These Clinical Guidelines have been created using resources that were current as of the "Reviewed" date noted at the beginning of the document. Clinicians should refer to the manufacturer's Prescribing Information (or equivalent) for the most up-to-date information. While CarepathRx has published these Clinical Guidelines after a close review of available literature and a clinical review process, given the evolving nature and complexity of modern pharmaceutical products, CarepathRx does not and cannot warrant or guarantee that these Clinical Guidelines reflect the objectively best or highest standard of care at any given time.

Nothing within these Clinical Guidelines is intended to supersede or interfere with any individual clinician's decision-making or professional judgment with respect to either (1) prescribing or dispensing the drug or product in question or (2) the overall treatment plan for an individual patient.

Reslizumab (Cinqair) Clinical Guideline for Home Intravenous Therapy

Section: Clinical Guideline
Compliance: ACHC Infusion Pharmacy
ACHC Standards: N/A
URAC Standards: N/A
Policy ID: CG010
Effective: 5/1/2024
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Revised: n/a
Approved by, Title and Date Approved: Kathleen Patrick, President, 5/1/24

I. BACKGROUND

Reslizumab is an interleukin-5 antagonist (IgG4 kappa) indicated for add-on maintenance treatment of patients with severe asthma aged 18 years and older, and with an eosinophilic phenotype. IL-5 is the major cytokine responsible for the growth and differentiation, recruitment, activation, and survival of eosinophils. Reslizumab works by binding to IL-5 and 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. Eosinophils are associated with inflammation and are a major contributor to 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. The following outlines the procedures for servicing patients in need of outpatient intravenous reslizumab infusions.

II. PATIENT ACCEPTANCE CRITERIA

A. All candidates for home care service must be evaluated by the clinician(s) and deemed appropriate to receive home care based upon the dispensing pharmacy's admission criteria.

B. The decision to administer a first dose in the home by a field nurse will be determined on a case-by-case basis and reviewed by nursing and pharmacy management. The following criteria will be evaluated:

1. Prescriber preference
2. Allergy profile
3. Age ≥18 years
4. Other relevant social and/or medical history

C. Physician orders for reslizumab must include:

1. Patient weight
2. Drug and dose (including weight-based dosing)
3. Route of administration
4. Frequency of administration
5. Emergency medications per protocol
6. Orders for pre-medications, if applicable
7. Line care protocol

D. Required prior to initiating therapy: Patients with pre-existing helminth infections should undergo treatment of the infection prior to initiating reslizumab therapy.

E. Additional recommended monitoring parameters (not required to begin therapy): CBC with differential prior to initiation of treatment and periodically thereafter.

F. Dispensing pharmacy treatment protocol for anaphylaxis will be instituted unless a more comprehensive patient-specific orders are provided by physician. See Appendix A (Nursing CarepathRx policy on *Management of Allergic/Anaphylactic Reactions*)

III. PHARMACOLOGY OVERVIEW

Refer to manufacturer's full Prescribing Information for most up to date information

A. Indications for use:

1. Add-on maintenance treatment of adults with severe eosinophilic asthma

B. Dosing

1. IV: 3 mg/kg once every 4 weeks* (maximum dose not established).
   **Dosing is based off actual body weight. Reslizumab has not been studied in extremes of body weights.*

C. Dose Adjustment: There are no dosage adjustments. No formal trial of the effect of hepatic or renal impairment on the PK of reslizumab was conducted.

D. Duration: Duration of therapy should be dependent on patient response and adverse reactions. A minimum of 4 months of treatment is suggested to determine efficacy.

E. Contraindications: Known hypersensitivity to reslizumab or any of its excipients.

F. Warnings and Precautions:

1. **Black Box Warning: Anaphylaxis:** Anaphylaxis was reported in 0.3% of patients in placebo-controlled studies. These events were observed during or within 20 minutes after completion of infusion and may occur as early as the second dose. Manifestations included dyspnea, decreased oxygen saturation, wheezing, vomiting, skin and mucosal involvement, including urticaria. Patients should be observed for an appropriate period of time after infusion. Healthcare professionals should be prepared to manage anaphylaxis that can be life-threatening. Discontinue reslizumab if anaphylaxis occurs and initiate appropriate treatment.
2. **Acute asthma symptoms or deteriorating disease:** Reslizumab should not be used to treat acute asthma symptoms or acute exacerbations. Do not use to treat acute bronchospasm or status asthmaticus. Patients should seek medical advice if their asthma remains uncontrolled or worsens after exposure to reslizumab.
3. **Malignancy:** In placebo-controlled studies, 0.6% of patients receiving reslizumab had at least 1 malignant neoplasm reported compared to 0.3% of patients in the placebo group. The observed malignancies were diverse with no predominant histologic type. The majority of malignancies were diagnosed within less than six months of exposure to reslizumab.

4. **Reduction of corticosteroid dosage:** No clinical studies have been conducted to assess reduction of maintenance corticosteroid dosages following administration of reslizumab. Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of therapy. Reductions in corticosteroid dose should be gradual, if appropriate. Clinicians should be aware that a reduction in corticosteroid dose may be associated with withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.
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 reslizumab will influence the immune response against parasitic infections. Treat patients with pre-existing helminth infections before initiating reslizumab. If patients become infected while receiving treatment with reslizumab, and do not respond to anti-helminth treatment, discontinue reslizumab until infection resolves.
6. **Pregnancy and Lactation:** 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 higher during the second and third trimester of pregnancy. Reslizumab has a long half-life which should be taken into consideration. Poorly controlled asthma or asthma exacerbations may have a greater fetal/maternal risk than what is associated with appropriately used asthma medications. Reslizumab was present in the milk of lactating mice following dosing during pregnancy. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for reslizumab and any potential adverse effects on the breastfed child from reslizumab or the underlying maternal condition. 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.
7. **Pediatrics:** Reslizumab is not indicated for use in pediatric patients less than 18 years of age. The safety and effectiveness in pediatric patients have not been established.
8. **Immunogenicity:** As with all therapeutic proteins, there is a potential for immunogenicity. In placebo-controlled studies, a treatment-emergent anti-reslizumab antibody responses developed in 53/983 (5.4%) of reslizumab treated patients. The antibody responses were of low titer and often transient. There was no detectable impact of the antibodies on the clinical pharmacokinetics, pharmacodynamics , clinical efficacy, and safety of reslizumab. Product specific IgE antibodies were not detected in patients who reported anaphylactic reactions.

G. Pharmacokinetics:

1. Distribution: Vd: ~5 L
2. Metabolism: Undergoes proteolytic degradation via enzymes into small peptides and amino acids
3. Half-life elimination: ~24 days

H. Adverse Reactions

1. >10%: Neuromuscular & skeletal: increased creatine phosphokinase (CPK) in blood specimen (20%)
2. 1% to 10%:
3. Immunologic: antibody development (5%)
4. Neuromuscular & skeletal: myalgia (1%)
5. Respiratory: oropharyngeal pain (3%)
6. <1%: Hypersensitivity: anaphylaxis, immunogenicity (5.4%)

I. Drug Interactions: Drug-drug interactions may exist. Consult interaction database for patient specific assessment. No formal clinical drug interaction studies have been performed with reslizumab.

IV. ADMINISTRATIVE GUIDELINES

A. Administration- IV infusions should be given immediately after reconstitution and dilution. Start infusion within 4 hours of preparation per current USP Immediate-Use Guidelines.

B. Reslizumab should be administered by a healthcare professional prepared to manage anaphylaxis

C. **Dilute prior to use. Infuse using an infusion set with an in-line, sterile, non-pyrogenic, low protein binding 0.2- micron filter.**

D. Do not infuse reslizumab concomitantly in the same IV line with other medications.

E. Reslizumab vials for IV infusion are for use in adult patients only.

V. NURSING PROCEDURE

A. Supplies may include but are not limited to:

1. Alcohol Swabs
2. Gloves
3. Tape
4. Peripheral IV access supplies for patients requiring peripheral IV access
    a. IV start Kit
    b. Peripheral IV catheter (ex. 22 Gauge x1" and 24 Gauge x ¾")
    c. Extension set 8" with needless connector
5. If applicable, Central Venous Access Catheter (CVAD) Dressing Change and needless
6. connectors if patient has a central line, and non-coring needle set if the CVAD is an implanted
7. port.
8. IV Pole
9. IV administration set (flow regulator [ex: dial-a-flow] or gravity) with in-line or add-on 0.22
10. micron low protein binding filter
11. Syringes (10mL, 20mL, or 30mL) with needles (20 G x 1")
12. Sharps container

B. Prescription items:

1. Reslizumab vials
2. Compounded 50 mL 0/9% Sodium Chloride for Injection bag
3. 50 mL 0.9% Sodium Chloride for Injection post infusion flush bag

C. How Supplied: 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.

D. Storage and Handling: Refrigerate vials at 2ºC to 8ºC (36ºF to 46ºF) in original carton and protected from light until time of use. Do not freeze. To avoid foaming, do not shake.

E. Compatibility

1. Compatible with 0.9% Sodium Chloride for Injection
2. Compatible with polyvinylchloride (PVC) or polyolefin infusion bags
3. Compatible with polyethersulfone (PES), polyvinylidene fluoride (PVDF), nylon, and cellulose acetate in-line infusion filters

F. Procedures:

1. Explain the reasoning for visit and use of reslizumab.
2. Don gloves.
3. Assess for signs and symptoms of infection prior to establishing venous access and preparing medication.
4. Establish venous access prior to preparation of drug.
5. Counsel patient on warnings, precautions, and potential side effects including but not limited to: hypersensitivity/anaphylaxis (skin or mucosal involvement, airway compromise, reduced blood pressure) and malignancy.
6. Prepare Infusion

    a. Before dilution, remove reslizumab from the refrigerator.
    b. Inspect visually for particulate matter and discoloration prior to administration. Since reslizumab 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.
    c. Withdraw the proper volume of reslizumab from the vial(s), based on the recommended weight-base dosage according to the following calculation:

    $$\text{Volume (mL)} = \frac{\text{body weight (kg) x prescribed dose (3 mg/kg)}}{\text{Concentration of reslizumab 10 mg/mL}}$$

    Use number of vials based on total volume needed (one vial contains 10 mL of solution) Discard any unused portion.

    d. Dispense syringe contents slowly into an infusion bag containing 50 mL of 0.9% Sodium Chloride Injection, to minimize foaming. Gently invert the bag to mix the solution. Do not shake. Do not mix or dilute with other drugs.

7. Infusion Rates

    a. Administer over 20-50 minutes.

8. Upon completion of the infusion, flush the administration tubing with 20-30 mL 0.9% Sodium Chloride Injection via flow regulated tubing at the same rate of the infusion to ensure that all reslizumab has been administered.

9. Post infusion monitoring: Monitor patient and vital signs periodically during the infusion and 30 minutes after the infusion is complete per CarepathRx policy on *Nursing Best Practice Administration Guidelines*.

VI. CLINICAL MONITORING

A. Prior to therapy

1. Signs and symptoms of parasitic (helminth) infection
    a. Consider CBC with diff

B. During therapy

1. Anaphylaxis/hypersensitivity reactions
2. Signs/symptoms of infection
3. Malignancy
4. Signs and symptoms of parasitic (helminth) infection
    a. Consider CBC with diff

C. Disease progression and therapy efficacy

1. Asthma symptoms/exacerbations
2. Lung function (FEV_1)
3. Improved quality of life

Please refer to the package insert for the most up to date guidance on this medication.

VII. REFERENCES:

1. Cinqair (reslizumab) [prescribing information]. West Chester, PA: Teva Respiratory, LLC; June 2022.
2. Reslizumab. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL.
3. United States Pharmacopeia (USP). General Chapter, <797> Pharmaceutical Compounding—Sterile Preparations. (2023) USP-NF. Rockville, MD: United States Pharmacopeia. Accessed November 29, 2023.
4. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. https://ginasthma.org/2023-gina-main-report/. Updated 2023. Accessed August 23, 2023.

APPENDIX A: ANAPHYLAXIS KIT INTRUCTIONS

Emergency Medication After Your Infusion

Please call your pharmacy if you have any questions or concerns. In the event of an emergency, always call 911.

Your nurse will tell you when you need to use Emergency Medications.
The epinephrine dose will be noted on the Anaphylaxis Protocol included with your kit.

Start with a clean work surface and clean hands.

Open the supply bag labeled Anaphylaxis Kit Contents.

You will need:

1. **Bag containing Pills** (2 Acetaminophen and 2 Diphenhydramine)
2. **Bag containing Alcohol Prep Pads**
3. **Bag labeled IM Epinephrine**

All other contents will not be needed.

Open the IM Epinephrine Bag

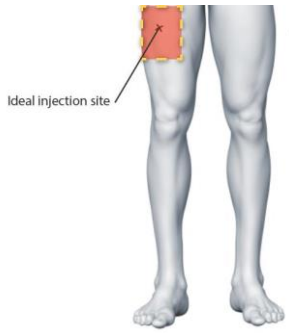
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampule use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampule of epinephrine

Prepare IM (intramuscular) injection of Epinephrine:

1. **Attach the brown filtered needle to syringe**
    a. Be careful to not touch the tip of the syringe or the needle.
2. Using an **alcohol swab, wipe the neck of the epinephrine ampule.**
3. Holding the ampule upright, **swirl and flick the ampule until all fluid flows to the bottom chamber** (the top chamber should be empty).
4. Using a new alcohol wipe, grasp the neck of the ampule and with your other hand grasp the bottom chamber of the ampule. **Quickly snap the top of the ampule off, directing the snap way from you.**

5. **Place the tip of the brown filter needle inside the ampule**. Tilting the ampule, **withdraw dose of medication into the syringe** by gently pulling back on the plunger. Be careful to not pull the plunger out of the syringe.
6. Remove the needle from the ampule and h**old the syringe upright** with the needle pointing upward. **Gently tap the side of the syringe to bring any air to the top of the syringe.**
7. **Push the air out of the syringe by gently pushing on the plunger**.
8. Replace the cap on the brown filter needle. Discard remainder in ampule.
9. **Remove the brown filter needle and place the black safety needle onto the syringe.**

Give your IM Epinephrine injection



1. **Grasp your leg muscle at the outer mid-thigh** and **cleanse the area** with a new alcohol wipe.
2. **Push the needle into your leg muscle straight** in at a 90-degree angle.
3. **Inject the medication** by depressing the plunger in a slow and steady motion.
4. **Remove the needle** and wipe the site with the alcohol wipe.
5. May repeat dose every 5 minutes (**maximum 3 doses**) if ordered per protocol.

Take the pills by mouth.

a. 2 – Acetaminophen
b. 2 – Diphenhydramine

Place all trash in the bag the pills came in and take with you when you seek medical care. **Give the bag to the nurse or EMT**, so your doctor will know what medication you already took. They will properly dispose of the syringe and needles.
Call 911 or have someone drive you to the emergency department.