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.

CAREPATHrx™
Specialty Pharmacy & Infusion Solutions

GUIDELINES FOR OUTPATIENT INTRAVENOUS KEYTRUDA (PEMBROLIZUMAB) THERAPY

Section: Nursing
Compliance: ACHC Infusion Pharmacy
ACHC Standards: N/A
URAC Standards: N/A
Policy ID: NUR253
Effective: 1/3/23
Reviewed:
Revised:
Approved by: Kathleen Patrick, President, 1/3/23

I. BACKGROUND

Keytruda (pembrolizumab) is a highly selective anti-PD-1 humanized monoclonal antibody which inhibits programmed cell death-1 (PD-1) activity by binding to the PD-1 receptor on T-cells to block PD-1 ligands (PD-L1 and PD-L2) from binding. PD-1 has a major involvement in suppressing the immune system during the formation of the PD-1/PD-L1 pathway, which transmits an inhibitory signal to reduce T cell activity. PD-L1 is often expressed in various malignant tumors. Blocking the PD-1 pathway inhibits the negative immune regulation caused by PD-1 receptor signaling. Anti-PD-1 antibodies reverse T-cell suppression and induce antitumor responses. Pembrolizumab is indicated and used in diseases associated with Melanoma, Non-Small Cell Lung Cancer, Head and Neck Squamous Cell Cancer, Classical Hodgkin Lymphoma, Primary Mediastinal Large B-Cell Lymphoma, Urothelial Carcinoma, Microsatellite Instability-High Cancer, Gastric Cancer, Cervical Cancer, Hepatocellular Carcinoma, and Merkel Cell Carcinoma. The following outlines the procedures for servicing patients in need of outpatient pembrolizumab 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 old
4. Ability to secure contracted nursing for subsequent infusions
5. Other relevant social and/or medical history

C. Pregnancy status

D. Physician orders for Pembrolizumab must include:
1. Drug and dose
2. Route of administration
3. Frequency of administration
4. Emergency medications
5. Line Care protocol
6. Orders for pre-medications, if applicable
7. Routine lab monitoring, if applicable

E. Baseline labs or tests recommended prior to starting therapy
1. LFTs
2. Renal function (i.e., serum creatinine)
3. Thyroid function
4. Blood cortisol

F. Dispensing pharmacy treatment protocol for anaphylaxis will be instituted unless a more comprehensive patient-specific orders are provided by physician. See policy NUR012 (Appendix A).

III. PHARMACOLOGY OVERVIEW

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

A. Indications, Dosing, Duration

Indication	Recommended Dosage of Pembrolizumab	Duration Timing of Treatment
Adult patients with unresectable or metastatic melanoma or RCC	200mg every 3 weeks or 400mg every 6 weeks	Until disease progression or unacceptable toxicity
Adjuvant treatment of adult patients with melanoma or RCC	200mg every 3 weeks or 400mg every 6 weeks	Until disease progression or unacceptable toxicity, or up to12 months
Adult patients with NSCLC, HNSCC, cHL, PMBCL, locally advanced or metastatic Urothelial Carcinoma, MSI-H or	200mg every 3 weeks or 400mg every 6 weeks	Until disease progression or unacceptable toxicity, or up to 24 months

dMMR Carcinoma, Esophageal Cancer, Cervical Cancer, HCC, MCC, TMB-H Cancer, cSCC, TNBC, or GC		
Adult patients with high-risk BCG-unresponsive NMIBC	200mg every 3 weeks or 400mg every 6 weeks	Until persistent or recurrent high-risk NMIBC, disease progression, unacceptable toxicity, or up to 24 months
Pediatric patients with cHL, PMBCL, MSI-H or dMMR Cancer, MCC, or TMB-H Cancer	2mg/kg every 3 weeks (up to max dose of 200mg)	Until disease progression, unacceptable toxicity, or up to 24 months
Pediatric patients (12 years and older) for adjuvant treatment of melanoma	2mg/kg every 3 weeks (up to max dose of 200mg)	Until disease progression, unacceptable toxicity, or up to 24 months

B. Dose Adjustments
   1. Renal and hepatic impairment **prior** to treatment initiation in children and adult patients.
      a. No dosage adjustments provided in the manufacturer's labeling.
   2. Renal and hepatic impairment **during** treatment in children and adult patients

Adverse Effect	Severity	Pembrolizumab Dosage Modification
Nephrotoxicity	Grade 2 or grade 3 serum creatinine elevation	Withhold pembrolizumab; resume pembrolizumab after complete or partial (to grade 0 or 1) resolution after corticosteroid taper. Permanently discontinue pembrolizumab if no complete or partial response within 12 weeks of initiating corticosteroids, or if unable to reduce corticosteroid dose to the equivalent of prednisone ≤10 mg/day in adults within 12 weeks of corticosteroid initiation.
	Grade 4 serum creatinine elevation	Permanently discontinue pembrolizumab.

Hepatitis without tumor involvement of the liver	AST or ALT >3 up to 8 times ULN or total bilirubin >1.5 up to 3 times ULN	Withhold pembrolizumab treatment. Resume pembrolizumab treatment with complete or partial resolution (to grade 0 or 1) of hepatitis after corticosteroid taper
	AST or ALT >8 times ULN or total bilirubin >3 times ULN:	Discontinue pembrolizumab permanently.
Hepatitis with tumor involvement of the liver (Note: If AST and ALT are ≤ ULN at baseline, follow recommendations for hepatitis without tumor involvement of the liver)	If baseline AST or ALT >1 up to 3 times ULN and increases to >5 up to 10 times ULN or baseline AST or ALT >3 up to 5 times ULN and increases to >8 up to 10 times ULN	Withhold pembrolizumab treatment. Resume pembrolizumab treatment with complete or partial resolution (to grade 0 or 1) of hepatitis after corticosteroid taper.
	AST or ALT increases to >10 times ULN or total bilirubin increases to >3 times ULN	Discontinue pembrolizumab permanently
Adult patients ONLY: Hepatitis when used in combination with axitinib (for renal cell carcinoma)	AST or ALT ≥3 to <10 times ULN without concurrent total bilirubin ≥2 times ULN	Withhold pembrolizumab (and axitinib) treatment until recovery to grade 0 or 1. After recovery, consider re-challenge with a single drug (either pembrolizumab or axitinib) or sequential re-challenge with both pembrolizumab and axitinib; axitinib may require a dose reduction
	AST or ALT ≥10 times ULN or >3 times ULN with concurrent total bilirubin ≥2 times ULN	Discontinue pembrolizumab (and axitinib) permanently

3. Recommended Dosage Modifications for other adverse reactions **during** treatment in adult patients only.

Adverse Effect	Severity	Pembrolizumab Dosage Modification
Immune-mediated adverse reactions	Severe, Grade 3	Withhold therapy. If interruption or discontinuation is required, administer systemic corticosteroid therapy (prednisone 1 to 2 mg/kg/day or equivalent) until improvement to Grade 1 or less Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroid therapy
	Grade 4 reactions or recurrent severe Grade 3 reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to prednisone 10 mg or less per day (or equivalent) within 12 weeks of initiating steroids	Permanently discontinue pembrolizumab
Cardiovascular toxicity: Myocarditis	Grade 2, 3, or 4	Permanently discontinue pembrolizumab.
Dermatologic toxicity	Mild or moderate non-exfoliative rash	May be managed with topical emollients and/or topical corticosteroids.
	Exfoliative dermatologic conditions: Suspected Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), or drug rash with eosinophilia and systemic symptoms (DRESS)	Withhold pembrolizumab; resume pembrolizumab after complete or partial (to grade 0 or 1) resolution after corticosteroid taper. Permanently discontinue pembrolizumab if no complete or partial response within 12 weeks of initiating corticosteroids, or if unable to reduce prednisone to ≤10 mg/day (or equivalent)

		within 12 weeks of corticosteroid initiation.
	Confirmed SJS, TEN, or DRESS	Permanently discontinue pembrolizumab.
Endocrinopathies	Grade 3 or 4	Withhold pembrolizumab until clinically stable or permanently discontinue depending on severity.
	Adrenal insufficiency, ≥ grade 2	Initiate symptomatic management (including hormone replacement as clinically indicated).
	Diabetes, type 1	Initiate insulin as clinically indicated. Long-term insulin therapy may be required.
	Hypophysitis	Withhold or discontinue pembrolizumab (depending on the severity). Initiate medical management as clinically indicated.
	Hyperthyroidism/Thyroiditis	Withhold or discontinue pembrolizumab (depending on the severity). Initiate medical management as clinically indicated.
	Hypothyroidism	Withhold pembrolizumab (depending on the severity). Initiate thyroid hormone replacement therapy as clinically indicated.
GI toxicity: Colitis	Grade 2 or 3	Withhold pembrolizumab; resume pembrolizumab after complete or partial (to grade 0 or 1) resolution after corticosteroid taper. Permanently discontinue pembrolizumab if no complete or partial response within 12 weeks of initiating corticosteroids, or if unable to reduce prednisone to ≤10 mg/day (or equivalent) within 12 weeks of corticosteroid initiation.
	Grade 4	Permanently discontinue pembrolizumab.
Hematologic toxicity (in	Grade 4	Withhold pembrolizumab until

patients with classical Hodgkin lymphoma or primary mediastinal large B-cell lymphoma)		resolution to grade 0 or 1.
Neurologic toxicities	Grade 2	Withhold pembrolizumab; resume pembrolizumab after complete or partial (to grade 0 or 1) resolution after corticosteroid taper. Permanently discontinue pembrolizumab if no complete or partial response within 12 weeks of initiating corticosteroids, or if unable to reduce prednisone to ≤10 mg/day (or equivalent) within 12 weeks of corticosteroid initiation.
	Grade 3 or 4	Permanently discontinue pembrolizumab.
Ocular disorders: Vogt-Koyanagi-Harada-like syndrome		May require systemic corticosteroids to reduce the risk of permanent vision loss.
Pulmonary toxicity: Pneumonitis	Grade 2	Withhold pembrolizumab; resume pembrolizumab after complete or partial (to grade 0 or 1) resolution after corticosteroid taper. Permanently discontinue pembrolizumab if no complete or partial response within 12 weeks of initiating corticosteroids, or if unable to reduce prednisone to ≤10 mg/day (or equivalent) within 12 weeks of corticosteroid initiation.
	Grade 3 or 4	Permanently discontinue pembrolizumab.
Other Adverse Reactions		
Infusion reactions	Grade 1 or 2	Interrupt or slow the rate of pembrolizumab infusion.
	Grade 3 or 4	Stop infusion and permanently discontinue pembrolizumab.

C. Contraindications

1. **There are no contraindications listed in the manufacturer's US labeling.**

D. Warnings and Precautions
    1. Pulmonary toxicity
        a. Immune-mediated pneumonitis has been observed, including grades 2 to 4, and fatal cases. Many patients required management with systemic corticosteroids. Pneumonitis resolved in over half of the affected patients. In cases where pembrolizumab was withheld for pneumonitis, all reinitiated pembrolizumab after symptom improvement; pneumonitis recurred in ~25% of patients. Pneumonitis occurred more frequently in patients with a history of prior thoracic radiation.
    2. GI toxicity
        a. Immune-mediated colitis has occurred (may present with diarrhea), including cases of grade 2 to 4 colitis. Systemic corticosteroids were administered to the majority of patients for immune-mediated colitis; additional immunosuppressant therapy was necessary in some patients. Most patients with colitis experienced resolution. In cases where pembrolizumab was withheld for colitis, all reinitiated treatment after symptom improvement; colitis recurred in ~25% of patients. Pancreatitis (including increased serum amylase and lipase levels), gastritis, and duodenitis have also been reported.
    3. Hepatotoxicity
        a. Immune-mediated hepatitis has occurred with pembrolizumab monotherapy (grades 2 to 4 hepatitis). Monitor patients for changes in liver function. Hepatitis has led to pembrolizumab treatment interruption or discontinuation. Systemic corticosteroids were used to manage immune-mediated hepatitis in many patients; additional immunosuppressants were necessary in some cases. Hepatitis resolved in a majority of patients. In cases where pembrolizumab was withheld for hepatitis, all reinitiated treatment after symptom improvement with no recurrence of hepatitis.
    4. Endocrinopathies
        a. Adrenal insufficiency:
            a. Primary and secondary adrenal insufficiency have occurred, including cases of ≥ grade 2 adrenal insufficiency. Over 75% of cases were managed with systemic corticosteroids; the majority of patients remained on corticosteroid therapy. In cases where pembrolizumab was withheld for adrenal insufficiency, all reinitiated treatment after symptom improvement.
        b. Diabetes mellitus:
            a. Type 1 diabetes mellitus has occurred (which may present with diabetic ketoacidosis).
        c. Hypophysitis:
            a. Immune-mediated hypophysitis has occurred (grades 2, 3,

and 4), and may present with acute mass effect symptoms (headache, photophobia, or visual field defects). Hypophysitis may lead to hypopituitarism. Most hypophysitis cases were managed with systemic corticosteroids; the majority of patients remained on corticosteroid therapy. In cases where pembrolizumab was withheld for hypophysitis, all reinitiated treatment after symptom improvement.

d. Thyroid disorders:
    a. Hyperthyroidism occurred in a small percentage of patients, including grade 2 and 3 events. Discontinuation or treatment interruption due to hyperthyroidism were required in a small number of patients. In cases where pembrolizumab was withheld, all reinitiated treatment after symptom improvement.
    b. Hypothyroidism has occurred, including grade 2 and 3 cases. Hypothyroidism may follow hyperthyroidism. Discontinuation or treatment interruption due to hypothyroidism were required in a small number of patients; in cases where pembrolizumab was withheld, all reinitiated treatment. Most patients required long-term thyroid replacement therapy.
    c. Thyroiditis may present with or without endocrinopathy. Thyroiditis occurred rarely, and did not result in permanent discontinuation, although treatment was interrupted occasionally.

5. Nephrotoxicity
    a. Immune-mediated nephritis with kidney dysfunction has occurred, including grade 2 to grade 4 cases. Monitor patients for changes in renal function. Most patients required systemic corticosteroids. In cases where pembrolizumab was withheld for nephritis, all reinitiated treatment after symptom improvement with no recurrence of nephritis. Nephritis resolved in over one-half of affected patients.

6. Dermatologic toxicity
    a. Immune-mediated rash or dermatitis may occur. Immune-mediated dermatologic adverse reactions (including grade 2 and 3 events) occurred with pembrolizumab. Exfoliative dermatitis, including Stevens-Johnson syndrome, drug rash with eosinophilia and systemic symptoms, and toxic epidermal necrolysis has occurred with anti-PD-1/PD-L1 monoclonal antibodies. Immune-mediated dermatologic reactions were treated with systemic corticosteroids in 40% of patients, and reactions resolved in ~80% of patients. In cases where

pembrolizumab was withheld, all reinitiated treatment after symptom improvement; immune-mediated dermatologic toxicity recurred in some patients.

7. Infusion-related reactions:
    a. Infusion-related reactions (including severe and life-threatening cases) have occurred. Signs/symptoms of a reaction included rigors, chills, wheezing, pruritus, flushing, rash, hypotension, hypoxemia, and fever.

8. Other Immune Mediated Adverse Reactions (immune-mediated):
    a. Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue in patients receiving pembrolizumab. While immune-mediated adverse reactions usually occur during treatment with PD-1/PD-L1 blocking antibodies, they may occur after discontinuation of treatment. For suspected immune-mediated adverse reactions, ensure adequate evaluation to confirm etiology or exclude other causes.
    b. The following clinically significant, immune-mediated adverse reactions occurred in patients treated with pembrolizumab: arthritis, uveitis, myositis, Guillain Barré syndrome, myasthenia gravis, vasculitis, pancreatitis, hemolytic anemia, sarcoidosis, and encephalitis. In addition, myelitis and myocarditis were reported in other trials, including cHL, and post marketing use.

9. Hypersensitivity
    a. Hypersensitivity and anaphylaxis have been observed (rare).

10. Complications of Allogeneic HSCT
    a. Immune-mediated complications, including fatal events, occurred in patients who underwent allogeneic hematopoietic stem cell transplantation (HSCT) after being treated with Pembrolizumab. These complications may occur despite intervening therapy between PD-1 blockade and allogeneic HSCT.
    b. In patients with a history of allogeneic HSCT, acute GVHD, including fatal GVHD, has been reported after treatment with pembrolizumab. Patients who experienced GVHD after their transplant procedure may be at increased risk for GVHD after treatment with pembrolizumab. Consider the benefit of treatment with pembrolizumab versus the risk of possible GVHD in patients with a history of allogeneic HSCT.

11. Increased Mortality in Patients with Multiple Myeloma when pembrolizumab is Added to a Thalidomide Analogue and Dexamethasone

a. In two randomized trials in patients with multiple myeloma, the addition of pembrolizumab to a thalidomide analogue plus dexamethasone, a use for which no PD-1 or PD-L1 blocking antibody is indicated, resulted in increased mortality. Treatment of patients with multiple myeloma with a PD-1 or PD-L1 blocking antibody in combination with a thalidomide analogue plus dexamethasone is not recommended outside of controlled trials.

12. Embryo-Fetal Toxicity
    a. Based on its mechanism of action, pembrolizumab can cause fetal harm when administered to a pregnant woman. Animal models link the PD-1/PD-L1 signaling pathway with maintenance of pregnancy through induction of maternal immune tolerance to fetal tissue. Advise women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with pembrolizumab and for 4 months after the last dose.

E. Pharmacokinetics
    1. Distribution: Vd: 6L
    2. Half-life elimination: 22 days

F. Adverse Reactions
    1. Common
        a. Cardiovascular: Hypertension
        b. Dermatologic: Alopecia, Pruritis, Rash
        c. Endocrine metabolic: Hypercholesterolemia, Hyperglycemia, Hypertriglyceridemia, Hypoalbuminemia, Hyponatremia
        d. Gastrointestinal: Constipation, Decrease in appetite, Diarrhea, Nausea
        e. Hematologic: Leukopenia, Thrombocytopenia
        f. Hepatic: Alkaline phosphatase elevations, Aspartate aminotransferase serum level elevations
        g. Musculoskeletal: Arthralgia, Disorder of musculoskeletal system, Musculoskeletal pain
        h. Neurologic: Neuropathy
        i. Renal: Proteinuria
        j. Respiratory: Cough, Dyspnea
        k. Other: Fatigue
    2. Serious
        a. Cardiovascular: Myocardial ischemia, Myocarditis, Pericarditis, right ventricular dysfunction, Vasculitis, Vasculitis
        b. Dermatologic: Drug reaction with eosinophilia and systemic symptoms, Hand-foot syndrome due to cytotoxic therapy, Stevens-Johnson syndrome, Stevens Johnson syndrome AND

toxic epidermal necrolysis overlap, Toxic epidermal necrolysis

c. Endocrine metabolic: Adrenal insufficiency, Hyperthyroidism, Hypoparathyroidism, Hypophysitis, Hypothyroidism, Thyroiditis, Type 1 diabetes mellitus
d. Gastrointestinal: Colitis, Duodenitis, Gastritis, Gastrointestinal obstruction, Malignant, Gastrointestinal perforation, Lower gastrointestinal hemorrhage, Pancreatitis
e. Hematologic: Anemia, Grade 3 or 4, Aplastic anemia, Febrile neutropenia, Hemolytic anemia, Hemophagocytic lymphohistiocytosis, Immune thrombocytopenia
f. Hepatic: Hepatitis, Hepatotoxicity, Veno-occlusive disease of the liver
g. Immunologic: Anaphylaxis, Graft versus host disease, Histiocytic necrotizing lymphadenitis, Hypersensitivity reaction, Sarcoidosis, Systemic inflammatory response syndrome, Transplanted organ rejection, Vogt-Koyanagi-Harada disease
h. Musculoskeletal: Eaton-Lambert syndrome, Myasthenia gravis, Myositis, Polymyalgia rheumatica, Polymyositis, Rhabdomyolysis
i. Neurologic: Confusion, Demyelination of spinal cord, Encephalitis, Guillain-Barre syndrome, Meningitis, Myelitis, Nerve palsy
j. Ophthalmic: Iritis, Myasthenia gravis, ocular, Optic neuritis, Uveitis, Visual impairment
k. Renal: Acute injury of kidney, Nephritis, Renal failure
l. Respiratory: Pleural effusion, Pneumonia, Pneumonitis, Pulmonary embolism, Respiratory failure
m. Other: Cardiorespiratory arrest, Disorder characterized by fever, Steroid-requiring, Fever, Infusion reaction, Infusion reaction, Multiple organ failure, Sepsis

G. Drug Interactions

1. Significant drug interactions exist, requiring dose/frequency adjustment or avoidance. Consult drug interactions database for more information.
2. Avoid concomitant use with Thalidomide analogs (thalidomide, pomalidomide, and lenalidomide).
    a. Pembrolizumab may enhance the adverse/toxic effect of Thalidomide analogs - mortality may be increased when this combination is used for treatment of refractory multiple myeloma
3. Acetaminophen, antibiotics, and PPIs: may diminish the therapeutic effect of immune checkpoint inhibitors.
4. Axitinib: may enhance the hepatotoxic effect of Pembrolizumab and diminish the therapeutic effect of immune checkpoint inhibitors.
5. Desmopressin: hyponatremia-associated agents may enhance the hyponatremic effect of Desmopressin.

6. Efgartigimod Alfa: may diminish the therapeutic effect of Fc Receptor-Binding Agents.
7. Ketoconazole (Systemic): immune checkpoint inhibitors may enhance the hepatotoxic effect of Ketoconazole

IV. ADMINISTRATIVE GUIDELINES

A. If following NIOSH and USP <800> recommendations for handling and preparation, Prepare the preparation under aseptic conditions in a containment primary engineering control.

B. IV: Infuse over 30 minutes through a **0.2 to 5 micron** sterile, non-pyrogenic, low-protein binding inline or add-on filter. Do not infuse other medications through the same infusion line.

C. Preparation of product
   1. Visually inspect the solution for particulate matter and discoloration. The solution is clear to slightly opalescent, colorless to slightly yellow. Discard the vial if visible particles are observed.
   2. Withdraw the required volume from the vial(s) of pembrolizumab and transfer into an intravenous (IV) bag containing 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP.
   3. Mix diluted solution by gentle inversion. The final concentration of the diluted solution should be between 1 mg/mL to 10 mg/mL
   4. Discard any unused portion left in the vial
   5. Diluted solutions are stable for 6 hours at room temperature and 96 hours under refrigeration if mixed under aseptic conditions with a primary engineering control

D. Hazardous handling
   1. **It is the responsibility of the dispensing pharmacy to ensure medication handling is in compliance with organizational policies and procedures.** This medication may meet the definitions of a hazardous drug as outlined by NIOSH. It is the responsibility of the dispensing pharmacy to ensure medication handling is in compliance with organizational policies and procedures.

E. Infusion Rates
   1. Infusions are administered over 30 minutes
   2. Do not infuse other agents concomitantly with pembrolizumab in the same IV line.

V. NURSING PROCEDURE

A. If following NIOSH and USP <800> recommendations for handling,

administration, and disposal, supplies may include but are not limited to:

1. Alcohol Swabs
2. Chemo gloves/prep pad/ gown
3. Chemo spill kit
4. Chemo waste bin
5. Dressing change kit
6. IV Pole
7. IV Start Kit
8. Peripheral IV catheter
9. Port access needle
10. Tape
11. Extension set 8”
12. IV injection cap
13. IV administration set (dial-a-flow or gravity) with in-line or add-on 0.22-micron filter
14. Normal Saline (0.9%) saline flushes

B. How Supplied
    1. Pembrolizumab injection (clear to slightly opalescent, colorless to slightly yellow solution): carton containing one 100 mg/4 mL (25 mg/mL), single-dose vial (NDC 0006-3026-02)

C. Storage and Handling
    1. Store vials under refrigeration at 2°C to 8°C (36°F to 46°F) in original carton to protect from light. Do not freeze. Do not shake.

D. Procedures
    1. Explain the reasoning for visit and use of Pembrolizumab.
    2. Don gloves.
    3. Establish venous access prior to preparation of drug if applicable.
    4. Counsel patient on warnings, precautions, and potential side effects including but not limited to:
        a. Fatigue, musculoskeletal pain, rash, diarrhea, pyrexia, cough, decreased appetite, pruritis, dyspnea, constipation, abdominal pain, and nausea
        b. Embryofetal Toxicity
            i. Pembrolizumab can cause fetal harm when administered to a pregnant woman. Advise women of this potential risk. In females of reproductive potential, verify pregnancy status prior to initiating therapy and advise them to use effective contraception during treatment and for 4 months after the last dose.
    5. Infuse over 30 minutes using an in line 0.2 to 5 in micron filter.
    6. The nurse should remain with the patient for 30 minutes following medication administration to monitor vital signs and response to therapy

VI. CLINICAL MONITORING

A. **Prior** to therapy:
   1. Labs/Radiology
      a. LFT's, CBC with differential, serum Cr, thyroid function test, blood glucose tests, cortisol levels
   2. Additional suggested monitoring recommended by American Society of Clinical Oncology (ASCO) prior to initiating Pembrolizumab:
      a. Serum chemistries
      b. Comprehensive clinical assessment including performance status, weight, BMI, heart rate, BP, and oxygen saturation
      c. Consider chest x-ray, ECG, and CT scan
      d. Assess history of autoimmune conditions, organ-specific disease, endocrinopathies, neuropathy, and infectious disease; assess bowel habits, respiratory symptoms, skin (for rash), arthralgias, and neurologic symptoms

B. **During** therapy:
   1. Monitor necessary lab work including LFT's, CBC with differential, serum Cr, thyroid function test, blood glucose tests, cortisol levels, and bone mineral density (with long-term therapy)
   2. Monitor patients for signs and symptoms of infusion-related reactions including rigors, chills, wheezing, pruritus, flushing, rash, hypotension, hypoxemia, and fever.
   3. Assessment of signs/symptoms of adverse effects:
      a. Adrenal insufficiency
      b. Diarrhea/colitis
      c. Dermatologic toxicity
      d. Nephrotoxicity
      e. Diabetes mellitus
      f. Hypophysitis
      g. Ocular disorders
      h. Thyroid disorders
      i. Pneumonitis
      j. Other immune-mediated adverse reactions
   4. Monitor ocular toxicity through regularly scheduled eye exams including intraocular pressure 6 weeks after starting therapy.
   5. If received/receiving hematopoietic stem cell transplant, monitor closely for early signs/symptoms of transplant-related complications.
   6. Monitor PD-L1 expression, tumor specimen microsatellite instability-high (MSI-H) status, mismatch repair deficient (dMMR) status, mismatch repair proficient status, and/or tumor mutational burden-high (TMB-H) status (if applicable).
   7. Additional suggested monitoring recommended by ASCO:
      a. Assess BP, weight, heart rate, and oxygen saturation

b. Assess for infections
c. Serum chemistries

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

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APPENDIX A: ANAPHYLAXIS KIT INTRUCTIONS FOR IV INFUSION

Emergency Medication after Your Infusion

Please call 1-800-755-4704 if you have any questions or concerns. We are available 24 hours a day, 7 days a week. In the event of an emergency, always call 911.

Your nurse will tell you when you need to use Emergency Medications.

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

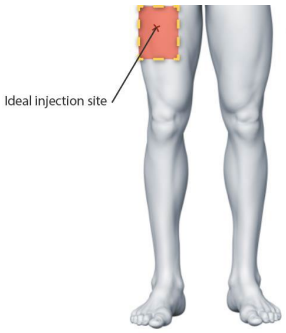
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampule of epinephrine

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, **withdrawal all the 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.
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.

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.