HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use CINQAIR safely and effectively. See full prescribing information for CINQAIR.

CINQAIR® (reslizumab) injection, for intravenous use
Initial U.S. Approval: 2016

WARNING: ANAPHYLAXIS
See full prescribing information for complete boxed warning.
• Anaphylaxis occurred with CINQAIR infusion in 0.3% of patients in placebo-controlled studies (5.1)
• Patients should be observed for an appropriate period of time after CINQAIR infusion; healthcare professionals should be prepared to manage anaphylaxis that can be life-threatening (5.1)
• Discontinue CINQAIR immediately if the patient experiences anaphylaxis (5.1)

INDICATIONS AND USAGE
CINQAIR is an interleukin-5 antagonist monoclonal antibody (IgG4 kappa) indicated for add-on maintenance treatment of patients with severe asthma aged 18 years and older, and with an eosinophilic phenotype (1).

Limitations of Use: CINQAIR is not indicated for:
• treatment of other eosinophilic conditions (1)
• relief of acute bronchospasm or status asthmaticus (1)

DOSAGE AND ADMINISTRATION
• CINQAIR is for intravenous infusion only. Do not administer as an intravenous push or bolus (2.1)
• CINQAIR should be administered in a healthcare setting by a healthcare professional prepared to manage anaphylaxis (2.2)
• Recommended dosage regimen is 3 mg/kg once every 4 weeks by intravenous infusion over 20-50 minutes (2.1)

FULL PRESCRIBING INFORMATION: CONTENTS*
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Dosing
2.2 Preparation and Administration Instructions
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINdicATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Anaphylaxis
5.2 Acute Asthma Symptoms or Deteriorating Disease
5.3 Malignancy
5.4 Reduction of Corticosteroid Dosage
5.5 Parasitic (Helminth) Infection
6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
6.2 Immunogenicity
7 DRUG INTERACTIONS

FULL PRESCRIBING INFORMATION

WARNING: ANAPHYLAXIS
Anaphylaxis has been observed with CINQAIR infusion in 0.3% of patients in placebo-controlled clinical studies. Anaphylaxis was reported as early as the second dose of CINQAIR (see Warnings and Precautions (5.1), Adverse Reactions (6)). Anaphylaxis can be life-threatening. Patients should be observed for an appropriate period of time after CINQAIR administration by a healthcare professional prepared to manage anaphylaxis. Discontinue CINQAIR immediately if the patient experiences signs or symptoms of anaphylaxis (see Dosage and Administration (2.2), Warnings and Precautions (5.1)).

1 INDICATIONS AND USAGE
CINQAIR® is indicated for the add-on maintenance treatment of patients with severe asthma aged 18 years and older with an eosinophilic phenotype (see Clinical Studies (14)).

Limitation of Use: CINQAIR is not indicated for:
• treatment of other eosinophilic conditions (1)
• relief of acute bronchospasm or status asthmaticus (1)

2 DOSAGE AND ADMINISTRATION
2.1 Dosing
CINQAIR is for intravenous infusion only. Do not administer as an intravenous push or bolus. The recommended dosage regimen is 3 mg/kg once every 4 weeks administered by intravenous infusion over 20-50 minutes [see Dosage and Administration (2.2)]. Discontinue the infusion immediately if the patient experiences a severe systemic reaction, including anaphylaxis [see Contraindications (4), Warnings and Precautions (5.1)].

2.2 Preparation and Administration Instructions
CINQAIR is provided as a solution in a single-use vial for intravenous infusion only and should be prepared by a healthcare professional using aseptic technique as follows: Preparation of intravenous infusion
1. Remove CINQAIR from the refrigerator. To minimize foaming, do not shake CINQAIR.
2. Inspect visually for particulate matter and discoloration prior to administration. CINQAIR solution is clear to slightly hazy/opalescent, colorless to slightly yellow liquid. Since CINQAIR is a protein, proteinaceous particles may be present in the solution that appear as translucent to white, amorphous particulates. Do not administer if discolored or if other foreign particulate matter is present.
3. Withdraw the proper volume of CINQAIR from the vial(s), based on the recommended weight-based dosage. Discard any unused portion.
4. Dissolve the lyophilized contents slowly into an infusion bag containing 50 mL of 0.9% Sodium Chloride Injection, USP to minimize foaming of CINQAIR (CINQAIR is compatible with polyvinylchloride (PVC) or polyolefin infusion bags). Gently invert the bag to mix the solution. Do not shake. Do not mix or dilute with other drugs.
5. Administer immediately after preparation. If not used immediately, store diluted solutions of CINQAIR in the refrigerator at 2°C to 8°C (36°F to 46°F) or at room temperature up to 25°C (77°F), protected from light, for up to 16 hours. The time between preparation of CINQAIR and administration should not exceed 16 hours.
6. Observe the patient over the infusion and for an appropriate period of time following administration instructions:
1. CINQAIR should be administered in a healthcare setting by a healthcare professional prepared to manage anaphylaxis [see Warnings and Precautions (5.1)].
2. If refrigerated prior to administration, allow the diluted CINQAIR solution to reach room temperature.
3. Use an infusion set with an in-line, low protein-binding filter (pore size of 0.2 micron). CINQAIR is compatible with polyethersulfone (PES), polyvinylidene fluoride (PVDF), nylon, and cellulose acetate in-line infusion filters.
4. Infuse the diluted solution of CINQAIR intravenously, over a 20-50 minute period. Infusion time may vary depending on the total volume to be infused as based upon patient weight.
5. Do not infuse CINQAIR concomitantly in the same intravenous line with other agents. No physical or biochemical compatibility studies have been conducted to evaluate the co-administration of CINQAIR with other agents.
6. Observe the patient over the infusion and for an appropriate period of time following infusion.
7. Upon completion of the infusion, flush the intravenous administration set with 0.9% Sodium Chloride Injection, USP to ensure that all CINQAIR has been administered.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.4 Pediatric Use
8.5 Geriatric Use

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

14 CLINICAL STUDIES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.
CINQAIR® (reslizumab) injection

3 DOSAGE FORMS AND STRENGTHS
Injection: 100 mg/10 mL (10 mg/mL), clear to slightly hazy/opalescent, colorless to slightly yellow solution in single-use vials.

4 CONTRAINDICATIONS
CINQAIR is contraindicated in patients who have known hypersensitivity to reslizumab or any of its excipients [see Warnings and Precautions (5.1)].

5 WARNINGS AND PRECAUTIONS
5.1 Anaphylaxis
Anaphylaxis to CINQAIR was reported in 0.3% of asthma patients in placebo-controlled clinical studies [see Adverse Reactions (6.1)]. These events were observed during or within 20 minutes after completion of the CINQAIR infusion and reported as early as the second dose of CINQAIR. Manifestations included dyspnea, decreased oxygen saturation, wheezing, vomiting, and skin and mucosal involvement, including urticaria. In 3 cases, CINQAIR was discontinued.

Anaphylaxis can be life-threatening. CINQAIR should be administered in a healthcare setting by a healthcare professional prepared to manage anaphylaxis. Patients should be observed for an appropriate period of time after CINQAIR administration. If severe systemic reactions, including anaphylaxis, occur, stop administration of CINQAIR immediately and provide appropriate medical treatment. Prior to discharge, inform patients of the signs and symptoms of anaphylaxis and instruct them to seek immediate medical care if symptoms occur. Discontinue CINQAIR use permanently if the patient experiences signs or symptoms of anaphylaxis [see Contraindications (5.1)].

CINQAIR should not be used to treat acute asthma symptoms or acute exacerbations. Do not use CINQAIR to treat acute bronchospasm or status asthmaticus. Patients should seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with CINQAIR.

5.2 Acute Asthma Symptoms or Deteriorating Disease
CINQAIR is not recommended for use in the acute treatment of asthma.[see Warnings and Precautions (5.3)].

5.3 Malignancy
Malignancy also occurred more commonly in the placebo group compared to the CINQAIR group [see Warnings and Precautions (5.4)].

In placebo-controlled studies, the population studied was 12 to 76 years of age, 62% female, and 73% of which were in the placebo-controlled studies. In the placebo-controlled asthma studies, the majority of malignancies were diagnosed within less than six months of exposure to CINQAIR.

6 ADVERSE REACTIONS
CINQAIR is not recommended for use in the acute treatment of asthma. CINQAIR should not be used to treat acute asthma symptoms or acute exacerbations. Do not use CINQAIR to treat acute bronchospasm or status asthmaticus. Patients should seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with CINQAIR.

5.4 Reduction of Corticosteroid Dosage
No clinical studies have been conducted to assess reduction of maintenance corticosteroid dosages following administration of CINQAIR. Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of therapy with CINQAIR. Reductions for in corticosteroid dose, if appropriate, should be gradual and performed under the supervision of a physician. Reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.

5.5 Parasitic (Helminth) Infection
Eosinophils may be involved in the immunological response to some helminth infections. Patients with known parasitic infections were excluded from participation in clinical studies. It is unknown if CINQAIR will influence the immune response against parasitic infections. Treat patients with pre-existing helminth infections before initiating therapy with CINQAIR and do not respond to anti-helminth treatment, discontinue treatment with CINQAIR and infuse until infection resolves.

6 ADVERSE REACTIONS
CINQAIR is not recommended for use in the acute treatment of asthma. CINQAIR should not be used to treat acute asthma symptoms or acute exacerbations. Do not use CINQAIR to treat acute bronchospasm or status asthmaticus. Patients should seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with CINQAIR.

The following adverse reactions are discussed in other sections of the labeling:

- Anaphylaxis [see Warnings and Precautions (5.1)].
- Malignancy [see Warnings and Precautions (5.3)].

6.1 Clinical Trials Experience
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 clinical practice.

Overall, 2195 subjects received at least 1 dose of CINQAIR. The data described below reflect exposure to CINQAIR in 1611 patients with asthma, including 1120 exposed for up to 16 weeks, 1006 exposed for 6 months, 759 exposed for 1 year, and 479 exposed for greater than 2 years. The adverse events occurring with CINQAIR are not unexpected given the use of CINQAIR in clinical trials. In the placebo-controlled studies, 1596 patients received the 3 mg/kg dose, 1028 in the placebo-controlled studies. Of the 1611 patients, 2195 patients received at least 1 dose of CINQAIR. The data described includes patients who were included in at least 1 clinical trial. The data described for a drug cannot be directly compared to the data described for another drug because different methodologies, sample handling, timing of sample collection, concomitant medication, and underlying disease. For these reasons, comparison of the incidence of antibodies to reslizumab with the incidence of antibodies to other products may be misleading.

6.2 Immunogenicity
As with all therapeutic proteins, there is a potential for immunogenicity. In placebo-controlled studies, a treatment-emergent anti-reslizumab antibody response developed in 53/983 (5.4%) of CINQAIR-treated patients (3 mg/kg). In the long-term, open-label study, treatment-emergent anti-reslizumab antibodies were detected in 49/1014 (4.8%) of CINQAIR-treated (3 mg/kg) asthma patients over 36 months. The antibody responses were of low titer and often transient. Neutralizing antibodies and product-specific IgG antibodies were not evaluated. There was no detectable impact of the antibodies on the clinical pharmacokinetics, pharmacodynamics, clinical efficacy, and safety of CINQAIR [see Clinical Pharmacology (12.2)]. The data reflect the percentage of patients whose test results were positive for antibody response to reslizumab in specific assays. The observed incidence of antibody response is highly dependent on several factors, including assay sensitivity and specificity, assay methodology, sample handling, timing of sample collection, concomitant medication, and underlying disease. For these reasons, comparison of the incidence of antibodies to reslizumab with the incidence of antibodies to other products may be misleading.

7 DRUG INTERACTIONS
No formal clinical drug interaction studies have been performed with CINQAIR.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Risk Summary
The data on pregnancy exposure from the clinical trials are insufficient to inform on drug-associated risk. Monoclonal antibodies, such as reslizumab, are transported across the placenta and may have the potential to affect the developing fetus. Data from animal studies indicate that the estimated background risk of major birth defects and miscarriage for the indicated population is similar to that of the general population. All pregnancies have a background risk of major birth defects, miscarriage, and other pregnancy-related problems. A woman should not be pregnant while receiving CINQAIR.

Animal Data
In 2 separate embryo-fetal development studies, pregnant mice and rabbits received a single reslizumab dose during the period of organogenesis to pregnant mice and rabbits at doses that produced exposures up to approximately 6 times the exposure at the maximum recommended human dose (MRHD) in mice and approximately 17 times the exposure at the MRHD in rabbits [see Data]. The estimated background risk of major birth defects and miscarriage for the indicated population is similar to that of the general population. The incidence of major birth defects in humans is approximately 2% to 4% and the incidence of miscarriage in the general population is approximately 15 to 20%, respectively. In animal studies, reslizumab was present in the mammary gland in lactating rats. Anaphylaxis can be life-threatening. CINQAIR should be administered only to pregnant women if the potential benefit justifies the potential risk to the fetus. There are no adequate and well-controlled studies in pregnant women. If CINQAIR is used during pregnancy, or if the patient becomes pregnant while taking CINQAIR, instruct the patient of the potential risk to the fetus. Pregnant women should be closely monitored in pregnancy and treatment adjusted as necessary to maintain optimal control.

Data
Animal Data
In 2 separate embryo-fetal development studies, pregnant mice and rabbits received a single reslizumab dose during the period of organogenesis to pregnant mice and rabbits at doses that produced exposures up to approximately 6 times the exposure at the maximum recommended human dose (MRHD) in mice and approximately 17 times the exposure at the MRHD in rabbits [see Data]. The estimated background risk of major birth defects and miscarriage for the indicated population is similar to that of the general population. All pregnancies have a background risk of major birth defects, miscarriage, and other pregnancy-related problems. A woman should not be pregnant while receiving CINQAIR.

8.2 Lactation
Risk Summary
It is not known whether reslizumab is present in human milk, and the effects of reslizumab on the breastfed infant and on milk production are not known. However, human IgG is known to be present in human milk. Reslizumab was present in the milk of lactating mice following dosing during pregnancy [see Data]. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for CINQAIR and any potential adverse effects on the breastfed child from CINQAIR or the underlying maternal condition.
CINQAIR® (reslizumab) injection

Data
Reslizumab was excreted in milk of lactating CD-1 mice that received reslizumab at 10 or 50 mg/kg (1.5 and 6 times the exposures achieved at the MRHD on an AUC basis) during pregnancy on gestation days 6 and 18 and on postnatal day 14. Levels of reslizumab in milk were approximately 5-7% of maternal serum concentrations.

8.4 Pediatric Use
CINQAIR is not indicated for use in pediatric patients less than 18 years of age. The safety and effectiveness in pediatric patients (aged 17 years and younger) have not been established.

CINQAIR was evaluated in 39 patients aged 12 to less than 18 years with asthma in two 52-week exacerbation studies and one 16-week lung function study. In the exacerbation studies, patients were required to have at least 1 asthma exacerbation requiring systemic corticosteroid use in the year prior to study entry. In these studies, the asthma exacerbation rate was higher in adolescent patients treated with CINQAIR than placebo (CINQAIR = 14, rate 2.86, 95% CI [1.02 to 8.09] and placebo = 11, rate 1.37, 95% CI [0.57 to 3.28]; rate ratio 2.09, 95% CI [0.82 to 5.36]).

8.5 Geriatric Use
CINQAIR was evaluated in 122 patients aged 65 years and older with asthma in two 52-week exacerbation studies and two 16-week lung function studies. No overall differences in safety or effectiveness were observed between these patients and younger patients. Based on available data, no adjustment of the dosage of CINQAIR in geriatric patients is necessary.

10 OVERDOSAGE
Single doses of up to 732 mg have been administered intravenously to subjects in clinical trials without evidence of dose-related toxicities. There is no specific treatment for an overdose with CINQAIR. If overdose occurs, the patient should be treated supportively with appropriate monitoring as necessary.

11 DESCRIPTION
CINQAIR (reslizumab) is a humanized interleukin-5 antagonist monoclonal antibody (IgG4κ). Reslizumab is produced by recombinant DNA technology in murine myeloma non-secret ing (NS0) cells. Reslizumab has a molecular weight of approxi mately 147 kDa.

CINQAIR is a sterile, preserve-free, clear to slightly hazy/opalescent, colorless to slightly yellow solution (injectable) for intravenous infusion. Since CINQAIR is a protein, proteinaceous particles may be present in the solution that appear as translucent to white, amorphous particulates. Each single-use vial contains 100 mg reslizumab in 10 mL. Each mL contains 10 mg of reslizumab, glacial acetic acid (0.12 mg), sodium acetate trihydrate (2.45 mg), and sucrose (76 mg), with a pH of 5.5.

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
Reslizumab is an interleukin-5 antagonist (IgG4, kappa). IL-5 is the major cytokine responsible for the growth and differentiation, recruitment, activation, and survival of eosinophils. Reslizumab binds to IL-5 with a dissociation constant of 61 pM, inhibiting the bioactivity of IL-5 by blocking its binding to the alpha chain of the IL-5 receptor complex expressed on the eosinophil surface. Inflammation is an important component in the pathogenesis of asthma. Multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, cytokines) are involved in inflammation. Reslizumab, by inhibiting the action of IL-5, reduces the production and survival of eosinophils; however, the mechanism of reslizumab action in asthma has not been definitively established.

12.2 Pharmacodynamics
In clinical studies with CINQAIR 3 mg/kg, reductions in blood eosinophil counts were observed following the first dose and maintained through 52 weeks of treatment with no signs of tachyphylaxis. Mean eosinophil counts were 696 cells/mcL (n=245) and 764 cells/mcL at baseline, and were 55 cells/mcL (92% reduction, n=212) at 52 weeks. Studies I and II were 52-week studies in 953 patients with asthma who were required to have a blood eosinophil count of at least 400/mcL (within 3 to 4 weeks of dosing), and at least 1 asthma exacerbation requiring systemic corticosteroid use over the past 12 months. The majority of patients (82%) were on medium-high dose inhaled corticosteroids plus a long-acting beta agonist (ICS/LABA) at baseline. Maintenance oral corticosteroids (OCS) (up to 10 mg of prednisone per day or equivalent) were allowed; 106 (11%) patients were on OCS at baseline. CINQAIR 3 mg/kg administered once every 4 weeks for a total of 12 doses was evaluated compared with placebo.

Study III
Study IV
Study V
Study IV was a 16-week study in 496 patients unselected for baseline blood eosinophil count of less than 400/mcL. Maintenance OCS were not allowed. CINQAIR 3 mg/kg or 0.3 mg/kg administered once every 4 weeks for a total of 4 doses was evaluated compared with placebo. While 2 doses of CINQAIR were studied, CINQAIR 3 mg/kg is the only recommended dose [see Dosage and Administration (2.1)].

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
In a 6-month bioassay, reslizumab was administered intravenously once every 2 weeks for 26 consecutive weeks (14 total doses) to Tg.rash2 mice at doses up to 516 mg/kg/dose. There was no evidence of carcinogenicity.

Published literature using animal models suggests that IL-5 and eosinophils are part of an early inflammatory reaction at the site of tumorigenesis and can promote tumor rejection. However, other reports indicate that eosinophil infiltration into tumors can promote tumor growth. Therefore, the malignancy risk in humans from an antibody to IL-5 such as reslizumab is unknown.

13.2 Nonclinical Toxicity
In a fertility study, administration of reslizumab to parental mice at doses up to 50 mg/kg (approximately 6 times the MRHD on an AUC basis) had no effects on male or female mating or fertility.

14 CLINICAL STUDIES
The asthma development program for CINQAIR 3 mg/kg (administered once every 4 weeks) included 4 randomized, double-blind, placebo-controlled studies (Studies I-IV) in clinical trials that included 981 patients 12 years of age and older. While patients aged 12 to 17 years were included in these trials, CINQAIR is not approved for use in this age group [see Use in Specific Populations (8.4)]. All subjects continued their background asthma therapy throughout the duration of the studies.

Studies I and II
Studies III and IV were 52-week studies in 953 patients with asthma who were required to have a blood eosinophil count of at least 400/mcL (within 3 to 4 weeks of dosing), and at least 1 asthma exacerbation requiring systemic corticosteroid use over the past 12 months. The majority of patients (82%) were on medium-high dose inhaled corticosteroids plus a long-acting beta agonist (ICS/LABA) at baseline. Maintenance oral corticosteroids (OCS) (up to 10 mg of prednisone per day or equivalent) were allowed; 106 (11%) patients were on OCS at baseline. CINQAIR 3 mg/kg administered once every 4 weeks for a total of 13 doses was evaluated compared with placebo.

Study I
Study II
Study III
Study IV
Study V
Study IV was a 16-week study in 496 patients unselected for baseline blood eosinophil levels (approximately 80% of patients had a screening [within 3 to 4 weeks of dosing] blood eosinophil count of less than 400/mcL). Maintenance OCS were not allowed. CINQAIR 3 mg/kg administered once every 4 weeks for a total of 4 doses was evaluated compared with placebo. The demographics and baseline characteristics of these 4 studies is provided in Table 1.
The time to first asthma exacerbation was significantly longer for the groups receiving CINQAIR 3 mg/kg compared to placebo in both Studies I and II. A representative figure from Study I is shown below (Figure 1). Study II showed similar results.

### Table 1: Demographics and Baseline Characteristics of Patients in Asthma Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Study I</th>
<th>Study II</th>
<th>Study III</th>
<th>Study IV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=489)</td>
<td>(N=464)</td>
<td>(N=315)</td>
<td>(N=498)</td>
</tr>
<tr>
<td>Mean age (yr)</td>
<td>47</td>
<td>47</td>
<td>44</td>
<td>45</td>
</tr>
<tr>
<td>Female (%)</td>
<td>63</td>
<td>63</td>
<td>58</td>
<td>64</td>
</tr>
<tr>
<td>White (%)</td>
<td>73</td>
<td>73</td>
<td>81</td>
<td>67</td>
</tr>
<tr>
<td>Duration of asthma, mean (yr)</td>
<td>19</td>
<td>18</td>
<td>20</td>
<td>26</td>
</tr>
<tr>
<td>Baseline Pre-bronchodilator FEV₁, mean % predicted</td>
<td>64</td>
<td>69</td>
<td>70</td>
<td>67</td>
</tr>
<tr>
<td>Baseline Reversibility, mean % ΔFEV₁ post-SABA</td>
<td>26</td>
<td>28</td>
<td>25</td>
<td>26</td>
</tr>
<tr>
<td>Baseline mean blood eosinophil count/mL</td>
<td>660</td>
<td>649</td>
<td>614</td>
<td>280</td>
</tr>
<tr>
<td>Mean number of exacerbations in previous year</td>
<td>1.99</td>
<td>1.94</td>
<td>2.03</td>
<td>1.86</td>
</tr>
</tbody>
</table>

* Baseline for lung function and eosinophil count is the day of randomization. FEV₁=forced expiratory volume in 1 second; SABA=short-acting beta agonist.

### Table 2: Frequency of Asthma Exacerbations during the 52-Week Treatment Period in Patients with Severe Asthma with an Eosinophilic Phenotype (Studies I and II)*

<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>Asthma Exacerbation Rate</th>
<th>Rate Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CINQAIR 3 mg/kg (N=245)</td>
<td>0.90</td>
<td>0.5 (0.37, 0.67)</td>
</tr>
<tr>
<td>Placebo (N=244)</td>
<td>1.80</td>
<td>1.60 (0.82, 0.95)</td>
</tr>
<tr>
<td>CINQAIR 3 mg/kg (N=232)</td>
<td>0.86</td>
<td>0.41 (0.28, 0.59)</td>
</tr>
<tr>
<td>Placebo (N=232)</td>
<td>2.11</td>
<td>2.22 (1.08, 4.54)</td>
</tr>
</tbody>
</table>

* Randomized patients

### Exacerbations requiring systemic corticosteroid use

<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>Asthma Exacerbation Rate</th>
<th>Rate Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CINQAIR 3 mg/kg (N=245)</td>
<td>0.72</td>
<td>0.45 (0.33, 0.62)</td>
</tr>
<tr>
<td>Placebo (N=244)</td>
<td>1.60</td>
<td>1.36 (0.94, 1.93)</td>
</tr>
<tr>
<td>CINQAIR 3 mg/kg (N=232)</td>
<td>0.65</td>
<td>0.39 (0.27, 0.58)</td>
</tr>
<tr>
<td>Placebo (N=232)</td>
<td>1.66</td>
<td>1.72 (1.14, 2.56)</td>
</tr>
</tbody>
</table>

### Exacerbations resulting in a hospitalization AND/OR emergency room visit

<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>Asthma Exacerbation Rate</th>
<th>Rate Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CINQAIR 3 mg/kg (N=245)</td>
<td>0.14</td>
<td>0.66 (0.32, 1.36)</td>
</tr>
<tr>
<td>Placebo (N=244)</td>
<td>0.21</td>
<td>0.55 (0.29, 0.96)</td>
</tr>
<tr>
<td>CINQAIR 3 mg/kg (N=232)</td>
<td>0.03</td>
<td>0.69 (0.29, 1.65)</td>
</tr>
<tr>
<td>Placebo (N=232)</td>
<td>0.05</td>
<td>1.06 (0.49, 2.31)</td>
</tr>
</tbody>
</table>

* Study IV studied asthma patients unscreened for blood eosinophils.

Lung Function

The effect of CINQAIR 3 mg/kg administered once every 4 weeks on spirometry was assessed in all 4 studies (Table 3). FEV₁ was the primary endpoint in the 16-week lung function studies (Study IV and Study IV). Study III also studied a lower dose, CINQAIR 0.3 mg/kg, that produced significant but numerically smaller changes in FEV₁ and blood eosinophil reduction compared to placebo. While 2 doses of CINQAIR were studied, CINQAIR 3 mg/kg is the only recommended dose (see Dosage and Administration (2.1)). Study IV was the only study to test CINQAIR 3 mg/kg in asthmatic patients unscreened for blood eosinophils (measured 3 to 4 weeks prior to dosing); association of treatment effect (i.e., difference between CINQAIR and placebo in the change in FEV₁ at Week 16) and baseline blood eosinophils was not observed.

### Table 3: Mean Change (95% CI) from Baseline in FEV₁ in mL Over 16 Weeks

<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>FEV₁ Change in mL (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CINQAIR 3 mg/kg (N=245)</td>
<td>0.90 (0.37, 0.67)</td>
</tr>
<tr>
<td>Placebo (N=244)</td>
<td>1.80 (0.33, 0.62)</td>
</tr>
<tr>
<td>CINQAIR 3 mg/kg (N=232)</td>
<td>0.86 (0.28, 0.59)</td>
</tr>
<tr>
<td>Placebo (N=232)</td>
<td>2.11 (0.41, 0.80)</td>
</tr>
<tr>
<td>CINQAIR 0.3 mg/kg (N=232)</td>
<td>0.65 (0.27, 0.58)</td>
</tr>
<tr>
<td>Placebo (N=232)</td>
<td>2.16 (0.41, 0.80)</td>
</tr>
<tr>
<td>CINQAIR 0.03 mg/kg (N=232)</td>
<td>0.03 (0.29, 1.65)</td>
</tr>
<tr>
<td>Placebo (N=232)</td>
<td>2.04 (0.33, 0.62)</td>
</tr>
</tbody>
</table>

* Study IV studied asthma patients unscreened for blood eosinophils.

Improvements in FEV₁ were observed at 4 weeks following the first dose of CINQAIR for Studies I and II and maintained through Week 52.

The Asthma Control Questionnaire-7 (ACQ-7) and Asthma Quality of Life Questionnaire (AQLQ) were both assessed in Studies I, II, and III. The responder rate for both measures was defined as an improvement in score of 0.5 or more as threshold over 16 weeks.

- For ACQ-7, the responder rate for those randomized to CINQAIR vs. placebo was 69% vs. 65% for Study I, 70% vs. 58% for Study II, and 64% vs. 58% for Study III.
- For AQLQ, the responder rate for those randomized to CINQAIR vs. placebo was 58% vs. 58% for Study I, 76% vs. 55% for Study II, and 64% vs. 48% for Study III.

### Figure 1: Time to First Asthma Exacerbation by Treatment Group in Patients with Severe Asthma with an Eosinophilic Phenotype (Study I)

#### Figure 2: Mean Change from Baseline in FEV₁ in Patients with Severe Asthma with an Eosinophilic Phenotype (Study III)

The Asthma Control Questionnaire-7 (ACQ-7) and Asthma Quality of Life Questionnaire (AQLQ) were both assessed in Studies I, II, and III. The responder rate for both measures was defined as an improvement in score of 0.5 or more as threshold over 16 weeks.

- For ACQ-7, the responder rate for those randomized to CINQAIR vs. placebo was 69% vs. 65% for Study I, 70% vs. 58% for Study II, and 64% vs. 58% for Study III.
- For AQLQ, the responder rate for those randomized to CINQAIR vs. placebo was 58% vs. 58% for Study I, 76% vs. 55% for Study II, and 64% vs. 48% for Study III.

### 16 HOW SUPPLIED/STORAGE AND HANDLING

CINQAIR (reslizumab) injection, 100 mg/10 mL (10 mg/mL), is supplied as a preservative-free, sterile, clear to slightly hazy/opalescent, colorless to slightly yellow solution in single-use vials.
17 PATIENT COUNSELING INFORMATION

See FDA approved patient labeling (Patient Information).

Hypersensitivity/Anaphylaxis

Inform patients that hypersensitivity reactions, including anaphylaxis, have occurred with administration of CINQAIR. Educate patients on the signs and symptoms of hypersensitivity reactions and anaphylaxis (e.g., skin or mucosal involvement, airway compromise, reduced blood pressure). Instruct patients to contact their healthcare professional immediately if they experience symptoms of an allergic reaction after they have received their infusion of CINQAIR [see Warnings and Precautions (5.1)].

Not for Acute Symptoms or Deteriorating Disease

Inform patients that CINQAIR does not treat acute asthma symptoms or acute exacerbations. Inform patients to seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with CINQAIR [see Warnings and Precautions (5.2)].

Malignancy

Counsel CINQAIR-treated patients about the risk of malignancies [see Warnings and Precautions (5.3)].

Reduction of Corticosteroid Dosage

Inform patients not to discontinue systemic or inhaled corticosteroids except under the direct supervision of a physician. Inform patients that reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy [see Warnings and Precautions (5.4)].

PATIENT INFORMATION

CINQAIR® (reslizumab) injection

(reslizumab) injection for intravenous use

What is the most important information I should know about CINQAIR?

CINQAIR can cause serious side effects, including:

Serious allergic reactions (anaphylaxis). Serious allergic reactions can happen right after you receive your CINQAIR infusion. These reactions can cause death. Allergic reactions sometimes do not happen right away. Your healthcare provider will watch you during and after you receive your CINQAIR infusion for any signs of a reaction. Tell your healthcare provider right away if you have any of the following symptoms that may be associated with an allergic reaction:

• breathing problems
• paleness
• flushing
• skin rash (hives)
• itching
• swelling of your face, lips, mouth, or tongue
• symptoms of low blood pressure (fainting, dizziness, light headedness, confusion, fast heart beat)
• nausea or abdominal discomfort

What is CINQAIR?

CINQAIR is a prescription medicine used with other asthma medicines for the maintenance treatment of asthma in people aged 18 years of age and older whose asthma is not controlled with the current asthma medicines. When added to other medicines for asthma, CINQAIR helps prevent severe asthma attacks (exacerbations) and can improve your breathing. Medicines such as CINQAIR reduce blood eosinophils. Eosinophils are a type of white blood cell that may contribute to your asthma.

• CINQAIR is not used to treat other problems caused by eosinophils.
• CINQAIR is not used to treat sudden breathing problems.

It is not known if CINQAIR is safe and effective in children less than 18 years of age.

What are the possible side effects of CINQAIR?

CINQAIR may cause serious side effects, including:

• See “What is the most important information I should know about CINQAIR?”
• abnormal growth of cells or tissue in your body that may or may not be cancer (malignancy)

The most common side effects of CINQAIR include:

• throat pain
• swelling of your face, lips, mouth, or tongue
• runny nose
• sneezing
• cough
• cold symptoms
• stomach pain
• vomiting
• diarrhea
• abdominal pain
• anemia

How will I receive CINQAIR?

You will be given CINQAIR by a healthcare provider using a needle placed in a vein (intravenous infusion) 1 time every 4 weeks. It will take about 20 to 50 minutes to receive the full dose of CINQAIR.

Before receiving CINQAIR, tell your healthcare provider about all of your medical conditions, including if you:

• are taking oral or inhaled corticosteroid medicines. Do not stop taking your corticosteroid unless your healthcare provider tells you to stop. This may cause other symptoms that were controlled by the corticosteroid medicine to come back.
• have or have had cancer (malignancy).
• have a parasitic (helminth) infection.
• are pregnant or plan to become pregnant. It is not known if CINQAIR will harm your unborn baby. Tell your healthcare provider if you become pregnant during your treatment with CINQAIR.
• are breastfeeding or plan to breastfeed. It is not known if CINQAIR passes into your breast milk. You and your healthcare provider should decide if you will receive CINQAIR and breastfeed. Talk to your healthcare provider about the best way to feed your baby if you receive CINQAIR.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of CINQAIR.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use CINQAIR for a condition for which it was not prescribed. You can ask your pharmacist or healthcare provider for information about CINQAIR that is written for healthcare professionals.

What are the ingredients in CINQAIR?

Active ingredient: reslizumab

Inactive ingredients: sodium acetate, acetic acid, sucrose

What is the most important information I should know about CINQAIR?

CINQAIR can cause serious side effects, including:

• See “What is the most important information I should know about CINQAIR?”
• abnormal growth of cells or tissue in your body that may or may not be cancer (malignancy)

The most common side effects of CINQAIR include:

• throat pain
• swelling of your face, lips, mouth, or tongue
• runny nose
• sneezing
• cough
• cold symptoms
• stomach pain
• vomiting
• diarrhea
• abdominal pain
• anemia

What will I receive CINQAIR as an injection for?

CINQAIR is an injection that is given into your vein (intravenous infusion).

How do I receive CINQAIR?

• CINQAIR is given as an injection into a vein every 4 weeks. Your healthcare provider will tell you how many injections to receive and when to receive them.

Do not receive CINQAIR if you are allergic to reslizumab or any of the ingredients in CINQAIR. See the end of this leaflet for a complete list of ingredients in CINQAIR.

What are the possible side effects of CINQAIR?

CINQAIR may cause serious side effects, including:

• See “What is the most important information I should know about CINQAIR?”
• abnormal growth of cells or tissue in your body that may or may not be cancer (malignancy)

The most common side effects of CINQAIR include:

• throat pain
• swelling of your face, lips, mouth, or tongue
• runny nose
• sneezing
• cough
• cold symptoms
• stomach pain
• vomiting
• diarrhea
• abdominal pain
• anemia

How will I receive CINQAIR?

• CINQAIR is given as an injection into a vein every 4 weeks. Your healthcare provider will tell you how many injections to receive and when to receive them.

Do not receive CINQAIR if you are allergic to reslizumab or any of the ingredients in CINQAIR. See the end of this leaflet for a complete list of ingredients in CINQAIR.

Before receiving CINQAIR, tell your healthcare provider about all of your medical conditions, including if you:

• are taking oral or inhaled corticosteroid medicines. Do not stop taking your corticosteroid unless your healthcare provider tells you to stop. This may cause other symptoms that were controlled by the corticosteroid medicine to come back.
• have or have had cancer (malignancy).
• have a parasitic (helminth) infection.
• are pregnant or plan to become pregnant. It is not known if CINQAIR will harm your unborn baby. Tell your healthcare provider if you become pregnant during your treatment with CINQAIR.
• are breastfeeding or plan to breastfeed. It is not known if CINQAIR passes into your breast milk. You and your healthcare provider should decide if you will receive CINQAIR and breastfeed. Talk to your healthcare provider about the best way to feed your baby if you receive CINQAIR.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

What are the possible side effects of CINQAIR?

CINQAIR may cause serious side effects, including:

• See “What is the most important information I should know about CINQAIR?”
• abnormal growth of cells or tissue in your body that may or may not be cancer (malignancy)

The most common side effects of CINQAIR include:

• throat pain
• swelling of your face, lips, mouth, or tongue
• runny nose
• sneezing
• cough
• cold symptoms
• stomach pain
• vomiting
• diarrhea
• abdominal pain
• anemia

What will I receive CINQAIR as an injection for?

CINQAIR is an injection that is given into your vein (intravenous infusion).

How do I receive CINQAIR?

• CINQAIR is given as an injection into a vein every 4 weeks. Your healthcare provider will tell you how many injections to receive and when to receive them.

Do not receive CINQAIR if you are allergic to reslizumab or any of the ingredients in CINQAIR. See the end of this leaflet for a complete list of ingredients in CINQAIR.

Before receiving CINQAIR, tell your healthcare provider about all of your medical conditions, including if you:

• are taking oral or inhaled corticosteroid medicines. Do not stop taking your corticosteroid unless your healthcare provider tells you to stop. This may cause other symptoms that were controlled by the corticosteroid medicine to come back.
• have or have had cancer (malignancy).
• have a parasitic (helminth) infection.
• are pregnant or plan to become pregnant. It is not known if CINQAIR will harm your unborn baby. Tell your healthcare provider if you become pregnant during your treatment with CINQAIR.
• are breastfeeding or plan to breastfeed. It is not known if CINQAIR passes into your breast milk. You and your healthcare provider should decide if you will receive CINQAIR and breastfeed. Talk to your healthcare provider about the best way to feed your baby if you receive CINQAIR.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.