HTA Austria
Austrian Institute for Health Technology Assessment GmbH

Datopotamab deruxtecan (Datroway®)

for the treatment of unresectable or metastatic hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2–) breast cancer

General information [1]

INN	®		ATC Code	Substance class	Type of indication [1]
Datopotamab deruxtecan	Datroway®	Daiichi Sankyo Europe GmbH (MAH)	L01FX35	Antineoplastic agents	New indication

Mechanism of action [2]	Dosing & administration [2]	Setting in Austria [2]
Datopotamab deruxtecan is a TROP2-directed antibody-drug conjugate linking a humanised anti-TROP2 antibody to the topoisomerase I inhibitor deruxtecan (DXd) via a cleavable linker. After binding and internalisation in TROP2-expressing tumour cells, DXd is released, causing DNA damage and apoptosis. Additional indirect cytotoxic effects occur through antibody-dependent cellular cytotoxicity, antibody-dependent cellular phagocytosis, and bystander mechanisms.	The recommended dose of datopotamab deruxtecan is 6 mg/kg (up to a maximum of 540 mg for patients with a body weight of >90 kg) administered as an intravenous (IV) infusion once every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity occurs.	☒ Hospital ☐ Interface between hospital and outpatient sector ☐ Outpatient sector

Indication [1]

Datopotamab deruxtecan as monotherapy is indicated for the treatment of adult patients with unresectable or metastatic HR+, HER2- breast cancer who have received endocrine therapy and at least one line of chemotherapy in the advanced setting.

EMA approval status [1]	FDA approval status [3]
☒ **Approved for this indication** ✓ Positive CHMP opinion on 30th January 2025 ✓ Marketing authorisation issued on 4th April 2025 ✓ Additional monitoring ongoing ☐ **Approved for other indications:** ✓ none	☒ **Approved for this indication** ✓ FDA approval on 17th January 2025 (indication identical with CHMP) ☐ **Approved for other indications:** ✓ none

Disease

Description [2, 4]	Prevalence & incidence in Austria	Mortality in Austria
HR+, HER2- advanced breast cancer is defined by the presence of oestrogen and/or progesterone receptor expression (≥1 % positive cells by immunohistochemistry), and the absence of HER2 gene amplification or protein overexpression. Diagnosis relies on histopathologic confirmation from tumour or metastatic tissue, including assessment of oestrogen receptor, progesterone receptor, and HER2 status. At the metastatic stage, molecular testing is conducted to identify actionable mutations. This subtype represents the most common form of advanced breast cancer, typically exhibiting a more indolent course and sensitivity to endocrine therapy. However, many patients eventually develop endocrine therapy resistance, defined by disease progression or clinical deterioration during hormonal treatment, new or enlarging metastases, or shortened duration of response to prior endocrine therapy.	2023 [5]: ❖ 6,971 persons were newly diagnosed with breast cancer. ❖ The age-standardised incidence rate was 137.2/100,000 in women and 1.6/100,000 in men. ❖ Breast cancer was the most diagnosed cancer among women, accounting for ~30 % of all female cancer cases. At the end of 2022, 89,188 women and 742 men were living with a breast cancer diagnosis, representing the largest cancer survivor group in Austria [6]. Given that approximately 70% of all breast cancer cases are HR+/HER2-, it is estimated that around 4,600 individuals in Austria are diagnosed with this subtype each year [7].	2023 [5]: ❖ The age-standardised mortality rate was 29.8/100,000 in women and 0.4/100,000 in men. ❖ Breast cancer was the second leading cause of cancer death among women (16.3 % of all female cancer deaths).

[1] New indication/extension to an existing indication/first-in-class.

Current treatment

The current treatment algorithms for unresectable and metastatic HR+, HER2- breast cancer are based on the ESMO Living Guideline for metastatic breast cancer [8], which is continuously updated to reflect emerging evidence. Specific recommendations for first-line treatment are provided in the Appendix below [9].

Evidence

Trial name NCT number	Trial characteristics	Population size (n)	Intervention (I)	Control (C)	Follow-up	Treatment duration (I vs. C)
TROPION-Breast01 **[10]** NCT05104866	Global, open-label randomised, phase III study	732 (1:1)	Datopotamab deruxtecan 6 mg/kg administered IV every 3 weeks until disease progression, unacceptable toxicity, or withdrawal	Single-agent chemotherapy[2] every 3 weeks (capecitabine, gemcitabine, eribulin, vinorelbine)	10.8 months at the interim analysis and 22.8 months at the final analysis	6.7 vs. 4.1 months

Main efficacy outcomes (I vs. C) [2]

Overall survival (OS), median (months): 18.6 (95% CI 17.3-20.1) vs. 18.3 (95% CI 17.3-20.5) Hazard ratio (HR): 1.01 (95% CI 0.83-1.22); p-value=0.9445

Progression-free survival (PFS), median (months), by blinded independent central review (BICR): 6.9 (95% CI 5.7-7.4) vs. 4.9 (95% CI 4.2-5.5)
HR: 0.63 (95% CI 0.52-0.76); p-value<0.0001
ORR by BICR: 133 patients (36.5%) vs. 84 (22.9%)
Duration of response, median (months): 6.7 (95% CI 5.6-9.8) vs. 5.7 (95% CI 4.9-6.8)
Time to first subsequent therapy: n/a

Main safety outcomes (I vs. C) [2]

Adverse events (AEs) of grade ≥3: 35.0% vs. 55.6%
Serious adverse events (SAEs): 17.2% vs. 19.1%
Discontinuation due to AEs: 4.2% vs. 3.1%
Deaths due to AEs : 0.6% vs. 0.9%
TRAEs≥3: 4.7% vs. 8.8%

Patient-reported outcomes (PROs)

- A mixed-method model was used to evaluate secondary patient-reported outcome endpoints.
- Health-related quality of life (HRQoL) was assessed by using EORT QLQ-C30 and EORT QLQ IL116 questionnaires.
- Statistical analyses showed numerical improvements favouring datopotamab deruxtecan over investigator's choice chemotherapy (ICC) across pain, physical functioning, and global health status/QoL domains however, these improvements did not reach statistical significance.

Limitations

- Evolving treatment landscape: During the trial, the therapeutic landscape for endocrine-refractory HR+ metastatic breast cancer changed, which may have influenced treatment choices and relevance.
- Treatment allocation: A slightly higher number of patients in the ICC arm did not receive their assigned therapy, likely reflecting patient preference to avoid standard chemotherapy.
- Mouthwash use: Prophylactic steroid-based mouthwash was recommended but not mandatory (due to limited global availability), making it difficult to assess its effect on the prevention of stomatitis, as the study was not designed for this purpose.

ESMO-MCBS version 2.0

Scale	Int.	Form	MG ST	MG	HR (95% CI)	Score calculation	PM	Toxicity	QoL	AJ	FM
Original [11]	Non-curative	2b	< 6 months	PFS: +2.0 months	0.63 (0.52-0.76)	HR ≤0.65 and gain ≥1.5 months	3	-	-	No adjustment	**3**
Adapted [12]	Non-curative	2b	< 6 months	PFS: +2.0 months	0.63 (0.52-0.76)	HR ≤0.65 and gain ≥1.5 months	3	-	-	No adjustment	**3**

Risk of bias – randomised controlled trial (RCT) [13, 14]

Adequate generation of randomisation sequence	Adequate allocation concealment	Blinding	Incomplete outcome data	Selective outcome reporting unlikely	Other aspects increasing the RoB	Risk of bias
yes low risk	yes low risk	no[3] high risk	yes low risk	yes low risk	yes[4] unclear risk	**unclear risk**

[2] Investigator's choice of chemotherapy (ICC)
[3] Open-label trial design.
[4] Changes in treatment landscape during study; ongoing study.

Ongoing trials [15]		
NCT number	Description	Estimated completion date
NCT05104866	Please see above.	12/25
HTA reports		
Institution	Status	Link
Agency for Care Effectiveness (ACE)	Datopotamab deruxtecan for previously treated unresectable or metastatic HR+, HER2-negative breast cancer – completed (decision: not recommended)	Guidance datopotamab deruxtecan
Gemeinsamer Bundesausschuss (GBA), Germany	Nutzenbewertungsverfahren zum Wirkstoff Datopotamab deruxtecan (Mammakarzinom, HR+, HER2-, nach min. 1 Vortherapie) – decision in preparation	Nutzenbewertungsverfahren
National Institute for Health and Care Excellence (NICE)	In development - appraisal in progress (publication expected in 2026)	Project information | Datopotamab deruxtecan | NICE

Costs

Costs per patient per		Costs for expected patient population in Austria (n~530 patients) per		Additional cost categories	
Cycle	Year	Cycle	Year	Diagnostics	Monitoring
€8,571 Datroway® powder for IV infusion 100mg = €2,041[5] [16]	Per median treatment duration (i.e., 6.7 months, ~9 cycles) €77 thsd. Per year €149 thsd. [2, 16]	€4.5 million Estimated based on the national breast cancer incidence data with published proportions of HR+/HER2- tumours that are metastatic or unresectable, receive endocrine therapy, and subsequently undergo at least one line of chemotherapy [5, 7, 16-20]. No other drugs with the same indication were considered.	€77 million Based on the assumption that ~17 subsequent cycles can be conducted per year.	▪ HR and HER2 testing, biopsy for receptor status ▪ Radiological assessment	▪ Regular laboratory monitoring (blood counts, liver/kidney function) ▪ Monitoring of interstitial lung diseases ▪ Ophthalmological exams
				Additional medication	
				▪ Pre-medication (antiemetic agents, antihistamine, paracetamol)	

Other aspects and conclusions

- Datopotamab deruxtecan offers an alternative therapy for patients with unresectable or metastatic HR+/HER2- breast cancer after prior endocrine therapy and at least one line of chemotherapy. In TROPION-Breast01, it demonstrated a significant PFS benefit but no OS improvement compared with ICC.
- Compared with ICC, datopotamab deruxtecan was associated with less haematologic and neurotoxicity, but higher rates of stomatitis/mucositis and ocular events. Interstitial lung disease occurred infrequently but required careful monitoring and management.
- PROs indicated numerical improvements in pain, physical functioning, and global health status/QoL in favour of datopotamab deruxtecan over ICC, although differences were not statistically significant.
- Beyond drug acquisition costs, routine monitoring (laboratory tests, imaging, ophthalmologic exams), preventive measures (mouthwash, eye drops), and management of intestinal lung diseases represent additional costs and resource demands for hospitals.
- The study's open-label design entails potential performance bias. The rapidly evolving treatment landscape for endocrine-refractory HR+/HER2- disease during recruitment may have influenced comparator choice; therefore, the overall risk of bias remains unclear.
- TROP2 is widely expressed across HER2- breast cancers, yet no validated predictive cut-off or standardised assay has been established. Recent evidence indicates that TROP2 expression levels are not clearly correlated with clinical response to TROP2-directed antibody–drug conjugates. Accordingly, no companion diagnostic is currently required. Ongoing research explores TROP2-targeted PET tracers and circulating assays to enhance patient selection and therapy monitoring [21-24].

[5] German list price shown. No official Austrian price available as of October 2025.

- Besides datopotamab deruxtecan, a TROP2-directed antibody-drug-conjugate sacituzumab govitecan was approved in the EU and US for metastatic triple-negative and HR+/HER2- breast cancer, and under investigation for urothelial, lung, and gastrointestinal cancers [25, 26].

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Abbreviations : AE…Adverse events, AJ…adjustment,, BICR…blinded independent central review, C….comparator, CHMP.…Committee for Medicinal Products for Human Use, CI….confidence interval, Dxd…deruxtecan, EMA…European Medicines Agency, ESMO-MCBS…European Society of Medical Oncology – Magnitude of Clinical Benefit Scale, EU…European Union, FDA…Food and Drug Administration, FM…final magnitude, HR…hazard ratio, HR+…hormone receptor positive, HER2-…human epidermal growth factor receptor 2-negative, HRQoL…health-related quality of life, I…intervention, ICC…investigator's choice of chemotherapy, INN…international non-proprietary name, IV….intravenous(ly), MAH…marketing authorisation holder, MG…median gain, n…number, NICE…National Institute for Health and Care Excellence, ORR…objective response rate, OS…overall survival, , PFS….Progression-free survival, PM…preliminary magnitude, PRO….patient-reported outcome, RCT…randomised controlled trial, SAE…serious adverse event, ST…standard treatment, TROP2…trophoblast cell surface antigen 2

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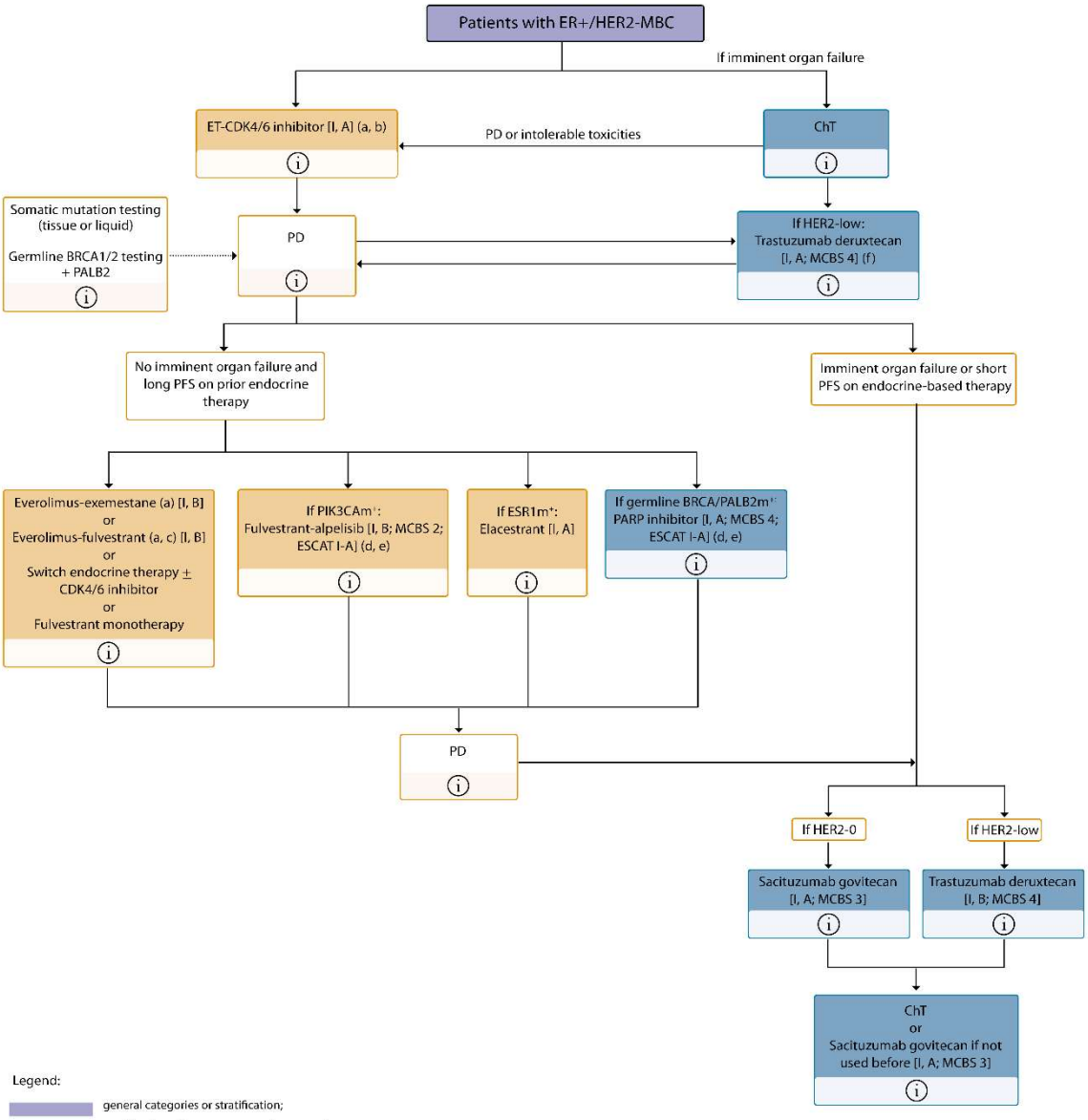
Appendix:

ESMO metastatic breast cancer living guideline : ER-positive HER2-negative breast cancer



AI, aromatase inhibitor; CDK4/6, cyclin-dependent kinase 4 and 6; ChT, chemotherapy; EMA, European Medicines Agency; ER, estrogen receptor; ESCAT, ESMO Scale for Clinical Actionability of Molecular Targets; ESR1, estrogen receptor 1; ET, endocrine therapy; FDA, Food and Drug Administration; HER2, human epidermal growth factor receptor 2; m, mutation; MBC, metastatic breast cancer; MCBS, ESMO-Magnitude of Clinical Benefit Scale; OFS, ovarian function suppression; PALB2, partner and localiser of BRCA2; PARP, poly (ADP-ribose) polymerase; PD, progressive disease; PFS, progression-free survival; PIK3CA, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha.

(a) OFS if the patient is premenopausal.

(b) If relapse <12 months after end of adjuvant AI: fulvestrant–CDK4/6 inhibitor (a); if relapse >12 months after end of adjuvant AI: AI–CDK4/6 inhibitor (a).

(c) Preferred if the patient is ESR1 mutation positive [ESCAT score: II-A]. (d)

(d) ESMO-MCBS v1.1 (Cherny, 2017) was used to calculate scores for new therapies/indications approved by the EMA or FDA. The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee (https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-evaluation-forms).

(e) ESCAT scores apply to genomic alterations only. These scores have been defined by the guideline authors and validated by the ESMO Translational Research and Precision Medicine Working Group. (Mateo, 2018)

(f) Trastuzumab deruxtecan can also be given following adjuvant ChT in the setting of fast progression (DESTINY-Breast04/EMA indication)