patients from **4 to 87 years** of age (in JIA and RA[8])

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LOOK AHEAD
WITH CONFIDENCE

- PASI 75 response **sustained** through 6 months—even after dose reduction[1,11]
- Response was **more rapid** in a group initially treated with 50 mg twice weekly for 12 weeks vs 25 mg once weekly[1,11]
- **More patients** in this group achieved PASI 75, even after the dose was reduced to 25 mg twice weekly at week 12[1,11]
- PASI 75 at week 12:

ENBREL 50 mg twice weekly 49%

ENBREL 25 mg twice weekly 34%

Placebo 3%

($P<0.0001$ for each ENBREL group vs placebo)[1,11]

In the double-blind part of a two-part study, 583 patients received either ENBREL 25 mg, ENBREL 50 mg, or placebo twice weekly for 3 months. Upon completion of the 3-month study, patients entered an open-label treatment period in which all patients received ENBREL 25 mg twice weekly for another 6 months. PASI responses were analyzed using a last-observation-carried-forward approach.

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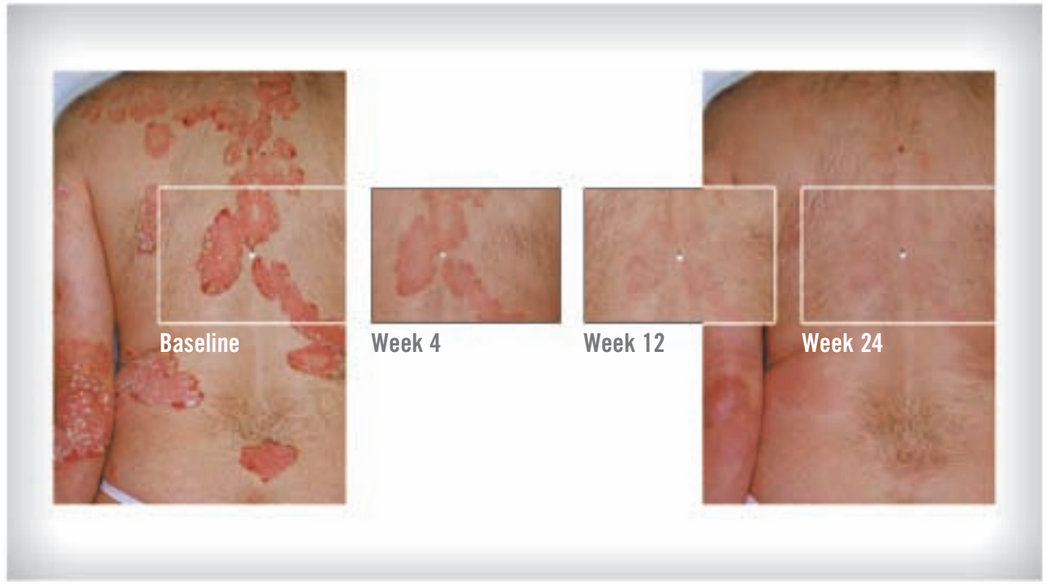
EXPECT
SUSTAINABLE RESPONSE



Example of improved skin lesions in a patient treated with ENBREL who was enrolled in a psoriasis clinical trial. This patient was initially treated with ENBREL 50 mg twice weekly and stepped down to 25 mg weekly at 12 weeks. Individual results may vary.

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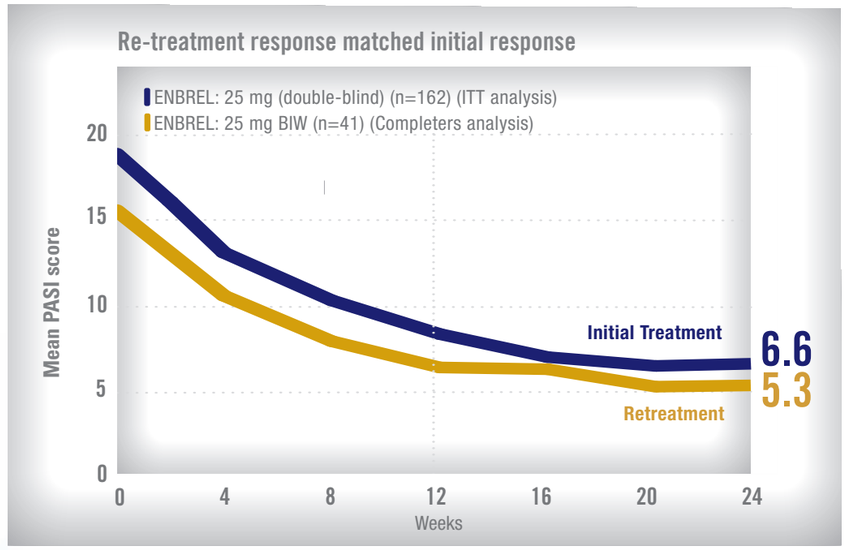
LOOK AT
REPEATED SUCCESS

- With **re-treatment**, PASI 75 rates were similar to those attained during the initial treatment course[2,10]
- No association with rebound, conversion of disease type, or worsening psoriasis after discontinuation[10]
- After discontinuation, mean time to loss of response was approximately 3 months[10]
- **No evidence** of neutralizing antibodies, no efficacy decay, no increase in dose over time[8]

EXPECT
RELIABLE RESPONSE

After treatment interruption



A double-blind study evaluated 652 patients with chronic plaque psoriasis involving 10% of body surface area and with a minimum PASI 10. Patients were randomized to receive ENBREL 25 mg once weekly, ENBREL 25 mg twice weekly, ENBREL 50 mg twice weekly, or placebo. After 12 weeks, patients receiving placebo began treatment with blinded ENBREL 25 mg twice weekly, and patients receiving active treatment continued on their original dose through week 24.[2,11] Patients who achieved a PASI 50 response at 24 weeks were discontinued from treatment and evaluated until relapse during the withdrawal period. Relapse was defined as a loss of at least half of the improvement achieved through week 24. Following relapse, patients were re-treated with blinded ENBREL at the same dose they were receiving at week 24.[10]

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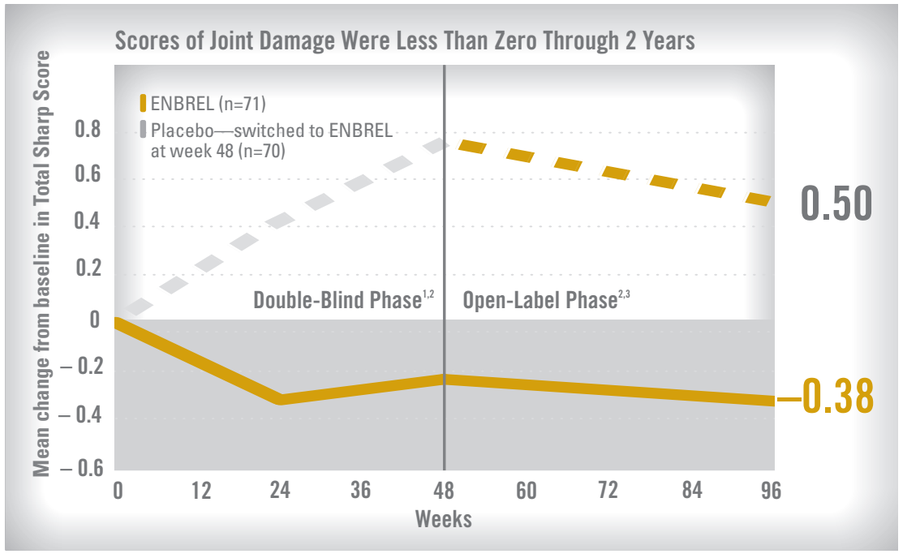
LOOK BENEATH *THE SKIN*

You can diagnose and treat psoriatic arthritis early, before potential joint damage can occur

- 30% of your psoriasis patients may have psoriatic arthritis[12]
- Skin symptoms usually manifest first in these patients—who risk long term joint damage[13,14]

EXPECT SUSTAINED *INHIBITION OF JOINT DAMAGE*

- Joint damage was substantially inhibited over the long term[1]



Multicenter, double-blind, phase 3 trial of 205 patients with active psoriatic arthritis. Mean duration of arthritic disease was about 9.1 years, and mean duration of plaque psoriasis was about 19.0 years (with a qualifying target skin lesion). Patients were randomized to receive subcutaneous injections of ENBREL 25 mg (n = 101) or placebo (n = 104) administered twice weekly over the 24-week blinded treatment period. After the 24-week period, patients continued therapy in a maintenance period until all patients completed double-blind therapy. After the maintenance period, all patients received ENBREL 25 mg twice weekly in an open-label period of 48 weeks. The data were stratified by absence or presence of concurrent MTX (either ENBREL alone [n = 57] vs placebo [n = 58] or ENBREL + MTX [n = 44] vs placebo + MTX [n = 46]). Stable use of corticosteroids and/or NSAIDs was allowed. Of the 205 patients in the blinded study, 169 patients (81 originally receiving placebo, 88 originally receiving ENBREL) entered the open-label extension. Linear extrapolation was utilized for the radiographic data. Nonresponder imputation analysis was conducted during the double-blind portion for ACR response and skin lesion clearing while parameters assessed during the open-label period were analyzed based on the observed population at each time point.

- At week 12, 59% of ENBREL patients achieved the primary score of joint improvement (ACR 20) vs 15% of placebo patients ($P < 0.0001$)[1,15]

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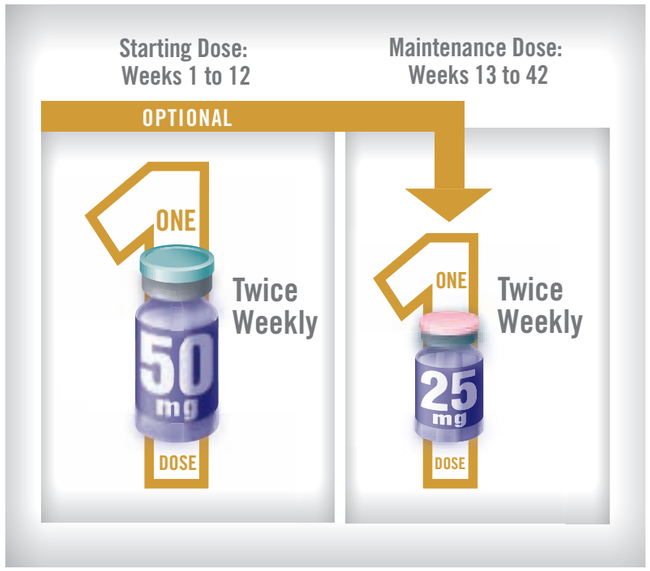
SEE THE ADVANTAGE OF

DOSING FLEXIBILITY

- Treat with the recommended dose for psoriasis—25 mg twice weekly—for up to 24 weeks or until remission is achieved[8]
  - — Alternatively, treat with 50 mg twice weekly for up to 12 weeks
    - – Achieve rapid and stronger response[2,9]
    - – Response sustained after step-down to 25 mg[2,9]
- Re-treat for 24-week intervals when psoriasis symptoms recur[8]



Treatment with ENBREL should continue until remission is achieved, for up to 24 weeks. Treatment should be discontinued in patients who show no response after 12 weeks. If re-treatment with ENBREL is indicated, the above guidance on treatment duration should be followed. The dose should be 25 mg twice weekly.

Now in psoriatic arthritis, treat continuously with 50 mg once-weekly dosing

25 mg twice-weekly dosing is still an option.

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Indications

ENBREL can be used alone or in combination with methotrexate for the treatment of active rheumatoid arthritis in adults when the response to disease-modifying antirheumatic drugs, including methotrexate (unless contraindicated), has been inadequate.

ENBREL is also indicated in the treatment of severe, active and progressive rheumatoid arthritis in adults not previously treated with methotrexate.

In patients with rheumatoid arthritis, ENBREL used alone or in combination with methotrexate has been shown to slow the progression of disease-associated structural damage as measured by X-ray.

Treatment of active polyarticular-course juvenile idiopathic arthritis in children aged 4 to 17 years who have had an inadequate response to, or who have proved intolerant of, methotrexate. ENBREL has not been studied in children aged less than 4 years.

Treatment of active and progressive psoriatic arthritis in adults when the response to previous disease-modifying antirheumatic drug therapy has been inadequate.

Treatment of adults with severe active ankylosing spondylitis who have had an inadequate response to conventional therapy.

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 cyclosporine, methotrexate or PUVA.

Important Safety Information

In postmarketing use, serious infections and sepsis, including fatalities, have been reported. 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.

Cases of CNS demyelinating disorders have been reported, although the causal relationship to ENBREL remains unclear. Rare cases of pancytopenia, including aplastic anemia, some fatal, have been reported in patients with rheumatoid arthritis (RA). Exercise caution in patients who have a previous history of significant hematologic abnormalities. Although the causal relationship to ENBREL remains unclear, advise patients to seek immediate medical attention if they develop signs or symptoms of blood dyscrasias or infection. If significant hematologic abnormalities are confirmed, discontinue ENBREL. Long-term effects of ENBREL therapy on the development or course of infection and malignancy are unknown.

The most frequent adverse events in five double-blind, controlled clinical trials in patients with RA were infections (49% of patients), injection-site reactions (31%), headaches (12%), and respiratory disorders (10%). Malignancies were rare.

The types of adverse events observed in the psoriatic arthritis and ankylosing spondylitis trials were similar to those reported in RA clinical trials.

The most common adverse events observed during the double-blind, placebo-controlled portions of three clinical trials in patients with psoriasis were infections (27%-29% of patients), injection-site reactions (14%-16%), headaches (9%-12%), and injection-site ecchymoses (6%-8%). There were no reports of opportunistic infections or tuberculosis during 662 patient exposure years.

Twenty-three (23) malignancies were reported in patients with plaque psoriasis treated with ENBREL in double-blind and open-label studies of up to 15 months involving 1,261 patients treated with ENBREL.

References: 1. Data on file, Amgen. **2.** Data on file, Wyeth Pharmaceuticals. **3.** Smith CH, Anstey AV, Barker JNWN, et al. British Association of Dermatologists guidelines for use of biological interventions in psoriasis 2005. *Br J Dermatol*. 2005:153;486-497. **4.** Elewski B, Leonardi C, Gottlieb A, et al. Sustained long-term clinical efficacy and safety for up to 2.5 years of etanercept in patients with psoriasis. Presented at the European Academy of Dermatology and Venereology. February 9-12, 2006, Saariselkä, Finland. P39. **5.** Randazzo B, Griffiths C, Guillet G, Vanderham R, Stichering M. Analysis of etanercept safety based on data from phase 2 and phase 3 clinical trials in patients with psoriasis. Presented at: European Academy of Dermatology and Venereology; April 29 – May 1, 2004; Budapest, Hungary. P100. **6.** Tyring S, Poulin Y, Langley R, et al. A 2-year phase 3 study of safety and efficacy of etanercept 50 mg twice weekly in patients with psoriasis: 48-week results. Presented at: American Academy of Dermatology; July 20-24, 2005; Chicago, Illinois. P134. **7.** Weinblatt ME, Genovese MC, Moreland LW, et al. Efficacy and safety of over 8 years of etanercept (Enbrel®) therapy in North American patients with early and long-standing rheumatoid arthritis. *Arthritis Rheum*. 52(9 (Supplement)):S541 2005. **8.** ENBREL Summary of Product Characteristics, Wyeth Pharmaceuticals **9.** Papp K, Tyring S, Lahfa M, et al. A global phase III randomized controlled trial of etanercept in psoriasis: safety, efficacy, and effect of dose reduction. *Br J Dermatol*. 2005;152:1304-13. **10.** Gordon K, Gottlieb A, Leonardi C, et al. Clinical response in psoriasis patients discontinued from and then reinitiated on etanercept therapy. *J Dermatol Treat*. 2006;17:9-17. **11.** Leonardi CL, Powers JL, Matheson RT, et al. Etanercept as monotherapy in patients with psoriasis. *N Engl J Med*. 2003;349:2012-2020 **12.** Zachariae H, Zachariae R, Blomqvist K, et al. Quality of life and prevalence of arthritis reported by 5,795 members of the Nordic Psoriasis Associations: data from the Nordic Quality of Life Study. *Acta Derm Venereol*. 2002;82:108-113. **13.** Stern RS. The epidemiology of joint complaints in patients with psoriasis. *J Rheumatol*. 1985;12:315-320. **14.** Helliwell PS, Wright V. Psoriatic arthritis: clinical features. In: Klippel JH, Dieppe PA, eds. Rheumatology. 2nd ed. Philadelphia, Pa: Mosby; 1998;21.1-21.8. **15.** Lebwohl M, Gottlieb AB, Goffe BS, Jahreis A. Etanercept in psoriatic arthritis: sustained improvement in skin and joint disease and inhibition of radiographic progression at 2 years. Poster presented at the 63rd Annual Meeting of the American Academy of Dermatology; February 18-22, 2005; New Orleans, La.

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MORE THAN *WHAT YOU SEE*

- World-wide experience—over 14 years of study
- Safety profile established in over 2 years of psoriasis studies
- Sustainable response
- Repeatable response
- Treats both skin and joints
- Flexible treatment options

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