Phase 3 Clinical Trials Support STELARA® (ustekinumab) for the Treatment of Moderate to Severe Plaque Psoriasis

By Jack Alan McCain Jr.

A review of recently published data with a commentary for managed care decision makers

By Jeffrey M. Sobell, MD

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Please see Important Safety Information on pages 8-9 and accompanying Full Prescribing Information and Medication Guide for STELARA® on pages 10-15.


Phase 3 Clinical Trials Support STELARA® (ustekinumab) for the Treatment of Moderate to Severe Plaque Psoriasis

STELARA®, is a subcutaneously administered biologic approved by the US Food and Drug Administration in September 2009 for the treatment of adult patients (18 years or older) with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy. This Clinical Brief summarizes the 2 phase 3 multicenter, randomized, double-blind, placebo-controlled trials that demonstrated the efficacy and safety of STELARA®.

PHOENIX 1

PHOENIX 1 examined the efficacy and safety of STELARA® vs placebo over 12 weeks in patients with moderate to severe plaque psoriasis. To assess the efficacy and safety of long-term usage for up to 76 weeks, a randomized-withdrawal design was used. The primary endpoint was the proportion of patients who achieved a Psoriasis Area and Severity Index (PASI 75) at Week 12. PASI 75 represents a 75% improvement from baseline PASI score. Major secondary endpoints included the proportion of patients with a Physician's Global Assessment (PGA) score of Cleared or Minimal at Week 12, and in the randomized withdrawal phase, time to loss of PASI 75 response in the group receiving maintenance therapy with STELARA® compared with the group withdrawn from treatment at Week 40. The eligibility criteria for PHOENIX 1 are presented in Table 1.

**TABLE 1. Eligibility criteria for PHOENIX 1 and PHOENIX 2**

<table>
<thead>
<tr>
<th>Key inclusion criteria</th>
<th>Key exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men and women ≥18 years of age</td>
<td>Nonplaque psoriasis</td>
</tr>
<tr>
<td>Diagnosis of plaque psoriasis for ≥6 months</td>
<td>Recent serious systemic or local infection</td>
</tr>
<tr>
<td>Eligible for phototherapy or systemic therapy</td>
<td>Malignancy (excluding treated basal or squamous cell skin cancer ≥5 years)</td>
</tr>
<tr>
<td>Plaques covering ≥10% body surface area (BSA)</td>
<td>Previous treatment with agents targeting IL-12 or IL-23</td>
</tr>
<tr>
<td>PASI score ≥12</td>
<td>Biological or investigational agents within the previous 3 months</td>
</tr>
<tr>
<td>No history or symptoms of active tuberculosis (TB)*</td>
<td>Conventional systemic psoriasis therapy or phototherapy within the previous 4 weeks</td>
</tr>
</tbody>
</table>

*The PASI divides the body into 4 regions and assesses each separately for redness, thickness, and scaliness on a scale of 0 to 4. Scores range from 0 to 72. Higher scores indicate greater severity of disease. PASI 50 and PASI 75 represent ≥50% and ≥75% improvement overall, respectively, in PASI score.†‡

†Patients with latent TB (a positive Mantoux tuberculin skin test without radiologic evidence of TB at screening) were allowed to enroll if they began appropriate therapy for TB according to local country guidelines for immunocompromised patients prior to, or concurrently with, the first administration of study agent.纪念馆

4 At Week 28, non-responders (PASI<50) in all groups discontinued STELARA®, partial responders (PASI 50 to <75) initiated dosing every 8 weeks, and PASI responders (PASI ≥75) were treated every 12 weeks.3

5 At Week 40, patients in Group 1 and Group 2 who responded to dosing every 12 weeks were randomized to receive either placebo or continued treatment with STELARA® every 12 weeks at their original dose. Individuals in Group 3 were treated with placebo. Upon loss of therapeutic effect, patients receiving placebo were retreated at their dosing regimen before withdrawal. Across all groups, non-responders or partial responders were adjusted to dosing every 8 weeks. Patients already receiving dosing every 8 weeks continued this dosing schedule.3

**Results**

Significantly more patients in both the STELARA® 45 mg and 90 mg groups achieved the primary endpoint—PASI 75 at Week 12—than the patients in the placebo group (*P*<0.0001; Figure 2). Efficacy was achieved rapidly, with significantly higher proportions of patients treated with STELARA® achieving PASI 50, or a 50% improvement from baseline PASI score, by Week 2 and PASI 75 by Week 4. Cleared or Minimal disease as measured by the PGA was achieved by significantly more patients receiving STELARA® than by those receiving placebo at Week 12 (*P*<0.0001; Figure 2). Patients taking STELARA® consistently showed greater improvement in their psoriasis compared with patients taking placebo, as measured by PASI or PGA scores through Week 12. Efficacy continued well after the placebo-controlled portion of the study. Patients randomized to receive placebo at baseline achieved similar response rates after crossover at Week 12.3

Maximum efficacy was observed in both STELARA® 45 mg and 90 mg groups at Week 24. At Week 28, >90% of patients in both groups treated with STELARA® achieved PASI 50, >70% achieved PASI 75, and approximately 50% achieved PASI 90 (Figure 2). These response rates were generally maintained through Week 40, at which point long-term responders underwent randomized withdrawal.3

Among patients rerandomized at Week 40, maintenance of PASI 75 (defined as the time to loss of PASI 75 response) was better in patients receiving maintenance therapy than in patients withdrawn from therapy through 1 year (*P*<0.0001). Patients on maintenance therapy maintained PASI 50, PASI 75, PASI 90, and PGA responses up to at least Week 76. In contrast, the withdrawal groups showed a decline in PASI improvement, which began gradually by Week 44. The rate of decline in PASI score accelerated after Week 52, finally decreasing from over 96% in both withdrawal groups at Week 40 to about 40% at Week 64. In the patients withdrawn from treatment, the median time to loss of PASI 75 response was about 15 weeks. Rebound psoriasis was not reported in patients who were withdrawn from treatment. Eighty-six percent of patients who reinitiated STELARA® achieved PASI 75 within 12 weeks of reinitiation, with similar response rates observed in all treatment groups.3
Adverse events

In PHOENIX 1, adverse events were generally mild, not serious, and did not require treatment adjustments (Table 2). The most commonly reported adverse events were upper respiratory tract infections, nasopharyngitis, headache, and arthralgia. Serious adverse events occurred in 2 patients receiving placebo (1 patient with pneumonia and 1 patient with a psychotic disorder); 2 patients receiving STELARA® 45 mg (1 patient with a stroke and 1 patient with hypertension); and 4 patients receiving STELARA® 90 mg (2 patients with serious infections, 1 patient with coronary artery disease, and 1 patient with worsening psoriasis). No malignancies were reported during the placebo-controlled phase. Patterns of common adverse events were similar during the placebo-crossover and randomized-withdrawal phases. The most common serious adverse events observed during these phases included infections (3 patients), malignancies (2 patients), cardiovascular events (2 patients), and a stroke (1 patient). No dose response was seen in the rates of adverse events, serious adverse events, or adverse events leading to study agent discontinuation. The percentage of patients with abnormal hematologic and chemistry laboratory measures, including liver and renal function tests, were low and generally comparable between the groups treated with STELARA® and placebo.3


†An adverse event that resulted in any of the following outcomes: death, a life-threatening condition, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, or a congenital anomaly or birth defect, irrespective of its relationship to study agent.

**TABLE 2. Adverse events reported through Week 12 in PHOENIX 1**

<table>
<thead>
<tr>
<th></th>
<th>STELARA® 45 mg (n=255)</th>
<th>STELARA® 90 mg (n=255)</th>
<th>Placebo (n=255)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthralgia</td>
<td>3%</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>Headache</td>
<td>6%</td>
<td>5%</td>
<td>2%</td>
</tr>
<tr>
<td>Infections</td>
<td>31%</td>
<td>26%</td>
<td>27%</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>10%</td>
<td>8%</td>
<td>9%</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>7%</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Serious infections</td>
<td>0</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Serious adverse events†</td>
<td>&lt;1%</td>
<td>2%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Adverse events leading to withdrawal of STELARA®</td>
<td>&lt;1%</td>
<td>2%</td>
<td>2%</td>
</tr>
</tbody>
</table>


†An adverse event that resulted in any of the following outcomes: death, a life-threatening condition, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, or a congenital anomaly or birth defect, irrespective of its relationship to study agent.

**Please see Important Safety Information on pages 8-9 and accompanying Full Prescribing Information and Medication Guide for STELARA® on pages 10-15.**
PHOENIX 2

PHOENIX 2 was the second, major clinical trial that sought to assess the efficacy and safety of STELARA® in patients with moderate to severe plaque psoriasis for up to 52 weeks. In addition, PHOENIX 2 looked to determine if dosing intensification would improve response in patients who had a partial response to initial treatment. The primary endpoint was the proportion of PASI 75 responders at Week 12. Major secondary endpoints included the proportion of patients with a PGA score of Cleared or Minimal at Week 12, and the proportion of partial responders rerandomized between Weeks 40 and 52 who demonstrated PASI 75 response every 8 weeks vs every 12 weeks. The eligibility criteria for PHOENIX 2 are presented in Table 1.4

Study design

PHOENIX 2 was divided into 3 phases: (1) a placebo-controlled phase from Weeks 0 to 12, (2) a placebo-crossover and active-treatment phase during Weeks 12 to 28, and (3) a randomized-dose-intensification phase during Weeks 28 to 52 (Figure 3). At baseline, patients were randomly assigned to receive STELARA® 45 mg or STELARA® 90 mg at Weeks 0 and 4, and then every 12 weeks, or placebo. Of the patients receiving placebo, half were randomized to cross over to STELARA® 45 mg at Weeks 12, 16, and every 12 weeks thereafter; the other half received STELARA® 90 mg according to the same schedule.4

At Week 28, those responders who had initially been randomized to receive STELARA® and achieved PASI ≥50, but PASI <75, were rerandomized to continue to either receive the drug every 12 weeks or intensified dosing every 8 weeks. Patients not achieving PASI 50 at Week 28 discontinued treatment, and patients achieving PASI 75 at Week 28 continued to receive STELARA® every 12 weeks. Efficacy and safety parameters were assessed through Week 52.4

Results

Significantly more patients treated with STELARA® achieved PASI 75 in both groups (67% and 76%, respectively) compared with 4% in the placebo group (P<0.0001; Figure 4). At Week 12, a PGA assessment score of Cleared or Minimal was achieved by 68% and 74% of patients who received STELARA® 45 mg or STELARA® 90 mg, respectively, vs 5% of patients in the placebo group (P<0.0001; Figure 4). PASI 50, PASI 75, PASI 90, and PASI 100 were achieved by a significantly greater proportion of patients treated with STELARA® at Week 12 than those patients who had been given placebo. After Week 12, response rates in the patients who crossed over from placebo to active treatment with STELARA® were similar to those seen in the patients initially randomized to the respective STELARA® dose at baseline.4
At Week 28, more than 90% of all patients treated with STELARA® achieved PASI $\geq 50$ response. Patients who were PASI 75 responders at Week 28 and continued to receive STELARA® every 12 weeks typically sustained response until Week 52.4 Twenty-three percent (93 patients) in the STELARA® 45 mg group and 16% (65 patients) in the 90 mg group were partial responders at Week 28.4 When compared with those patients who responded to dosing every 12 weeks, partial responders tended to have a higher body weight and more marked or severe disease as measured by the PGA. For patients weighing $\leq 100$ kg (220 lbs), the recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks. For patients weighing $>100$ kg (220 lbs), the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks. In patients weighing $>100$ kg, 45 mg was also shown to be efficacious. However, 90 mg resulted in greater efficacy in these patients.1,4

*At Week 28, non-responders (PASI <50) discontinued treatment with STELARA®, Partial responders (PASI 50 to <75) treated with STELARA® were randomly assigned to receive treatment either every 8 or 12 weeks. Responders (PASI $\geq 75$) continued treatment every 12 weeks. All partial responders who were initially assigned to receive placebo received doses every 8 weeks at Week 28.*

**FIGURE 4. Percentage of patients who responded at Weeks 12 and 28 in PHOENIX 2**

1$P<0.0001$ vs placebo.
Adverse events

In PHOENIX 2, adverse events were generally mild and did not require modification of treatment. During the placebo-controlled phase, rates of infections were the same across all 3 groups (Table 3). Serious adverse events occurred in 8 of 410 patients receiving placebo (2 instances of cellulitis, and 1 case each of psoriatic arthropathy cervicobrachial syndrome, hepatocellular cancer, chest pain, asthma, and pityriasis rubra pilaris); 8 of 409 patients receiving STELARA® 45 mg (2 cases of intervertebral disc protrusion, and 1 case each of angina, dactylitis, clavicular fracture, sciatica, nephrolithiasis, and seroma of an amputation stump); and 5 of 411 patients receiving STELARA® 90 mg (nonischemic sudden cardiac death in a patient with underlying dilated cardiomyopathy, cellulitis, benign meningioma, alcohol withdrawal syndrome, and a complex of symptoms including transient palpitations, ventricular extrasystoles, vertigo, and hypertension). Cutaneous malignancies were reported in 2 patients: 1 patient in the placebo group with squamous cell cancer and 1 patient in the STELARA® 90 mg group with basal cell cancer. Rates of laboratory abnormalities were similar between treatment groups, and no differences in liver aminotransferase concentrations, fasting glucose, or hemoglobin A1c levels were noted between treatment groups.4

During the dose intensification phase, adverse events were more common in patients receiving dosing every 8 weeks. Higher rates of serious adverse events were reported in patients treated with every–12-week dosing than with every–8-week dosing. By Week 52, no dose response was observed in rates of adverse events, serious adverse events, or those leading to discontinuation of treatment. The most common serious adverse events in those patients treated with STELARA® were infections (9 patients) and cardiac disorders (9 patients). Injection-site reactions were mild in all but one case. No cases of anaphylactic or serum-sickness–like reactions, tuberculosis, lymphoma, or demyelinating disease were reported.4

TABLE 3. Adverse events reported through Week 12 in PHOENIX 2

<table>
<thead>
<tr>
<th></th>
<th>STELARA® 45 mg (n=409)</th>
<th>STELARA® 90 mg (n=411)</th>
<th>Placebo (n=410)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthralgia</td>
<td>3%</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>Cough</td>
<td>&lt;1%</td>
<td>1%</td>
<td>2%</td>
</tr>
<tr>
<td>Headache</td>
<td>5%</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Injection-site erythema</td>
<td>2%</td>
<td>2%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Infections</td>
<td>22%</td>
<td>22%</td>
<td>20%</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>7%</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>4%</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Serious adverse events†</td>
<td>2%</td>
<td>1%</td>
<td>2%</td>
</tr>
<tr>
<td>Adverse events leading to withdrawal of STELARA®</td>
<td>&lt;1%</td>
<td>2%</td>
<td>2%</td>
</tr>
</tbody>
</table>


†Adverse events that resulted in any of the following outcomes: death, a life-threatening condition, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, or a congenital anomaly or birth defect, irrespective of its relationship to study agent.
Indications

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

Dosing

STEVALA® is administered by subcutaneous injection.1

- For patients weighing ≤100 kg (220 lbs), the recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks
- For patients weighing >100 kg (220 lbs), the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks

In patients weighing >100 kg, 45 mg was also shown to be efficacious. However, 90 mg resulted in greater efficacy in these patients.7

The safety and efficacy of STEVALA® have not been evaluated beyond two years.1

Infections

STEVALA® may increase the risk of infections and reactivation of latent infections. Serious bacterial, fungal, and viral infections were reported. Infections requiring hospitalization included cellulitis, diverticulitis, osteomyelitis, gastroenteritis, pneumonia, and urinary tract infections. STEVALA® should not be given to patients with a clinically important active infection and should not be administered until the infection resolves or is adequately treated. Instruct patients to seek medical advice if signs or symptoms suggestive of an infection occur. Exercise caution when considering use of STEVALA® in patients with a chronic infection or a history of recurrent infection.

Theoretical Risk for Vulnerability to Particular Infections

Individuals genetically deficient in IL-12/IL-23 are particularly vulnerable to disseminated infections from mycobacterium, Salmonella, and Bacillus Calmette-Guerin (BCG) vaccinations. Serious infections and fatal outcomes have been reported in such patients. It is not known whether patients with pharmacologic blockade of IL-12/IL-23 from treatment with STEVALA® will be susceptible to these types of infections. Consider appropriate diagnostic testing as dictated by clinical circumstances.

Pre-Treatment Evaluation of Tuberculosis (TB)

Evaluate patients for TB prior to initiating treatment with STEVALA®. STEVALA® should not be given to patients with active TB. Initiate treatment of latent TB before administering STEVALA®. Patients should be monitored closely for signs and symptoms of active TB during and after treatment with STEVALA®.

Malignancies

STEVALA® is an immunosuppressant and may increase the risk of malignancy. Malignancies were reported among patients who received STEVALA® in clinical studies. The safety of STEVALA® has not been evaluated in patients who have a history of malignancy or who have a known malignancy.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS)

One case of RPLS has been reported in a STEVALA®-treated patient. If RPLS is suspected, discontinue STEVALA® and administer appropriate treatment.

RPLS is a neurological disorder, which is not caused by an infection or demyelination. RPLS can present with headache, seizures, confusion, and visual disturbances. RPLS has been associated with fatal outcomes.

Please see Important Safety Information continued on page 9 and accompanying Full Prescribing Information and Medication Guide for STEVALA® on pages 10-15.
CONCLUSION

STELARA® is a human IgG1κ monoclonal antibody that binds with high affinity and specificity to the p40 protein subunit used by both the IL-12 and IL-23 cytokines, which may play a role in the immunopathophysiology of psoriasis. The PHOENIX 1 and PHOENIX 2 clinical trials demonstrated that treatment with STELARA® 45 mg or STELARA® 90 mg provided rapid and significant improvements in patients with moderate to severe plaque psoriasis, as measured by the PASI and PGA scores.1,3,4 The safety profile of STELARA® was generally comparable to that of placebo during the placebo-controlled portions of the trials. Adverse events typically were mild and included upper respiratory tract infections, nasopharyngitis, headache, and arthralgia. Serious adverse events included serious infections, malignancies, and 1 case of RPLS. No active cases of tuberculosis were reported.1,3,4 With rapid and sustained efficacy outcomes, a benefit/risk profile, and a convenient dosing schedule (every 12 weeks after 2 starter doses), STELARA® is a noteworthy new therapeutic option for patients with moderate to severe plaque psoriasis.1,3,4

REFERENCES

INDICATIONS AND USAGE

• Concomitant therapy: The safety of concomitant use of STELARA™ with

• Live vaccines: Live vaccines should not be given with STELARA™. (7.1)

-----------------------------------DRUG INTERACTIONS ----------------------------------
outcomes have been reported in such patients. Bacillus Calmette-Guerin (BCG) vaccinations. Serious infections and fatal environmental mycobacteria), salmonella (including nontyphi strains), and viral infections, gastroenteritis, pneumonia, and urinary tract infections. STELARA™ in patients with a chronic infection or a history of recurrent infection. STELARA™ should not be administered until the infection resolves or is inactive. STELARA™ is an immunosuppressant and may increase the risk of malignancy. Malignancies were reported among subjects who received STELARA™ in clinical studies [see Adverse Reactions (6.1)]. In rodent models, inhibition of IL-12/IL-23p40 increased the risk of malignancy [see Nonclinical Toxicology (13)]. The safety of STELARA™ has not been evaluated in patients who have a history of malignancy or who have a known malignancy.

5.5 Reversible Posterior Leukoencephalopathy Syndrome

One case of reversible posterior leukoencephalopathy syndrome (RPLS) was observed during the clinical development program which included 3523 STELARA™-treated subjects. The subject, who had received 12 doses of STELARA™ over approximately two years, presented with headache, seizures and confusion. No additional STELARA™ injections were administered and the subject fully recovered with appropriate treatment.

RPLS is a neurological disorder, which is not caused by demyelination or a known infectious agent. RPLS can present with headache, seizures, confusion and visual disturbances. Conditions with which it has been associated include pre eclampsia, eclampsia, acute hypertension, cytotoxic agents and immunosuppressive therapy. Fatal outcomes have been reported. If RPLS is suspected, STELARA™ should be discontinued and appropriate treatment administered.

5.6 Immunizations

Prior to initiating therapy with STELARA™, patients should receive all immunizations appropriate for age as recommended by current immunization guidelines. Patients being treated with STELARA™ should not receive live vaccines. BCG vaccines should not be given during treatment with STELARA™ or for one year prior to initiating treatment or one year following discontinuation of treatment. Caution is advised when administering live vaccines to household contacts of patients receiving STELARA™ because of the potential risk for shedding from the household contact and transmission to patient. Non-live vaccinations received during a course of STELARA™ may not elicit an immune response sufficient to prevent disease.

5.7 Concomitant Therapies

The safety of STELARA™ in combination with other immunosuppressive agents or phototherapy has not been evaluated. Ultraviolet-induced skin cancers developed earlier and more frequently in mice genetically manipulated to be deficient in both IL-12 and IL-23 or IL-12 alone [see Nonclinical Toxicology (13)].

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed elsewhere in the label:

- Infections [see Warnings and Precautions (5.1)]
- Malignancies [see Warnings and Precautions (5.4)]
- Reversible Posterior Leukoencephalopathy Syndrome [see Warnings and Precautions (5.5)]

6.1 Clinical Studies Experience

The safety data reflect exposure to STELARA™ in 2286 psoriasis subjects, including 1970 exposed for at least 6 months, 1285 exposed for at least one year, and 373 exposed for at least 18 months. Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. Table 1 summarizes the adverse reactions that occurred at a rate of at least 1% and at a higher rate in the STELARA™ groups than the placebo group during the placebo-controlled period of STUDY 1 and STUDY 2.

It is not known whether patients with pharmacologic blockade of IL-12/IL-23 from treatment with STELARA™ will be susceptible to these types of infections. Appropriate diagnostic testing should be considered, e.g., tissue culture, stool culture, as dictated by clinical circumstances.
Table 1. Adverse reactions reported by ≥1% of subjects through Week 12 in STUDY 1 and STUDY 2

<table>
<thead>
<tr>
<th>Subjects treated</th>
<th>Placebo 45 mg</th>
<th>STELARATM 90 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharyngitis</td>
<td>51 (8%)</td>
<td>56 (8%)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>30 (5%)</td>
<td>36 (5%)</td>
</tr>
<tr>
<td>Headache</td>
<td>23 (3%)</td>
<td>33 (5%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>14 (2%)</td>
<td>18 (3%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>12 (2%)</td>
<td>13 (2%)</td>
</tr>
<tr>
<td>Back pain</td>
<td>8 (1%)</td>
<td>9 (1%)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>8 (1%)</td>
<td>14 (2%)</td>
</tr>
<tr>
<td>Pharyngolaryngeal pain</td>
<td>7 (1%)</td>
<td>9 (1%)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>9 (1%)</td>
<td>10 (2%)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>4 (1%)</td>
<td>7 (1%)</td>
</tr>
<tr>
<td>Depression</td>
<td>3 (&lt;1%)</td>
<td>4 (1%)</td>
</tr>
</tbody>
</table>

Adverse drug reactions that occurred at rates less than 1% included: cellulitis and certain injection site reactions (pain, swelling, pruritus, induration, hemorrhage, bruising, and irritation). One case of RPLS occurred during clinical trials [see Warnings and Precautions (5.5)].

Infections

In the placebo-controlled period of clinical studies of psoriasis subjects (average follow-up of 12.6 weeks for placebo-treated subjects and 12.4 weeks for STELARATM-treated subjects), 27% of STELARATM-treated subjects reported infections (1.39 per subject-year of follow-up) compared with 24% of placebo-treated subjects (1.21 per subject-year of follow-up). Serious infections occurred in 0.3% of STELARATM-treated subjects (0.01 per subject-year of follow-up) and in 0.4% of placebo-treated subjects (0.02 per subject-year of follow-up) [see Warnings and Precautions (5.1)].

In the controlled and non-controlled portions of psoriasis clinical trials, 61% of STELARATM-treated subjects reported infections (1.24 per subject-year of follow-up). Serious infections were reported in 0.9% of subjects (0.01 per subject-year of follow-up).

Malignancies

In the controlled and non-controlled portions of psoriasis clinical trials, 0.4% of STELARATM-treated subjects reported malignancies excluding non-melanoma skin cancers (0.36 per 100 subject-years of follow-up). Non-melanoma skin cancer was reported in 0.8% of STELARATM-treated subjects (0.02 per 100 subject-years of follow-up) [see Warnings and Precautions (5.1)].

Serious malignancies included breast, colon, head and neck, kidney, prostate, and thyroid cancers.

Immunogenicity

The presence of ustekinumab in the serum can interfere with the detection of anti-ustekinumab antibodies resulting in inconclusive results due to assay interference. In STUDIES 1 and 2, antibody testing was done at time points when ustekinumab may have been present in the serum. Table 2 summarizes the antibody results from STUDIES 1 and 2. In STUDY 1 the last ustekinumab injection was between Weeks 28 and 48 and the last test for anti-ustekinumab antibodies was at Week 52. In STUDY 2 the last ustekinumab injection was at Week 16 and the last test for anti-ustekinumab antibodies was at Week 24.

Table 2

<table>
<thead>
<tr>
<th>Antibody Results</th>
<th>STUDY 1 (N=473)</th>
<th>STUDY 2 (N=3198)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>38 (5%)</td>
<td>53 (3%)</td>
</tr>
<tr>
<td>Negative</td>
<td>51 (47%)</td>
<td>90 (8%)</td>
</tr>
<tr>
<td>Inconclusive</td>
<td>354 (48%)</td>
<td>1075 (90%)</td>
</tr>
</tbody>
</table>

The data reflect the percentage of subjects whose test results were positive for antibodies to ustekinumab in a bridging immunoassay, and are highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody positivity in an assay may be influenced by several factors, including sample handling, timing of sample collection, concomitant medications and underlying disease. For these reasons, comparison of the incidence of antibodies to ustekinumab with the incidence of antibodies to other products may be misleading.

7 DRUG INTERACTIONS

Drug interaction studies have not been conducted with STELARATM.

7.1 Live Vaccines

Live vaccines should not be given concurrently with STELARATM [see Warnings and Precautions (5.6)].

7.2 Concomitant Therapies

The safety of STELARATM in combination with immunosuppressive agents or phototherapy has not been evaluated [see Warnings and Precautions (5.7)].

7.3 CYP450 Substrates

The formation of CYP450 enzymes can be altered by increased levels of certain cytokines (e.g., IL-1, IL-6, TNFα, IFN) during chronic inflammation. Thus, ustekinumab could normalize the formation of CYP450 enzymes. A role for IL-12 or IL-23 in the regulation of CYP450 enzymes has not been reported. However, upon initiation of ustekinumab in patients who are receiving concomitant CYP450 substrates, particularly those with a narrow therapeutic index, monitoring for therapeutic effect (e.g., for warfarin or drug concentration (e.g., for cyclosporine) should be considered and the individual dose of the drug adjusted as needed [see Clinical Pharmacology (12.3)].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B

There are no studies of STELARATM in pregnant women. STELARATM should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. No teratogenic effects were observed in the developmental and reproductive Toxicology studies performed in cynomolgus monkeys at doses up to 45 mg/kg ustekinumab, which is 45 times (based on mg/kg) the highest intended clinical dose in psoriasis patients (approximately 1 mg/kg based on administration of a 90 mg dose to a 90 kg psoriasis patient).

Ustekinumab was tested in two embryo-fetal development toxicity studies. Pregnant cynomolgus monkeys were administered ustekinumab at doses up to 45 mg/kg during the period of organogenesis either twice weekly via subcutaneous injections or weekly by intravenous injections. No significant adverse developmental effects were noted in either study.

In an embryo-fetal development and pre- and post-natal development toxicity study, three groups of 20 pregnant cynomolgus monkeys were administered subcutaneous doses of 0, 22.5, or 45 mg/kg ustekinumab twice weekly from the beginning of organogenesis in cynomolgus monkeys to Day 33 after delivery. There were no treatment-related effects on mortality, clinical signs, body weight, food consumption, hematologic, or serum biochemistry in dams. Fetal losses occurred in six control monkeys, six 22.5 mg/kg-treated monkeys, and five 45 mg/kg-treated monkeys. Neonatal deaths occurred in one 22.5 mg/kg-treated monkey and in one 45 mg/kg-treated monkey. No ustekinumab-related abnormalities were observed in the neonates from birth through six months of age in clinical signs, body weight, hematologic, or serum biochemistry. There were no treatment-related effects on functional development until weaning, functional development after weaning, morphological development, immunological development, and gross and histopathological examinations of offspring by the age of 6 months.

8.3 Nursing Mothers

Caution should be exercised when STELARATM is administered to a nursing woman. The unknown risks to the infant from gastrointestinal or systemic exposure to ustekinumab should be weighed against the known benefits of breast-feeding. Ustekinumab is excreted in the milk of lactating monkeys administered ustekinumab. IgG is excreted in human milk, so it is expected that STELARATM will be present in human milk. It is not known if ustekinumab is absorbed systemically after ingestion; however, published data suggest that antibodies in breast milk do not enter the neonatal and infant circulation in substantial amounts.

8.4 Pediatric Use

Safety and effectiveness of STELARATM in pediatric patients have not been evaluated.

8.5 Geriatric Use

Of the 2266 psoriasis subjects exposed to STELARATM, a total of 131 were 65 years or older, and 14 subjects were 75 years or older. Although no differences in safety or efficacy were observed between older and younger subjects, the number of subjects aged 65 and over is not sufficient to determine whether they respond differently from younger subjects.

10 OVERDOSAGE

Single doses up to 4.5 mg/kg intravenously have been administered in clinical studies without dose-limiting toxicity. In case of overdosage, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions or effects and appropriate symptomatic treatment be instituted immediately.

11 DESCRIPTION

STELARATM is a human IgG1x monoclonal antibody against the p40 subunit of the IL-12 and IL-23 cytokines. Using DNA recombinant technology, STELARATM is produced in a well characterized recombinant cell line and is purified using standard bio-processing technology. The manufacturing process contains steps for the clearance of viruses. STELARATM is comprised of 1326 amino acids and has an estimated molecular mass that ranges from 148,079 to 149,690 Daltons. STELARATM is available as: 45 mg of ustekinumab in 0.5 mL and 90 mg of ustekinumab in 1 mL STELARATM is supplied as a sterile solution in a single-use prefilled syringe with a 27 gauge fixed ½ inch needle, or a single-use 2 mL Type I glass vial with a coated stopper. The syringe is fitted with a passive needle guard and a needle cover that is manufactured using a dry natural rubber (a derivative of latex).

12
Each 45 mg ustekinumab prefilled syringe also contains: L-histidine and L-histidine monochloride monohydrate (0.5 mg), Polysorbate 80 (0.02 mg), and sucrose (38 mg) to fill to a final volume of 0.5 mL.

Each 90 mg ustekinumab prefilled syringe also contains: L-histidine and L-histidine monochloride monohydrate (0.5 mg), Polysorbate 80 (0.02 mg), and sucrose (38 mg) to fill to a final volume of 0.5 mL.

Each 45 mg ustekinumab vial also contains: L-histidine and L-histidine monochloride monohydrate (0.5 mg), Polysorbate 80 (0.02 mg), and sucrose (38 mg) to fill to a final volume of 0.5 mL.

Each 90 mg ustekinumab vial also contains: L-histidine and L-histidine monochloride monohydrate (1 mg), Polysorbate 80 (0.04 mg), and sucrose (76 mg) to fill to a final volume of 1 mL.

The STELARA™ solution is colorless to slightly yellow in appearance and has a pH of 5.7-6.3. STELARA™ does not contain preservatives.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Ustekinumab is a human IgG1 monoclonal antibody that binds with high affinity and specificity to the p40 protein subunit used by both the interleukin (IL)-12 and IL-23 cytokines. IL-12 and IL-23 are naturally occurring cytokines that are involved in inflammatory and immune responses, such as natural killer cell activation and CD4+ T-cell differentiation and activation. In in vivo models, ustekinumab was shown to disrupt IL-12 and IL-23 mediated signaling and cytokine cascades by disrupting the interaction of these cytokines with a shared cell-surface receptor chain, IL-12 Rb1.

12.2 Pharmacodynamics

In a small exploratory study, a decrease was observed in the expression of mRNA of its molecular targets IL-12 and IL-23 in lesional skin biopsies measured at baseline and up to two weeks post-treatment in psoriatic subjects.

12.3 Pharmacokinetics

Absorption

In psoriatic subjects, the median time to reach the maximum serum concentration (Tmax) was 13.5 days and 7 days, respectively, after a single subcutaneous administration of 45 mg (N=22) and 90 mg (N=24) of ustekinumab. In healthy subjects (N=30), the median Tmax value (8.5 days) following a single subcutaneous administration of 90 mg of ustekinumab was comparable to that observed in psoriasis subjects. Following multiple subcutaneous doses of STELARA™, the steady-state serum concentrations of ustekinumab were achieved by Week 28. The mean (±SD) steady-state trough serum concentration ranged from 0.31 ± 0.33 mcg/mL (45 mg) to 0.64 ± 0.64 mcg/mL (90 mg). There was no apparent accumulation in serum ustekinumab concentration over time when given subcutaneously every 12 weeks.

Distribution

Following subcutaneous administration of 45 mg (N=18) and 90 mg (N=21) of ustekinumab to psoriasis subjects, the mean (±SD) apparent volume of distribution during the terminal phase (Vz/F) was 161 ± 65 mL/kg and 179 ± 85 mL/kg, respectively. The mean (±SD) volume of distribution during the terminal phase (Vz) following a single intravenous administration to subjects with psoriasis ranged from 58.1 ± 8.5 to 92.1 ± 23.8 mL/kg.

Metabolism

The metabolic pathway of ustekinumab has not been characterized. As a human IgG1 monoclonal antibody ustekinumab is expected to be degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgG.

Elimination

The mean (± SD) systemic clearance (CL/F) following a single intravenous administration of ustekinumab to psoriasis subjects ranged from 1.90 ± 0.28 to 2.23 ± 0.63 mL/day/kg. The mean (±SD) half-life ranged from 4.13 ± 4.60 to 90.2 days across all psoriasis studies following intravenous and subcutaneous administration.

Weight

When given the same dose, subjects weighing > 100 kg had lower median serum ustekinumab concentrations compared with those subjects weighing ≤ 100 kg.

Hepatic and Renal Impairment

No pharmacokinetic data are available in patients with hepatic or renal impairment.

Elderly

A population pharmacokinetic analysis (N=108/1937 subjects greater than or equal to 65 years old) was performed to evaluate the effect of age on the pharmacokinetics of ustekinumab. There were no apparent changes in pharmacokinetic parameters (clearance and volume of distribution) in subjects older than 65 years old.

Drug-Drug Interactions

Upon initiation of ustekinumab in patients who are receiving concomitant CYP450 substrates, particularly those with narrow therapeutic index, monitoring for therapeutic effect (e.g., for warfarin) or drug concentration (e.g., for cyclosporine) should be considered and the individual dose of the drug adjusted as needed [see Drug Interactions (17.3)].

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies have not been conducted to evaluate the carcinogenic or mutagenic potential of STELARA™. Published literature showed that administration of murine IL-12 caused an anti-tumor effect in mice that contained transplanted tumors and IL-12/IL-23p40 knockout mice or mice treated with anti-IL-12/IL-23p40 antibody had decreased host defense to tumors. Mice genetically manipulated to be deficient in both IL-12 and IL-23 or IL-12 alone developed UV-induced skin cancers earlier and more frequently compared to wild-type mice. The relevance of these experimental findings in mouse models for malignancy risk in humans is unknown.

A male fertility study was conducted with only 6 male monkeys per group administered subcutaneous doses of 0, 22.5, or 45 mg/kg ustekinumab twice weekly prior to mating and during the mating period for 13 weeks, followed by a 13-week treatment-free period. Although fertility and pregnancy outcomes were not evaluated in mated females, there were no treatment-related effects on parental toxicity or male fertility parameters.

A female fertility study was conducted in mice using an analogous IL-12/IL-23p40 antibody by subcutaneous administration at doses up to 50 mg/kg, twice weekly, beginning 15 days before cohabitation and continuing through GD 7. There were no treatment-related effects on maternal toxicity or female fertility parameters.

13.2 Animal Toxicology and/or Pharmacology

In a 26-week toxicity study, one out of 10 monkeys subcutaneously administered 45 mg/kg ustekinumab twice weekly for 26 weeks had a bacterial infection.

14 CLINICAL STUDIES

Two multicenter, randomized, double-blind, placebo-controlled studies (STUDY 1 and STUDY 2) enrolled a total of 1996 subjects 18 years of age and older with plaque psoriasis who had a minimum body surface area involvement of 10%, and Psoriasis Area and Severity Index (PASI) score ≥12, and who were candidates for phototherapy or systemic therapy. Subjects with guttate, erythrodermic, or pustular psoriasis were excluded from the studies.

STUDY 1 enrolled 766 subjects and STUDY 2 enrolled 1230 subjects. The studies had the same design through Week 28. In both studies, subjects were randomized in equal proportion to placebo, 45 mg or 90 mg of STELARA™. Subjects randomized to STELARA™ received 45 mg or 90 mg doses, regardless of weight, at Weeks 0, 4, and 16. Subjects randomized to receive placebo at Weeks 0 and 4 crossed over to receive STELARA™ (either 45 mg or 90 mg) at Weeks 12 and 16.

In both studies, the endpoints were the proportion of subjects who achieved at least a 75% reduction in PASI score (PASI 75) from baseline to Week 12 and treatment success (cleared or minimal) on the Physician’s Global Assessment (PGA). The PGA is a 6-category scale ranging from 0 (cleared) to 5 (severe) that indicates the physician’s overall assessment of psoriasis focusing on plaque thickness/induration, erythema, and scaling.

In both studies, subjects in all treatment groups had a median baseline PASI score ranging from approximately 17 to 18. Baseline PGA score was marked or severe in 44% of subjects in STUDY 1 and 40% of subjects in STUDY 2. Approximately two-thirds of all subjects had received prior phototherapy, 69% had received either prior conventional systemic or biologic therapy for the treatment of psoriasis, with 56% receiving prior conventional systemic therapy and 43% receiving prior biologic therapy. A total of 28% of study subjects had a history of psoriatic arthritis.

Clinical Response

The results of STUDY 1 and STUDY 2 are presented in Table 3 below.

Table 3. Clinical Outcomes STUDY 1 and STUDY 2

<table>
<thead>
<tr>
<th>Week 12</th>
<th>STUDY 1</th>
<th>STUDY 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>STELARA™</td>
</tr>
<tr>
<td>Subjects randomized</td>
<td>255</td>
<td>255</td>
</tr>
<tr>
<td>PASI 75 response</td>
<td>8 (3%)</td>
<td>171 (67%)</td>
</tr>
<tr>
<td>PGA of Cleared or Minimal</td>
<td>10 (4%)</td>
<td>151 (59%)</td>
</tr>
<tr>
<td>Examination of age, gender, and race subgroups did not identify differences in response to STELARA™ among these subgroups.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In subjects who weighed < 100 kg, response rates were similar with both the 45 mg and 90 mg doses; however, in subjects weighing > 100 kg, higher response rates were seen with 90 mg dosing compared with 45 mg dosing (Table 4 below).

Table 4. Clinical Outcomes Study 1 and Study 2

<table>
<thead>
<tr>
<th>Week 12</th>
<th>STUDY 1</th>
<th>STUDY 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>STELARA™</td>
</tr>
<tr>
<td>Subjects randomized</td>
<td>255</td>
<td>255</td>
</tr>
<tr>
<td>PASI 75 response</td>
<td>8 (3%)</td>
<td>273 (67%)</td>
</tr>
<tr>
<td>PGA of Cleared or Minimal</td>
<td>10 (4%)</td>
<td>277 (68%)</td>
</tr>
</tbody>
</table>

Examination of age, gender, and race subgroups did not identify differences in response to STELARA™ among these subgroups.
Table 4. Clinical Outcomes by Weight STUDY 1 and STUDY 2

<table>
<thead>
<tr>
<th>STUDY 1</th>
<th>STUDY 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
</tr>
<tr>
<td>Subjects randomized</td>
<td>255</td>
</tr>
<tr>
<td>Week 12</td>
<td></td>
</tr>
<tr>
<td>PASI 75 response</td>
<td></td>
</tr>
<tr>
<td>≤ 100 kg</td>
<td>4%</td>
</tr>
<tr>
<td>&gt;100 kg</td>
<td>2%</td>
</tr>
<tr>
<td>PGA of Cleared or Minimal</td>
<td></td>
</tr>
<tr>
<td>≤ 100 kg</td>
<td>4%</td>
</tr>
<tr>
<td>&gt;100 kg</td>
<td>3%</td>
</tr>
</tbody>
</table>

Subjects in STUDY 1 were evaluated through Week 52. At Week 40, those who were PASI 75 responders at both Weeks 28 and 40 were re-randomized to either continued dosing of STELARA™ (STELARA™ at Week 40) or to withdrawal of therapy (placebo at Week 40). At Week 52, 89% (144/162) of subjects re-randomized to STELARA™ treatment were PASI 75 responders compared with 63% (100/159) of subjects re-randomized to placebo (treatment withdrawal after Week 28 dose).

16 HOW SUPPLIED/STORAGE AND HANDLING

STELARA™ does not contain preservatives. STELARA™ is available in prefilled syringes or single-use vials containing 45 mg or 90 mg of ustekinumab. Each prefilled syringe is equipped with a needle safety guard.

The NDC number for the 45 mg prefilled syringe is 57894-060-03.

The NDC number for the 90 mg prefilled safety guard is 57894-061-03.

The NDC number for the 45 mg vial is 57894-060-02.

The NDC number for the 90 mg vial is 57894-061-02.

Storage and Stability

Store STELARA™ upright and refrigerated at 2ºC to 8ºC (36ºF to 46ºF). Keep the product in the original carton to protect from light until the time of use. Do not freeze. Do not shake. STELARA™ does not contain a preservative; discard any unused portion.

17 PATIENT COUNSELING INFORMATION

Instruct patients to read the Medication Guide before starting STELARA™ therapy and to reread the Medication Guide each time the prescription is renewed.

Infections

Inform patients that STELARA™ may lower the ability of their immune system to fight infections. Instruct patients of the importance of communicating any history of infections to the doctor, and contacting their doctor if they develop any symptoms of infection.

Malignancies

Patients should be counseled about the risk of malignancies while receiving STELARA™.

Prefilled Syringe Manufactured by:

Centocor Ortho Biotech Inc.,
Horsham, PA 19044, License No. 1821 at Baxter Pharmaceutical Solutions,
Bloomington, IN 47403

Vial Manufactured by:

Centocor Ortho Biotech Inc.,
Horsham, PA 19044, License No. 1821 at Cilag AG,
Schaaffhausen, Switzerland
Cancers:
STELARATM may decrease the activity of your immune system and increase your risk for certain types of cancers. Tell your doctor if you have ever had any type of cancer.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS):
RPLS is a rare condition that affects the brain and can cause death. The cause of RPLS is not known. If RPLS is found early and treated, most people recover. Tell your doctor right away if you have any new or worsening medical problems including:
• headache
• seizures
• confusion
• vision problems

What is STELARATM?
STELARATM is a prescription medicine used to treat adults 18 years and older with moderate or severe psoriasis that involves large areas or many areas of their body, who may benefit from taking injections or pills (systemic therapy) or phototherapy (treatment using ultraviolet light alone or with pills).
STELARATM may improve your psoriasis but may also lower the ability of your immune system to fight infections. This may also increase your risk for certain types of cancer.
It is not known if STELARATM is safe and effective in children.
It is not known if taking STELARATM for more than 2 years is safe and effective.

What should I tell my doctor before receiving STELARATM?
Before receiving STELARATM, tell your doctor if you:
• have any of the conditions or symptoms listed in the section “What is the most important information I should know about STELARATM?”
• have recently received or are scheduled to receive an immunization (vaccine). People who take STELARATM should not receive live vaccines. Tell your doctor if anyone in your house needs a vaccine. The viruses used in some types of vaccines can spread to people with a weakened immune system, and can cause serious problems. You should not receive the BCG vaccine during the one year before taking STELARATM or one year after you stop taking STELARATM.
• receive phototherapy for your psoriasis.
• have any other medical conditions.
• are pregnant or planning to become pregnant. It is not known if STELARATM will harm your unborn baby. You and your doctor should decide if you will take STELARATM.
• are breast-feeding or plan to breast-feed. It is thought that STELARATM passes into your breast milk. You should not breast-feed while taking STELARATM without first talking with your doctor.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. Especially tell your doctor if you take:
• other medicines that affect your immune system.
• certain medicines that can affect how your liver breaks down other medicines.
Ask your doctor or pharmacist if you are not sure if your medicine is one that is listed above.

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How will I receive STELARATM?
• STELARATM is given by injection under the skin (subcutaneous injection).
• STELARATM should only be given by a healthcare provider as directed by your doctor.
• Your doctor will decide the right dose of STELARATM for you and how often you should receive it.
• Be sure to keep all of your scheduled follow-up appointments.

What should I avoid while receiving STELARATM?
You should not receive a live vaccine while taking STELARATM. See “What should I tell my doctor before taking STELARATM?”

What are the possible side effects of STELARATM?
STELARATM can increase your chances of having serious side effects. See “What is the most important information I should know about STELARATM?”

Common side effects of STELARATM include:
• upper respiratory infections
• headache
• tiredness

These are not all of the possible side effects of STELARATM. Tell your doctor about any side effect that bothers you or that does not go away. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or to Centocor Ortho Biotech Inc. at 1-800-457-6399.

General information about STELARATM
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide.

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

What are the ingredients in STELARATM?
Active ingredient: ustekinumab
Inactive ingredients: L-histidine, L-histidine monohydrochloride monohydrate, polysorbate 80, and sucrose.

Prefilled Syringe Manufactured by:
Centocor Ortho Biotech Inc.,
Horsham, PA 19044, License No. 1821 at Baxter Pharmaceutical Solutions,
Bloomington, IN 47403

Vial Manufactured by:
Centocor Ortho Biotech Inc.,
Horsham, PA 19044, License No. 1821 at Cilag AG,
Schaffhausen, Switzerland

Revised December 2009

This Medication Guide has been approved by the U.S. Food and Drug Administration.

U.S. License No. 1821

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