Rosacea is a chronic skin disease that often requires continuous treatment, but data about healthcare utilization and the costs associated with its management have been lacking, especially for relatively newer therapies. James D. Kendall, PharmD, and Norman J. Preston, PhD, of Galderma Laboratories, LP, recently addressed this information gap in a poster presentation at the 2013 Academy of Managed Care Pharmacy Nexus meeting.

This retrospective analysis was based on claims data from the IMS LifeLink Health Plan Claims Database between July 1, 2006, and June 30, 2011. This database contains 79 managed care health plans encompassing more than 70 million members who are primarily commercially insured.

Patients with rosacea were identified if they received any prescription drug for the treatment of rosacea. Patients were aged ≥30 years and had at least 1 diagnosis of rosacea. The index date was the time of first prescription for rosacea. A 1-year period after the index date was used to capture pharmacy and medical claims to assess utilization patterns and associated costs.

Dr Kendall and Dr Preston documented the medication possession ratio (MPR), which measures the percentage of time the patient has access to the medication (patients with only 1 prescription had an MPR of zero); therapy changes; and prescribing trends for rosacea and costs associated with the specialty of the prescribing physician (ie, dermatologist or nondermatologist).

Database of Nearly 100,000 Patients
A total of 99,894 patients met the inclusion criteria for the analysis. The majority (73.2%) of the patients were women (mean age, 52.4 years). Overall, 81.7% of the patients were treated with a single agent—57.3% received a topical agent and 24.6% received an oral antibiotic. Combination therapy with ≥2 medications was prescribed for 18.3% of patients.

The topical medications included metronidazole, aze- laic acid, and sulfacetamide sulfur. The oral antibiotics included doxycycline, minocycline, and tetracycline.

Among the patients who received a topical medica-
tion, 70% had only 1 prescription filled. “The high one-
time fill of topical medication suggests that patients self-dose based on self-diagnosis of rosacea flares,” the researchers commented. Another reason for the high one-time fill of topical medications is that patients may have erythematotelangiectatic rosacea, for which none of the topical therapies has shown a significant effect.

The MPR for monotherapy was higher for oral medications (37.8%) than for topical agents (18.2%). A higher proportion (27%) of patients who were prescribed oral drugs changed therapy than those prescribed a topical agent (17.5%; \(P < .001\)).

Costs Associated with Rosacea Treatment
The treatment of rosacea incurred primarily pharmacy rather than medical costs. The median annual pharmacy costs, by type of therapy, were:
- $285 for combination therapy
- $142 for a topical medication
- $63 for an oral antibiotic agent.

The median annual rosacea-related medical costs were $0. Of note, prescribing patterns varied according to the medical specialty of the treating physician. Dermatologists were more likely to prescribe oral antibiotics and combination therapies, whereas nondermatologists were more likely to prescribe topical therapies.

Treatment by a dermatologist also was associated with higher costs overall. The median annual pharmacy-related costs per patient were $154 for dermatologists and $137 for nondermatologists; the median rosacea-related medical costs were $37 for dermatologists and $0 for nondermatologists.

When considered by type of drug prescribed, the median annual cost per drug type was significantly different, based on the type of prescriber:
- Oral antibiotic: $83 when prescribed by a dermatologist versus $46 (\(P < .001\)) by a nondermatologist
- Topical medications: $143 versus $137 (\(P < .001\)), respectively
- Combination therapy: $302 versus $256 (\(P < .001\)), respectively.

The various cost and utilization analyses in this study
show that “specialist care was associated with more complex treatments, higher costs, and additional physician visits,” Dr Kendall and Dr Preston concluded.

The various cost and utilization analyses in this study show that “specialist care was associated with more complex treatments, higher costs, and additional physician visits.”

**Skin Conditions Top Reason for Medical Visits**

Dermatologic conditions are often not on a payer’s radar, because the management of skin conditions has not been perceived as a major driver of healthcare utilization and costs. However, the results of a new study may require payers to revise their approach to skin conditions, in light of this new study, which indicates that the general public’s concern about skin conditions is the most common reason to visit a physician in the United States.

Researchers from the Mayo Clinic conducted an extensive review of a large database of 142,377 residents of Olmsted County, MN, in 2009. The study captured adult residents in 2009 and reached a rather unpredictable conclusion—more patients seek medical help for skin disorders than for back pain, colds, arthritis, and other common ailments.² The researchers were surprised to find that the most prevalent nonacute conditions are not age-related chronic conditions, such as diabetes or heart disease, but are instead conditions that affect men and women equally at all age-groups.

These disorders include, in this order, skin disorders, osteoarthritis and joint disorders, back problems, lipid disorders, and upper respiratory tract disease (excluding asthma).² “Unexpectedly, almost half of the Olmsted County population of all ages received a diagnosis of skin disorders within approximately 5 years,” Sauver and colleagues observed. “Skin disorders are not typically major drivers of disability or death but may be important determinants of healthcare utilization and cost.”² They also noted that many dermatologic conditions require continued follow-up and treatment.

When grouped according to age, skin disorders were the most prevalent (32.9%) for the youngest age-group (ie, newborn-18 years) in both sexes. This frequency steadily rose across the life span; resulting in 38.2% for the 19- to 29-year age-group, 41.3% for the 30- to 49-year age-group, 50.4% for the group aged 50 to 64 years, and 65.7% for patients aged ≥65 years.²

According to the investigators, the “finding that skin and back problems are major drivers of healthcare utilization affirms the importance of moving beyond the commonly recognized health care priorities….Our findings highlight opportunities to improve healthcare and decrease costs related to common nonacute conditions as we move forward through the changing healthcare landscape.”²

This study sheds new light on the potential role of dermatologic conditions in healthcare utilization and costs and may suggest that payers reexamine their approach to skin conditions, including rosacea, as an increasing and significant driver of healthcare utilization and costs, especially in light of the introduction of new therapies for a variety of skin conditions.

**Reference**

1. Kendall JD, Preston NJ. Treatment patterns and costs associated with rosacea in the United States. Poster presented at the Academy of Managed Care Pharmacy Nexus meeting; San Antonio, TX; October 15-18, 2013.
In the fight against active, autoantibody-positive systemic lupus erythematosus (SLE) in adult patients receiving standard therapy

Add BENLYSTA to Help Make SLE More Manageable

When added to standard therapy, BENLYSTA significantly reduced disease activity vs standard therapy alone at Week 521

- BENLYSTA 10 mg/kg + standard therapy demonstrated superior efficacy vs placebo + standard therapy in reducing disease activity at Week 52 in 2 Phase III trials (Total N=1684)1-3
- The primary endpoint was the percentage of patients meeting the SLE Responder Index (SRI) at Week 52. The SRI components measure reduction in disease activity defined as clinical improvement (SELENA-SLEDAI*) with no significant worsening in any organ system (BILAG†) and no worsening in overall patient condition (PGA‡)1
  - A Phase II trial (Total N=449) did not meet the prespecified co-primary endpoints of percent change in SELENA-SLEDAI at Week 24 and time to first flare over 52 weeks. The Phase II trial led to the selection of a targeted autoantibody-positive population in the Phase III trials (28% of the Phase II trial population was autoantibody negative at baseline)4
- In Phase II and III clinical trials, 1458 patients with SLE have been exposed to BENLYSTA for a total of 1516 patient-years2-5

* SELENA-SLEDAI (Safety of Estrogens in Lupus Erythematosus: National Assessment Version of the Systemic Lupus Erythematosus Disease Activity Index).
† BILAG (British Isles Lupus Assessment Group).
‡ PGA (Physician’s Global Assessment).

Indication
BENLYSTA is indicated for the treatment of adult patients with active, autoantibody-positive, systemic lupus erythematosus (SLE) who are receiving standard therapy.

Limitations of Use: The efficacy of BENLYSTA has not been evaluated in patients with severe active lupus nephritis or severe active central nervous system lupus. BENLYSTA has not been studied in combination with other biologics or intravenous cyclophosphamide. Use of BENLYSTA is not recommended in these situations.

How supplied: BENLYSTA is available as 120 mg in a 5-mL single-use vial and 400 mg in a 20-mL single-use vial for injection, for intravenous use only.

Important Safety Information for BENLYSTA

CONTRAINDICATION
BENLYSTA is contraindicated in patients who have had anaphylaxis with belimumab.

WARNINGS AND PRECAUTIONS

MORTALITY
There were more deaths reported with BENLYSTA than with placebo during the controlled period of the clinical trials. Out of 2133 patients in 3 clinical trials, a total of 14 deaths occurred in the following groups: 3/675 in placebo, 5/673 in BENLYSTA 1 mg/kg, 0/111 in BENLYSTA 4 mg/kg, and 6/674 in BENLYSTA 10 mg/kg. No single cause of death predominated. Etiologies included infection, cardiovascular disease, and suicide.

SERIOUS INFECTIONS
Serious and sometimes fatal infections have been reported in patients receiving immunosuppressive agents, including BENLYSTA. Caution should be exercised when considering use in patients with a history of chronic infections. Patients receiving therapy for a chronic infection should not receive BENLYSTA. Consider interrupting BENLYSTA therapy in patients who develop a new infection while receiving BENLYSTA. The most frequent serious infections included pneumonia, urinary tract infection, cellulitis, and bronchitis.

Please see additional Important Safety Information for BENLYSTA on following page.
Please see Brief Summary of Prescribing Information for BENLYSTA on adjacent pages.
Important Safety Information for BENLYSTA (cont’d)

WARNINGS AND PRECAUTIONS (cont’d)

MALIGNANCY
The impact of treatment with BENLYSTA on the development of malignancies is not known. As with other immunomodulating agents, the mechanism of action of BENLYSTA could increase the risk of malignancies.

HYPERSENSITIVITY REACTIONS (INCLUDING ANAPHYLAXIS) AND INFUSION REACTIONS
Hypersensitivity reactions, including anaphylaxis and death, have been reported with BENLYSTA. Delay in the onset of acute hypersensitivity reactions has been observed. Patients with a history of multiple drug allergies or significant hypersensitivity may be at increased risk. Some patients received premedication; however, there is insufficient evidence to determine whether premedication diminishes the frequency or severity of these reactions.

Healthcare providers should be aware of the risk of hypersensitivity reactions, which may present as infusion reactions, and monitor patients closely. Manifestations of hypersensitivity included hypotension, angioedema, urticaria or other rash, pruritus, and dyspnea. In the event of a serious hypersensitivity reaction, discontinue BENLYSTA immediately and administer appropriate medical therapy. Infusion-associated adverse events were also reported. Serious infusion reactions included bradycardia, myalgia, headache, rash, urticaria, and hypotension. In the event of an infusion reaction, the infusion rate may be slowed or interrupted.

Patients should be informed of the signs and symptoms of a hypersensitivity reaction and instructed to seek immediate medical care should a reaction occur.

DEPRESSION
In clinical trials, psychiatric events (primarily depression, insomnia, and anxiety) were reported more frequently with BENLYSTA than with placebo. Serious psychiatric events, serious depression, and two suicides were also reported. It is unknown if BENLYSTA treatment is associated with increased risk for these events. Instruct patients to contact their healthcare provider if they experience new or worsening depression, suicidal thoughts, or other mood changes.

IMMUNIZATION
Live vaccines should not be given for 30 days before or concurrently with BENLYSTA. BENLYSTA may interfere with the response to immunizations.

USE WITH BIOLOGIC THERAPIES OR IV CYCLOPHOSPHAMIDE
BENLYSTA has not been studied in combination with other biologic therapies, including B-cell targeted therapies, or IV cyclophosphamide. Therefore, use of BENLYSTA is not recommended in combination with these therapies.

ADVERSE REACTIONS
The most commonly reported adverse reactions (≥5%) were nausea, diarrhea, pyrexia, nasopharyngitis, bronchitis, insomnia, pain in extremity, depression, migraine, and pharyngitis.

Other Important Information for BENLYSTA

USE IN SPECIFIC POPULATIONS

Pregnancy: Category C. BENLYSTA should be used during pregnancy only if the potential benefit outweighs the risk. Women of childbearing potential should use adequate contraception during BENLYSTA treatment and for at least 4 months after the last dose.

Pregnancy Registry: Healthcare professionals are encouraged to register patients and pregnant women are encouraged to enroll themselves by calling 1-877-681-6296.

Effect in black/African American patients: In exploratory analyses of 2 Phase III trials, response rates were lower for black patients (N=148) in the BENLYSTA group relative to black patients in the placebo group. In the Phase II trial, black patients (N=106) in the BENLYSTA group did not appear to have a different response than the rest of the study population. Although no definitive conclusions can be drawn from these analyses, caution should be used when considering BENLYSTA for black/African American patients.


Please see Brief Summary of Prescribing Information for BENLYSTA on adjacent pages.
INDICATIONS AND USAGE

BENLYSTA® (belimumab) is indicated for the treatment of adult patients with active, autoantibody-positive, systemic lupus erythematosus (SLE) who are receiving standard therapy.

Limitations of Use

The effect of BENLYSTA has not been evaluated in patients with severe active lupus nephritis or severe active central nervous system lupus. BENLYSTA has not been studied in combination with other biologics or intravenous cyclophosphamide. Use of BENLYSTA is not recommended in these situations.

CONTRAINDICATIONS

BENLYSTA is contraindicated in patients who have had anaphylaxis with belimumab.

WARNINGS AND PRECAUTIONS

Mortality

There were more deaths reported with BENLYSTA than with placebo during the controlled period of the clinical trials. Out of 2133 patients in 3 clinical trials, a total of 14 deaths occurred during the placebo-controlled, double-blind treatment periods: 3/675 (0.4%), 5/673 (0.7%), 0/111 (0%), and 6/674 (0.9%) deaths in the placebo, BENLYSTA 1 mg/kg, BENLYSTA 4 mg/kg, and BENLYSTA 10 mg/kg groups, respectively. No single cause of death predominated. Etiologies included infection, cardiovascular disease and suicide.

Serious Infections

Serious and sometimes fatal infections have been reported in patients receiving immunosuppressive agents, including BENLYSTA. Physicians should exercise caution when considering the use of BENLYSTA in patients with chronic infections. Patients receiving any therapy for chronic infection should not begin therapy with BENLYSTA. Consider interrupting BENLYSTA therapy in patients who develop a new infection while undergoing treatment with BENLYSTA and monitor these patients closely.

In the controlled clinical trials, the overall incidence of infections was 71% in patients treated with BENLYSTA compared with 67% in patients who received placebo. The most frequent infections (>5% of patients receiving BENLYSTA) were upper respiratory tract infection, sinusitis, bronchitis, and pneumonia. The most frequent serious infections included pneumonia, urinary tract infection, cellulitis, and bronchitis. Infections leading to discontinuation of treatment occurred in 0.7% of patients receiving BENLYSTA and 1.0% of patients receiving placebo. Infections resulting in death occurred in 0.3% (4/1458) of patients treated with BENLYSTA and in 0.1% (1/675) of patients receiving placebo.

Malignancy

The impact of treatment with BENLYSTA on the development of malignancies is not known. In the controlled clinical trials, malignancies (including non-melanoma skin cancers) were reported in 0.4% of patients receiving BENLYSTA and 0.4% of patients receiving placebo. In the controlled clinical trials, malignancies, excluding non-melanoma skin cancers, were observed in 0.2% (3/1458) and 0.3% (2/675) of patients receiving BENLYSTA and placebo, respectively. As with other immunomodulating agents, the mechanism of action of BENLYSTA could increase the risk for the development of malignancies.

Hypersensitivity Reactions, including Anaphylaxis

Hypersensitivity reactions, including anaphylaxis and death, have been reported in association with BENLYSTA. Delay in the onset of acute hypersensitivity reactions has been observed. Limited data suggest that patients with a history of multiple drug allergies or significant hypersensitivity may have a more frequent or severe reaction at increased risk. In the controlled clinical trials, hypersensitivity reactions (occurring on the same day of infusion) were reported in 13% (191/1458) of patients receiving BENLYSTA and 11% (76/675) of patients receiving placebo. Anaphylaxis was observed in 0.6% (9/1458) of patients receiving BENLYSTA and 0.4% (3/675) of patients receiving placebo. Manifestations included hypotension, angioedema, urticaria or other rash, pruritus, and dyspnea. Due to overlap in signs and symptoms, it was not possible to distinguish between hypersensitivity reactions and infusion reactions requiring infusion therapy.

Some patients (13%) received prednisone, which may have mitigated or masked a hypersensitivity response, however, there is insufficient evidence to determine whether predmedication diminishes the frequency or severity of hypersensitivity reactions.

BENLYSTA should be administered by healthcare providers prepared to manage anaphylactic reactions. In the event of a serious reaction, administration of BENLYSTA must be discontinued immediately and appropriate medical therapy administered. Patients should be monitored during and for an appropriate period of time after administration of BENLYSTA. Patients should be informed of the signs and symptoms of a hypersensitivity reaction and instructed to seek immediate medical care should a reaction occur.

Infusion Reactions

In the controlled clinical trials, adverse events associated with the infusion (occurring on the same day of the infusion) were reported in 17% (251/1458) of patients receiving BENLYSTA and 15% (99/675) of patients receiving placebo. Serious infusion reactions (excluding hypersensitivity reactions) were reported in 0.5% of patients receiving BENLYSTA and 0.4% of patients receiving placebo and included bradycardia, myalgia, headache, rash, urticaria, and hypotension. The most common infusion reactions (≥ 3% of patients receiving BENLYSTA) were headache, nausea, and skin reactions. Due to overlap in signs and symptoms, it was not possible to distinguish between hypersensitivity reactions and infusion reactions in all cases [see Warnings and Precautions]. Some patients (13%) received premedication, which may have mitigated or masked an infusion reaction; however there is insufficient evidence to determine whether predmedication diminishes the frequency or severity of infusion reactions [see Adverse Reactions].

BENLYSTA should be administered by healthcare providers prepared to manage infusion reactions. The infusion rate may be slowed or interrupted if the patient develops an infusion reaction. Healthcare providers should be aware of the risk of hypersensitivity reactions, which may present as infusion reactions, and monitor patients closely.

Depression

In the controlled clinical trials, psychiatric events were reported more frequently with BENLYSTA (16%) than with placebo (12%), related primarily to depression-related events (6.3% BENLYSTA and 4.7% placebo), insomnia (6.0% BENLYSTA and 5.3% placebo), and anxiety (3.9% BENLYSTA and 2.6% placebo). Serious psychiatric events were reported in 0.6% of patients receiving BENLYSTA (0.6% and 1.2% with 1 and 10 mg/kg, respectively) and 0.4% of patients receiving placebo. Serious depression was reported in 0.4% (6/1458) of patients receiving BENLYSTA and 0.1% (1/675) of patients receiving placebo. Two suicides (0.1%) were reported in patients receiving BENLYSTA. The majority of patients who reported serious depression or suicide had a history of depression or other mood disorders, and most were receiving psychoactive medications. It is unknown if BENLYSTA treatment is associated with increased risk for these events.

Patients receiving BENLYSTA should be instructed to contact their healthcare provider if they experience new or worsening depression, suicidal thoughts, or other mood changes.

Immunization

Live vaccines should not be given for 30 days before or concurrently with BENLYSTA. This safety data has not been established. No data are available on the secondary transmission of infection from persons receiving live vaccines to patients receiving BENLYSTA or the effect of BENLYSTA on new immunizations. Because of its mechanism of action, BENLYSTA may interfere with the response to immunizations.

Concomitant Use with Other Biologic Therapies or Intravenous Cyclophosphamide

BENLYSTA has not been studied in combination with other biologic therapies, including B-cell targeted therapies, or intravenous cyclophosphamide. Therefore, use of BENLYSTA is not recommended in combination with biologic therapies or intravenous cyclophosphamide.

ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Clinical Trials Experience

The data described below reflect exposure to BENLYSTA plus standard of care compared with placebo plus standard of care in 2133 patients in 3 controlled studies. Patients received BENLYSTA at doses of 1 mg/kg (N=673), 4 mg/kg (N=111; Trial 1 only), or 10 mg/kg (N=674) or placebo (N=675) intravenously over a 1-hour period on Days 0, 14, 28, and then every 28 days. In two of the studies (Trial 1 and Trial 3), treatment was given for 48 weeks, while in the other study (Trial 2) treatment was given for 72 weeks [see Clinical Studies]. Because there was no apparent dose-related increase in the majority of adverse events observed with BENLYSTA, the data summarized below are presented for the 3 doses pooled, unless otherwise indicated; the adverse reaction table displays the results for the recommended dose of 10 mg/kg compared with placebo.

The population had a mean age of 39 (range 18-75), 94% were female, and 52% were Caucasian. In these trials, 93% of patients treated with BENLYSTA reported an adverse reaction compared with 92% treated with placebo.

The most common serious adverse reactions were serious infections (6.0% and 5.2% in the groups receiving BENLYSTA and placebo, respectively) [see Warnings and Precautions]. The most commonly-reported adverse reactions, occurring in ≥5% of patients in clinical trials worldwide, included: fatigue, dyspnea, headache, nausea, arthralgia, abdominal pain, and upper respiratory tract infection.

The proportion of patients who discontinued treatment due to any adverse reaction during the controlled clinical trials was 6.2% for patients receiving BENLYSTA and 7.1% for patients receiving placebo. The most common adverse reactions resulting in discontinuation of treatment (≥1% of patients receiving BENLYSTA or placebo) were infections (1.6% BENLYSTA and 0.9% placebo), lupus nephritis (0.7% BENLYSTA and 1.2% placebo), and infections (0.7% BENLYSTA and 1.0% placebo).

Brief summary of Prescribing Information continued on reverse.
Table 1 lists adverse reactions, regardless of causality, occurring in at least 3% of patients with SLE who received BENLYSTA 10 mg/kg and at an incidence at least 1% greater than that observed with placebo in the 3 controlled studies.

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>BENLYSTA 10 mg/kg + Standard of Care (n = 674) %</th>
<th>Placebo + Standard of Care (n = 675) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>Pyrexia</td>
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<td>8</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
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<td>7</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Insomnia</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>6</td>
<td>4</td>
</tr>
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<td>2</td>
</tr>
<tr>
<td>Gastroenteritis viral</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>

Immunogenicity

In Trials 2 and 3, anti-belimumab antibodies were detected in 4 of 563 (0.7%) patients receiving BENLYSTA 10 mg/kg and in 27 of 559 (4.8%) patients receiving BENLYSTA 1 mg/kg. The reported frequency for the group receiving 10 mg/kg may underestimate the actual frequency due to lower assay sensitivity in the presence of high drug concentrations. Neutralizing antibodies were detected in patients receiving BENLYSTA 1 mg/kg. Three patients with anti-belimumab antibodies experienced mild infusion reactions of nausea, erythema, rash, pruritus, eyelid edema, headache, and dyspnea; none of the reactions was life-threatening. The clinical relevance of the presence of anti-belimumab antibodies is not known.

The data reflect the percentage of patients whose test results were positive for antibodies to belimumab in specific assays. The observed incidence of antibody positivity in an assay is highly dependent on several factors, including assay sensitivity and specificity, assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to belimumab with the incidence of antibodies to other products may be misleading.

DRUG INTERACTIONS

Formal drug interaction studies have not been performed with BENLYSTA. In clinical trials of patients with SLE, BENLYSTA was administered concomitantly with other drugs, including corticosteroids, antimalarials, immunomodulatory and immunosuppressive agents (including azathioprine, methotrexate, and mycophenolate), angiotensin pathway antagonists, HMG-CoA reductase inhibitors (statins), and NSAIDs without evidence of a clinically meaningful effect of these concomitant medications on belimumab pharmacokinetics. The effect of belimumab on the pharmacokinetics of other drugs has not been evaluated (see Pharmacokinetics).

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category C. There are no adequate and well-controlled clinical studies using BENLYSTA in pregnant women. Immunglobulin G (IgG) antibodies, including BENLYSTA, can cross the placenta. Because animal reproduction studies are not always predictive of human response, BENLYSTA should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus. Women of childbearing potential should be advised of the potential for fetal harm if belimumab is administered during pregnancy. Women of childbearing potential should be asked if they have a history of delivery before the final treatment. Nonclinical reproductive studies have been performed in pregnant cynomolgus monkeys receiving belimumab at doses of 0, 5, and 150 mg/kg by intravenous infusion (the high dose was approximately 9 times the anticipated maximum human exposure) every 2 weeks from gestation day 20 to 150. Belimumab was shown to cross the placenta. Belimumab was not associated with direct or indirect teratogenicity under the conditions tested. Fetal deaths were observed in 14%, 24%, and 15% of pregnant females in the 0, 5, and 150 mg/kg groups, respectively. Infant deaths occurred with an incidence of 0%, 8%, and 5%. The cause of fetal and infant deaths is not known. The relevance of these findings to humans is not known. Other treatment-related findings were limited to the expected reversible reduction of B cells in both dams and infants and reversible reduction of IgM in infant monkeys. B-cell numbers recovered after the cessation of belimumab treatment by about 1 year post-partum in adult monkeys and by 3 months of age in infant monkeys. IgM levels in infants exposed to belimumab in utero recovered by 6 months of age.

Pregnancy Registry: To monitor maternal-fetal outcomes of pregnant women exposed to BENLYSTA, a pregnancy registry has been established. Healthcare professionals are encouraged to register patients and pregnant women are encouraged to enroll themselves by calling 1-877-681-6296.

Nursing Mothers

It is not known whether BENLYSTA is excreted in human milk or absorbed systemically after ingestion. However, belimumab was excreted into the milk of cynomolgus monkeys. Because maternal antibodies are excreted in human breast milk, a decision should be made whether to discontinue breastfeeding or to discontinue the drug, taking into account the importance of breastfeeding to the infant and the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness of BENLYSTA have not been established in children.

Geriatric Use

Clinical studies of BENLYSTA did not include sufficient numbers of subjects aged 65 or over to determine whether they respond differently from younger subjects. Use with caution in elderly patients.

Race

In Trial 2 and Trial 3, response rates for the primary endpoint were lower for black subjects in the BENLYSTA group relative to black subjects in the placebo group (see Clinical Studies). Use with caution in black/African-American patients.

OVERDOSAGE

There is no clinical experience with overdosage of BENLYSTA. Two doses of up to 20 mg/kg have been given by intravenous infusion to humans with no increase in incidence or severity of adverse reactions compared with doses of 1, 4, or 10 mg/kg.

PATIENT COUNSELING INFORMATION

See Medication Guide.

Advice for the Patient

Patients should be given the Medication Guide for BENLYSTA and provided an opportunity to read it prior to each treatment session. It is important that the patient’s overall health be assessed at each infusion visit and any questions resulting from the patient’s reading of the Medication Guide be discussed.

Mortality: Patients should be advised that more patients receiving BENLYSTA in the main clinical trials died than did patients receiving placebo treatment [see Warnings and Precautions].

Serious Infections: Patients should be advised that BENLYSTA may decrease their ability to fight infections. Patients should be asked if they have a history of chronic infections and if they are currently on any therapy for an infection [see Warnings and Precautions]. Patients should be instructed to tell their healthcare provider if they develop signs or symptoms of an infection.

Hypersensitivity/Anaphylactic and Infusion Reactions: Educate patients on the signs and symptoms of anaphylaxis, including wheezing, difficulty breathing, peri-oral or lingual edema, and rash. Patients should be instructed to immediately tell their healthcare provider if they experience symptoms of an allergic reaction during or after the administration of BENLYSTA [see Warnings and Precautions].

Depression: Patients should be instructed to contact their healthcare provider if they experience new or worsening depression, suicidal thoughts or other mood changes. [see Warnings and Precautions].

Immunizations: Patients should be informed that they should not receive live vaccines while taking BENLYSTA. Response to vaccinations could be impaired by BENLYSTA [see Warnings and Precautions].

Pregnancy and Nursing Mothers: Patients should be informed that BENLYSTA has not been studied in pregnant women or nursing mothers so the effects of BENLYSTA on pregnant women or nursing infants are not known. Patients should be instructed to tell their healthcare provider if they are pregnant, become pregnant, or are thinking about becoming pregnant [see Use in Specific Populations]. Patients should be instructed to tell their healthcare provider if they plan to breastfeed their infant [see Use in Specific Populations].

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Manufactured by: Human Genome Sciences, Inc.
Rockville, Maryland 20850
U.S. License No. 1820
Marketed by: GlaxoSmithKline
Research Triangle Park, NC 27709

Table 2: Incidence of Adverse Reactions Occurring in at Least 3% of Patients Treated With BENLYSTA 10 mg/kg Plus Standard of Care and at Least 1% More Frequently Than in Patients Receiving Placebo plus Standard of Care in 3 Controlled SLE Studies

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<td>Bronchitis</td>
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