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DOSING AND ADMINISTRATION GUIDE

INCLUDED IN PRESCRIBING INFORMATION: Dose escalation in HER2+ eBC and mBC[1]

This guide is not a substitute for the Full Prescribing Information

Dose escalation of neratinib (NERLYNX®) for HER2+ eBC is included in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer[2,*]

*** Useful in certain circumstances for patients with HER2+ eBC.[2]**

eBC: early-stage breast cancer; HER2+: human epidermal growth factor receptor 2–positive; mBC: metastatic breast cancer; NCCN: National Comprehensive Cancer Network® (NCCN®).
NCCN makes no warranties of any kind whatsoever regarding its content, use, or application and disclaims any responsibility for how its content is applied or used, in any way.

INDICATIONS: NERLYNX® (neratinib) tablets, for oral use, is a kinase inhibitor indicated:

- As a single agent, for the extended adjuvant treatment of adult patients with early-stage HER2-positive breast cancer, to follow adjuvant trastuzumab-based therapy.
- In combination with capecitabine, for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 based regimens in the metastatic setting.

Select IMPORTANT SAFETY INFORMATION

Diarrhea: Manage diarrhea through either NERLYNX dose escalation or loperamide prophylaxis. If diarrhea occurs despite recommended prophylaxis, treat with additional antidiarrheals, fluids, and electrolytes as clinically indicated.

Hepatotoxicity: Monitor liver function tests monthly for the first 3 months of treatment, then every 3 months while on treatment and as clinically indicated.

Embryo-Fetal Toxicity: NERLYNX can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception.

Please see additional IMPORTANT SAFETY INFORMATION throughout this piece and Full Prescribing Information.

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EXTENDED ADJUVANT

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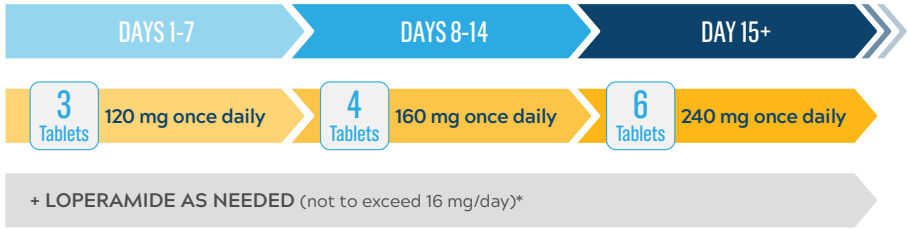
DOSE ESCALATION OVERVIEW

START NERLYNX AT A LOWER DOSE AND TITRATE UP TO THE FULL RECOMMENDED DOSE TO HELP MANAGE DIARRHEA[1,3]

!

It is important to titrate up to the full dose of **NERLYNX** when using dose escalation[1,3]

NERLYNX dose escalation[1]



- For patients in the dose-escalation arm (DE1) of CONTROL (n=60)[1,3,†]:
  - Median time to first onset of grade ≥3 diarrhea was 45 days (range: 15-132 days)
  - Median cumulative duration of grade ≥3 diarrhea was 2.5 days (range: 1-6 days)
  - Grade 3 diarrhea occurred in 13% of patients in the dose-escalation arm

* If diarrhea occurs, treat with antidiarrheal medications, fluids, and electrolytes as clinically indicated. NERLYNX dose interruptions and dose reductions may also be required to manage diarrhea.[1]

† Dose-escalation arm (DE1): NERLYNX 120 mg/day on days 1-7, 160 mg/day on days 8-14, 240 mg/day from days 15-364.[3]

Select IMPORTANT SAFETY INFORMATION

Diarrhea: Manage diarrhea through either NERLYNX dose escalation or loperamide prophylaxis. If diarrhea occurs despite recommended prophylaxis, treat with additional antidiarrheals, fluids, and electrolytes as clinically indicated. Withhold NERLYNX in patients experiencing severe and/or persistent diarrhea. Permanently discontinue NERLYNX in patients experiencing Grade 4 diarrhea or Grade ≥2 diarrhea that occurs after maximal dose reduction.

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DOSING OVERVIEW

NERLYNX IS AN ORAL ONCE-DAILY THERAPY[1]

When not using dose escalation, initiate loperamide prophylaxis with the first dose of NERLYNX[1]:

- 4 mg TID days 1-14
- 4 mg BID days 15-56
- 4 mg PRN day 57 onward*

*Loperamide 4 mg as needed not to exceed 16 mg per day; titrate dosing to achieve 1-2 bowel movements per day.
† A 2-week dose escalation for NERLYNX may be initiated. See page 3 for details.
BID: twice daily; PRN: as needed; TID: three times daily.

The recommended daily dose of NERLYNX is six 40-mg tablets (240 mg total), taken continuously for 1 year[1,†,‡]

TAKE 6 TABLETS	ONCE A DAY	CONTINUOUSLY FOR UP TO 1 YEAR	MANAGEMENT OF DIARRHEA
			
40-mg TABLETS	WITH FOOD	OR UNTIL DISEASE RECURRENCE	LOPERAMIDE

‡ Taken continuously for 1 year or until disease recurrence, whichever is shorter.

PATIENT COUNSELING INFORMATION[1]


Take NERLYNX at approximately the same time every day with food


Do not chew, crush, or split tablets


If a dose is missed, resume NERLYNX at the regular scheduled time the next day


Avoid grapefruit in any form

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DOSE ESCALATION

DOSE ESCALATION WAS INVESTIGATED IN THE CONTROL STUDY[1]

CONTROL[3]
A phase 2, open-label, multicohort, multinational study to evaluate the effect of dose escalation or antidiarrheal prophylaxis on diarrhea associated with NERLYNX. NERLYNX dose-escalation arm (DE1): n=60; 120 mg/day on days 1-7, 160 mg/day on days 8-14, 240 mg/day from days 15-364.*

ExteNET[1,4]
A pivotal phase 3, global, multicenter, randomized, double-blind, placebo-controlled study. NERLYNX arm in ExteNET: n=1408; 240 mg/day for up to 1 year. Antidiarrheals were not protocol mandated.

A DESCRIPTIVE COMPARISON OF THE DOSE-ESCALATION ARM IN CONTROL (n=60)* VS NERLYNX ARM IN ExteNET (n=1408)[1]

>65% **lower rate of grade 3 diarrhea**[1]
Rate of grade 3 diarrhea:
13% with NERLYNX dose escalation in CONTROL*
vs **40%** with NERLYNX in ExteNET.

50% **fewer median days of grade ≥3 diarrhea**[1]
Median cumulative days of grade ≥3 diarrhea:
2.5 days with NERLYNX dose escalation in CONTROL*
vs **5 days** with NERLYNX in ExteNET.

>80% **lower rate of discontinuations due to diarrhea**[1]
Treatment discontinuations due to diarrhea:
3.3% with NERLYNX dose escalation in CONTROL*
vs **17%** with NERLYNX in ExteNET.

- Loperamide-prophylaxis arm of CONTROL: 32% grade 3 diarrhea (n=109),[1] 3-day median cumulative duration of grade ≥3 diarrhea (n=137),[3] and 18% rate of discontinuation due to diarrhea (n=109)[1]

* Data from NERLYNX dose-escalation arm DE1 in CONTROL. There was an additional NERLYNX dose-escalation arm, DE2, studied in CONTROL. Data from DE2 are not included in the USPI.[1,3]

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DOSE ESCALATION

MORE PATIENTS START NERLYNX TREATMENT WITH DOSE ESCALATION[5]

In patients with HER2+ eBC

~65%

of patients started NERLYNX treatment with dose escalation[5,*,†]

* Data captured from specialty pharmacy claims between 1/1/22 to 9/30/22.[5]

† Data calculation does not include Specialty Distributor Network (eg, clinic in-house pharmacies, hospital pharmacies). It includes on-label patients. Metastatic patients were excluded.[5]

eBC: early-stage breast cancer; HER2+: human epidermal growth factor receptor 2–positive.

NERLYNX is available in a 133-tablet bottle for patients starting treatment with dose escalation[1]

NERLYNX IS AVAILABLE IN 2 QUANTITIES:

133-COUNT BOTTLE:
NDC 70437-240-33

180-COUNT BOTTLE:
NDC 70437-240-18

This guide is not a substitute for the Full Prescribing Information. Please see additional IMPORTANT SAFETY INFORMATION throughout this piece and Full Prescribing Information.

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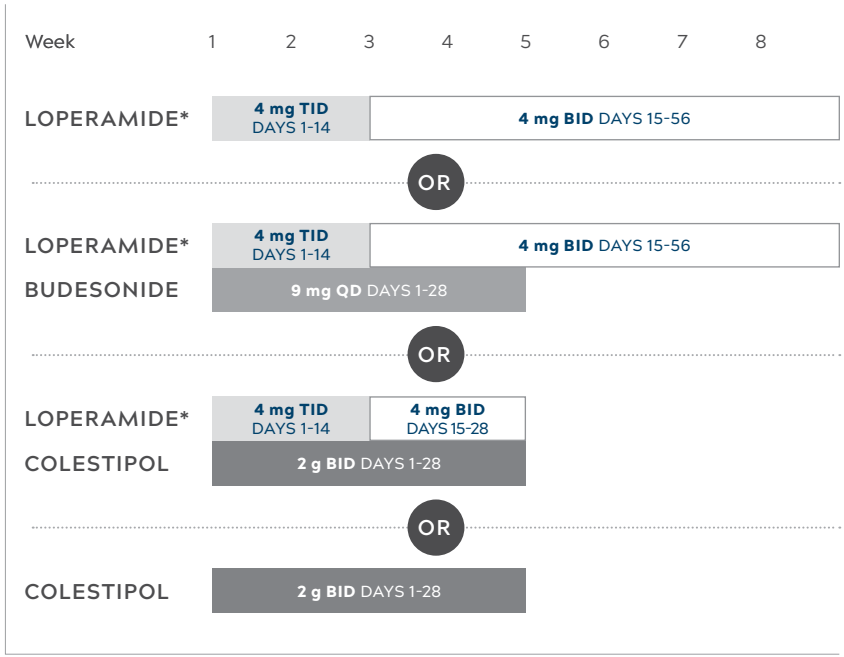
ANTIDIARRHEAL PROPHYLAXIS REGIMENS

PROPHYLAXIS REGIMENS STUDIED IN CONTROL[3]

Proactive diarrhea management with dose escalation and/or antidiarrheal prophylaxis has been shown to lower the incidence of grade 3 diarrhea and NERLYNX discontinuations due to diarrhea[3]

NERLYNX 240 mg QD FOR 1 YEAR + LOPERAMIDE PRN (UP TO 16 mg/DAY)



* Loperamide 4 mg initial dose.

BID: twice daily; PRN: as needed; QD: once daily; TID: three times daily.

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ANTIDIARRHEAL PROPHYLAXIS

If diarrhea occurs despite prophylaxis, treat with additional antidiarrheals, fluids, and electrolytes as clinically indicated[1]

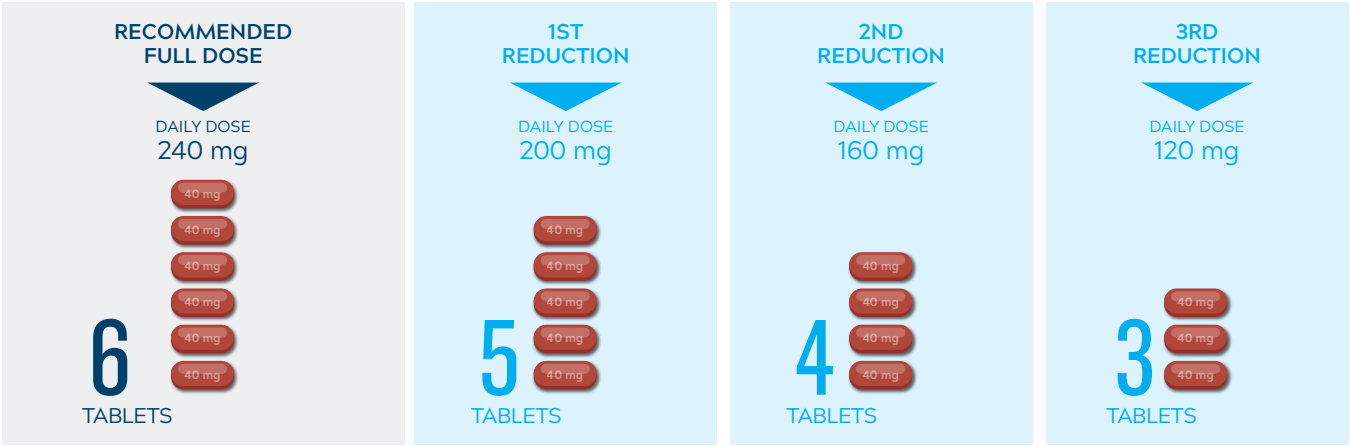
A voucher program for up to 3 months' free supply of antidiarrheals is available to all patients

- Proactive diarrhea management should be initiated with the first dose of NERLYNX[1]
- Medications that help manage diarrhea have different mechanisms of action; if one doesn't work, another might
- Dietary changes or NERLYNX dose modifications may also help manage diarrhea[1]

MEDICATION	MECHANISM
BUDESONIDE[6] *Anti-inflammatory*	• Budesonide is a high-potency glucocorticoid (corticosteroid) that reduces inflammation
COLESTIPOL[7] *Bile acid sequestrant*	• Colestipol hydrochloride binds bile acids in the intestine, forming a complex that is excreted in the feces • Constipation is the most common adverse reaction of colestipol treatment • **Patients should take colestipol ≥4 hours before or ≥1 hour after NERLYNX**
LOPERAMIDE[8] *Antidiarrheal*	• Loperamide reduces propulsive peristalsis, incontinence and urgency, and daily fecal volume • Loperamide increases intestinal transit time, fecal viscosity, and bulk density • Loperamide diminishes the loss of fluid and electrolytes

DOSE MODIFICATIONS

NERLYNX dose adjustments for adverse events when used as a single agent[1]



- NERLYNX dose modifications are recommended based on individual safety and tolerability; adjust the dose as clinically indicated[1]
- Some adverse reactions may require dose interruption, reduction, or discontinuation[1]
- Discontinue NERLYNX for patients who fail to recover to grade ≤1 or baseline from treatment-related toxicity, for toxicities that result in a treatment delay >3 weeks, for patients who are unable to tolerate 120 mg daily, or for any grade 4 toxicities[1]

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DOSE MODIFICATIONS: MANAGEMENT OF DIARRHEA

Management of diarrhea may require antidiarrheals, dietary changes, supportive care, and appropriate dose modifications[1]

SEVERITY OF DIARRHEA*

- Grade 1
- Grade 2 lasting ≤5 days
- Grade 3 lasting ≤2 days

→ Adjust antidiarrheal treatment†

- Any grade with complicated features‡
- Grade 2 lasting >5 days§
- Grade 3 lasting >2 days§

→ Interrupt NERLYNX†

- Diarrhea resolves to grade ≤1 in ≤1 week → Resume NERLYNX at the same dose
- Diarrhea resolves to grade ≤1 in >1 week → Resume NERLYNX at a reduced dose

- Grade 4
- Grade ≥2 recurring at 120 mg daily

→ Permanently discontinue NERLYNX treatment

Once resolved to grade ≤1 or baseline, start loperamide 4 mg with each subsequent NERLYNX administration

* Based on CTCAE.
† Institute the following: diet modifications, maintain ~2 L fluid intake per day.
‡ Complicated features include dehydration, fever, hypotension, renal failure, or grade 3 or 4 neutropenia.
§ Despite being treated with optimal medical therapy.
CTCAE: Common Terminology Criteria for Adverse Events.

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METASTATIC

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DOSE ESCALATION OVERVIEW

DOSE ESCALATION IS APPROVED TO HELP MANAGE DIARRHEA AND IMPROVE PATIENT TOLERANCE OF NERLYNX[1]

NERLYNX is available in a 133-tablet bottle for patients starting treatment with dose escalation[1]

Cycle 1—NERLYNX dose escalation[1]

DAYS 1-7	DAYS 8-14	DAYS 15-21
3 Tablets: 120 mg once daily	4 Tablets: 160 mg once daily	6 Tablets: 240 mg once daily

CAPECITABINE 750 mg/m² twice daily (DAYS 1-14)*

+ LOPERAMIDE AS NEEDED (not to exceed 16 mg/day)†

Cycle 2 and beyond—full recommended NERLYNX dose[1]

DAYS 1-7	DAYS 8-14	DAYS 15-21
6 Tablets: 240 mg once daily		

CAPECITABINE 750 mg/m² twice daily (DAYS 1-14)*

+ LOPERAMIDE AS NEEDED (not to exceed 16 mg/day)†

*** Refer to the capecitabine Prescribing Information when NERLYNX is used in combination with capecitabine.**

† If diarrhea occurs, treat with antidiarrheal medications, fluids, and electrolytes as clinically indicated.

Select IMPORTANT SAFETY INFORMATION

Diarrhea: Manage diarrhea through either NERLYNX dose escalation or loperamide prophylaxis. If diarrhea occurs despite recommended prophylaxis, treat with additional antidiarrheals, fluids, and electrolytes as clinically indicated. Withhold NERLYNX in patients experiencing severe and/or persistent diarrhea. Permanently discontinue NERLYNX in patients experiencing Grade 4 diarrhea or Grade ≥2 diarrhea that occurs after maximal dose reduction.

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DOSING OVERVIEW

NERLYNX + CAPECITABINE IS ADMINISTERED ON A 21-DAY DOSING CYCLE[1]

When not using dose escalation, initiate loperamide prophylaxis with the first dose of NERLYNX[1]:

- 4 mg TID days 1-14
- 4 mg BID days 15-56
- 4 mg PRN day 57 onward*

*Loperamide 4 mg as needed not to exceed 16 mg per day; titrate dosing to achieve 1–2 bowel movements per day.

† A 2-week dose escalation for NERLYNX may be initiated. See page 12 for details.

BID: twice daily; PRN: as needed; TID: three times daily.

The recommended daily dose of NERLYNX is six 40-mg tablets (240 mg total), plus capecitabine twice daily on days 1-14 of a 21-day cycle, until disease progression or unacceptable toxicities[1,†]

TAKE 6 TABLETS	ONCE A DAY	UNTIL DISEASE PROGRESSION		MANAGEMENT OF DIARRHEA
			+	
40-mg TABLETS	WITH FOOD	OR UNACCEPTABLE TOXICITIES		LOPERAMIDE

- Instruct patients to take capecitabine with water within 30 minutes after a meal on days 1 to 14 of each 21-day cycle[5]

PATIENT COUNSELING INFORMATION[1]

Take NERLYNX at approximately the same time every day with food

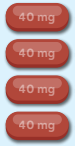
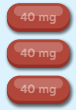
Do not chew, crush, or split tablets

If a dose is missed, resume NERLYNX at the regular scheduled time the next day

Avoid grapefruit in any form

DOSE MODIFICATIONS

NERLYNX dose adjustments for adverse events when used in combination with capecitabine[1]

RECOMMENDED FULL DOSE	1ST REDUCTION	2ND REDUCTION
DAILY DOSE 240 mg	DAILY DOSE 160 mg	DAILY DOSE 120 mg
 6 TABLETS	 4 TABLETS	 3 TABLETS

- NERLYNX dose modifications are recommended based on individual safety and tolerability; adjust the dose as clinically indicated[1]
- Some adverse reactions may require dose interruption, reduction, or discontinuation[1]
  - Refer to the capecitabine Prescribing Information when NERLYNX is used in combination with capecitabine
- Discontinue NERLYNX for patients who fail to recover to grade ≤1 or baseline from treatment-related toxicity, for toxicities that result in a treatment delay >3 weeks, for patients who are unable to tolerate 120 mg daily, or for any grade 4 toxicities[1]

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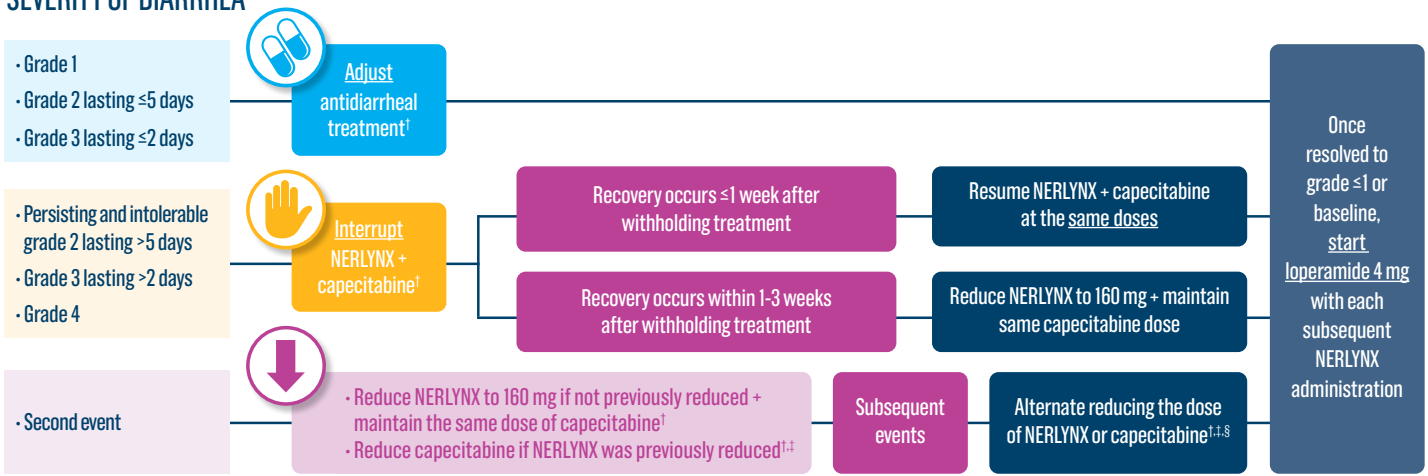
DOSE MODIFICATIONS: MANAGEMENT OF DIARRHEA

Management of diarrhea may require antidiarrheals, dietary changes, supportive care, and appropriate dose modifications[1]

SEVERITY OF DIARRHEA*



* Based on CTCAE.
† Institute the following: diet modifications, maintain ~2 L fluid intake per day.
‡ Refer to the capecitabine Prescribing Information when NERLYNX is used in combination with capecitabine.
§ Reduce capecitabine if NERLYNX was previously reduced or reduce NERLYNX if capecitabine was previously reduced.
CTCAE: Common Terminology Criteria for Adverse Events.

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GENERAL INFORMATION

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DIET MODIFICATIONS

WAYS TO HELP PATIENTS TAKE CONTROL

Proactively discuss dietary adjustments that may help minimize diarrhea

Instruct patients to take NERLYNX with food and consider dietary modifications, including but not limited to[1,9,10]:

- Stopping all lactose-containing products
- Drinking 8-10 large glasses (approximately 2 liters) of clear liquids per day
- Eating smaller, more frequent meals

WHAT TO EAT		WHAT TO AVOID	
Foods that are low in fiber Visit familydoctor.org and search BRAT diet to learn more.	eg, bananas, white rice, applesauce, white bread	Other dairy products	eg, milk, cheese, ice cream
Foods that are high in protein	eg, beef, skinless chicken, turkey, eggs	Alcohol, caffeinated drinks, and sugary sodas	eg, beer, wine, coffee, soda
Foods that are high in potassium	eg, bananas, skinless potatoes, avocados, asparagus tips	Greasy, fatty, and spicy foods	eg, fried chicken, pizza, peppers
Yogurt Yogurt contains "good" bacteria known as probiotics, which can shorten the duration of diarrhea.	yogurt	Foods that are high in fiber	eg, popcorn, pickles, whole-grain bread, brown rice
		Foods that cause intestinal gas	eg, broccoli, cabbage, beans, cauliflower
		Grapefruit and grapefruit products	grapefruit
		Foods that contain sorbitol Foods with artificial sweeteners and certain fruits.	eg, sugar-free candies and cookies, stone and dried fruits

Perform stool cultures as clinically indicated to exclude infectious causes of grade 3 or 4 diarrhea or diarrhea of any grade with complicated features[1,*]

CTCAE v5.0 grading for diarrhea[11]

GRADE 1	**Increase of <4 stools per day over baseline;** mild increase in ostomy output compared to baseline
GRADE 2	**Increase of 4-6 stools per day over baseline;** moderate increase in ostomy output compared to baseline; limiting instrumental ADL
GRADE 3	**Increase of ≥7 stools per day over baseline;** hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self-care ADL
GRADE 4	**Life-threatening consequences;** urgent intervention indicated

ADL: activities of daily living; CTCAE: Common Terminology Criteria for Adverse Events.

HYPOTHETICAL PATIENT CASE (EXTENDED ADJUVANT)[1]

*Complicated features include dehydration, fever, or neutropenia.
†Institute the following: diet modifications, maintain ~2 L fluid intake per day.
‡Once diarrhea resolves to grade ≤1 or baseline, start loperamide 4 mg with each subsequent NERLYNX administration (not to exceed 16 mg/day).

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DOSE MODIFICATIONS: ADVERSE EVENTS[1]

HEPATIC IMPAIRMENT

- **Reduce the NERLYNX starting dose to 80 mg** in patients with severe hepatic impairment (Child-Pugh C)
- **No dose modifications are recommended** for patients with mild to moderate hepatic impairment (Child-Pugh A or B)

HEPATOTOXICITY

- **Perform liver function tests** in patients who experience grade ≥3 diarrhea or any signs or symptoms of hepatotoxicity, such as worsening of fatigue, nausea, vomiting, right upper quadrant tenderness, fever, rash, or eosinophilia
- Total bilirubin, AST, ALT, and alkaline phosphatase should be measured prior to starting treatment with NERLYNX, monthly for the first 3 months of treatment, then every 3 months while on treatment and as clinically indicated

HEPATOTOXICITY SEVERITY*	RECOMMENDED ACTION
Grade 3 ALT or AST (>5–20×ULN) OR Grade 3 bilirubin (>3–10×ULN)	• **Hold NERLYNX** until recovery to grade ≤1 • Evaluate alternative causes • **Resume NERLYNX at the next lower dose level if recovery to grade ≤1 occurs within 3 weeks.** If grade 3 ALT, AST, or bilirubin occurs again despite one dose reduction, permanently discontinue NERLYNX
Grade 4 ALT or AST (>20×ULN) OR Grade 4 bilirubin (>10×ULN)	• **Discontinue NERLYNX permanently** • Evaluate alternative causes

OTHER TOXICITIES†

TOXICITY SEVERITY*	RECOMMENDED ACTION
GRADE 3	**Hold NERLYNX** until recovery to grade ≤1 or baseline within 3 weeks of stopping treatment, then resume NERLYNX at the next lower dose level
GRADE 4	**Discontinue NERLYNX permanently**

* Based on CTCAE.
† Also refer to diarrhea dose modifications in this guide.

ALT: alanine aminotransferase; AST: aspartate aminotransferase; CTCAE: Common Terminology Criteria for Adverse Events; ULN: upper limit of normal.

EFFECTS OF OTHER DRUGS ON NERLYNX[1]

GASTRIC ACID–REDUCING AGENTS		• **Avoid concomitant administration of NERLYNX with proton pump inhibitors, eg, esomeprazole, lansoprazole, omeprazole, pantoprazole.** When patients require gastric acid–reducing agents, use an H_2-receptor antagonist or antacid • NERLYNX should be taken at least 2 hours before or 10 hours after H_2-receptor antagonists, eg, cimetidine, famotidine • NERLYNX should be taken at least 3 hours after antacids
STRONG CYP3A4 INHIBITORS	Clinical Impact	• Concomitant use of NERLYNX with strong CYP3A4 inhibitors may increase NERLYNX concentrations • Increased NERLYNX concentrations may increase the risk of toxicity
	Prevention	• **Avoid concomitant use**
	Examples	• Clarithromycin, itraconazole, ketoconazole, ritonavir
P-GP AND MODERATE CYP3A4 DUAL INHIBITORS	Clinical Impact	• Concomitant use of NERLYNX with P-gp and moderate CYP3A4 dual inhibitors may increase NERLYNX concentrations • Increased NERLYNX concentrations may increase the risk of toxicity
	Prevention	• **Avoid concomitant use**
	Examples	• Diltiazem, dronedarone, erythromycin, verapamil
STRONG OR MODERATE CYP3A4 INDUCERS	Clinical Impact	• Concomitant use of NERLYNX with strong or moderate CYP3A4 inducers may decrease NERLYNX concentrations • Decreased NERLYNX concentrations may reduce NERLYNX activity
	Prevention	• **Avoid concomitant use**
	Examples	• Carbamazepine, phenobarbital, phenytoin, rifampin, St John's wort

P-gp: P-glycoprotein.

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EFFECT OF NERLYNX ON OTHER DRUGS[1]

CERTAIN P-GP SUBSTRATES	• Concomitant use of NERLYNX with digoxin, a P-gp substrate, increased digoxin concentrations • Increased concentrations of a P-gp substrate may increase the risk of adverse reactions • Monitor for adverse reactions of certain P-gp substrates for which minimal concentration change may lead to serious adverse reactions when used concomitantly with NERLYNX

TOXICITY WARNINGS[1]

HEPATOTOXICITY	• NERLYNX has been associated with hepatotoxicity characterized by increased liver enzymes • Monitor liver function tests monthly for the first 3 months of treatment, then every 3 months while on treatment and as clinically indicated
EMBRYO-FETAL TOXICITY	• NERLYNX can cause fetal harm when administered to a pregnant woman; advise pregnant women of the potential risk to a fetus • Advise females of reproductive potential to use effective contraception during treatment and for at least 1 month after the last dose

DIARRHEA ASSESSMENT QUESTIONS

If your patients report having diarrhea after starting treatment with NERLYNX, consider asking:

- What changes they have experienced in stool consistency, frequency, or volume compared to baseline
- Whether they have avoided foods that might aggravate diarrhea
- Whether they may be taking any medications or supplements that might have a laxative or stool-softening effect
- Whether the consistency of the diarrhea is related to or caused by inflammatory etiologies, secretory etiologies, or bile-acid malabsorption

P-gp: P-glycoprotein.

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PATIENT SUPPORT

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ACCESS & COVERAGE

PumaPatientLynx™
SUPPORTIVE CARE VOUCHER PROGRAM*

- Up to 3 months' free supply of antidiarrheal products
- Available to all patients
- Used at the dispensing pharmacy, with prescription(s) at a local retail pharmacy or through the Puma Specialty Pharmacy Network
- Access via:
  - Patient starter kits provided by specialty pharmacy when the first prescription is dispensed
  - Hard copy provided by your Puma Clinical Specialist
  - Telephone at 1-855-816-5421, Monday to Friday, 9 AM to 8 PM ET

PumaPatientLynx™

BENEFITS VERIFICATION & PRIOR AUTHORIZATION ASSISTANCE

This program provides comprehensive support, including benefits investigation to verify insurance coverage and assistance with prior authorization.

NERLYNX QUICK START

Provides a free 3-week supply of NERLYNX to eligible patients experiencing delays in gaining access to therapy.

CO-PAY ASSISTANCE

Eligible patients treated with NERLYNX may pay as little as $10 per prescription. Patients will be enrolled through their specialty pharmacy or through the Access and Support page on nerlynx.com.

FINANCIAL SUPPORT INFORMATION

For patients with financial needs, we will work to find appropriate sources for support.

* Puma Patient Lynx programs are subject to change or to be discontinued without notice. Limitations apply and certain programs are subject to eligibility criteria. For full terms and conditions, visit nerlynxHCP.com or call 1-855-816-5421.

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ONGOING TREATMENT

For more information on the Puma Patient Lynx Support Program:

nerlynxHCP.com/access-and-support

1-855-816-5421
Monday to Friday, 9 AM to 8 PM ET

PumaPatientLynx™

NERLYNX MENTOR PROGRAM

Patient mentors provide confidential support for patients who are considering or currently taking NERLYNX.*
Bilingual mentors are available.

NURSE CALL CENTER

Our staff of registered nurses by training are available to speak with patients and healthcare providers to answer questions about NERLYNX.†
The call center is open Monday to Friday, 9 AM to 8 PM ET, for your convenience.
Call 1-855-816-5421 (when prompted, press 2).
Bilingual nurses are available.

PRODUCT SUPPORT

Our specialty pharmacy network will provide patients with product education and side effect counseling to help them better understand and manage their NERLYNX therapy.

TEXT MESSAGE SUPPORT

Patients can sign up to receive medication reminders and motivational messages to support treatment adherence.

* Mentors are compensated for their time.
† This is an informational service. Call center nurses do not offer medical advice.

nerlynx® (neratinib) tablets

NERLYNX—THE FIRST AND ONLY HER2-DIRECTED SMALL MOLECULE APPROVED IN BOTH EARLY-STAGE AND METASTATIC HER2+ BREAST CANCER[1]

Visit nerlynxHCP.com to learn more

INDICATIONS: NERLYNX® (neratinib) tablets, for oral use,

is a kinase inhibitor indicated:

- As a single agent, for the extended adjuvant treatment of adult patients with early-stage HER2-positive breast cancer, to follow adjuvant trastuzumab-based therapy.
- In combination with capecitabine, for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 based regimens in the metastatic setting.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS: None

WARNINGS AND PRECAUTIONS:

- **Diarrhea:** Manage diarrhea through either NERLYNX dose escalation or loperamide prophylaxis. If diarrhea occurs despite recommended prophylaxis, treat with additional antidiarrheals, fluids, and electrolytes as clinically indicated. Withhold NERLYNX in patients experiencing severe and/or persistent diarrhea. Permanently discontinue NERLYNX in patients experiencing Grade 4 diarrhea or Grade ≥2 diarrhea that occurs after maximal dose reduction.
- **Hepatotoxicity:** Monitor liver function tests monthly for the first 3 months of treatment, then every 3 months while on treatment and as clinically indicated. Withhold NERLYNX in patients experiencing Grade 3 liver abnormalities and permanently discontinue NERLYNX in patients experiencing Grade 4 liver abnormalities.
- **Embryo-Fetal Toxicity:** NERLYNX can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception.

ADVERSE REACTIONS: The most common adverse reactions (reported in ≥5% of patients) were:

- NERLYNX as a single agent: diarrhea, nausea, abdominal pain, fatigue, vomiting, rash, stomatitis, decreased appetite, muscle spasms, dyspepsia, AST or ALT increased, nail disorder, dry skin, abdominal distention, epistaxis, weight decreased, and urinary tract infection.
- NERLYNX in combination with capecitabine: diarrhea, nausea, vomiting, decreased appetite, constipation, fatigue/asthenia, weight decreased, dizziness, back pain, arthralgia, urinary tract infection, upper respiratory tract infection, abdominal distention, renal impairment, and muscle spasms.

To report SUSPECTED ADVERSE REACTIONS, contact Puma Biotechnology, Inc. at 1-844-NERLYNX (1-844-637-5969) or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

DRUG INTERACTIONS:

- Gastric acid reducing agents: Avoid concomitant use with proton pump inhibitors. Separate NERLYNX by at least 2 hours before or 10 hours after H_2-receptor antagonists. Or separate NERLYNX by at least 3 hours after antacids.
- Strong CYP3A4 inhibitors: Avoid concomitant use.
- P-gp and moderate CYP3A4 dual inhibitors: Avoid concomitant use.
- Strong or moderate CYP3A4 inducers: Avoid concomitant use.
- Certain P-gp substrates: Monitor for adverse reactions of P-gp substrates for which minimal concentration change may lead to serious adverse reactions when used concomitantly with NERLYNX.

USE IN SPECIFIC POPULATIONS:

- **Lactation:** Advise women not to breastfeed.

Please see Full Prescribing Information.

HER2+: human epidermal growth factor receptor 2–positive; NCCN: National Comprehensive Cancer Network® (NCCN®).

References: 1. NERLYNX [package insert]. Los Angeles, CA: Puma Biotechnology, Inc. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V4.2023. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed April 6, 2023. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **3.** Chan A, Ruiz-Borrego M, Marx G, et al. Final findings from the CONTROL trial: strategies to reduce the incidence and severity of neratinib-associated diarrhea in patients with HER2-positive early-stage breast cancer. *Breast*. 2023;67:94-101. doi:10.1016/j.breast.2022.12.003 **4.** Chan A, Moy B, Mansi J, et al. Final efficacy results of neratinib in HER2-positive hormone receptor-positive early-stage breast cancer from the phase III ExteNET trial. *Clin Breast Cancer*. 2021;21(1):80-91.e7. doi:10.1016/j.clbc.2020.09.014 **5.** Puma Biotechnology, Inc. Data on file. **6.** ENTOCORT [package insert]. Elan Pharma International Limited. **7.** COLESTID [package insert]. New York City, NY: Pfizer Inc. **8.** IMODIUM [package insert]. Johnson & Johnson Consumer Inc. **9.** Ustaris F, Saura C, Di Palma J, et al. Effective management and prevention of neratinib-induced diarrhea. *Am J Hematol Oncol*. 2015;11(11):13-22. **10.** Stanford Cancer Nutrition Services. Diarrhea Nutrition Tips. Accessed June 11, 2021. https://stanfordhealthcare.org/medical-clinics/cancer-nutrition-services/managing-side-effects/diarrhea.html **11.** US Department of Health and Human Services. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. November 27, 2017. Accessed June 9, 2021. https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf

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