This material was developed by Knight Therapeutics as part of the Risk Management Plan for NERLYNX®.
It is not intended for promotional use.

NERLYNX® Appropriate Use

NERLYNX® (neratinib) is indicated:[1]

- **For the extended adjuvant treatment of women with early-stage hormone receptor positive, HER2-overexpressed/amplified breast cancer within one year after completion of trastuzumab-based adjuvant therapy.**
- **In combination with capecitabine for the treatment of patients with metastatic HER2-overexpressed/amplified breast cancer, who have received two or more prior anti-HER2-based regimens in the metastatic setting.**

Dear Healthcare Professional,

Please take careful note of this important safety information regarding NERLYNX® (neratinib). This information is being provided to assist you in the appropriate use of NERLYNX® and to facilitate the discussion with your patient pertaining to the specific important risks listed below:

- Diarrhea
- Stomatitis
- Hepatotoxicity
- Skin toxicity: rash* and nail disorders**

The accompanying **NERLYNX® PRESCRIBER CHECKLIST** includes detailed information and actions on managing these risks in clinical practice.

You should discuss the risks associated with NERLYNX® therapy with patients or their caregivers. Additionally, please provide the patient or caregiver with the **NERLYNX® PATIENT CHECKLIST.**

REPORTING ADVERSE EVENTS: Please report to Knight Therapeutics any medication errors and/or adverse events suspected to be associated with the use of NERLYNX® by telephone at 1-844-483-5636 or by email at medinfo@knighttx.com.

Refer to the NERLYNX® Product Monograph for complete prescribing information.

The Product Monograph is available online at www.gud-knight.com, by telephone at 1-844-483-5636, or by email at medinfo@knighttx.com.

* Includes rash, rash erythematous, rash follicular, rash generalised, rash maculo-papular, rash pruritic, rash pustular.
** Includes nail bed inflammation, nail bed tenderness, nail discolouration, nail disorder, nail pitting, onychalgia, onychoclasis, paronychia.

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NERLYNX® Prescriber Checklist

Please take careful note of this important safety information regarding NERLYNX® (neratinib). This information is being provided to assist you in the appropriate use of NERLYNX® and to facilitate the discussion with your patient pertaining to the specific important risks listed below.

Diarrhea

In the clinical trial, 95% of patients receiving NERLYNX® reported diarrhea (40% Grade 3, 0.1% Grade 4). Severe diarrhea and sequelae, such as dehydration, hypotension and renal failure have been reported.[1]

- ☐ **Either a NERLYNX® dose escalation or antidiarrheal prophylaxis with loperamide is recommended,** as per the Product Monograph.
- ☐ **Manage diarrhea proactively** with adequate oral hydration, avoiding aggravating foods, and treating with additional antidiarrheal therapy.[1]
- ☐ **Dose modifications are recommended for patients with diarrhea,** as per the Product Monograph.[1]
- ☐ Advise patients of the risk of diarrhea, and instruct them to watch for signs and symptoms accordingly.

Stomatitis

In the clinical trial, 14% of patients receiving NERLYNX® reported stomatitis (0.6% Grade 3+).[1]

- ☐ **Recommend dental examination prior to and during NERLYNX® therapy.** Regular dental prophylaxis and treatment should also be considered if indicated.[2]
- ☐ Educate patients on oral hygiene, including regular brushing, flossing and mouth rinsing.[2]
- ☐ Advise patients of the risk of stomatitis, and instruct them to avoid irritants such as tobacco, alcohol, spicy, acidic or very hot food.[2]

Hepatotoxicity

NERLYNX® has been associated with hepatotoxicity, characterized by increased liver enzymes. In the clinical trial, 12% of patients receiving NERLYNX® reported hepatotoxicity (1.7% Grade 3+).[1]

- ☐ **Conduct liver function tests prior to and during NERLYNX® therapy.** Patients who experience Grade >3 diarrhea, requiring IV fluid treatment, or any signs or symptoms of hepatotoxicity should be evaluated for changes in liver function tests.[1]
- ☐ **Dose modifications or treatment discontinuation are recommended for patients with treatment-emergent hepatotoxicity,** as per the Product Monograph.[1]
- ☐ **Avoid concomitant use of NERLYNX® with strong or moderate CYP3A4 inhibitors.**[1]
- ☐ Advise patients of the risk of hepatotoxicity, and instruct them to watch for signs and symptoms accordingly.

Skin toxicity (rash and nail disorders)

Rash: In the clinical trial, 21.3% of patients reported rash (0.6% Grade 3).[1]

- ☐ Advise patients of the risk of rash and instruct them to watch for signs and symptoms accordingly.
- ☐ Advise patients to maintain a good skin hygiene by applying sunscreen and moisturizer.[3]
- ☐ **Patients with symptomatic skin and subcutaneous tissue disorders should be carefully monitored.**

Nail disorders: In the clinical trial, 8.0% of patients experienced nail disorder events (0.3% Grade 3).[1]

- ☐ Advise patients of the risk of nail disorders.
- ☐ Instruct patients to wear comfortable shoes, avoid aggressive manicuring, wear gloves while cleaning (e.g., household, dishes).[3]

Refer to the NERLYNX® Product Monograph for complete prescribing information.

The Product Monograph is available online at www.gud-knight.com, by telephone at 1-844-483-5636, or by email at medinfo@knighttx.com.

References:

1. NERLYNX® Product Monograph, Knight Therapeutics Inc. July 16, 2021.
2. BC Cancer. Symptom Management Guidelines. http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management Accessed July 5, 2021.
3. National Cancer Institute. Skin and Nail Changes during Cancer Treatment. https://www.cancer.gov/about-cancer/treatment/side-effects/skin-nail-changes.Accessed March 10, 2022.