swissmedic

Date: 15 September 2025
Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

DATROWAY

International non-proprietary name: datopotamab deruxtecan

Pharmaceutical form:	Powder for concentrate for solution for infusion
Dosage strength(s):	100 mg
Route(s) of administration:	intravenous use
Marketing authorisation holder:	Daiichi Sankyo (Schweiz) AG
Marketing authorisation no.:	69801
Decision and decision date:	approved on 28 May 2025

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

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1 Terms, Definitions, Abbreviations

1L	First-line
2L	Second-line
ADA	Anti-drug antibody
ADME	Absorption, distribution, metabolism, elimination
AE	Adverse event
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
API	Active pharmaceutical ingredient
ATC	Anatomical Therapeutic Chemical Classification System
AUC	Area under the plasma concentration-time curve
$AUC_{0\text{-}24h}$	Area under the plasma concentration-time curve for the 24-hour dosing interval
CI	Confidence interval
C_{max}	Maximum observed plasma/serum concentration of drug
CYP	Cytochrome P450
DDI	Drug-drug interaction
DOR	Duration of response
ECOG	Eastern Cooperative Oncology Group
EMA	European Medicines Agency
ERA	Environmental risk assessment
FDA	Food and Drug Administration (USA)
GLP	Good Laboratory Practice
HPLC	High-performance liquid chromatography
IC/EC_{50}	Half-maximal inhibitory/effective concentration
ICH	International Council for Harmonisation
Ig	Immunoglobulin
INN	International non-proprietary name
ITT	Intention-to-treat
LoQ	List of Questions
MAH	Marketing Authorisation Holder
Max	Maximum
Min	Minimum
MRHD	Maximum recommended human dose
MTD	Maximum tolerated dose
N/A	Not applicable
NCCN	National Comprehensive Cancer Network
NO(A)EL	No observed (adverse) effect level
ORR	Objective response rate
OS	Overall survival
PBPK	Physiology-based pharmacokinetics
PD	Pharmacodynamics
PFS	Progression-free survival
PIP	Paediatric Investigation Plan (EMA)
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
PSP	Pediatric study plan (US FDA)
RMP	Risk management plan
SAE	Serious adverse event
SwissPAR	Swiss Public Assessment Report
TEAE	Treatment-emergent adverse event
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)

TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)
TROP2	Trophoblast cell-surface antigen-2

2 Background information on the procedure

2.1 Applicant's request(s) and information regarding procedure

New active substance status
The applicant requested new active substance status for datopotamab deruxtecan in the above-mentioned medicinal product.

Work-sharing procedure
The applicant requested a work-sharing procedure with Singapore's Health Sciences Authority (HSA) and Australia's Therapeutic Goods Administration (TGA).
The Access NAS (new active substance) work-sharing initiative is a collaboration between regulatory authorities – specifically Australia's Therapeutic Goods Administration (TGA), Health Canada (HC), Singapore's Health Sciences Authority (HSA), the UK Medicines & Healthcare products Regulatory Agency (MHRA) and Swissmedic – and the pharmaceutical industry.
The work-sharing initiative involves the coordinated assessment of NAS applications that have been filed in at least two jurisdictions.

2.2 Indication and dosage

2.2.1 Requested indication

Breast cancer

DATROWAY is indicated for the treatment of adult patients with unresectable or metastatic hormone receptor (HR)-positive, HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have received prior systemic therapy for unresectable or metastatic disease.

2.2.2 Approved indication

DATROWAY is indicated as monotherapy for the treatment of adult patients with unresectable or metastatic hormone receptor positive (HR+), HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have already received an endocrine therapy and at least one chemotherapy in the unresectable or metastatic setting and have progressed on the last therapy line (see "Clinical efficacy").

2.2.3 Requested dosage

Summary of the requested standard dosage:

The recommended dose is 6mg/kg and is administered by intravenous infusion once every 3 weeks (cycles of 21-days) until disease progression or until the occurrence of unacceptable toxicity.

2.2.4 Approved dosage

(See appendix)

2.3 Regulatory history (milestones)

Application	29 March 2024

Formal control completed	14 May 2024
List of Questions (LoQ)	18 September 2024
Response to LoQ	18 November 2024
Second LoQ	22 January 2025
Response to second LoQ	05 February 2025
Preliminary decision	01 April 2025
Response to preliminary decision	16 April 2025
Final decision	28 May 2025
Decision	approval

3 Quality aspects

3.1 Drug substance

Swissmedic has not assessed the primary data relating to quality aspects for the drug substance submitted with this application and relies on the assessment of the foreign reference authority, Australia's TGA (see section 2.1 Applicant's request / Work-sharing procedure).

3.2 Drug product

Datopotamab deruxtecan drug product is a sterile, preservative-free, white to yellowish white lyophilised powder, supplied in a single-dose vial. The dose strength of datopotamab deruxtecan drug product is 100 mg/vial. Prior to administration, the datopotamab deruxtecan drug product is reconstituted with 5.0 mL sterile water for injection. The composition of reconstituted datopotamab deruxtecan drug product is 20 mg/mL datopotamab deruxtecan, histidine buffer, sucrose and polysorbate 80 at pH 6.0. The reconstituted vial is further diluted with 5% dextrose for intravenous (IV) administration.

All excipients used in the datopotamab deruxtecan drug product (histidine, sucrose, polysorbate 80 and water for injection) are tested in accordance with current compendial methods to the corresponding compendial specification. In addition, there are no novel excipients or excipients of human or animal origin in the datopotamab deruxtecan drug product.

Several drug product dosage forms, strengths, and filling facilities were used during clinical development. However, comparability studies, which included batch release data, extended characterisation data, and forced degradation data, demonstrated comparability of the relevant quality attributes between the different processes. Compatibility studies were conducted to establish the in-use stability of diluted drug product with the intended materials and conditions of use.

The drug product manufacturing process consists of drug substance thawing, compounding, sterile filtration, aseptic filling, lyophilisation, and capping followed by visual inspection, labelling, and secondary packaging. The drug product manufacturing process was validated with several consecutive batches. The data demonstrated consistent production.

The specifications for release and stability of the drug product include relevant tests and acceptance criteria, e.g., for identity, purity and impurities, quantity, potency, appearance, pH, osmolality, visible and subvisible particles, bacterial endotoxins, and sterility. The drug product specifications comply with current compendial or regulatory guidelines.

Batch analysis data for several batches of the drug product, including development batches, clinical batches, and process validation batches, were provided. All batch release data comply with the drug product specifications that were valid at the time of batch release. All specific analytical methods have been validated.

The container closure system consists of an amber type I glass vial, a grey fluoro-resin laminated butyl rubber stopper, and an aluminum seal with flip-off cap. The materials in the type I glass vial and rubber stopper meet compendial requirements.

The vials are stored at 2°C to 8°C. The stability data support a shelf life of 36 months.

3.3 Quality conclusions

Satisfactory and consistent quality of the drug substance and drug product has been demonstrated. Safety of the product with regard to viral and non-viral contaminants has been adequately addressed.

4 Nonclinical aspects

4.1 Pharmacology

Datopotamab deruxtexan (Dato-DXd) bound to trophoblast cell-surface antigen-2 (TROP2) of cynomolgus monkeys and humans (KD values 110.42 ng/mL and 97.65 ng/mL). It did not bind to mouse or rat TROP2. There was also no binding activity to EpCAM, the second human TROP family protein. Dato-DXd inhibited cell growth in the two human TROP2-positive cancer cell lines CFPAC-1 and BxPC3 (IC50 values 706 and 75 ng/mL), but not in TROP2-negative Calu-6-cells. It induced DNA damage and apoptosis in CFPAC-1 cells in the same manner as DXd, suggesting that these changes were caused by the topoisomerase I inhibition of DXd released from Dato-DXd. Dato-DXd and unconjugated datopotamab showed in vitro antibody-dependent cellular cytotoxicity (ADCC) activity against the TROP2-expressing human NCI-H322 cancer cell line; EC50 values were within clinical exposure range. The applicant does not consider that ADCC activity contributes significantly to the anti-tumour activity of Dato-DXd because unconjugated datopotamab showed no activity in mouse tumour models.
Dato-DXd (10 mg/kg, single intravenous (IV) administration) showed significant anti-tumour activity in vivo in mouse xenograft models with TROP2-positive human cancer cells. Both NSCLC and breast cancer tumour models were used in the experiments.
In conclusion, the mode of action of Dato-DXd, targeting TROP2-expressing tumours and showing anti-tumour efficacy, was sufficiently characterised in pharmacology studies.
DXd did not show affinity towards a selection of receptors, channels, transporters, and enzymes at a concentration of 10 µmol/L.
In vitro, DXd had no effect on hERG currents at concentrations up to 10 µmol/L (>1600 times human Cmax at clinical dose). Dato-DXd did not show any effect on the cardiovascular, respiratory, and central nervous systems in cynomolgus monkeys at doses up to 80 mg/kg IV – an exposure approximately 10 times the clinical exposure based on Cmax and AUC.

4.2 Pharmacokinetics

Elimination half-life of Dato-DXd ranged from 1.5 to 2 days in cynomolgus monkeys after single IV administration of doses from 0.2 to 6 mg/kg. At doses above 6 mg/kg, half-life was longer (2.4 to 7.9 days) and comparable to the human value (4.8 days). Cmax and AUC values of Dato-DXd and total anti-TROP2 antibody generally increased with the dose after single and repeated IV dosing in rats (20-200 mg/kg) and monkeys (10-80 mg/kg). In rats, there was also a dose-dependent increase in free DXd in plasma, whereas no dose-dependent effect on DXd, Cmax, and AUC21d was seen in monkeys.
ADA formation reduced exposure during the repeat-dose toxicity study in some monkeys at the middle dose of 10 mg/kg. Since no high-dose animal showed an ADA response in the toxicity studies, the validity of these studies was not affected.
In quantitative whole body autoradiography studies with 14C-labelled free DXd in pigmented rats and cynomolgus monkeys, radioactivity was quickly and widely distributed throughout the body and cleared steadily from the tissues. High concentrations (at least double the plasma Cmax) were found in the gastrointestinal tract, urinary bladder, kidney, liver, and aorta. In addition, monkeys showed high concentrations in fat tissues, pigmented skin, seminal vesicle, and parts of the eye (ciliary body and sclera). Concentrations in the brain, lens, and spinal cord were below the limit of quantification at all time points.
Plasma protein binding of DXd in vitro was highest in humans, followed by rats, mice, and monkeys. Mean free plasma fractions were 8.6% in mice, 4.3% in rats, 12.5% in monkeys, and 2.6% in humans. In all species, DXd concentrations were higher in plasma than in blood.
The stability of Dato-Dxd was examined in plasma. Release rates of DXd were not dependent on concentration. The highest mean release of DXd was 6%, observed in monkey plasma, followed by 4.4% in humans, 1.8% in rats and 1.5% in mice. CYP3A4 was the main enzyme involved in DXd metabolism in vitro. DXd's metabolic stability against UGT enzymes was high. DXd was the main

component in urine, faeces, and bile after single IV administration to rats and monkeys. No data were generated on metabolites in plasma, but this is acceptable on the basis of ICH S9.
The major excretion pathway of DXd in rats and monkeys was faeces, whereas urinary excretion was minor.

4.3 Toxicology

Dato-DXd was administered IV once every three weeks, in line with the intended clinical route and schedule of administration. Repeat-dose toxicity studies were conducted in rats (3 months) and cynomolgus monkeys (up to 3 months). The duration of treatment was appropriate for the indication of advanced cancer. The monkey was identified as pharmacologically relevant species. In addition, two repeat-dose toxicity studies were conducted in rats and monkeys with DXd alone, the drug moiety of Dato-DXd.
No mortality or moribundity occurred in either species up to the maximum doses of 200 mg/kg in rats and 80 mg/kg in monkeys. Dato-DXd induced lung toxicity, which was more pronounced in monkeys, with inflammatory changes in histopathology, pulmonary consolidation in computed tomography examination of the chest, and decreased blood gas parameters. Further target organs of toxicity in both species were the eyes, skin, intestines, lymphatic/haematopoietic organs, and kidney. Additional targets of toxicity were the liver in monkeys and the reproductive organs (see below) and incisor teeth in rats. In general, the findings are in line with known risks for the payload DXd and/or published expression of TROP2 in epithelia. Except for the liver, kidney and teeth, the target organs identified in the toxicity studies correlate with the findings from the clinical studies with Dato-DXd. There is no safety margin for the effects observed in the livers of Dato-DXd-treated monkeys. The safety margin for kidney-related findings with Dato-DXd is 4 in rats and 2.9 in monkeys. The tooth toxicity in rats is not considered clinically relevant because the proposed indications are only for adult patients.
DXd was not mutagenic in the bacterial reverse mutation assay, but was clastogenic in vitro and in vivo. Genotoxicity to mammalian cells is a known characteristic of topoisomerase I inhibitors. On the basis of ICH S9, no genotoxicity and carcinogenicity studies have been conducted with Dato-DXd .
On the basis of ICH S9, the applicant did not conduct studies of reproductive and developmental toxicity. Dato-DXd and/or DXd showed toxicity in tissues with rapidly dividing cells (lymphatic/haematopoietic organs, intestines, or testes) in rats and monkeys, and DXd is genotoxic. Therefore, it is possible that Dato-DXd will cause embryo-fetal damage. In rats, non-reversible effects were found in the testes and epididymis of rats, which suggests impaired male reproductive function and fertility. The risks are adequately addressed in the Information for healthcare professionals.
Tissue cross-reactivity studies of Dato-DXd with a panel of normal human and monkey tissues showed specific staining of epithelia in different tissues. The staining pattern was similar between the two species and largely consistent with published data on TROP2 expression.
DXd was phototoxic in vitro, but no phototoxic reaction was observed in vivo in pigmented rats at the highest dose tested (3 mg/kg; exposure approximately 29 times the clinical exposure at the 6 mg/kg dose based on Cmax).
No dedicated studies on local tolerance have been conducted. No relevant effects were observed in the repeat-dose toxicity studies at the IV injection sites.
In in vitro cytokine release assays, human peripheral blood mononuclear cells showed an increased cytokine release in response to DXd compared to Dato-DXd. Cellular activation was not shown. There was no cytokine release in a second in vitro assay in human whole blood. In the clinical studies, infusion-related reactions were a common adverse event with Dato-DXd treatment.
All relevant nonclinical safety findings are adequately described in the nonclinical part of the safety specification in the RMP.
The excipients in the Dato-DXd product give no cause for concern.
Based on the ERA, any risk to the environment is unlikely.

4.4 Nonclinical conclusions

The submitted nonclinical documentation is considered adequate to support the approval of Dato-DXd in the proposed indications. The pharmacological properties as well as the pharmacokinetic and toxicity profiles of Dato-DXd were adequately characterised. All nonclinical data that are relevant for safety are included in the Information for healthcare professionals. From the nonclinical standpoint, there is no objection to approval.

5 Clinical aspects

Swissmedic has not assessed the primary data relating to clinical aspects submitted with this application and relies on the assessment of the foreign reference authority HSA Singapore (see section 2.1 Applicant’s request / Work-sharing procedure).

6 Risk management plan summary

The RMP summaries contain information on the medicinal products′ safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

7 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for DATROWAY was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo.ch).

Note:
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected new or serious adverse reactions. See the "Undesirable effects" section for advice on the reporting of adverse reactions.

DATROWAY® 100 mg powder for concentrate for solution for infusion

Composition

Active substances

Datopotamab Deruxtecan is composed of an antibody (produced in Chinese hamster ovary cells by recombinant DNA technology) conjugated via a linker to the topoisomerase I inhibitor DXd.

Excipients

L-histidinum, L-histidini hydrochloridum monohydricum, saccharum, polysorbatum 80.

Pharmaceutical form and active substance quantity per unit

Powder for concentrate for solution for infusion.
White to yellowish white lyophilised powder.
One vial of lyophilised powder for concentrate for solution for infusion contains 100 mg of datopotamab deruxtecan.

Indications/Uses

Breast Cancer

DATROWAY is indicated as monotherapy for the treatment of adult patients with unresectable or metastatic hormone receptor positive (HR+), HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have already received an endocrine therapy, and at least one chemotherapy in the unresectable or metastatic setting and have progressed on the last therapy line (see “Clinical Efficacy”).

Dosage/Administration

DATROWAY should be prescribed by a physician and used under the supervision of a physician experienced in the use of anti-cancer drugs.

Patient selection for HER2-negative metastatic breast cancer

Patients for treatment of unresectable locally advanced or metastatic hormone receptor (HR)-positive, HER2-negative breast cancer should be selected on the basis of HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH-) tumour status as assessed by a validated test.

Premedication and Prophylactic Medications

Prior to each infusion of DATROWAY, a premedication regimen for the prevention of infusion-related reactions that consists of an antihistamine agent and paracetamol (with or without glucocorticoids) is recommended.

It is also recommended that patients receive prophylactic antiemetic agents (dexamethasone with 5-HT3 antagonists as well as other medicinal products, such as NK1 receptor antagonists), prior to infusion of DATROWAY and on subsequent days as needed.

For prophylactic treatment for keratitis and stomatitis, please refer to Warnings and Precautions for Use (see section “Warnings and precautions”).

Posology

The recommended dose of DATROWAY is 6 mg/kg given as an intravenous infusion once every three weeks (21-day cycle) until disease progression or unacceptable toxicity.

First infusion: Administer infusion over 90 minutes. Observe patients during the infusion and for at least 30 minutes following the initial dose, for signs or symptoms of infusion-related reactions.

Subsequent infusions: Administer infusion over 30 minutes if prior infusions were tolerated. Observe patients during the infusion and for at least 30 minutes after infusion.

To ensure traceability of biotechnological medicinal products, it is recommended that DATROWAY and batch number should be documented for each treatment.

Dose Modifications

Dose modifications for infusion-related reactions

Slow or interrupt the infusion rate if the patient develops an infusion-related reaction. Permanently discontinue DATROWAY for life-threatening infusion-related reactions.

Dose modifications for adverse reactions

Management of adverse reactions may require dose delay, dose reduction, or treatment discontinuation per guidelines provided in Tables 1 and 2.

Do not re-escalate the DATROWAY dose after a dose reduction is made.

Table 1: Dose Reductions for Adverse Reactions

Recommended starting dose	6 mg/kg
First dose reduction	4 mg/kg
Second dose reduction	3 mg/kg
Third dose reduction	Permanently discontinue treatment

Table 2: Dosage Modifications for Adverse Reactions

Adverse Reaction	Severity[a]	Dose Modification
Interstitial Lung Disease (ILD)/Pneumonitis (see sections “Warnings and precautions” and “Undesirable Effects”)	Asymptomatic ILD/pneumonitis Grade 1	Delay dose of DATROWAY until resolved to Grade 0[b], then: • if resolved in 28 days or less from date of onset, maintain dose. • if resolved in greater than 28 days from date of onset, reduce dose one level (see Table 1). • consider corticosteroid treatment as soon as ILD/pneumonitis is suspected.
	Symptomatic ILD/pneumonitis (Grade 2 or greater)	• Permanently discontinue DATROWAY. • Promptly initiate corticosteroid treatment as soon as ILD/pneumonitis is suspected.

Keratitis (see sections “Warnings and precautions” and “Undesirable Effects”)	Grade 2	• Delay dose of DATROWAY until resolved to Grade 1 or less, then maintain dose.
	Grade 3	• Delay dose of DATROWAY until resolved to Grade 1 or less, then reduce the dose by 1 level (see Table 1).
	Grade 4	• Permanently discontinue DATROWAY.
Stomatitis (see sections “Warnings and precautions” and “Undesirable Effects”)	Grade 2	• Delay dose of DATROWAY until resolved to Grade 1 or less. • Restart treatment with DATROWAY at the same dose for first occurrence. • Consider restarting treatment with DATROWAY at reduced dose level (see Table 1) if recurrent.
	Grade 3	• Delay dose of DATROWAY until resolved to Grade 1 or less. • Restart treatment with DATROWAY at reduced dose level (see Table 1).

	Grade 4	• Permanently discontinue DATROWAY.

[a] Per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 5.0

[b] Grade 0 refers to full resolution of ILD/pneumonitis, including the disappearance of radiological findings associated with active ILD/pneumonitis. Residual scarring or fibrosis following recovery of ILD/pneumonitis is not considered to be active disease.

Delayed or Missed Dose

If a planned dose is delayed or missed, it should be administered as soon as possible without waiting until the next planned cycle. The schedule of administration should be adjusted to maintain a 3-week interval between doses.

Special Populations

Elderly patients

No dose adjustment of DATROWAY is required in patients aged 65 years or older.

Children and adolescents

DATROWAY is not authorised for the use in the paediatric population as the safety and efficacy in children and adolescents below 18 years of age have not been established.

Patients with renal impairment

No dose adjustment is required in patients with mild to moderate (creatinine clearance [CLcr] 30 to <90 ml/min) renal impairment. The recommended dosage of DATROWAY has not been established in patients with severe renal impairment.

Patients with hepatic impairment

No dose adjustment is required in patients with mild (total bilirubin ≤ULN and any AST >ULN or total bilirubin >1 to 1.5 times ULN and any AST) hepatic impairment. There are limited data to make a recommendation on dose adjustment in patients with moderate (total bilirubin >1.5 to 3 times ULN and any AST) and severe (total bilirubin >3 times ULN and any AST) hepatic impairment.

Method of Administration

DATROWAY is for intravenous use. It must be reconstituted and diluted by a healthcare professional and administered as an intravenous infusion. DATROWAY must not be administered as an intravenous push or bolus.

For instructions on reconstitution and dilution of DATROWAY before administration, see section “Instructions and special precautions for handling and disposal”.

Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section “Composition”.

Warnings and precautions

Interstitial lung disease/pneumonitis

Cases of interstitial lung disease (ILD), including pneumonitis, have been reported in patients treated with DATROWAY (see section “Undesirable Effects”). Fatal outcomes have been observed.
Patients with a history of ILD/pneumonitis requiring steroid treatment or present or suspected ILD/pneumonitis at the time of screening and patients with clinically severe pulmonary impairment were not included in the pivotal studies.
Patients should be advised to immediately report cough, dyspnea, fever, and/or any new or worsening respiratory symptoms. Patients should be monitored for signs and symptoms of ILD/pneumonitis. Evidence of ILD/pneumonitis should be promptly investigated. Patients with suspected ILD/pneumonitis should be evaluated by radiographic imaging. Consultation with a pulmonologist should be considered. For asymptomatic (Grade 1) ILD/pneumonitis, consider corticosteroid treatment (e.g., ≥0.5 mg/kg/day prednisolone or equivalent). DATROWAY should be delayed until recovery to Grade 0 and may be resumed according to instructions in Table 2 (see section “Dosage/Administration”). For symptomatic ILD/pneumonitis (Grade 2 or greater), promptly initiate systemic corticosteroid treatment (e.g., ≥1 mg/kg/day prednisolone or equivalent) and continue for at least 14 days followed by gradual taper for at least 4 weeks. DATROWAY should be permanently discontinued in patients who are diagnosed with symptomatic (Grade 2 or greater) ILD/pneumonitis (see section “Dosage/Administration”). Patients with a history of ILD/pneumonitis may be at increased risk of developing ILD/pneumonitis and should be monitored carefully.

Keratitis

DATROWAY can cause ocular surface events including keratitis. Signs and symptoms of keratitis may include dry eye, increased lacrimation, photophobia, and detrimental changes to vision (see section “Undesirable Effects”). The majority of these events were mild to moderate in severity.

Advise patients to use preservative-free lubricant eye drops several times daily for prophylaxis. Advise patients to avoid use of contact lenses unless directed by an eye care professional. Promptly refer patients to an eye care professional for any new or worsening ocular signs and symptoms that could suggest keratitis. Monitor for keratitis and if diagnosis is confirmed, dose delay, dose reduce, or permanently discontinue DATROWAY (see section “Dosage/Administration”).
Patients with clinically significant corneal disease were excluded from the clinical studies.

Stomatitis

Stomatitis, including mouth ulcers and oral mucositis, have been reported in patients being treated with DATROWAY.

In addition to practicing good oral hygiene, when starting DATROWAY and throughout treatment, daily use of a steroid-containing mouthwash (e.g., dexamethasone oral solution 0.1 mg/mL 4 times daily or a similar steroid-containing mouthwash regimen) is recommended for prophylaxis and treatment. Where clinically indicated, antifungal agents may be considered in accordance with local guidelines. In the absence of a prophylactic steroid-containing mouthwash, use of bland mouth rinses (e.g., a nonalcoholic and/or bicarbonate-containing mouthwash) per local guidelines is recommended. Ice chips or ice water held in the mouth throughout the infusion may also be considered. If stomatitis does occur, frequency of mouthwashes may be increased and/or other topical treatments may be used. Based on the severity of the adverse reaction, dose delay, dose reduce, or permanently discontinue DATROWAY (see section “Dosage/Administration”).

Embryo-fetal toxicity

Based on findings in animals and its mechanism of action, the topoisomerase I inhibitor component of DATROWAY can cause embryofoetal harm when administered to a pregnant woman (see section ”Pregnancy, lactation”).
The pregnancy status of females of reproductive potential should be verified prior to the initiation of DATROWAY. The patient should be informed of the potential risks to the fetus. Females of reproductive potential should be advised to use effective contraception during treatment and for at least 7 months following the last dose of DATROWAY. Male patients with female partners of reproductive potential should be advised to use effective contraception during treatment with

DATROWAY and for at least 4 months after the last dose of DATROWAY (see section “Pregnancy, lactation”).

Interactions

Effects of other medicinal products on the pharmacokinetics of DATROWAY

No clinical drug interaction studies with DATROWAY have been conducted.
Based on PBPK modeling, coadministration with ritonavir, a dual inhibitor of OATP1B/CYP3A, or with itraconazole, a strong CYP3A inhibitor, is not predicted to have a clinically meaningful increase in exposures of datopotamab deruxtecan or released DXd. No dose adjustment is required during coadministration of DATROWAY with drugs that are inhibitors of OATP1B or CYP3A.

No clinically meaningful interaction is expected with drugs that are inhibitors of P-glycoprotein (P-gp), MATE2-K, MRP1, or BCRP transporters.

Effects of DATROWAY on the pharmacokinetics of other medicinal products

In vitro studies indicate that DXd does not inhibit or induce major CYP450 enzymes.

Pregnancy, lactation

Women of childbearing potential / contraception in males and females

Pregnancy status of women of childbearing potential should be verified prior to initiation of DATROWAY.
Women of childbearing potential should use effective contraception during treatment with DATROWAY and for at least 7 months following the last dose.
Men with female partners of childbearing potential should use effective contraception during treatment with DATROWAY and for at least 4 months following the last dose.

Pregnancy

There are no available data on the use of DATROWAY in pregnant women. However, based on findings in animals and its mechanism of action, the topoisomerase I inhibitor component of DATROWAY can cause embryo-foetal harm when administered to a pregnant woman (see section “Warnings and precautions” and “Preclinical data”).

DATROWAY must not be used during pregnancy unless clearly necessary. If DATROWAY is administered during pregnancy or if a woman becomes pregnant during treatment or within 7 months after the last dose of DATROWAY, the possibility of damage to the foetus must be pointed out.

Breastfeeding

It is not known if DATROWAY is excreted in human milk. Since many medicinal products are excreted in human milk and because of the potential for serious adverse reactions in breastfeeding infants, women should discontinue breastfeeding prior to initiating treatment with DATROWAY. Women may begin breastfeeding 1 month after concluding treatment.

Fertility

No dedicated fertility studies have been conducted with datopotamab deruxtecan. Based on results from animal toxicity studies, DATROWAY may impair reproductive function and fertility (see section “Preclinical data”).

It is not known whether datopotamab deruxtecan or its metabolites are found in seminal fluid. Before starting treatment, male patients should be advised to seek counseling on sperm storage. Male patients must not freeze or donate sperm throughout the treatment period, and for at least 4 months after the final dose of DATROWAY.

Effects on ability to drive and use machines

DATROWAY may have a minor influence on the ability to drive and use machines. Patients should be advised to use caution when driving or operating machinery in case the experience fatigue or vision changes during treatment with DATROWAY (see section “Undesirable effects”).

Undesirable effects

Summary of the safety profile

The pooled safety population has been evaluated for patients who received at least one dose of DATROWAY 6 mg/kg (n = 927) in TROPION-PanTumor01 (NCT03401385), TROPION-Lung05 (NCT04484142), TROPION-Lung01 (NCT04656652), and TROPION-Breast01 (NCT05104866) clinical studies, which included 484 patients with NSCLC and 443 patients with breast cancer. The median duration of treatment in this pool was 5.5 months (range: 0.7 to 29.9 months).

The most common adverse reactions were stomatitis (60.5%), nausea (51.3%), fatigue (44.2%), alopecia (37.9%), constipation (27.3%), decreased appetite (22.3%), and vomiting (21.5%).

The most common Grade 3 or higher adverse reactions were stomatitis (7.2%), fatigue (4.5%), anemia (3.8%), nausea (1.9%), decreased appetite (1.4%), vomiting (1.2%), and keratitis (1.1%). Grade 5 was reported in 0.9% of patients and was due to ILD.

The most common serious adverse reaction was ILD (2.6%).

The frequency of treatment discontinuation due to adverse reactions was 4.5% in patients treated with DATROWAY. The most common adverse reactions leading to treatment discontinuation was ILD (2.7%). The frequency of dose interruptions due to adverse reactions was 14.2%. The most common adverse reactions leading to dose interruption were stomatitis (4.7%), fatigue (2.5%), ILD (1.6%), infusion-related reactions (1.4%), keratitis (1.3%), and anemia (1.2%). The frequency of dose reductions due to adverse reactions was 16.5%. The most common adverse reactions leading to dose reductions were stomatitis (10.7%), fatigue (3%), and nausea (2.4%).

Tabulated List of Adverse Reactions

Table 3 presents adverse reactions reported with DATROWAY. Adverse reactions are listed by System Organ Class and frequency category.

The severity of adverse drug reactions was assessed based on the Common Terminology Criteria for Adverse Events (CTCAE), defining Grade 1=mild, Grade 2=moderate, Grade 3=severe, Grade 4=life threatening, and Grade 5=death.

Frequency categories are defined as very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), and not known (cannot be estimated from the available data).

Table 3: Adverse Reactions in Patients Treated with DATROWAY 6 mg/kg

MedDRA System Organ Class	**Frequency Category**	**All Grades (%)**	**Grade 3 or 4 (%)**
Blood and lymphatic system disorders			
Anaemia	Very Common	153 (16.5)	35 (3.8)
Metabolism and nutrition disorders			
Decreased appetite	Very Common	207 (22.3)	13 (1.4)
Eye disorders			
Dry eyes	Very Common	145 (15.6)	2 (0.2)
Keratitis[a]	Very Common	99 (10.7)	10 (1.1)
Conjunctivitis[b]	Common	55 (5.9)	1 (0.1)
Lacrimation increased	Common	55 (5.9)	0
Vision blurred	Common	39 (4.2)	0
Blepharitis	Common	27 (2.9)	0
Meibomian gland dysfunction	Common	24 (2.6)	0
Visual impairment[c]	Uncommon	9 (1.0)	1 (0.1)
Photophobia	Uncommon	8 (0.9)	0

Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease[d]	Common	46 (5.0)	7 (0.8)
Gastrointestinal disorders			
Stomatitis[e]	Very Common	561 (60.5)	67 (7.2)
Nausea	Very Common	476 (51.3)	18 (1.9)
Constipation	Very Common	253 (27.3)	1 (0.1)
Vomiting	Very Common	199 (21.5)	11 (1.2)
Diarrhea	Very Common	111 (12.0)	3 (0.3)
Dry mouth	Common	51 (5.5)	1 (0.1)
Skin and subcutaneous tissue disorders			
Alopecia	Very Common	351 (37.9)	1 (0.1)
Rash[f]	Very Common	145 (15.6)	2 (0.2)
Pruritus	Common	67 (7.2)	1 (0.1)
Dry skin[g]	Common	63 (6.8)	0
Skin hyperpigmentation[h]	Common	44 (4.7)	0
Madarosis	Uncommon	7 (0.8)	0
General disorders and administration site conditions			
Fatigue[i]	Very Common	410 (44.2)	42 (4.5)
Injury, poisoning and procedural complications			
Infusion-related reactions[j]	Very Common	110 (11.9)	3 (0.3)

MedDRA = Medical Dictionary for Regulatory Activities

Events were graded using NCI CTCAE version 5.0

a. Including keratitis, punctate keratitis, ulcerative keratitis
b. Including conjunctivitis, conjunctival disorder, conjunctival hyperemia, conjunctival irritation
c. Including visual impairment, reduced visual acuity
d. Interstitial lung disease includes events that were reported by the investigator which were adjudicated as drug-related ILD for DATROWAY: interstitial lung disease, pneumocystis jirovecii pneumonia, pneumonia, bacterial pneumonia, pneumonitis, pulmonary toxicity, respiratory failure
e. Including stomatitis, aphthous ulcer, glossitis, mouth ulceration, odynophagia, oral pain, oropharyngeal pain, pharyngeal inflammation
f. Including rash, erythematous rash, maculo-papular rash, pruritic rash
g. Including dry skin, xerosis
h. Including skin hyperpigmentation, pigmentation disorder, skin discoloration
i. Including fatigue, asthenia, lethargy, malaise
j. Infusion-related reaction includes as any reaction occurring (infusion-related reaction, anaphylactic reaction, bronchospasm, chills, flushing, hypersensitivity, hypotension, infusion related hypersensitivity reaction, pruritus, pyrexia, rash, maculo-papular rash, urticaria, wheezing) within the same day as DATROWAY infusion.

Description of selected undesirable effects and additional information

ILD/Pneumonitis

In the NSCLC pooled patient population, ILD occurred in 7% of patients treated with DATROWAY 6 mg/kg, as determined by independent review. Most ILD cases were Grade 1 (0.8%) and Grade 2 (3.7%). Grade 3 and Grade 4 ILD each occurred in 0.4% of patients. Grade 5 ILD occurred in 1.7% of patients in the overall NSCLC population and 1.2% of patients with non-squamous histology. Median time to first onset was 1.4 months (range: 0.2 to 9).

In the breast cancer pooled patient population, ILD occurred in 2.9% of patients treated with DATROWAY 6 mg/kg, as determined by independent review. Most ILD cases were Grade 1 (1.1%) and Grade 2 (0.9%). Grade 3 ILD occurred in 0.7% of patients and no Grade 4 ILD were observed. Grade 5 ILD occurred in 0.2% of patients. Median time to first onset was 2.5 months (range: 1.1 to 8.3).

Keratitis

Keratitis occurred in 10.7% of the pool of patients treated with DATROWAY 6 mg/kg, of which 7.3% were Grade 1, 2.3% were Grade 2 and 1.1% were Grade 3. No Grade 4 keratitis was reported. The median time to onset for keratitis was 4.1 months (range: 0.3 to 19.1). Discontinuation due to keratitis occurred in 0.4% of patients.

Stomatitis

Stomatitis occurred in 60.5% of the pool of patients treated with DATROWAY 6 mg/kg, of which 29.1% were Grade 1, 24.2% were Grade 2, 7.1% were Grade 3, and 0.1% were Grade 4. Median time to first onset was 0.5 months (range:0.03 to 10.3 months). Discontinuation due to stomatitis occurred in 0.5% of patients.

Specific populations

Elderly patients

Of the 234 non-squamous patients in TROPION-Lung01 randomized to DATROWAY 6 mg/kg, 46.2% were 65 years or older and 6% were 75 years or older. Of 365 patients in TROPION-Breast01 randomized to DATROWAY 6 mg/kg, 24.9% were 65 years of age or older.

Of the 927 patients treated with DATROWAY 6 mg/kg in the clinical studies, 32.8% were 65 years of age or older. No clinically meaningful differences in safety were observed between patients ≥65 years of age and younger patients.

Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity.

During the median 5.5-month treatment period across clinical studies in patients treated with DATROWAY at 6 mg/kg, the incidence of anti-datopotamab deruxtecan antibodies was 16% (146 out of 912) and the incidence of neutralizing antibodies against datopotamab deruxtecan was 2.5% (23 out of 912).
There was no apparent effect of anti-drug antibodies on the pharmacokinetics, or effectiveness of datopotamab deruxtecan. No clinically meaningful impact on the safety of datopotamab deruxtecan was observed.

Reporting suspected adverse reactions after authorisation of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions online via the ElViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

Overdose

There is no information on overdose with datopotamab deruxtecan. In the event of overdose, patients should be monitored, and appropriate supportive care should be given.

Properties/Effects

ATC code

L01FX35

Mechanism of action

DATROWAY, datopotamab deruxtecan, is a TROP2-directed antibody-drug conjugate (ADC). The antibody is a humanized anti-TROP2 IgG1 attached to deruxtecan, a topoisomerase I inhibitor (DXd) bound by a tetrapeptide-based cleavable linker. Following binding to TROP2 on tumor cells, datopotamab deruxtecan undergoes internalization and intracellular linker cleavage by lysosomal enzymes that are upregulated in cancer cells. Upon release, the membrane-permeable DXd causes DNA damage and apoptotic cell death. DXd, an exatecan derivative, is approximately 10 times more potent than SN-38, the active metabolite of irinotecan.

Pharmacodynamics

The administration of doses of datopotamab deruxtecan ranging from 0.27 to 10 mg/kg did not show any clinically meaningful effect on the QTc interval in an open-label study in 195 patients with NSCLC.

Clinical efficacy

Breast Cancer *(HR+/HER2- breast cancer)*

TROPION-Breast01 (NCT 05104866)

The efficacy of DATROWAY was evaluated in study TROPION-Breast01, a multicenter, open-label, randomized study of 732 patients with unresectable or metastatic HR-positive, HER2-negative (IHC 0, IHC1+ or IHC2+/ISH-) breast cancer. Patients must have progressed on and been unsuitable for endocrine therapy. Patients were required to have received 1 to 2 lines of prior chemotherapy in the unresectable or metastatic disease setting.
Patients with clinically inactive brain metastases were included in the study. Patients were excluded for a history of ILD/pneumonitis requiring treatment with steroids, ongoing ILD/pneumonitis, or clinically significant corneal disease at screening. Patients were also excluded for ECOG performance status >1.

A total of 732 patients were randomized 1:1 to receive either DATROWAY 6 mg/kg (N=365) by intravenous infusion every 3 weeks or physician's choice of chemotherapy (N=367, eribulin 59.9%, capecitabine 20.7%, vinorelbine 10.4%, or gemcitabine 9.0%) until unacceptable toxicity or disease progression. Randomization was stratified by previous lines of chemotherapy (one or two), prior treatment with a CDK4/6 inhibitor (yes or no), and geographical region. Tumor imaging was obtained every 6 weeks until disease progression.

The dual primary efficacy outcomes were progression-free survival (PFS) as assessed by blinded independent central review (BICR) based on Response Evaluation Criteria in Solid Tumors (RECIST) v.1.1 and overall survival (OS).

Baseline demographics and disease characteristics were similar between treatment arms. The median age was 55 years (range 28-86); 22.3% were ≥65 years and 98.8% were female; 47.8% were White, 1.5% were Black or African American, 40.7% were Asian, and 11.3% were of Hispanic/Latino ethnicity; 57% had ECOG PS 0 and 42.3% had ECOG PS of 1; 97.3% had visceral disease, 71.9% had liver metastases and 7.9% had stable brain metastases at baseline at the time of randomization.

There were 60.2% of patients who received prior endocrine therapy in the (neo) adjuvant setting, 88.5% received prior endocrine therapy in the unresectable or metastatic setting and all patients received prior chemotherapy regimens in the unresectable or metastatic setting. Overall, 80.7% of patients had received prior taxanes and 63.8% had received prior anthracyclines. There were 62% of patients who had 1 prior chemotherapy regimen and 37.7% of patients had 2 prior chemotherapy

regimens for treatment of unresectable or metastatic disease. 82.5% of patients had prior treatment with a CDK4/6 inhibitor.

The study met its primary endpoint and demonstrated a statistically significant improvement in PFS in patients randomized to DATROWAY compared to chemotherapy. OS did not reach statistical significance at final analysis.

Efficacy results are shown in Table 4.

Table 4: Efficacy Results by BICR in TROPION-Breast01

Efficacy Parameter	DATROWAY (n=365)	Chemotherapy (n=367)
Progression-Free Survival by BICR[a]		
Number of events (%)	212 (58.1)	235 (64.0)
Median, months (95% CI)	6.9 (5.7, 7.4)	4.9 (4.2, 5.5)
Hazard ratio (95% CI)	0.63 (0.52, 0.76)	
p-value[b]	< 0.0001	
Overall Survival[c, d]		
Number of events (%)	223 (61.1)	213 (58.0)
Median, months (95% CI)	18.6 (17.3, 20.1)	18.3 (17.3, 20.5)
Hazard ratio (95% CI)	1.01 (0.83, 1.22)	
p-value[e]	0.9445	

[a] Data cutoff 17 July 2023.

[b] Predefined p-value boundary was 0.01.

[c] Data cutoff 24 July 2024.

[d] 12.3% and 24.0% of patients in the datopotamab deruxtecan and ICC arms, respectively, received subsequent treatment with trastuzumab deruxtecan and/or sacituzumab govitecan post discontinuation.

[e] Predefined p-value boundary was 0.0403.

The improvement in PFS by BICR was consistent amongst the prespecified subgroups of patients including by geographic region, prior use of CDK4/6 inhibitor, and previous line of therapy.

Pharmacokinetics

The pharmacokinetics of datopotamab deruxtecan was evaluated in 729 patients.

At the recommended dosage of DATROWAY, the geometric mean (coefficient of variation [CV]%) Cmax of datopotamab deruxtecan and DXd were 154 µg/mL (20.3%) and 2.82 ng/mL (58.1%),

respectively, and the corresponding AUC were 671 µg*day/mL (31.4%) and 18.5 ng*day/mL (42.6%) after the first dose in cycle 1.

Distribution

The steady state volume of distribution of datopotamab deruxtecan is 3.52L.
In vitro, across the concentration range of 10 ng/mL to 100 ng/mL, the mean human plasma protein binding of DXd was 96.8 to 98.0%, and the blood-to-plasma concentration ratio of DXd was 0.59–0.62.

Metabolism

Datopotamab deruxtecan undergoes intracellular cleavage by lysosomal enzymes to release DXd.

The humanized TROP2 IgG1 monoclonal antibody is expected to be degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgG.
In vitro metabolism studies in human liver microsomes indicate that DXd is primarily metabolized by CYP3A4 via oxidative pathways and does not undergo significant metabolism by UGT or other CYP enzymes.

Elimination

The clearance of datopotamab deruxtecan was estimated to be 0.57 L/day. The median elimination half-life ($t_{1/2}$) of datopotamab deruxtecan was 4.82 days and apparent median $t_{1/2}$ of released DXd was approximately 5.50 days. *In vitro*, DXd was a substrate of P-gp, OATP1B1, OATP1B3, MATE2-K, MRP1, and BCRP. No accumulation of datopotamab deruxtecan was observed at the 6 mg/kg dose between cycle 1 and cycle 3.

Following intravenous administration of DXd to rats and monkeys, the major excretion pathway was feces via the biliary route. DXd was the most abundant component in urine, feces, and bile.

Linearity/non-linearity

The exposure of datopotamab deruxtecan and released DXd when administered intravenously increased in proportion to dose in the 4 mg/kg to 10 mg/kg dose range (approximately 0.7 to 1.7 times the recommended dose).

Specific patient groups

Age (26–86 years), race (Asian, White, Black and others), region/country (Japan, Mainland China, US, Europe, and rest of world), body weight (35.6-156 kg), and sex did not have a clinically meaningful effect on exposure of datopotamab deruxtecan or DXd.

Patients with renal impairment

No dedicated renal impairment study was conducted. Based on population pharmacokinetic analysis including patients with mild to moderate (creatinine clearance [CLcr] 30 to <90 mL/min) renal impairment, the pharmacokinetics of datopotamab deruxtecan or DXd was not affected by mild to moderate renal impairment as compared to normal renal function (CLcr ≥90 mL/min).

Patients with hepatic impairment

No dedicated hepatic impairment study was conducted. Based on population pharmacokinetic analysis including patients with mild hepatic impairment (total bilirubin ≤ULN and any AST >ULN or total bilirubin >1 to 1.5 times ULN and any AST), the pharmacokinetics of datopotamab deruxtecan or DXd was not affected by mild hepatic impairment as compared to normal hepatic function. There are limited data in patients with moderate (total bilirubin >1.5 to 3 times ULN and any AST) or severe hepatic impairment (total bilirubin >3 times ULN and any AST) to draw conclusions on the clinical impact of these changes.

Preclinical data

Repeated Dose Toxicity

In rats and cytomolgus monkeys, toxicities were observed following administration of datopotamab deruxtecan in clinically relevant exposures in the lympho-hematopoietic organ, intestine, lung, kidney, skin and cornea. In rats, additional toxicities were observed in male and female reproductive organs and incisor teeth, while monkeys showed additional toxicities in the liver and hip cartilage. In these animals, ADC exposure levels were similar or above clinical plasma exposure.

Genotoxicity

DXd was clastogenic in both an *in vivo* rat bone marrow micronucleus assay and an *in vitro* Chinese hamster lung chromosome aberration assay and was not mutagenic in an *in vitro* bacterial reverse mutation assay.

Carcinogenicity

Carcinogenicity studies have not been conducted with datopotamab deruxtecan.

Reproductive toxicity

Dedicated fertility studies have not been conducted with datopotamab deruxtecan. Based on the results from a general toxicity study in rats, datopotamab deruxtecan may impair male reproductive function and fertility.

Reproductive and developmental toxicity studies have not been conducted with datopotamab deruxtecan.

Based on results from general animal toxicity studies, datopotamab deruxtecan and DXd, were toxic to rapidly dividing cells (lymphohematopoietic organs, intestine, or testes), and DXd was genotoxic, suggesting the potential for embryotoxicity and teratogenicity.

Other information

Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.
Sodium chloride solution for infusion must not be used for reconstitution or dilution since it may cause particulate formation.

Shelf life

Do not use this medicine after the expiry date ("EXP") stated on the container.

Shelf life after opening

Reconstituted solution
It is recommended that the reconstituted solution be used immediately. If not used immediately, the reconstituted solution may be stored in a refrigerator at 2ºC to 8ºC for up to 24 hours, protected from light.

Diluted solution
It is recommended that the diluted solution be used immediately. If not used immediately, the diluted solution may be stored at room temperature for up to 4 hours or in a refrigerator at 2ºC to 8ºC for up to 24 hours, protected from light.

The maximum time from reconstitution of the vial through the end of administration should not exceed 24 hours. Discard if storage time exceeds these limits.

Special precautions for storage

Store in the refrigerator (2-8°C) until time of reconstitution.
Do not freeze.
Keep out of the reach of children.

For storage conditions after reconstitution and dilution of the medicinal product, see section “Other information”, “Shelf life after opening”.

Instructions and special precautions for handling and disposal

Appropriate procedures for the preparation of chemotherapeutic medicinal products should be used. Appropriate aseptic technique should be used for the following reconstitution and dilution procedures.

Reconstitution

- Reconstitute immediately before dilution.
- More than one vial may be needed for a full dose. Calculate the dose (mg), the total volume of reconstituted DATROWAY solution required, and the number of vial(s) of DATROWAY needed (see section “Dosage/Administration”).
- Reconstitute each 100 mg vial using a sterile syringe to slowly inject 5 mL of sterile water for injection into each vial to obtain a final concentration of 20 mg/mL.
- Swirl the vial gently until completely dissolved. Do not shake.
- If not used immediately, store the reconstituted DATROWAY vials in a refrigerator at 2ºC to 8ºC for up to 24 hours, protected from light. Do not freeze.
- The product does not contain a preservative. Discard unused reconstituted DATROWAY after 24 hours refrigerated.

Dilution

- Withdraw the calculated amount from the vial(s) using a sterile syringe. Inspect the reconstituted solution for particulates and discoloration. The solution should be clear and colorless to light yellow. Do not use if visible particles are observed or if the solution is cloudy or discolored.
- Dilute the calculated volume of reconstituted DATROWAY in an infusion bag containing 100 mL of 5% dextrose solution. Do not use sodium chloride solution. DATROWAY is compatible with an infusion bag made of polyvinyl chloride (PVC), or polyolefin (polypropylene (PP), copolymer of ethylene and propylene).

- Gently invert the infusion bag to thoroughly mix the solution. Do not shake.
- Cover the infusion bag to protect from light.
- If not used immediately, store at room temperature for up to 4 hours including preparation and infusion or in a refrigerator at 2ºC to 8ºC for up to 24 hours, protected from light. Do not freeze.
- Discard any unused portion left in the vial.

Administration

- The maximum time from reconstitution of the vial through the end of administration should not exceed 24 hours. Discard if storage time exceeds these limits.
- If the prepared infusion solution was stored refrigerated (2ºC to 8ºC), it is recommended that the solution be allowed to reach room temperature prior to administration, protected from light.
- Administer DATROWAY as an intravenous infusion only with an infusion line and tubing set made of PVC, polybutadiene (PBD), or low-density polyethylene (LDPE).
- Administer DATROWAY with a 0.2 micron in-line polytetrafluoroethylene (PTFE), polyethersulfone (PES) or nylon 66 filter.
- Do not administer as an intravenous push or bolus.
- Cover the infusion bag to protect from light.
- Do not mix DATROWAY with other medicinal products or administer other medicinal products through the same intravenous line.

Disposal

The reconstituted product contains no preservative and is intended for single use only. Discard any unused portion left in the vial.

Authorisation number

69801 (Swissmedic)

Packs

DATROWAY is provided in 10 mL Type 1 amber borosilicate glass vial sealed with a fluoro-resin laminated butyl rubber stopper, and a polypropylene/aluminium blue flip-off crimp cap.
Pack containing 1 vial with 100 mg of datopotomab deruxtecan (A)

Marketing authorisation holder

DAIICHI SANKYO (Schweiz) AG, Zürich

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April 2025