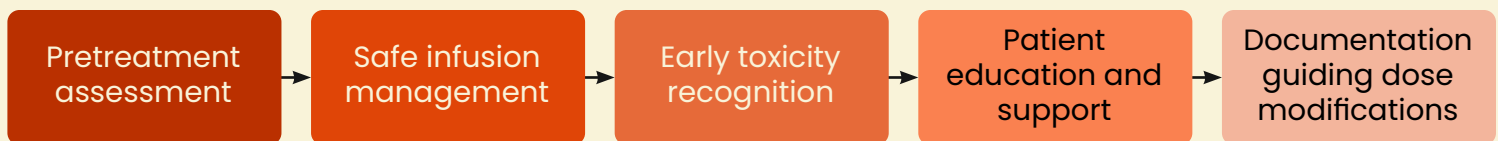


Roadmap to Maximizing Efficacy and Enhancing Tolerability With Antibody–Drug Conjugates in HER2-Negative Advanced Breast Cancer

This pocket guide is designed to assist oncology nurses in quickly identifying toxicity grade and managing adverse events associated with antibody–drug conjugates (ADCs) in the treatment of patients with HR-positive/HER2-negative MBC and metastatic TNBC

The Evolving Nursing Role for Patients With HER2-Negative MBC Receiving ADCs

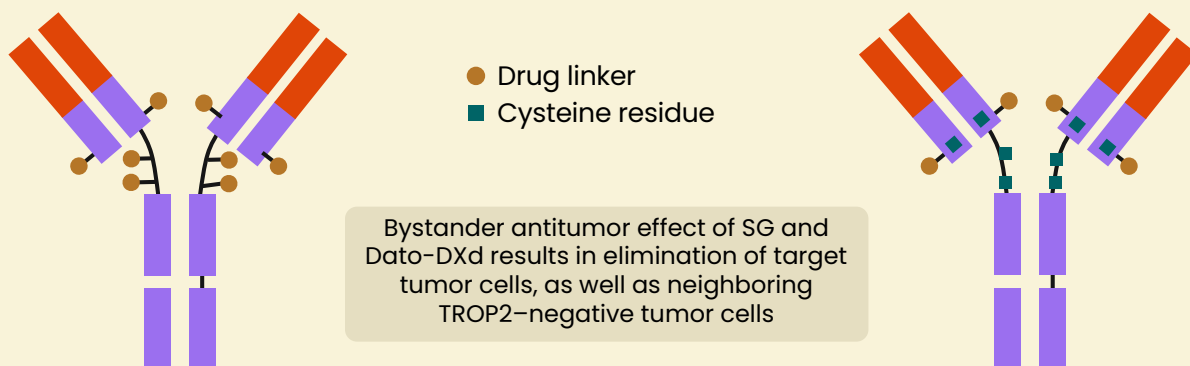
- ▲ With a rapidly evolving ADC landscape in HER2-negative MBC, it is important to continuously support oncology nurses' knowledge and competence in identifying and managing ADC-related AEs to maximize treatment efficacy and patients' quality of life while receiving treatment and after treatment discontinuation
 - There are currently 2 TROP2-directed ADCs that are approved by the FDA for patients with HER2-negative breast cancer:
 - Sacituzumab govitecan and datopotamab deruxtecan
 - These ADCs have distinct safety profiles requiring different nursing protocols
- ▲ Of importance, nurses are the frontline for:



What Nurses Must Know to Deliver Safe, High-Quality Care

FDA-Approved TROP2-Directed ADCs: Sacituzumab Govitecan and Datopotamab Deruxtecan

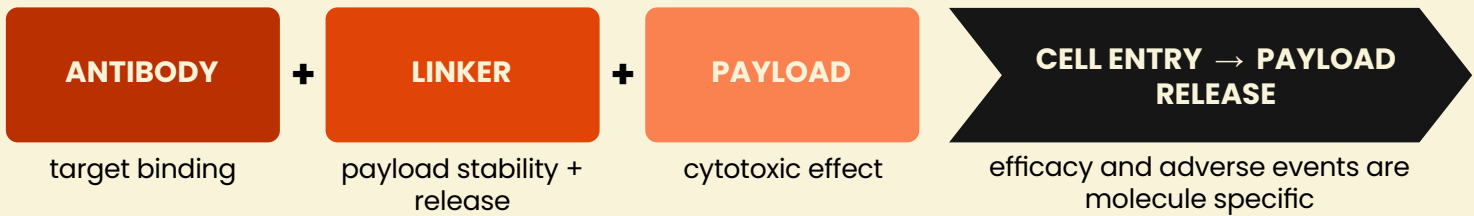
- ▲ SG
 - Humanized anti-TROP2 IgG mAb (RS7)
 - Attached to topoisomerase I inhibitor payload (camptothecin derivative; SN-38)
 - Proprietary cleavable hydrolyzable linker (CL2A)
- ▲ Dato-DXd
 - Humanized anti-TROP2 mAb (datopotamab)
 - Attached to topoisomerase I inhibitor payload (exatecan derivative)
 - Tetrapeptide-based cleavable linker



○ Drug-to-antibody ratio (7.6:1)

○ Drug-to-antibody ratio (4:1)

ADCs: Drug Design Predicts the Toxicity Pattern Nurses Will See



READ THE WHOLE LABEL

Do not use 1 "ADC class" checklist
→ Match screening, prophylaxis, and dose holds to the exact ADC

SG and Dato-DXd: FDA-Approved Indications in Unresectable, Advanced or MBC

1. Subtype	2. Treatment Context	3. FDA-Approved Option
mTNBC	First line • not eligible for PD-1/PD-L1 inhibitor (CPS <10)	SG or Dato-DXd
Ask about PD-(L)1 inhibitor eligibility and prior therapy	First line • PD-L1+ (CPS ≥10)	SG + pembrolizumab ± berahyaluronidase alfa-pmph
	After ≥2 systemic therapies (≥1 for MBC)	SG
HR+/HER2- (IHC 0, IHC 1+, or IHC 2+/ISH-)	After endocrine therapy + chemotherapy for advanced BC	Dato-DXd
Confirm Prior endocrine + systemic therapy	After endocrine therapy + ≥2 additional systemic therapies for MBC	SG

Nursing implication: verify subtype, immune eligibility, and prior therapy before administration

ADC CARE: A Nursing Memory Tool

7 nurse-led behaviors turn a complex therapy into safer, more patient-centered care



Earlier recognition → faster intervention → fewer avoidable treatment disruptions

Optimizing AE Recognition, Early Intervention, and QoL Preservation in Patients Receiving TROP2-Directed ADCs

Both ADCs Are Q3W, but the Nursing Workflow Differs

DOSE + CADENCE	PREPARE	INFUSE + OBSERVE	FOLLOW
SG 10 mg/kg IV Day 1 + Day 8 every 3 wk	PREMEDICATE Antiemetic • antipyretic H ₁ /H ₂ blockers • corticosteroid	FIRST → LATER 3 hr → 1–2 hr Observe ≥30 min after each infusion	MONITOR FOR • IRRs • CBCs/febrile neutropenia → G-CSF use if at risk • Diarrhea
Dato-DXd 6 mg/kg IV Every 3 wk (if <90 kg)	PREPARE + PROTECT Antiemetic • antipyretic • antihistamine Steroid mouthwash + preservative-free eye lubricant	FIRST → LATER 90 min → 30 min Observe ≥1 hr first; ≥30 min later	MONITOR FOR • IRRs • ILD/pneumonitis • Stomatitis • Ocular toxicities → preservative-free eye lubricant ≥4x/day

For both ADCs: monitor during and after infusion • dose reduce, interrupt or discontinue for IRRs based on grade

As ADCs Evolve, So Does the Nursing Watchlist

SG

AEs: HEMATOLOGIC + GI

Front-load CBC, hydration and bowel-pattern surveillance

64%

NEUTROPENIA

6% febrile neutropenia

62%

DIARRHEA

63%

NAUSEA

33% vomiting

Nursing priority → complete blood counts • infection • diarrhea • intake

Dato-DXd

AEs: ORAL + OCULAR + LUNG

Front-load mouth, eye, and respiratory symptom screening

63%

STOMATITIS

38%

OCULAR AEs
dry eye/keratitis

≤7%

**ILD/
PNEUMONITIS**

Nursing priority → mouth • vision • cough/dyspnea

BOTH

Fatigue
42%–59%

Alopecia
38%–47%

Nausea
51%–63%

Constipation
30%–37%

**Hypersensitivity/
IRR**
13%–28%

SG Requires 2 Parallel Early-Action Pathways

TOXICITY	1. MONITOR	2. CONFIRM	3. ACT
ANC NEUTROPENIA	CBC + INFECTION SCREEN CBC on Days 1 and 8 Teach fever/infection reporting Consider C1 G-CSF if increased risk	USE ANC THRESHOLDS Day 1: ANC $\geq 1500/\text{mm}^3$ Day 8: ANC $\geq 1000/\text{mm}^3$ Identify neutropenic fever	HOLD + TREAT PROMPTLY Withhold below thresholds or for fever Start anti-infective treatment without delay Use G-CSF as indicated
GI DIARRHEA	TREND THE BASELINE Ask about cramps + loose stools Track nausea/vomiting + intake Reinforce immediate reporting	GRADE + EXCLUDE INFECTION Compare stools with baseline Assess ADL impact Evaluate infectious causes	CONTROL + REHYDRATE If infection excluded: loperamide 4 mg, then 2 mg per episode (max 16 mg/day) Replace fluids + electrolytes

GRADE 3/4 OR RECURRENCE → withhold until recovery • reduce to 7.5 mg/kg, then 5 mg/kg • discontinue if 5 mg/kg is not tolerated

Interstitial Lung Disease Associated With Dato-DXd: Monitoring, Confirmation, and Management

MONITOR	CONFIRM	MANAGE
Suspected ILD Urge patients to immediately report new or worsening cough, dyspnea, fever, and/or new or worsening pulmonary symptoms • Monitor patients for signs/symptoms of ILD • Promptly investigate evidence of ILD • Evaluate patients with suspected ILD by radiographic imaging and assess	Assessments should include: • High-resolution CT • Pulmonologist consult; if indicated, ID consult • Blood culture and CBC; other blood tests as needed • Consider bronchoscopy and BAL if indicated and feasible • PFTs and pulse oximetry • Arterial blood gases if indicated • As soon as ILD is suspected, collect 1 blood sample for PK assessment, if feasible • Rule out other causes of ILD (eg, progression, infection, other drugs, radiotherapy) • All ILD events should be followed until resolution and after drug discontinuation	• Grade 1: Hold until resolved to grade 0, consider corticosteroids (0.5 mg/kg/day prednisolone), then: ◦ If resolved ≤ 28 days from onset: Maintain dose ◦ If resolved > 28 days after onset: Reduce dose by 1 level • Grades 2-4: Permanently discontinue treatment and promptly initiate systemic corticosteroid treatment (eg, ≥ 1 mg/kg/day prednisolone or equivalent for ≥ 14 days followed by taper for at least 4 wk)

Dato-DXd–Associated Stomatitis

TOXICITY	1. RECOGNIZE	2. CONFIRM /GRADE	3. ACT
ORAL STOMATITIS	PREVENT FROM DAY 1 Steroid mouth rinse 3–4×/day Oral hygiene + education Consider cryotherapy/ bland rinse	LOOK + GRADE Redness • sores • mouth pain Taste, chewing or swallowing change Grade by pain + oral intake	ESCALATE EARLY Report symptoms immediately Document intake + severity Trigger grade-based management

NURSING RULE → **teach prevention • assess every encounter • hold and escalate early**

Grade	Prophylaxis Status	Protocol Management Recommendations
1	With or without prophylaxis adherence	- Diet modification: avoid spicy, acidic and crunchy foods - Topical steroid gel: use for spot therapy directly to mouth ulcers - Steroid-containing mouth rinse: 3–4 times daily for 1–2 min
2	With prophylaxis adherence	- Delay Dato-DXd treatment until symptom improvement to grade ≤1 - Reinitiate Dato-DXd at a reduced dose: typically from 6 to 4 mg/kg - Use steroid-containing mouth rinse: 3–4 times daily for 1–2 min
	Without prophylaxis adherence	- Delay Dato-DXd treatment until symptom improvement to grade ≤1 - Use steroid-containing mouth rinse: 3–4 times daily for 1–2 min
3	With or without prophylaxis adherence	- Delay Dato-DXd treatment until symptom improvement to grade ≤1 - Consider reinitiating Dato-DXd at a reduced dose: typically from 6 to 4 mg/kg - Use steroid-containing mouth rinse: 3–4 times daily for 1–2 min
4	N/A	Permanently discontinue drug

Dato-DXd–Associated Ocular Toxicity: Symptoms and Management

	Dry eye - Eye redness - Stinging - Burning or scratchy sensation - Sensation of having something in eye	- Sensitivity to light - Blurred vision		Keratitis - Eye pain - Excess tears or discharge from eye - Difficulty opening eyelid due to pain or irritation - Decreased vision

Grade	Prophylaxis Status	Protocol Management Recommendations*
1: Asymptomatic		• Maintain dose • Ensure use of artificial tears • Consider ophthalmology assessment
2: Symptomatic with moderate decrease in visual acuity		• Obtain ophthalmology assessment • Delay dose until resolved to grade ≤ 1
3: Symptomatic with marked decrease in visual acuity limiting self-care ADL		• Obtain ophthalmology assessment • Delay dose until resolved to grade ≤ 1, then reduce by 1 dose level
4: Perforation; best corrected visual acuity of 20/200 or worse in affected eye		• Obtain ophthalmology assessment • Discontinue drug

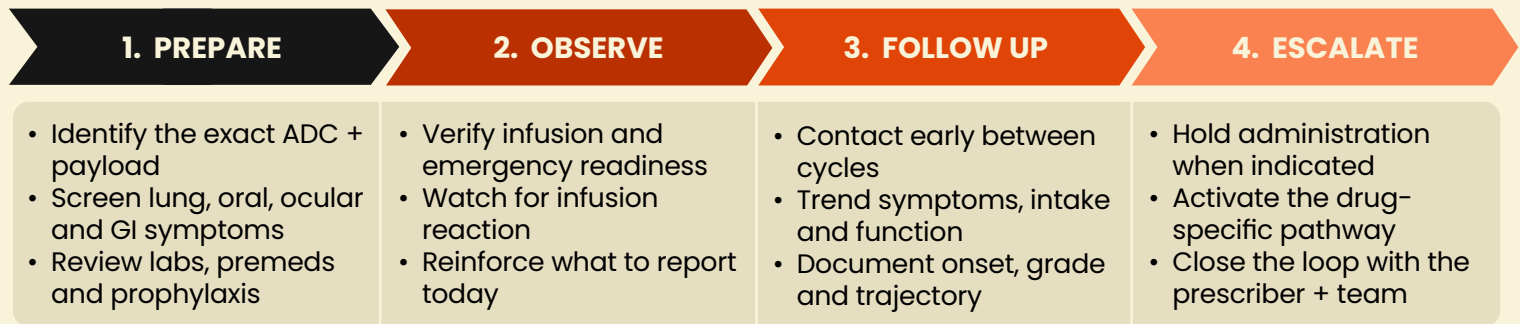
*Ensure that use of contact lenses is avoided.

Other Toxicities Associated With SG and Dato-DXd

WATCHLIST	1. PREPARE	2. ASSESS	3. ACT
IRR	Premedicate: acetaminophen + antihistamine + steroid	Monitor during + ≥ 30 min after Hypotension • wheeze • swelling	Emergency medicines ready for us Escalate severe reactions • discontinue for grade 4
FATIGUE	Document baseline + prior treatment burden Set expectations	Trend ADL impact Check anemia, intake, hydration, sleep + stress	Hydration + nutrition Mental health screen • activity + planned rest
ALOPECIA	Set expectations: partial or total loss Elicit patient preference	Monitor scalp dryness/ irritation Recognize eyebrow + lash distress	Wig/scarf/hat options SPF ≥ 30 • mild shampoo • natural oils
NAUSEA VOMITING	3-drug antiemetic premedication Plan for delayed onset	Confirm take-home antiemetics + instructions Assess hydration + severity	Antiemetics + supportive care High grade: hold until grade ≤ 1

ONE NURSING STANDARD → anticipate • detect early • promptly match action to toxicity

Role of Nurses in Providing Optimal Care for Patients Receiving ADCs



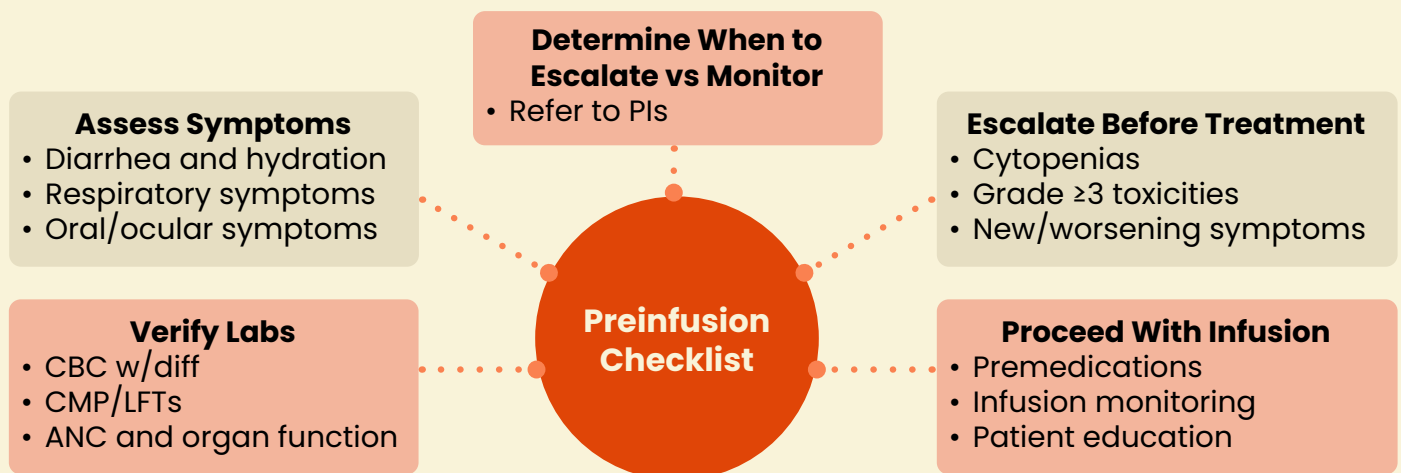
The safest protocol is agent-specific: verify the prescribing information before every cycle and after every new symptom

Role of nurses in ensuring safety is a continuous loop—not a preinfusion checklist

Nursing Interventions for Toxicity Management

- ▲ Nurses have a central role in the prevention and management of ADC-associated toxicities
 - Nurse-led early detection reduces ER visits, dose reductions, and treatment failure
 - Patients often report symptoms and toxicities to nurses first before other members of the care team
 - Most ADC-related toxicities begin as mild symptoms reported first to nurses
 - Rate of discontinuation of SG or Dato-DXd is ≤6%
 - Nurses have a critical role in monitoring and promoting patient safety during the course of ADC therapy
 - Nurses facilitate timely assessment, intervention, and escalation of treatment-related toxicities

Nursing Assessment Before ADC Administration



4 Red Flags That Should Never Wait for the Next Visit

Patient Reports	Nurse Hears/Sees	Same-Day Action
Breathing-related AEs	New or worsening cough, dyspnea, fever or chest symptoms	Hold treatment; notify prescriber and initiate urgent ILD/pneumonitis evaluation
Fever	Temperature $\geq 38^{\circ}\text{C}/100.4^{\circ}\text{F}$, chills, or infection symptoms	Urgent CBC and infection/neutropenia pathway; do not wait for the next appointment
Ocular AEs	Eye pain, photophobia, blurred vision, or new visual change	Notify promptly; arrange ophthalmic assessment and follow agent-specific hold criteria
GI AEs	Persistent diarrhea or vomiting, dizziness, low intake, or reduced urine	Same-day assessment; fluids/electrolytes and drug-specific antidiarrheal/antiemetic guidance

TEACH-BACK: “Call us the same day—even if the symptom feels mild”

Navigating the Healthcare Ecosystem: Equity and Real-world Access Considerations

- Oncology nurses and nurse navigators are an integral part of oncology treatment and patient care
 - Have important roles in empowering patients and their families to take charge of their health
 - Provide education, resources, and healthcare planning advice

Communication is important

- Optimize patient-provider communication
- Acknowledge and consider patient beliefs/values
- Minimize bias
- Acknowledge that cultural factors influence AE reporting
- Use digital tools for symptom reporting

Financial factors influence treatment

- Address avoidance due to financial concerns
- Monitor for transportation barriers
- Provide education and information on grants/financial assistance sources to cover transportation costs and dependent care

Utilize shared treatment decision-making approaches and provide appropriate patient/caregiver education to maximize outcomes and improve adherence

- Use health literacy assessment tools
- Ensure reliable transportation for clinic appointments
- Educate patients on differences between ADC-related AEs and chemo-related AEs
- Set expectations for monitoring frequency
- Help to avoid “silent suffering” leading to dose reductions (that can be prevented)
- Manage AEs proactively
- Provide return-to-work support to manage fatigue and stress
- Address barriers to care upfront

It is important to coordinate care with the MDT

Pharmacist
Medical Oncologist
APPs
Social Worker
Genetic Counselor
Oncology Nurse
Nurse Navigator
Nutritionist
Pulmonologist
Gastroenterologist
Ophthalmologist

Urgently contact the oncology team for fever, grade ≥ 3 cytopenias, new or worsening respiratory symptoms, mouth sores, vision/eye changes, jaundice, severe abdominal pain, changes in bowel movement, persistent nausea/vomiting, dehydration, suspected pregnancy, pregnancy planning, breastfeeding, major drug interaction, inability to obtain medication, IRRs, or any patient-directed treatment interruption

What Nurses Should Reinforce With ADCs

PLAN THE VISIT

Before each cycle

- Lab schedule
- Infusion cadence
- Premedication plan

Make the care plan concrete before treatment begins.

SG

PROTECT COUNTS USE NEUTROPENIA PROPHYLAXIS

Primary prophylaxis with G-CSF is recommended from cycle 1 for patients at increased risk of febrile neutropenia

INCREASED-RISK PATIENTS INCLUDE:

- Older patients
- History of neutropenia
- Poor performance status
- Organ dysfunction
- Multiple comorbidities

Dato-DXd

PROTECT ORAL + EYE HEALTH

- Steroid mouthwash for prevention
- Oral hygiene
- Preservative-free lubricant eye drops
- Avoid contact lens use
- Referral for ophthalmic exam

Reinforce at every touchpoint

At Every Visit

Patient Interaction Tips

- Use simple, plain language
- Use the teach-back method after every dose adjustment or major AE
- Encourage patients to call with new, worsening, or persistent symptoms
- Use interpreters and culturally responsive education to support equitable communication
- Provide written and verbal education

Questions to Ask Patients

- Have you experienced any of the following?
 - Fever
 - Bowel movement changes
 - Vision/eye changes
 - Mouth sores
 - New pulmonary symptoms
- Do you have issues with cost of treatment, transportation, or caregiver support?

Abbreviations

ADC, antibody–drug conjugate
ADL, activities of daily living
AE, adverse event
ANC, absolute neutrophil count
APP, advanced practice provider
BAL, bronchoalveolar lavage
BC, breast cancer
C1, cycle 1
CBC, complete blood count
CL2A, proprietary cleavable linker designation
CMP, comprehensive metabolic panel
CPS, combined positive score
CT, computed tomography

Dato-DXd, datopotamab deruxtecan
ER, emergency room
G-CSF, granulocyte colony-stimulating factor
GI, gastrointestinal
HR+, hormone receptor positive
ID, infectious disease
IgG, immunoglobulin G
IHC, immunohistochemistry
ILD, interstitial lung disease
IRR, infusion-related reaction
ISH, in situ hybridization
IV, intravenous
LFT, liver function test

mAb, monoclonal antibody
MBC, metastatic breast cancer
MDT, multidisciplinary team
mTNBC, metastatic triple-negative breast cancer
PFT, pulmonary function test
PI, prescribing information
PK, pharmacokinetics
Q3W, every 3 weeks
SG, sacituzumab govitecan
SPF, sun protection factor
TNBC, triple-negative breast cancer

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