Drug Monograph

Drug/Drug Class:	**Nerlynx® (neratinib) tablet/ Cancer**
Prepared for:	MO HealthNet
Prepared by:	Conduent

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms & Manufacturer:	Nerlynx® is available in a tablet containing 40 mg neratinib. Distributed by: Puma Biotechnology, Inc., Los Angeles, CA 90024
Summary of Findings:	The safety and efficacy of Nerlynx were investigated in the ExteNet trial, a multicenter, randomized, double-blind, placeb-controlled study of Nerlynx after adjuvant treatment with trastuzumab in women with HER2-positive breast cancer. 94.2% of patients taking Nerlynx 240 mg daily experienced invasive disease free survival compared to 91.9% of patients taking placebo.
Status Recommendation:	☐ Prior Authorization (PA) Required ☒ Open Access ☐ Clinical Edit ☐ PDL
Type of PA Criteria:	☐ Increased Risk of ADE ☐ Preferred Agent ☐ Appropriate Indications ☒ No PA Required

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Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payers are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction [2]

Human epidermal growth factor receptor 2 positive breast cancers tend to grow faster and are more likely to spread and come back compared to HER2-negative breast cancers. HER2 is overexpressed in 15-30% of invasive breast cancers. HER2 gene amplification is associated with shorter disease free and overall survival in breast cancer.

Dosage Form(s) [1]

Nerlynx® is available in a tablet containing 40 mg neratinib.

Manufacturer [1]

Distributed by: Puma Biotechnology, Inc., Los Angeles, CA 90024

Indication(s) [1]

Nerlynx® is indicated for the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer, to follow adjuvant trastuzumab based therapy.

Clinical Efficacy [1] (mechanism of action/pharmacology, comparative efficacy)

Nerlynx® is a kinase inhibitor that irreversibly binds to Epidermal Growth Factor Receptor (EGFR), Human Epidermal Growth Factor Receptor 2 (HER2), and HER4.

Pharmacokinetics:

	Nerlynx®
Protein Binding	>99%
Volume of Distribution	6,443 L
Metabolism	Primarily liver, via CYP3A4
Excretion	Urine, 1.1% Feces, 97.1%
Half-life	7 to 17 hours

ExteNET Trial

STUDY DESIGN	A multicenter, randomized, double-blind, placebo controlled study of Nerlynx after treatment with trastuzumab (N=2,840)

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INCLUSION CRITERIA	Women with early stage HER2 positive breast cancer within 2 years of completing treatment with adjuvant trastuzumab
EXCLUSION CRITERIA	Not specified.
TREATMENT REGIMEN	Patients were randomized to receive either Nerlynx 240 mg or placebo daily. Randomization was stratified by hormone receptor status, nodal status, and whether trastuzumab was given sequentially versus concurrently with chemotherapy.
RESULTS	The major efficacy major as invasive disease free survival (iDFS) defined as the time between the date of randomization to the first occurrence of invasive recurrence, distant recurrence, or death from any cause, with 2 years and 28 days of follow up. 94.2% of patients in the Nerlynx group at iDFS at 24 months compared to 91.9% in the placebo group.
SAFETY	The most common adverse events were diarrhea, nausea, and vomiting.

Contraindications [(1)]

- None

Warnings and Precautions [(1)]

- Severe diarrhea and sequelae, such as dehydration, hypotension, and renal failure, have been reporting during treatment with Nerlynx
- Nerlynx has been associated with hepatotoxicity characterized by increased liver enzymes
- Based on findings from animal studies and its mechanism of action, Nerlynx can cause fetal harm when administered to a pregnant woman.

Adverse Effects [(1)]

Most common, ≥ 5%	**Nerlynx® (n=1408)**	**Placebo (n=1408)**
Diarrhea	95%	35%
Nausea	43%	22%
Abdominal Pain	36%	15%
Vomiting	26%	8%
Stomatitis	14%	6%
Dyspepsia	10%	4%

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Abdominal distension	5%	3%
Fatigue	27%	20%
Alanine aminotransferase increased	9%	3%
Aspartate aminotransferase increased	7%	3%
Urinary tract infection	5%	2%
Weight decreased	5%	0.5%
Decreased appetite	12%	3%
Muscle spasms	11%	3%
Epistaxis	5%	1%
Rash	18%	9%
Dry skin	6%	2%
Nail disorder	8%	2%

Drug Interactions [(1)]

- PPI's – Avoid concomitant use
- H2 receptor antagonist – Avoid concomitant ues
- Antacids – Separate by 3 hours
- Strong and moderate CYP3A4 inhibitors; e.g. clarithromycin, diltiazem, itraconazole, ketoconazole, cimetidine, ciprofloxacin, erythromycin, danoprevir and ritonavir
- Strong and moderate CYP3A4 inducers; e.g. carbamazepine, phenytoin, rifampin. St. John's wort, bosentan efavirenz, etravirin, modafinil.

Dosage and Administration [(1)]

The FDA recommended dose of Nerlynx is 240 mg (6 tablets) given orally once daily with food, continuously for 1 year.

Cost

GENERIC NAME	BRAND NAME	MANUFACTURER	STRENGTH	DOSE	COST/ MONTH
Neratinib	Nerlynx	Puma	40 mg tablets	6 tablets daily	$10,499.40*
Lapatinib	Tykerb	GlaxoSmithKline	250 mg tablets	5 tablets daily	$6,864**

* Wholesale Acquisition Cost

** Maximum Allowable Cost

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Conclusion

Nerlynx® is a kinase inhibitor that irreversibly bind to EGFR, HER2, and HER4. It is indicated for the extended adjuvant treatment of adult patients with early stage HER2 overexpressed/amplified breast cancer, to follow adjuvant trastuzumab based therapy. In clinical studies, a higher percentage of patients taking Nerlynx experienced invasive disease free survival when compared to placebo. The most common adverse events were diarrhea, nausea, and vomiting.

Recommendation

MO HealthNet Division recommends Open Access status for this product.

References

1) Nerlynx. Retrieved 11/22/2017 from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=d1e41dcf-e82a-47c2-a0ad-6c6eef621834&audience=consumer

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