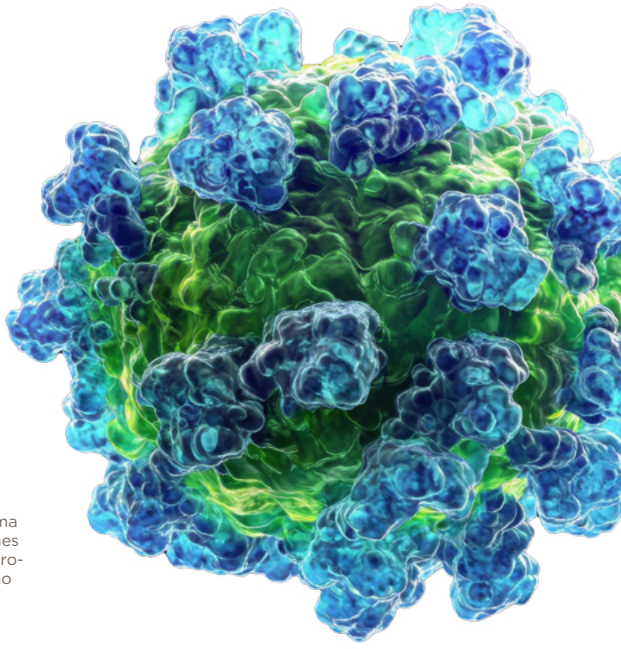
HIRSLANDEN
KLINIK HIRSLANDEN

CAR-T-CELL-THERAPY

for the treatment of relapsed/refractory multiple myeloma from 3L* onwards

BROCHURE FOR REFERRING PHYSICIANS

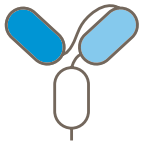
INFORMATION ON THERAPY WITH CARVYKTI®
AND PATIENT CARE



* CARVYKTI® is indicated for the treatment of adult patients with relapsed and refractory multiple myeloma (RRMM) who have previously received at least two lines of therapy, including an immunomodulatory drug, a proteasome inhibitor and an anti-CD38 antibody, and who are refractory to lenalidomide.[1]

WHAT CARVYKTI® IS AND WHAT IT IS USED FOR

TREATMENT OF RELAPSED AND REFRACTORY MULTIPLE MYELOMA (RRMM) WITH CARVYKTI® (CILTACABTAGENE AUTOLEUCEL) FROM THE 3rd* LINE OF THERAPY ONWARDS[2]



CARVYKTI® (ciltacabtagene autoleucel) is an immunotherapy carried out with autologous T cells that uses a chimeric antigen receptor (CAR), consisting of two single-domain antibodies directed against BCMA, to recognise and eliminate BCMA-expressing cells with high avidity. This distinguishes CARVYKTI® from idecabtagene vicleucel, with an anti-BCMA-scFv target domain.[3]

Since October 2024, CARVYKTI® has been approved and reimbursed after 2* lines of therapy for your adult patients with RRMM who:

- have previously received at least two lines of therapy, including an immunomodulatory drug (IMiD), a proteasome inhibitor (PI) and an anti-CD38 antibody, and who are refractory to lenalidomide.[1]
- have previously received at least three therapies with at least one PI, one IMiD and one anti-CD38 antibody, and who exhibited progression after the last therapy.[1]

CARVYKTI® is administered at a CAR-T-certified centre, such as the Klinik Hirslanden. It is important that you have all the information you need to refer and care for your patients with RRMM.

BCMA: B-cell maturation antigen; **CAR:** chimeric antigen receptor; **CD:** cluster of differentiation; **IMiD:** immunomodulatory drug; **MM:** multiple myeloma; **PI:** proteasome inhibitor; **RRMM:** relapsed/refractory multiple myeloma; **scFv:** single chain variable fragment.

IS YOUR PATIENT SUITABLE FOR CAR-T-CELL THERAPY?

For a referral, it is important that you have all the necessary information on eligibility criteria for your patients with RRMM[1]

SGH-SSH / SSMO Guideline recommendation includes the use from 3L* onwards[4]

For which of your patients in the 3rd* line, could CARVYKTI® be an option?

- ☑ 18 years or older
- ☑ Lenalidomide-refractory
- ☑ At least two previous lines of therapy, incl.
  - a PI
  - an IMiD
  - an anti-CD38 antibody
- ☑ No contraindications to CARVYKTI® or lymphodepleting chemotherapy
- ☑ Diagnosed with RRMM
- ☑ With or without BCMA-based pre-treatment

Not exhaustive. See full information in the current Information for Healthcare Professionals.

*CARVYKTI® is indicated for the treatment of adult patients with RRMM who have previously received at least two lines of therapy, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody, and who are refractory to lenalidomide.[1]

HOW DOES THE COOPERATION BETWEEN YOU AND THE KLINIK HIRSLANDEN WORK?

The course of therapy with CARVYKTI® in brief

Referring doctors (to Klinik Hirslanden)

Klinik Hirslanden as a certified CARVYKTI® centre

Referring physicians

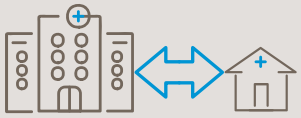
Referring physicians determine the indication and clarify the procedure regarding bridging therapy*, leukapheresis and other factors in consultation with the Klinik Hirslanden.

The Klinik Hirslanden covers:
- Initial examination
- Request for commitment to cover costs
- Patient Informed Consent
- Lymphodepletion and CAR-T therapy
- Monitoring and follow-up for up to 28 days
- etc.

Patients are referred back to the referring physician for long-term follow-up.

Recommendations for therapy planning at the Klinik Hirslanden

Contact the Klinik Hirslanden at an early stage if your patients with RRMM are showing the first signs of progression from the 2nd line of therapy onwards.



A joint decision is taken on whether a patient is suitable for CAR-T-cell therapy and if so, which bridging therapy* is necessary and when a T-cell toxic therapy should be avoided.

When choosing preceding therapies, please bear in mind any possible negative impact on subsequent CAR-T-cell therapy.

Requests for a commitment to cover costs are submitted by our experienced team at Klinik Hirslanden.

*For rapidly progressing disease: If indicated, short-term treatment after leukapheresis and before infusion of CARVYKTI® with a regimen that had previously at least led to stable disease.

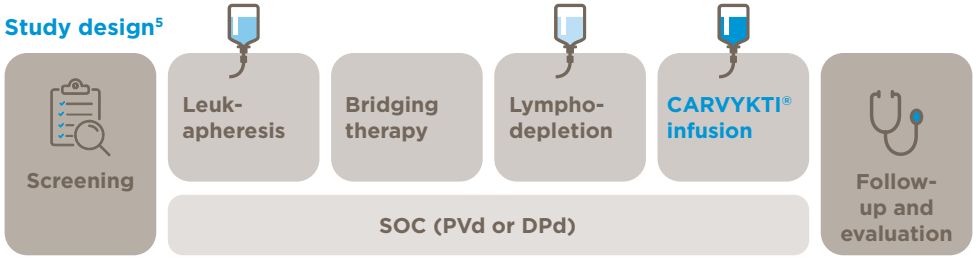
CARVYKTI® for 3*L RRMM – THE CARTITUDE-4 STUDY

CARTITUDE-4: Randomised Phase III study of CARVYKTI® for RRMM in comparison with an effective standard of care chosen by physicians (SOC: PVd or DPd). All patients had previously received 1*-3 lines of therapy.[5]

Important inclusion criteria[5]

- Lenalidomide-refractory
- 1*-3 lines of therapy, including a proteasome inhibitor and an immunomodulatory drug
- ECOG PS 0 or 1 before randomisation
- Previous ASCT and/or exposure to anti-CD38 was permitted but not required
- No prior CAR-T-cell therapy or BCMA-targeted treatment

Study design[5]



Important end points[5]

Primary endpoint
- PFS (defined as the time from randomisation to the first documentation of progression of the disease or death)

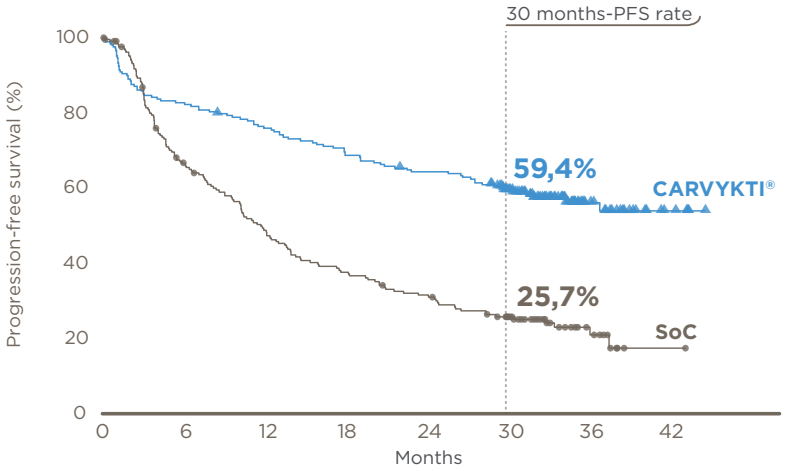
Important secondary endpoints
- CR or better
- ORR
- MRD negativity rate
- OS
- Worsening of patient-reported symptoms as assessed by the Multiple Myeloma Symptom and Impact Questionnaire
- Incidence and severity of Adverse Events

* CARVYKTI® (ciltacabtagene autoleucel) is not authorised in Switzerland for patients with RRMM and only one previous line of treatment. Further information can be found in the CARVYKTI® (ciltacabtagene autoleucel) Information for Health-care Professionals at www.swissmedicinfo.ch.
ASCT: autologous stem cell transplantation; **BCMA:** B-cell maturation antigen; **CAR:** chimeric antigen receptor; **CD:** cluster of differentiation; **CR:** complete response; **DPd:** daratumumab, pomalidomide and dexamethasone; **ECOG PS:** Eastern Cooperative Oncology Group Performance Status; **ITT:** intention-to-treat; **MRD:** minimal residual disease; **ORR:** overall response rate; **OS:** overall survival; **PFS:** progression-free survival; **PVd:** pomalidomide, bortezomib and dexamethasone; **SOC:** standard of care.

CARTITUDE-4 PRIMARY ENDPOINT: PFS BENEFIT vs SoC

CARVYKTI® SIGNIFICANTLY PROLONGED PFS VS SOC IN PATIENTS WITH RRMM (ITT POPULATION).[2,*]

After a single CARVYKTI® infusion, the median PFS for the CARTITUDE-4 study was not yet reached after 30 months



Patients at risk

CARVYKTI®	208	177	172	165	157	150	145	136	132	129	111	65	29	13	5	0
SoC	211	176	133	116	96	80	74	65	61	52	47	25	12	1	1	0

Adapted according to Mateos MV et al. 2024[2]

CARVYKTI® also showed a

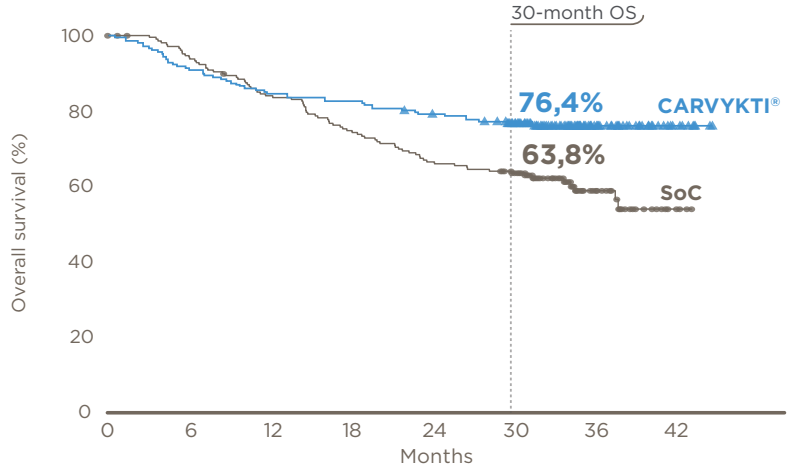
71% reduction in the risk of progression and mortality vs SOC*

(HR 0,29; 95% CI: 0,22-0,39; p<0,0001)

* vs. SoC: either PVd or DPd at the discretion of the doctors. p<0,0001[5]

CARTITUDE-4: OVERALL SURVIVAL UNDER CARVYKTI®

CARVYKTI® WAS THE FIRST CAR-T-CELL THERAPY IN THE RRMM TO SHOW A SIGNIFICANT OVERALL SURVIVAL BENEFIT VS. SOC (ITT POPULATION).[2,*]



Adapted according to Mateos MV et al. 2024[2]

CARVYKTI® also showed a

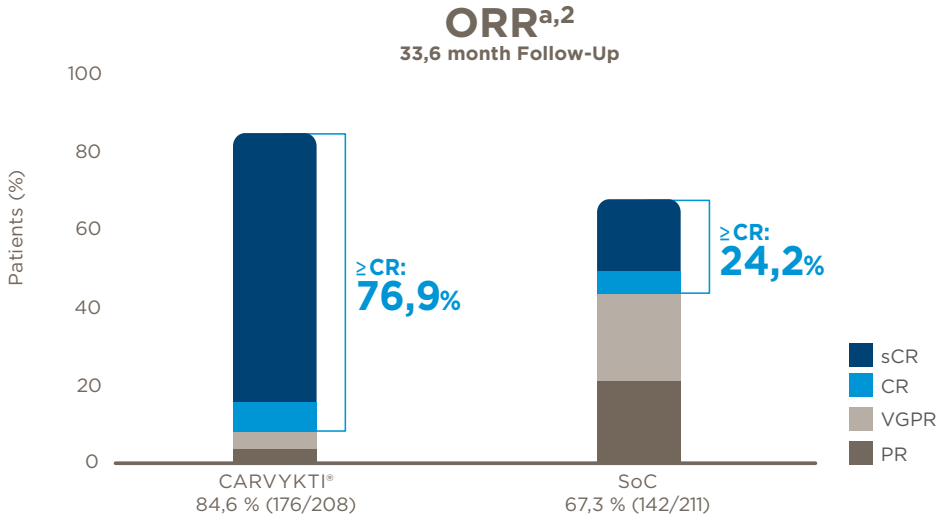
45% reduction in the risk of mortality vs SoC*

(HR 0,55; 95% CI: 0,39-0,79; p=0,0009)

* vs. SoC: either PVd or DPd at the discretion of the doctors. p<0,0009[5]

CARTITUDE-4: HIGH OVERALL RESPONSE RATES, MRD-NEGATIVITY AND SAFETY PROFILE

77 % of patients in the CARVYKTI® group achieved a complete response or better vs 24 % in the SOC group.[2]



Adapted according to Mateos MV et al. 2024[2]

MRD negativity after treatment with CARVYKTI®: Over 60% of patients who received CARVYKTI® achieved MRD negativity.[1,2]

The safety profile corresponded to that of the previous study programme[1]
Treatment-related adverse reactions occurred at a similar frequency in the CARVYKTI®and SOC groups[4]

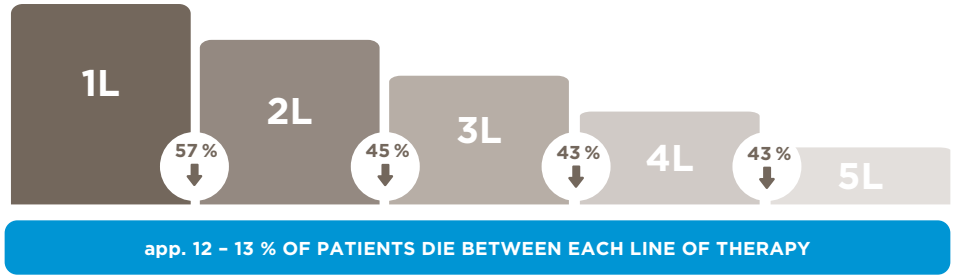
a: Assessment using a validated computerised algorithm; ORR is defined as the proportion of subjects who achieve a PR or better according to the IMWG criteria.
CR: complete response; **IMWG:** International Myeloma Working Group; **MRD:** minimal residual disease; **ORR:** overall response rate; **PR:** partial response; **sCR:** stringent complete response; **SOC:** standard of care; **VGPR:** very good partial response.

WHEN IS THE RIGHT TIME FOR CAR-T-CELL THERAPY?

ALMOST 6 OUT OF 10 PATIENTS WITH RRMM CANNOT RECEIVE A FURTHER LINE OF THERAPY.[6]

The depth of response, the time to disease progression and the duration of treatment decrease with each subsequent line of therapy.[6] In addition, patients of advanced age and/or with certain comorbidities are less likely to receive a further line of therapy.[6]

Attrition rates of transplant-ineligible patients with MM by LOT (US-Data).[6]



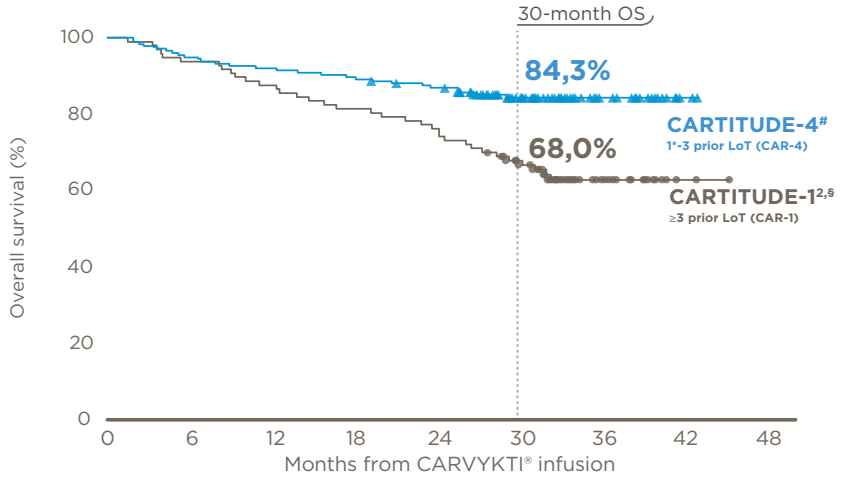
"CAR-T-cell therapy is a new type of immunotherapy that is based on the body's own defence cells. Treatment planning is complex and should take place as early on as possible in the course of treatment for better prospects of a good outcome."

Prof. Dr med. Christoph Renner, Klinik Hirslanden, Zurich

EARLY USE OF CARVYKTI® CAN PROVIDE A HIGHER BENEFIT

THE USE OF CARVYKTI® IN PREVIOUS LINES OF THERAPY SHOWED A NUMERICALLY BETTER OVERALL SURVIVAL.[2]

CARTITUDE-4 and CARTITUDE-1 studies: Patients who received CARVYKTI® as treatment (treated population)[2]



Patients at risk

CARTITUDE-4 1*–3 prior LoT	176	172	167	163	162	160	158	154	151	137	83	53	20	12	2	0	0
CARTITUDE-1 ≥3 prior LoT	97	96	91	88	85	81	79	77	74	69	59	33	19	10	2	1	0

Adapted according to Mateos MV et al. 2024[2]

* CARVYKTI® (ciltacabtagene autoleucel) is not authorised in Switzerland for patients with RRMM and only one previous line of treatment. Further information can be found in the CARVYKTI® (ciltacabtagene autoleucel) Information for Health-care Professionals at www.swissmedicinfo.ch. # For patients receiving CARVYKTI® as treatment (treated population), the start of treatment was set to the time of the CARVYKTI® infusion, with a median follow-up of 30.05 months.[2] Data from the CARTITUDE-4 randomised, open-label phase III study on the efficacy of CARVYKTI® vs SOC in 419 patients with lenalidomide-refractory MM who had all previously received 1*-3 lines of therapy (baseline ECOG PS 0 or 1).[4] § Data from the 33.4-month median follow-up[2] under CARVYKTI® of the open-label, multicentre phase Ib/II study CARTITUDE-1 with 97 patients with RRMM according to IMWG criteria with ≥3 previous lines of therapy or who were double refractory to a PI and IMiD (prior PI, IMiD and anti-CD38 mAb administration).[7]
LOT: line of therapy; **OS:** overall survival.

FOLLOW-UP IN CAR-T CENTRES AND SELECTED ADVERSE EVENTS OF CARVYKTI®

Short-term follow-up: Patients are monitored daily for the first 14 days after the infusion and then regularly for a further two weeks at the Klinik Hirslanden for signs and symptoms of Adverse Events.

Patients must be instructed to stay in the vicinity (maximum 2 hours away) of a CAR-T centre for at least 4 weeks after the infusion.

Cytokine release syndrome (CRS)[1]

Signs
and measures
See page on right

83%
(n=330/396)*
of the patients
under CARVYKTI®
exhibited CRS

Immune effector cell-associated neurotoxicity syndrome (ICANS)[1]

Signs
and measures
See page on right

11%
(n=45/396)*
of the patients
under CARVYKTI®
exhibited ICANS

CAR: chimeric antigen receptor; **CRS:** cytokine release syndrome; **ICANS:** immune effector cell-associated neurotoxicity syndrome.
* Incidences from pooled study data

COMMON SYMPTOMS OF CRS AND NEUROTOXICITY

Long-term follow-up: Long-term follow-up will take place on an outpatient basis with referring doctors, after consultation with the centre. Patients should continue to be reminded of the possible signs of CRS and neurotoxicity and be made aware that they should seek medical help immediately in such cases.

CRS: Fever (with or without rigor), chills, hypotension, hypoxia and elevated liver enzymes.

ICANS: Aphasia, slowed speech, dysgraphia, encephalopathy, impaired consciousness and confusion.

At the first signs of ICANS or CRS, immediate assessment for hospitalisation.
See www.swissmedicinfo.ch for more information.

Brief description of specific further neurotoxicities
Incidences from pooled study data[1]

Cranial nerve palsies[1]

Signs and possible measures
- e.g.: facial paresis
- Depending on severity, short-term treatment with systemic corticosteroids

7%
(n=27/396)
of patients treated
with CARVYKTI®
exhibited cranial
nerve palsy

Median time to
occurrence (incl. range)
22 days (17-101)
Median duration (incl. range)
56 days (1-209)

Parkinsonism[1]

Possible measures
- Supportive care measures
- In the CARTITUDE programme with 150 CARVYKTI® patients, risk reduction and management strategies reduced the incidence of exercise-related and neurocognitive toxicities from 5% to <1%.[8]

2%
(n=9/396)
of patients taking
CARVYKTI®
exhibited
symptoms of
Parkinsonism

Median time to
occurrence (incl. range)
38 days (14-914)
Duration (range)
Up to 996 days

All nine patients were male and had a history of previous CRS (mostly ICANS).

FURTHER SELECTED ADVERSE EVENTS OF CARVYKTI®

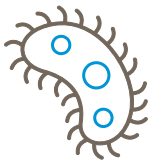
Cytopenias[1]

Possible measures
- Monitor blood count
- In cases of thrombocytopenia, consider supportive therapy measures with transfusions

Incidence of longer lasting cytopenias
Initially grade 3/4 (%) under CARVYKTI® and no improvement until ≤ grade 2 **by day 30**

Thrombocytopenia	**33%**
Neutropenia	**29%**
Lymphopenia	**25%**
Anaemia	**3%**

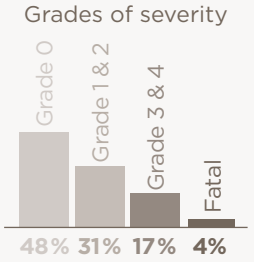
Infections[1]



Possible measures
- Monitor for signs
- In cases of febrile neutropenia, the infection should be investigated and treated accordingly with broad-spectrum antibiotics and supportive care.

52%

(n=206/396) of patients on CARVYKTI® had infections



Incidences from pooled study data

Secondary malignancies[1]

Possible measures
- Contact marketing authorisation holder for case registration and to receive instructions for taking patient samples for testing

For further measures, see the full Information for Healthcare Professionals for CARVYKTI®: www.swissmedicinfo.ch

REFERENCES BRIEF INFORMATION FOR PROFESSIONALS CARVYKTI®

References: 1. CARVYKTI® Information for Healthcare Professionals (February 2025) at www.swissmedicinfo.ch. **2.** Mateos M-V, et al. Presented at: 21st International Myeloma Society (IMS) Annual Meeting; 25–28 September 2024; Rio de Janeiro, Brazil. Overall Survival With Ciltacabtagene Autoleucel Versus Standard of Care in Lenalidomide-Refractory Multiple Myeloma: Phase 3 CARTITUDE-4 Study Update. **3.** Martin T, et al.Ciltacabtagene Autoleucel, an Anti-B-cell Maturation Antigen Chimeric Antigen Receptor T-Cell Therapy, for Relapsed/Refractory Multiple Myeloma: CARTITUDE-1 2-Year Follow-Up. Journal of Clinical Oncology. 2023; 41(6):1265–1274. **4.** Onkopedia guideline, Multiple myeloma, as of October 2024, at: onkopedia.com/en/onkopedia/guidelines/multiple-myeloma/@@guideline/html/index.html. Last accessed: 04/2025. **5.** San-Miguel J, et al. Cilta-cel or Standard Care in Lenalidomide-Refractory Multiple Myeloma. N Engl J Med 2023;389:335-47. **6.** Fonseca R, et al. Frontline treatment patterns and attrition rates by subsequent lines of therapy in patients with newly diagnosed multiple myeloma. BMC Cancer 2020;20:1087. **7.** Berdeja JG, et al. Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study. Lancet 2021; 398(10297): 314–324. **8.** Cohen AD, et al. Incidence and management of CAR-T neurotoxicity in patients with multiple myeloma treated with ciltacabtagene autoleucel in CARTITUDE studies. Blood Cancer J 2022;12(2):32.

Supporting documents are available on request from Janssen-Cilag AG, a Johnson & Johnson company.

Abbreviated Information for Professionals CARVYKTI®
CARVYKTI®: I: For the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least two prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody and are refractory to lenalidomide or who have received at least three prior therapies, with at least a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 antibody and have demonstrated disease progression on the last therapy. **D:** For autologous and intravenous use only. CARVYKTI® must be administered in a qualified treatment centre with direct access to appropriate intensive care units. A single dose of CARVYKTI is 0.5-1.0 × 10^6 CAR-positive viable T-cells per kg body weight up to a maximum of 1 × 10^8 CAR-positive viable T-cells in suspension. For more detailed information on recommendations for preparing patient for infusion, preparation of CARVYKTI® for infusion, monitoring after infusion, management of ADRs, refer to www.swissmedicinfo.ch **CI:** Hypersensitivity to the active substance or any of the excipients (Cryostor CS5 which contains dimethyl sulfoxide). CI to lymphodepleting chemotherapy must be considered. **SP:** Rapidly progressing disease, cytokine release syndrome (CRS), neurologic toxicities, ICANS, movement and neurocognitive toxicity with signs and symptoms of parkinsonism, Guillain-Barré syndrome, peripheral neuropathy, cranial nerve palsies, prolonged and recurrent cytopenias, serious infections and febrile neutropenia, viral reactivation, hypogammaglobulinemia, live vaccines, secondary malignancies, hypersensitivity, blood, organ, tissue and cell donation. **ADR:** *Very common:* Upper respiratory tract infection, viral infection, bacterial infection, pneumonia, neutropenia, thrombocytopenia, anemia, lymphopenia, leukopenia, coagulopathy, cytokine release syndrome, hypogammaglobulinemia, hypophosphatemia, hypokalemia, hypocalcemia, decreased appetite, hypomagnesemia, hypoalbuminemia, hyponatremia, hyperferritinemia, headache, motor dysfunction, dizziness, immune effector cell-associated neurotoxicity syndrome, encephalopathy, sleep disorder, tachycardia, hypotension, hypertension, hemorrhage, cough, dyspnea, hypoxia, diarrhea, nausea, constipation, vomiting, musculoskeletal pain, pyrexia, fatigue, edema, chills, pain, transaminase elevation, increased gamma-glutamyltransferase. *Common:* Sepsis, gastroenteritis, urinary tract infection, fungal infection, hematologic malignancy, febrile neutropenia, lymphocytosis, hemophagocytic lymphohistiocytosis, delirium, personality changes, cranial nerve palsies, neuropathy peripheral, aphasia, tremor, ataxia, neurotoxicity, paresis, cardiac arrhythmias, thrombosis, capillary leak syndrome, abdominal pain, hyperbilirubinemia, rash, renal failure, blood alkaline phosphatase increased and increased C-reactive protein. **IA:** No interaction studies have been performed with CARVYKTI®, some commercial HIV nucleic acid tests may yield false-positive results. For more information: www.swissmedicinfo.ch. **Packs:** Infusion bag individually packed in an aluminium cryo cassette. **Detailed information:** www.swissmedic.ch ou www.swissmedicinfo.ch. **Marketing authorisation holder:** Janssen-Cilag AG, Gubelstrasse 34, 6300 Zug (CH_ CP-508505)

▼ This medicinal product is subject to additional monitoring. For more information, see the product information (CARVYKTI®) at www.swissmedicinfo.ch

CONTACT

Use the adjacent QR code to find out more about CAR-T-cell therapy. For questions and referrals relating to cell therapy at the Klinik Hirslanden, please contact the medical team of the medical programme for cell therapy by phone on +41 44 387 37 80 or by email.

Hirslanden Emergency Centre Zurich,
Witellikerstrasse 40, 8032 Zurich
Available 24 hours a day on
phone no. +41 44 387 35 35

Prof. Dr med. Christoph Renner

Specialist in: Haematology, general internal medicine, medical oncology

christoph.renner@kho.ch

PD Dr med. Panagiotis Samaras

Specialist in: Medical oncology, general internal medicine

panagiotis.samaras@kho.ch

PD Dr med. Karin Hohloch

Specialist in: General internal medicine, medical oncology, haematology

karin.hohloch@kho.ch

Dr med. Ulf Petrausch

Specialist in: Medical oncology, general internal medicine, allergology and clinical immunology

ulf.petrausch@ozh.ch

in cooperation with:

HIRSLANDEN
KLINIK HIRSLANDEN

Johnson&Johnson

LEGEND BIOTECH

CP-517327_04/2025