Bristol Myers Squibb®

CAR T ACADEMY

CAR T Cell Infusion

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Journey Through the CAR T Cell Therapy Process

Icon indicates areas of collaboration between the non-CAR T and CAR T treatment teams

Manufacturing

Patient identification[1,2]

- Appropriate patients are identified for treatment at qualified treatment sites or referring sites
- Early collaboration may facilitate timely referral and eligibility evaluation
- Once a patient is confirmed as eligible, leukapheresis is scheduled

Apheresis[1-4]

- Before apheresis, patients undergo a washout of prior medications that may affect T cell health to ensure optimal collection
- Physicians, APPs, and nurse coordinators all play a role in ensuring a proper washout occurs before apheresis
- Patients then undergo apheresis, which involves collection of white blood cells
- The collected apheresis product is then sent to the manufacturer

Bridging[1,3]

- Bridging therapy may be given to maintain disease control during CAR T cell manufacturing
- Appropriate bridging therapy should be discussed and coordinated between the referring physicians and those treating with CAR T cell therapy

LDC and Infusion[1-3]

- LDC is administered prior to CAR T cell infusion to deplete endogenous T cells and create an environment for CAR T cell expansion
- Infusion will then occur at a qualified treatment center

Monitoring and long-term follow-up[1,2,5]

- After infusion, patients are closely monitored for at least 2 weeks at the CAR T cell therapy treatment site, and side effects are promptly managed
- After at least 2 weeks, patients may be discharged back to the referring physician's care
- Communication continues between the CAR T cell therapy treatment center and the primary hematologist/ oncologist as patients are monitored long-term

APP, advanced practice provider; CAR, chimeric antigen receptor; LDC, lymphodepleting chemotherapy.

References: 1. Beaupierre A, et al. *J Adv Pract Oncol.* 2019;10(Suppl 3):29-40. **2.** Beaupierre A, et al. *Clin J Oncol Nurs.* 2019;23:27-34. **3.** McGuirk J, et al. *Cytotherapy.* 2017;19(9):1015-1024. **4.** Qayed M, et al. *Cytotherapy.* 2022;S1465-3249(22)00641-7. **5.** US Food and Drug Administration. Accessed June 27, 2025. https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/fda-eliminates-risk-evaluation-and-mitigation-strategies-rems-autologous-chimeric-antigen-receptor

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01: HANDLING GUIDELINES

02: PATIENT PREPARATION

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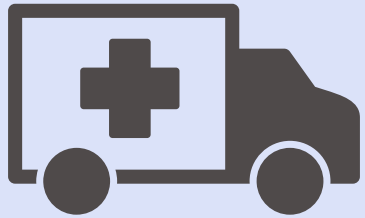
Please note: Each CAR T cell product is unique. Understanding the distinct features and toxicity profile for each product is essential for using these products in the clinic.

Shipment From Manufacturing Facility to Treatment Site

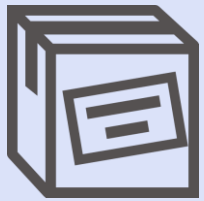
- Once successfully manufactured, CAR T cell products are formulated into a suspension and cryopreserved[1]
- Each product must pass quality tests before release for shipping as a frozen suspension[1–3]
- Each patient-specific product is typically packaged and stored in the vapor phase of liquid nitrogen[1,4]



The patient-specific product is then shipped to the treatment facility[1]

References: 1. Levine BL, et al. *Mol Ther - Methods Clin Dev*. 2017;4(March):92-101. **2.** Vormittag P, et al. *Curr Opin Biotechnol.* 2018;53:164-181. **3.** Li Y, et al. *Engineering*. 2019;5(1):122-131. doi:10.1016/j.eng.2018.12.003. **4.** Chen LN, et al. *Transfusion*. 2019;59(8):2506-2518.

Product Storage



CAR T cell products are delivered frozen and must be maintained in liquid nitrogen storage until being thawed immediately prior to use[2]

- Chain of Identity (COI) describes the ability to link a patient to their cells from the time of leukapheresis through product administration
- Throughout the CAR T cell therapy process, up through delivery to the treatment center and administration to the patient, it is critical that a CAR T cell product remains accurately linked to a specific patient at all times. Labels must be affixed to all product from collection to infusion to maintain COI[1,3,4]
  - Patient identifiers can include first name, last name, and date of birth
- If a site plans to store CAR T cell products on-site for a period of time, there may be regulatory or product-specific requirements for the site to meet in order to do so[2]

COI, chain of identity.

References: 1. Chen LN, et al. *Transfusion.* 2019;59(8):2506-2518. **2.** Yakoub-Agha I, et al. *Haematologica.* 2020;105(2):297-316. **3.** Perica K, et al. *Biol Blood Marrow Transplant.* 2018;24(6):1135-1141. **4.** Papathanasiou MM, et al. *Cancer Gene Ther.* 2020.

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Preparing the Patient for Treatment

Leading up to CAR T cell infusion day

- Administer the lymphodepleting chemotherapy regimen[1]
- Schedule the patient's CAR T cell infusion after completion of lymphodepleting chemotherapy[2]
- Avoid prophylactic use of systemic corticosteroids, as they may interfere with the activity of CAR T cell therapy[1]

Immediately before CAR T cell infusion

- Premedication with acetaminophen and diphenhydramine (or another H1 antihistamine) are generally recommended to minimize the risk of infusion reactions[1,3-9]

- **Reasons for potential delay of infusion include, but are not limited to[1,3-6,8-9]:**
  - Unresolved serious adverse reactions
  - Pulmonary reactions
  - Cardiac reactions
  - Hypotension
  - Active uncontrolled infections
  - Active graft-versus-host disease

References: 1. Yakoub-Agha I, et al. *Haematologica.* 2020;105(2):297-316. **2.** Perica K, et al. *Biol Blood Marrow Transplant.* 2018;24(6):1135-1141. **3.** National Institutes of Heath. DailyMed. Accessed August 5, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=594bb413-af3b-4b97-afb3-bfe2b174f2ed. **4.** National Institutes of Health. Accessed August 5, 2021. DailyMed. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b90c1fe7-f5cc-464e-958a-af36e9c26d7c. **5.** National Institutes of Health. DailyMed. Accessed August 10, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=aad3ba54-dfd3-4cb3-9e2b-c5ef89559189. **6.** National Institutes of Health. DailyMed. Accessed August 10, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=9b70606e-b99c-4272-a0f1-b5523cce0c59. **7.** National Institutes of Health. DailyMed. Accessed October 25, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a16108c2-7ca7-45af-965e-54bda4713022. **8.** National Institutes of Health. DailyMed. Accessed July 1, 2025. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=7d040b91-3fb8-41db-ba7f-60a36f06e2c2 **9.** National Institutes of Health. DailyMed. Accessed July 1, 2025. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4fef6986-b988-45e4-8c20-b14f0ef1f538

Pretreatment Considerations

Before you begin treatment with CAR T cell therapy, note the following:

- **Ensure that tocilizumab and emergency equipment are available prior to infusion and during the recovery period[1]**
- Monitor patients for signs and symptoms of infection before and after CAR T cell administration and treat appropriately.[2] CAR T cell therapy should not be administered to patients with clinically significant active systemic infections[3]
- Monitor complete blood counts prior to and after CAR T cell therapy administration[2]
- CAR T cell therapy may cause a false-positive HIV test result by some commercial tests[4,5]

HIV, human immunodeficiency virus

References: 1. Perica K, et al. *Biol Blood Marrow Transplant.* 2018;24(6):1135-1141. **2.** Beaupierre A, et al. *Clin J Oncol Nurs.* 2019;23(2):27-34. **3.** Yakoub-Agha I, et al. *Haematologica.* 2020;105(2):297-316. **4.** Hauser JR, et al. *J Clin Microbiol.* 2019;58:e01420-19. **5.** Ariza-Heredia EJ, et al. *Diagn Microbiol Infect Dis.* 2017;88(4):305-307.

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Product Preparation for Infusion[1-7]

Confirm the infusion time in advance, and adjust the start time of product thaw, if necessary

Match the patient's identity with the patient identifiers on the CAR T cell product documentation

Remove the CAR T cell product and verify that the contents match the product documentation

(continued on next slide)

References: 1. National Institutes of Heath. DailyMed. Accessed August 5, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=594bb413-af3b-4b97-afb3-bfe2b174f2ed. **2.** National Institutes of Health. DailyMed. Accessed August 5, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b90c1fe7-f5cc-464e-958a-af36e9c26d7c. **3.** National Institutes of Health. DailyMed. Accessed August 10, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=aad3ba54-dfd3-4cb3-9e2b-c5ef89559189. **4.** National Institutes of Health. DailyMed. Accessed August 10, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=9b70606e-b99c-4272-a0f1-b5523cce0c59. **5.** National Institutes of Health. DailyMed. Accessed October 25, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a16108c2-7ca7-45af-965e-54bda4713022. **6.** National Institutes of Health. DailyMed. Accessed July 1, 2025. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=7d040b91-3fb8-41db-ba7f-60a36f06e2c2 **7.** National Institutes of Health. DailyMed. Accessed July 1, 2025. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4fef6986-b988-45e4-8c20-b14f0ef1f538

Product Preparation for Infusion (cont.)

Inspect the product for any breaches of container integrity (breaks, cracks) and confirm appropriate patient identifiers upon receipt[1]

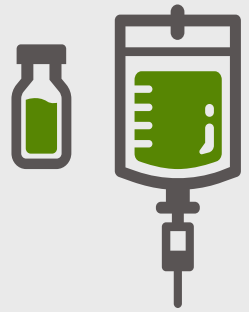
Thaw the CAR T cell product per the product manufacturer's specific guidance[2-8]

Refer to the product's specific prescribing information for the expiration time following thawing. Ensure that the dose is administered to the patient before the expiration period[2-8]

References: 1. Yakoub-Agha I, et al. *Haematologica.* 2020;105(2):297-316. **2.** National Institutes of Heath. DailyMed. Accessed August 5, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=594bb413-af3b-4b97-afb3-bfe2b174f2ed. **3.** National Institutes of Health. DailyMed. Accessed August 5, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b90c1fe7-f5cc-464e-958a-af36e9c26d7c. **4.** National Institutes of Health. DailyMed. Accessed August 10, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=aad3ba54-dfd3-4cb3-9e2b-c5ef89559189. 5. National Institutes of Health. DailyMed. Accessed August 10, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=9b70606e-b99c-4272-a0f1-b5523cce0c59. **6.** National Institutes of Health. DailyMed. Accessed October 25, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a16108c2-7ca7-45af-965e-54bda4713022. **7.** National Institutes of Health. DailyMed. Accessed July 1, 2025. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=7d040b91-3fb8-41db-ba7f-60a36f06e2c2 **8.** National Institutes of Health. DailyMed. Accessed July 1, 2025. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4fef6986-b988-45e4-8c20-b14f0ef1f538

Line Set Up and Infusion[1-7]

- Refer to the CAR T cell product's specific prescribing information for details on how to administer the particular CAR T cell product
- Before, during, and after administration, follow universal precautions and local biosafety guidelines for handling and disposal to avoid potential transmission of infectious diseases



Please refer to the product prescribing information for specific guidance regarding line set up and infusion[8]

IV, intravenous.

References: 1. National Institutes of Heath. DailyMed. Accessed August 5, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=594bb413-af3b-4b97-afb3-bfe2b174f2ed. **2.** National Institutes of Health. DailyMed. Accessed August 5, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b90c1fe7-f5cc-464e-958a-af36e9c26d7c. **3.** National Institutes of Health. DailyMed. Accessed August 10, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=aad3ba54-dfd3-4cb3-9e2b-c5ef89559189. **4.** National Institutes of Health. DailyMed. Accessed August 10, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=9b70606e-b99c-4272-a0f1-b5523cce0c59. **5.** National Institutes of Health. DailyMed. Accessed October 25, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a16108c2-7ca7-45af-965e-54bda4713022. **6.** National Institutes of Health. DailyMed. Accessed July 1, 2025. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=7d040b91-3fb8-41db-ba7f-60a36f06e2c2 **7.** National Institutes of Health. DailyMed. Accessed July 1, 2025. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4fef6986-b988-45e4-8c20-b14f0ef1f538 **8.** Beaupierre A, et al. *Clin J Oncol Nurs.* 2019;23(2):27-34.

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Sites of Infusion

Some clinical trials or products require inpatient admission for administration and post-infusion monitoring

- Inpatient admission may be necessary to manage the unique toxicities (eg, CRS, neurotoxicity) associated with CAR T cell therapy

Outpatient Centers

Certain CAR T cell products were administered in the outpatient setting in clinical trials

- Whether or not outpatient administration is appropriate will be up to the prescribing physician, dependent on what is appropriate for the patient, based on patient-specific considerations, including but not limited to severity of disease, caregiver support, and proximity to the treatment center
- Feasibility will also depend on the product and institutional infrastructure

CRS, cytokine release syndrome.

Reference: 1. Chow VA, et al. *Blood.* 2018;132:777-781.

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Team Coordination Is Key Before, During, and After CAR T Cell Infusion

Before Infusion[1]

Evaluate the patient for CAR T cell therapy based on physical assessment, medical records, laboratory assessment, treatment history, and other relevant information

During Infusion[1]

Infusion should be conducted by staff appropriately trained on the specific CAR T cell therapy

After Infusion[2]

Nursing staff, pharmacists, treating physicians, and primary hematologists should maintain close communication to identify patients experiencing toxicity and rapidly intervene

References: 1. McGuirk J, et al. *Cytotherapy.* 2017;19:1015-1024. **2.** Brudno JN, Kochenderfer JN. *Blood Rev.* 2019:34:45-55.

Summary

Handling Guidelines[1,2]

- Patient-specific CAR T cell products are typically cryopreserved, individually packaged, and shipped to the treatment facility
- The CAR T cell product typically will be stored frozen in the vapor phase of liquid nitrogen until ready for infusion

Patient Preparation[3-10]

- Lymphodepleting chemotherapy should be administered prior to CAR T cell infusion, with CAR T cell administration scheduled following completion
- Patients should be evaluated by a healthcare provider qualified in delivering CAR T cell therapy on the day of infusion to assess for any clinical concerns that might require a delay in treatment delivery
- To minimize risk of infusion reactions, patients should receive acetaminophen and H1 antihistamines just before CAR T cell product infusion

References: 1. Levine BL, et al. *Mol Ther - Methods Clin Dev*. 2017;4(March):92-101. **2.** Chen LN, et al. *Transfusion*. 2019;59(8):2506-2518. **3.** Yakoub-Agha I, et al. *Haematologica*. 2020;105(2):297-316. **4.** National Institutes of Heath. DailyMed. Accessed August 5, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=594bb413-af3b-4b97-afb3-bfe2b174f2ed. **5.** National Institutes of Health. Accessed August 5, 2021. DailyMed. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b90c1fe7-f5cc-464e-958a-af36e9c26d7c. **6.** National Institutes of Health. DailyMed. Accessed August 10, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=aad3ba54-dfd3-4cb3-9e2b-c5ef89559189. **7.** National Institutes of Health. DailyMed. Accessed August 10, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=9b70606e-b99c-4272-a0f1-b5523cce0c59. **8.** National Institutes of Health. DailyMed. Accessed October 25, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a16108c2-7ca7-45af-965e-54bda4713022. **9.** National Institutes of Health. DailyMed. Accessed July 1, 2025. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=7d040b91-3fb8-41db-ba7f-60a36f06e2c2 **10.** National Institutes of Health. DailyMed. Accessed July 1, 2025. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4fef6986-b988-45e4-8c20-b14f0ef1f538

Summary

Product Preparation[1-7]

- Because autologous CAR T cell products are patient-specific therapies, it is important to match the patient's identity to that of the product at all steps prior to infusion
- When the patient is ready to receive the CAR T cell product, the therapy must be thawed before use, which requires coordinated timing and reference to the product-specific guidance for thawing and preparation
- Intravenous line set up and infusion should be performed in accordance with product-specific labeling

Product Guidelines[8]

- CAR T cells can be administered at the treating physician's discretion in the inpatient and/or outpatient settings, depending on the product and patient considerations, as well as the capabilities of the treatment site

Multidisciplinary Team Coordination[9,10]

- Delivering optimal care to patients receiving CAR T cell therapy requires multidisciplinary collaboration before, during, and after CAR T cell infusion

References: 1. National Institutes of Heath. DailyMed. Accessed August 5, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=594bb413-af3b-4b97-afb3-bfe2b174f2ed. **2.** National Institutes of Health. Accessed August 5, 2021. DailyMed. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b90c1fe7-f5cc-464e-958a-af36e9c26d7c. **3.** National Institutes of Health. DailyMed. Accessed August 10, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=aad3ba54-dfd3-4cb3-9e2b-c5ef89559189. **4.** National Institutes of Health. DailyMed. Accessed August 10, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=9b70606e-b99c-4272-a0f1-b5523cce0c59. **5.** National Institutes of Health. DailyMed. Accessed October 25, 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a16108c2-7ca7-45af-965e-54bda4713022. **6.** National Institutes of Health. DailyMed. Accessed July 1, 2025. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=7d040b91-3fb8-41db-ba7f-60a36f06e2c2 **7.** National Institutes of Health. DailyMed. Accessed July 1, 2025. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4fef6986-b988-45e4-8c20-b14f0ef1f538 **8.** Chow VA, et al. *Blood.* 2018;132:777-781. **9.** McGuirk J, et al. Cytotherapy. 2017;19:1015-1024. **10.** Brudno JN, Kochenderfer JN. Blood Rev. 2019:34:45-55.

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