DRUG NAME: Pertuzumab-trastuzumab

SYNONYM(S):

COMMON TRADE NAME(S): PHESGO®

CLASSIFICATION: monoclonal antibody

Special pediatric considerations are noted when applicable, otherwise adult provisions apply.

MECHANISM OF ACTION:

Pertuzumab and trastuzumab are recombinant humanized immunoglobulin (Ig)G1κ monoclonal antibodies, which target the human epidermal growth factor receptor 2 (HER2). Pertuzumab and trastuzumab bind to distinct HER2 epitopes (subdomains II and IV respectively) and have complementary mechanisms for disrupting HER2 signaling. When pertuzumab and trastuzumab are given in combination, their anti-proliferative activity *in vitro* and *in vivo* is augmented. In addition, the Fc portion in each of their IgG1 framework provides for potent activation of antibody dependent cell-mediated cytotoxicity (ADCC), which is exerted preferentially on HER2-overexpressing cancer cells i*n vitro* compared with cancer cells that do not overexpress HER2.[1]

USES:

Primary uses:

*Breast cancer

Other uses:

*Health Canada approved indication

SPECIAL PRECAUTIONS:

Caution:

- subclinical and clinical ***cardiac failure*** associated with pertuzumab-trastuzumab can manifest as decreased LVEF and CHF[1]
- pertuzumab-trastuzumab for SC administration is ***NOT interchangeable*** with pertuzumab or trastuzumab formulations for intravenous administration; formulations differ in concentration and dosing
- in patients receiving ***taxanes***, pertuzumab-trastuzumab should be given prior to the taxane[1]
- in patients receiving ***anthracyclines***, pertuzumab-trastuzumab should be given after all planned cycles of the anthracycline[1]

SIDE EFFECTS:

The table includes adverse events that presented during drug treatment but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they were reported in more than 1% of patients in the product monograph or pivotal trials, and/or determined to be clinically important. When placebo-controlled trials are available, adverse events will generally be included if the incidence is ≥5% higher in the treatment group.

Developed: 1 March 2024
Revised:

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
blood and lymphatic system/ febrile neutropenia	***anemia*** (33%, severe 1%)
	febrile neutropenia (severe 7%)
	leukocytosis (3%)
	leukopenia (7%, severe 2%)
	lymphopenia (1%, severe <1%)
	neutropenia (21%, severe 14%)
	thrombocytopenia (4%)
cardiac	palpitations (2%)
	tachycardia (4%)
ear and labyrinth	vertigo (1%)
eye	blurry vision (1%)
	dry eye (5%, severe <1%)
	increased lacrimation (5%, severe <1%)
gastrointestinal	*emetogenic potential:* low[2]
	constipation (22%)
	diarrhea (58%, severe 7%); see paragraph following **Side Effects** table
	dry mouth (1%, severe <1%)
	dyspepsia (25%, severe <1%)
	gastroesophageal reflux disease (4%)
	hemorrhoids (8%)
	mouth ulceration (6%)
	nausea (59%, severe 2%)
	stomatitis (25%, severe 1%)
	vomiting (19%, severe 1%)
general disorders and administration site conditions	***asthenia, fatigue*** (26-29%, severe <2%)
	chest pain (2%)
	edema (2%)
	influenza like illness (4%)
	injection site reaction (7%)
	malaise (6%)
	mucosal inflammation (15%, severe 1%)
	pain (4%)
	peripheral edema (6%)
	pyrexia (11%)

Developed: 1 March 2024
Revised:

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
infections and infestations	conjunctivitis (2%)
	cystitis (2%)
	oral candidiasis (4%)
	oral herpes (1%)
	upper respiratory tract infection (19%)
	urinary tract infection (5%, severe <1%)
injury, poisoning, and procedural complications	***injection-related reaction*** (4%); see paragraph following **Side Effects** table
	procedural pain (11%)
	wound complication (2%)
investigations	alkaline phosphatase increase (2%)
	ALT increase (12%, severe 2%)
	AST increase (10%, severe 1%)
	ejection fraction decrease (2%)
	GGT increase (3%)
	LDH increase (3%)
	weight loss (9%, severe <1%)
metabolism and nutrition	***appetite decrease*** (15%, severe 1%)
	hyperchloremia (2%)
	hypercholesterolemia (2%)
	hyperglycemia (2%)
	hypertriglyceridemia (2%)
	hypokalemia (6%, severe 2%)
musculoskeletal and connective tissue	***arthralgia (***11%)
	back pain (7%)
	bone pain (7%)
	extremity pain (3%)
	muscle spasms (3%)
	musculoskeletal pain (3%, severe <1%)
	myalgia (19%, severe <1%)
nervous system	dizziness (6%)
	dysesthesia (1%)
	dysgeusia, taste disorder (3-16%)
	headache (14%)
	neurotoxicity (2%)

Developed: 1 March 2024
Revised:

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
	paresthesia (8%, severe 1%)
	peripheral neuropathy (26%, severe 2%)
	somnolence (<1%)
psychiatric	anxiety (3%)
	depression (2%)
	insomnia (13%)
renal and urinary	dysuria (4%)
reproductive system and breast disorders	breast pain (2%)
	irregular menses (2%, severe <1%)
	vulvovaginal dryness (1%)
respiratory, thoracic and mediastinal	cough (13%, severe <1%)
	dyspnea (9%, severe <1%)
	epistaxis (10%)
	nasal dryness (3%)
	oropharyngeal pain (4%)
	rhinorrhea (6%)
skin and subcutaneous tissue	***alopecia*** (77%, severe <1%)
	dermatitis (4%)
	dry skin (13%, severe <1%)
	erythema (4%)
	nail disorder (19%, severe <1%)
	palmar-plantar erythrodysesthesia syndrome (6%, severe 1%)
	paronychia (6%, severe <1%)
	pruritus (2%)
	rash (11%, severe <1%)
	rash, maculopapular (2%)
vascular	flushing, hot flushing (1-5%)
	hematoma (2%)
	hypertension (2%, severe 1%)
	hypotension (1%)

Adapted from standard reference[1] unless specified otherwise.

Pertuzumab-trastuzumab may cause severe ***diarrhea***. Patients 65 years and older have a higher risk of diarrhea compared with younger patients. Antidiarrheal treatment should be instituted at the first onset of severe diarrhea and, if no improvement is seen, pertuzumab-trastuzumab treatment interruption should be considered. Pertuzumab-trastuzumab can be restarted once the diarrhea is under control.[1]

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Revised:

Injection-related reactions have been reported with pertuzumab-trastuzumab and included symptoms such as fever, chills, and headache. Reactions are likely due to the release of cytokines that occurs within 24 hours of the administration of pertuzumab-trastuzumab. If a significant reaction occurs during administration, the rate of injection should be slowed down or paused while appropriate symptom management is administered. Permanent discontinuation should be considered for severe reactions.[1]

INTERACTIONS: no information found

SUPPLY AND STORAGE:

Injection: Hoffmann-La Roche Limited supplies pertuzumab-trastuzumab as ready-to-use, single-use (preservative free) vials. Loading doses are supplied in vials containing 1200 mg pertuzumab and 600 mg trastuzumab in 15 mL total volume per vial. Maintenance doses are supplied in vials containing 600 mg pertuzumab and 600 mg trastuzumab in 10 mL total volume per vial. Vials contain recombinant human hyaluronidase (rHuPH20). Refrigerate. Do not shake. Keep in original package to protect from light.[1]

For basic information on the current brand used at BC Cancer, see Chemotherapy Preparation and Stability Chart in Appendix.

SOLUTION PREPARATION AND COMPATIBILITY:

For basic information on the current brand used at BC Cancer, see Chemotherapy Preparation and Stability Chart in Appendix.

Additional information:

Compatibility: consult detailed reference

PARENTERAL ADMINISTRATION:

BC Cancer administration guideline noted in ***bold***, ***italics***

Subcutaneous[1]	Dose to be administered undivided in a single injection in the ***thigh*** (alternate injection site between right and left thigh) • ***loading dose***: over ***8 min*** • ***maintenance dose***: over ***5 min***
Intramuscular	no information found
Direct intravenous[1]	do not use
Intermittent infusion[1]	do not use
Continuous infusion	no information found
Intraperitoneal	no information found
Intrapleural	no information found
Intrathecal	no information found
Intra-arterial	no information found
Intravesical	no information found

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DOSAGE GUIDELINES:

Refer to protocol by which patient is being treated. Numerous dosing schedules exist and depend on disease, response and concomitant therapy. Guidelines for dosing also include consideration of absolute neutrophil count (ANC). Dosage may be reduced, delayed or discontinued in patients with bone marrow depression due to cytotoxic/radiation therapy or with other toxicities.

***Adults*:**

BC Cancer usual dose noted in ***bold, italics***

	Cycle Length:	
Subcutaneous:	***3 weeks***[1]:	***Loading dose: 1200 mg-600 mg SC for one dose*** on day 1 of first cycle ***Maintenance dose: 600 mg-600 mg SC for one dose on day 1*** of each subsequent cycle No dose reductions are recommended.

For treatment interruption of 6 weeks or longer: repeat loading dose of 1200 mg-600 mg, then resume maintenance dose of 600 mg-600 mg every three weeks thereafter. Refer to protocol by which patient is being treated.[1]

REFERENCES:

1. Hoffmann-La Roche Limited. PHESGO® product monograph. Mississauga, Ontario; January 5, 2022
2. BC Cancer. (SCNAUSEA) Guidelines for Prevention and Treatment of Chemotherapy-induced Nausea and Vomiting in Adults. Vancouver, British Columbia: BC Cancer; December 1 2018

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