CINQAIR® (reslizumab) injection, for intravenous use

INDICATIONS AND USAGE
CINQAIR is an interleukin-5 antagonist monoclonal antibody (IgG4 kappa) indicated for:

- the add-on maintenance treatment of patients with severe asthma aged 18 years and older, and with an eosinophilic phenotype (1).

Limitation of Use:

- CINQAIR is not indicated for treatment of other eosinophilic conditions (1).
- CINQAIR is not indicated for the relief of acute bronchospasm or status asthmaticus (1).

WARNINGS AND PRECAUTIONS

- Anaphylaxis: 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).

DOSAGE AND ADMINISTRATION

1. CINQAIR should be administered by a healthcare professional prepared to manage anaphylaxis. Discontinue CINQAIR immediately if the patient experiences a severe systemic reaction, including anaphylaxis [see Warnings and Precautions (5.1)].

2. Infuse the diluted solution of CINQAIR intravenously, over a 20 to 50 minute period. Seefull prescribing information for complete boxed warning.

3. Use an infusion set with an in-line, low protein-binding filter (pore size of 0.2 micron).

4. Dispense syringe contents slowly into an infusion bag containing 50 mL of 0.9% sodium chloride injection, USP to minimize foaming.

5. Keep the solution 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 from removal from the refrigerator to the start of infusion must be less than or equal to 16 hours. See full prescribing information for complete boxed warning.

6. Discard any unused portion.

ADVERSE REACTIONS

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)].

Indications

CINQAIR is indicated for the add-on maintenance treatment of patients with severe asthma aged 18 years and older, and with an eosinophilic phenotype. See full prescribing information for complete boxed warning.

Contraindications

- Known hypersensitivity to reslizumab or any of its excipients.

Warnings and Precautions

- Malignancy: Malignancies were observed in clinical studies. (5.3)
- Reduction in Corticosteroid Dosage: Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of therapy with CINQAIR. Decrease corticosteroids gradually, if appropriate. (5.4)
- Parasitic (Helminth) Infection: Treat patients with pre-existing helminth infections before therapy with CINQAIR. If patients become infected while receiving CINQAIR, do not discontinue CINQAIR and do not respond to anti-helminth treatment. Discontinue CINQAIR until the parasitic infection resolves. (5.5)

Reactions (6)

- Anaphylaxis: Anaphylaxis occurred with CINQAIR infusion in 0.3% of patients in placebo-controlled studies. [see Warnings and Precautions (5.1)].
- Inspect visually for particulate matter and discoloration prior to administration. (5.2)
- Dispense syringe contents slowly into an infusion bag containing 50 mL of 0.9% sodium chloride injection, USP to minimize foaming. (5.2)
- Do not shake CINQAIR. (5.2)
- CINQAIR solution is clear to slightly hazy/opalescent, colorless to slightly yellow colored. Discard any unused portion. (5.2)
- CINQAIR is compatible with polyethersulfone (PES), polyvinylidene fluoride (PVDF), nylon, and cellulose acetate in-line infusion filters. (5.2)
- CINQAIR is not compatible with polyvinyl chloride (PVC) or polyolefin infusion bags. (5.2)
- Gently invert the bag to mix the solution. Do not shake. Do not mix or dilute with other drugs. (5.2)
- 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. (5.2)
- The time between preparation of CINQAIR and administration should not exceed 16 hours. (5.2)
- Administration instructions: (5.2)
- CINQAIR should be administered by a healthcare professional prepared to manage anaphylaxis [see Warnings and Precautions (5.1)].
- Infuse the diluted solution of CINQAIR intravenously, over a 20 to 50 minute period. (5.2)
- Infusion time may vary depending on the total volume to be infused as based upon patient weight.

Full Prescribing Information: Contents

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*Sections or subsections omitted from the full prescribing information are not listed.
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.

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 all 3 cases, CINQAIR was discontinued.

Anaphylaxis can be life-threatening. CINQAIR should be administered 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 CINQAIR administration, 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 severe or lifethreatening anaphylaxis.

5.2 Acute Asthma Symptoms or Deteriorating Disease

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.

5.3 Malignancy

In placebo-controlled clinical studies, 6/1028 (0.6%) patients receiving 3 mg/kg CINQAIR had at least 1 malignant neoplasm reported compared to 2/730 (0.3%) patients in the placebo group. The observed malignancies in CINQAIR-treated patients were similar to those observed in patients receiving any other medication. The majority of malignancies were diagnosed within less than six months of exposure to 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 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 corticosteroids.

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, and CINQAIR will not influence the immune response to parasitic infections. Treat patients with pre-existing helminth infections before initiating CINQAIR. If patients become infected while receiving treatment with CINQAIR and do not respond to anti-helminth treatment, discontinue treatment with CINQAIR until infection resolves.

6 ADVERSE REACTIONS

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 249 exposed for longer than 2 years. The above referenced safety exposure for CINQAIR is derived from placebo-controlled studies ranging from 15 to 52 weeks in duration (CINQAIR 0.3 mg/kg and 3 mg/kg [n=1131] and placebo [n=730]) and 490 new CINQAIR 3 mg/kg exposures (previously on placebo) from a single open-label extension study. While a lower dose of CINQAIR 0.3 mg/kg (n=103) was included in a clinical trial, 3 mg/kg is the only recommended dose [see Dosage and Administration (2.1)]. Of the 1611 patients, 1596 received the 3 mg/kg dose, 1028 of which were in the placebo-controlled studies. In the placebo-controlled asthma studies, the population studied was 12 to 76 years of age, 62% female, and 73% white. While subjects 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)].

Serious adverse reactions that occurred in placebo-controlled studies in more than 1 subject and in a greater proportion of subjects treated with CINQAIR (n=1131) than placebo (n=730) included anaphylaxis (3 subjects vs. 0 subjects, respectively). The 3 subjects who experienced anaphylaxis were discontinued from the clinical studies [see Warnings and Precautions (5.1)]. Malignancy also occurred more commonly in patients treated with CINQAIR than placebo (0.6% and 0.3%, respectively) [see Warnings and Precautions (5.3)]. Adverse reactions that occurred at greater than or equal to 2% incidence and more commonly than in the placebo group included 1 event: oropharyngeal pain (2.6% vs. 2.2%).

CINQAIR is associated with muscle-related adverse reactions.

Elevated baseline creatine phosphokinase (CPK) was more frequent in patients randomized to CINQAIR (14%) versus placebo (9%). Transient CPK elevations in patients with normal baseline CPK values were observed more frequently with CINQAIR (20%) versus placebo (18%) during routine laboratory assessments. CPK elevations >10 x ULN, regardless of baseline CPK value, were 0.8% in the CINQAIR group compared to 0.4% in the placebo group. CPK elevations >10 x ULN were asymptomatic and did not lead to treatment discontinuation.

Myalgia was reported in 1% (10/1028) of patients in the CINQAIR 3 mg/kg group compared to 0.5% (4/730) of patients in the placebo group. On the day of infusion, musculoskeletal adverse reactions were reported in 2.2% and 1.5% of patients treated with CINQAIR 3 mg/kg and placebo, respectively. These reactions included but were not limited to musculoskeletal chest pain, neck pain, muscle spasms, extremity pain, muscle fatigue, and musculoskeletal pain.

6.2 Immunogenicity

Because CINQAIR is a recombinant protein, 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 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)]. Product-specific IgE antibodies were not detected in patients who reported anaphylactic reactions.

The data reflect the percentage of patients whose test results were positive for antibodies 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 in a linear fashion as pregnancy progresses; therefore, potential effects on a fetus are likely to be greater during the second and third trimester of pregnancy. Reslizumab has a long half-life [see Clinical Pharmacology (12.3)]. This half-life makes it less likely that the drug will be transferred to the fetus.

In animal reproduction studies, there was no evidence of embryo-fetal adverse developmental effects with intravenous administration of reslizumab during 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(s) are unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Clinical Considerations

Disease-Associated Maternal and/or Embryo-Fetal Risk

In women with poorly or moderately controlled asthma, evidence demonstrates that there is an increased risk of preeclampsia in the mother and prematurity, low birth weight, and small for gestational age in the neonate. The level of asthma control should be closely monitored in pregnant women 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 at 2, 10, and 50 mg/kg (0.4, 1.5, and 6 times the exposures achieved at the MRHD in mice on an AUC basis and 0.67, 3.3, and 17 times the exposures achieved at the MRHD in rabbits on a mg/kg basis). Reslizumab was not teratogenic in mice or rabbits. Embryo-fetal development of interleukin-5 (IL-5) deficient mice has been reported to be generally unaffected relative to wild-type mice.

In a prenatal and postnatal development study, pregnant CD-1 mice received reslizumab during organogenesis on gestation days 6 and 18 and on postnatal day 14 at 10 or 50 mg/kg (1.5 and 6 times the exposures achieved at the MRHD on an AUC basis). Reslizumab did not have any effects on fetal development up to
approximately 4 months after birth. Reslizumab crossed the placenta of pregnant mice. Serum concentrations in pups were approximately 6 to 8% of those in the dams (parental female mice) on postnatal day 14.

8.2 Lactation

Risk Summary

It is not known whether reslizumab is present in human milk, and the effects of reslizumab on the breast-fed 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 breast-fed child from CINQAIR or the underlying maternal condition.

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 exacerbation rate was higher in adolescent patients treated with CINQAIR than placebo (CINQAIR n=14, rate 2.86, 95% CI [1.02 to 8.09] and placebo n=11, rate 1.37, 95% CI [0.57 to 3.28]; ratio rate 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 1732 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-secreting 0 (NS0) cells. Reslizumab has a molecular weight of approximately 147 kDa.

CINQAIR is a sterile, preserve-free, clear to slightly hazy/opalescent, colorless to slightly yellow solution (injection) 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 (70 mg), with a pH of 5.5.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Reslizumab is an interleukin-5 antagonist (IgG4κ, 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 81 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 IL-5 signaling, reduces the production and survival of eosinophils; however, the mechanism of reslizumab action in asthma has not been definitively established.

12.2 Pharmacokinetics

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 624 cells/mcL (n=244) at baseline, and were 55 cells/mcL (92% reduction, n=212) and 496 cells/mcL (21% reduction, n=212) at the Week 52 visit for the CINQAIR and placebo treatment groups, respectively. Early eosinophil reduction was apparent in a subset of patients who had blood eosinophil counts assessed at days 2-3: 220 cells/mcL and 610 mcL for CINQAIR (n=35) and placebo (n=32), respectively. Eosinophils returned towards baseline in those CINQAIR-treated patients who completed a 50% follow-up assessment (n=35, 490 cells/mcL), approximately 120 days after the last dose of CINQAIR. Reductions of blood eosinophils were related to reslizumab serum levels, i.e., greater reductions of blood eosinophils were observed in subjects with higher reslizumab serum concentrations.

Treatment-emergent anti-reslizumab antibodies did not interfere with the blood eosinophil reduction effect by reslizumab.
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.

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

<table>
<thead>
<tr>
<th>Study</th>
<th>N=489</th>
<th>N=464</th>
<th>N=315</th>
<th>N=496</th>
</tr>
</thead>
<tbody>
<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 % predicteda</td>
<td>64</td>
<td>69</td>
<td>70</td>
<td>67</td>
</tr>
<tr>
<td>Baseline Reversibility, mean ΔFEV1, post-SABAa</td>
<td>26</td>
<td>28</td>
<td>25</td>
<td>26</td>
</tr>
<tr>
<td>Baseline mean blood eosinophil count/mla</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>

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

Exacerbations

The primary endpoint for Studies I and II was the frequency of asthma exacerbations for each patient during the 52-week treatment period. An asthma exacerbation was defined as a worsening of asthma that required at least 1 of the following medical interventions:

1) Either the use of a systemic corticosteroid, or 2-fold an increase in the use of ICS for 3 or more days, and/or
2) Asthma-related emergency treatment including at least 1 of the following: an unscheduled visit to their healthcare professional for nebulizer treatment or other urgent treatment to prevent worsening of asthma symptoms; a visit to the emergency room for asthma-related treatment; or an asthma-related hospitalization.

The medical intervention had to be corroborated with at least 1 of the following: 1) a decrease in forced expiratory volume in 1 second (FEV1) by 20% or more from baseline, 2) a decrease in peak expiratory flow rate (PEFR) by 30% or more from baseline on 2 consecutive days, or 3) worsening of symptoms or other clinical signs per physician evaluation of the event.

In Studies I and II, patients receiving CINQAIR 3 mg/kg administered once every 4 weeks had significant reductions in the rate of all asthma exacerbations compared to placebo (Table 2). Exacerbations requiring the use of a systemic corticosteroid (e.g., OCS) as well as exacerbations resulting in hospitalization or an emergency room visit were each reduced with CINQAIR 3 mg/kg.

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)a

<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>Asthma Exacerbation Rate</th>
<th>Rate Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All exacerbations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CINQAIR 3 mg/kg (n=245)</td>
<td>0.90</td>
<td>0.5</td>
</tr>
<tr>
<td>Placebo (n=244)</td>
<td>1.80</td>
<td>(0.37, 0.67)</td>
</tr>
<tr>
<td>Study II</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CINQAIR 3 mg/kg (n=232)</td>
<td>0.86</td>
<td>0.41</td>
</tr>
<tr>
<td>Placebo (n=232)</td>
<td>2.11</td>
<td>(0.28, 0.59)</td>
</tr>
</tbody>
</table>

| Exacerbations requiring systemic corticosteroid use |
| Study I |
| CINQAIR 3 mg/kg (n=245) | 0.72 | 0.45 |
| Placebo (n=244) | 1.60 | (0.33, 0.62) |
| Study II |
| CINQAIR 3 mg/kg (n=232) | 0.65 | 0.39 |
| Placebo (n=232) | 1.66 | (0.27, 0.58) |

| Exacerbations resulting in a hospitalization and/or emergency room visit |
| Study I |
| CINQAIR 3 mg/kg (n=245) | 0.14 | 0.66 |
| Placebo (n=244) | 0.21 | (0.32, 1.36) |
| Study II |
| CINQAIR 3 mg/kg (n=232) | 0.03 | 0.69 |
| Placebo (n=232) | 0.05 | (0.29, 1.65) |

a Randomized patients
CINQAIR® (reslizumab) injection

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. The following packaging configuration is available:
• NDC 59310-610-31: 100 mg/10 mL (10 mg/mL) single-use vial.
Storage and Stability: Refrigerate at 2 °C to 8°C (36°F to 46°F). Do not freeze. Do not shake. Protect the vials from light by storing in the original package until time of use.

17 PATIENT COUNSELING INFORMATION
See FDA approved patient labeling (Patient Information).

18 HOW SUPPLIED/STORAGE AND HANDLING
CINQAIR (reslizumab) injection for intravenous use

PATIENT INFORMATION
CINQAIR (sink-ayr’)(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
• 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.

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).
• 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.
Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.
Do not stop taking your other asthma medicines unless your healthcare provider tells you to.

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.
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.
These are not all the possible side effects of 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

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For more information, go to www.CINQAIR.com or call 1-888-483-8279.