DRUG NAME: Quinagolide

SYNONYM(S): CV 205 502[1]

COMMON TRADE NAME(S): NORPROLAC®

CLASSIFICATION: hormonal agent

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

MECHANISM OF ACTION:

Quinagolide is a non-ergot, selective dopamine-2 receptor agonist with long-lasting prolactin lowering activity. Quinagolide may decrease hormone production and the size of prolactin-dependent pituitary adenomas by inhibiting the release of prolactin from the anterior pituitary gland. Quinagolide is cell cycle phase-nonspecific. Quinagolide is not an immunosuppressive agent.[2]

PHARMACOKINETICS:

Oral Absorption	rapid; >95% of the dose	
Distribution	time to peak 30-60 minutes	
	cross blood brain barrier?	no information found
	volume of distribution	100 L
	plasma protein binding	90%
Metabolism	extensive first pass metabolism; sulfate and glucuronide conjugates are the major circulating metabolites	
	active metabolite(s)	N-desethyl analogue
	inactive metabolite(s)	sulfate or glucuronide conjugates and N,N-didesethyl analogue
Excretion	approximately equal via urine and feces; 95% as metabolites	
	urine	50%; sulfate or glucuronide conjugates, N-desethyl and N,N-didesethyl analogues
	feces	40%; unconjugated forms of sulfate or glucuronide conjugates, N-desethyl and N,N-didesethyl analogues
	terminal half life	17 h
	clearance	no information found

Adapted from standard reference[2] unless specified otherwise.

USES:

Primary uses:
*Pituitary tumour

*Health Canada approved indication

Other uses:

SPECIAL PRECAUTIONS:

Caution: use with caution in patients with severe hepatic or renal dysfunction; to date, studies have not been done in this patient population[3]

Carcinogenicity: Quinagolide demonstrates carcinogenic potential in animal studies. Due to species-specific differences in the regulation of the endocrine system and the role of prolactin, the relevance to humans is unknown.[4]

Mutagenicity: Not mutagenic in Ames test and mammalian *in vitro* mutation test. Quinagolide is not clastogenic in mammalian *in vitro* and *in vivo* chromosome tests.[2]

Fertility: Quinagolide may restore fertility in hyperprolactinemic patients. Women wishing to prevent pregnancy should use contraceptive measures.[2]

Pregnancy: Quinagolide is not available in the United States, therefore FDA Pregnancy Category has not been assigned. Animal-reproduction studies have not shown a fetal risk but there are no controlled studies in pregnant women.[2,4]

Breastfeeding: Quinagolide suppresses lactation due to its inhibitory effect on prolactin secretion.[2]

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.[5]

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
blood and lymphatic system/ febrile neutropenia	neutropenia (<1%)
cardiac	palpitation (1%)
eye	eye disorders (2%)
gastrointestinal	*emetogenic potential: low-moderate*[6]
	abdominal discomfort (3%)
	abdominal pain (3%)
	constipation (3%)
	diarrhea (1%)
	dyspepsia (2%)
	nausea (<60%)[7]; occurs early in treatment or with dose increases, tends to subside with continued treatment; see paragraph following **Side Effects** table
	vomiting (<35%)[7]; occurs early in treatment or with dose increases, tends to subside with continued treatment; see paragraph following **Side Effects** table
general disorders and administration site conditions	edema (2%)
	fatigue (20-50%)[7]; occurs early in treatment, tends to subside with continued treatment
	malaise (1%)
investigations	laboratory abnormalities (increased bilirubin, serum transaminases, creatine phosphokinases, potassium, and triglycerides; decreased hematocrit and hemoglobin); usually transient, rarely clinically significant
	weight gain (1%)
metabolism and nutrition	anorexia (2%)

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
musculoskeletal and connective tissue	extremity pain (1%)
nervous system	asthenia (3%)
	dizziness (20-50%)[7]; occurs early in treatment, tends to subside with continued treatment
	headache (20-50%)[7]; occurs early in treatment, tends to subside with continued treatment
	concentration impairment (1%)
	sedation (3%)
	syncope (1%)
	weakness (3%)
psychiatric	acute psychosis (<1%); reversible upon treatment discontinuation
	depression[7]
	insomnia (2%)
	mood lability (1%)
reproductive system and breast disorders	breast pain (1%)
respiratory, thoracic and mediastinal	nasal congestion (2%)
vascular	hypotension (1%); occurs early in treatment; transient[8]
	flushing (1-10%)
	orthostatic hypotension; occurs early in treatment, transient;[1,8] rarely results in syncope[2]

Adapted from standard reference[2] unless specified otherwise.

Nausea and vomiting is usually transient and occurs predominantly during the first few days of treatment or following dose increases. Although these effects tend to subside, in some patients they may prevent further dose increments or necessitate withdrawal.[7] Quinagolide may be taken at bedtime with a snack or a full glass of milk to reduce stomach irritation. Nausea and vomiting may be prevented by taking a peripheral dopaminergic antagonist (i.e., domperidone) for a few days, at least one hour before the ingestion of quinagolide.[2]

INTERACTIONS: No information found.

Quinagolide is a dopamine agonist, therefore, drugs with strong dopamine antagonist properties (i.e., neuroleptic agents, metoclopramide) may reduce the prolactin-lowering effect of quinagolide.[2] Monitor for signs of inadequate response to quinagolide.[2]

SUPPLY AND STORAGE:

Oral: Ferring Inc. supplies quinagolide as 0.025 mg, 0.05 mg, 0.075 mg, and 0.15 mg tablets. A six day starter pack containing three tablets each of 0.025 mg and 0.05 mg tablets is available. For maintenance dosing, 0.075 mg and 0.15 mg tablets are available. Tablets contain lactose. Store at room temperature.[9,10]

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*:**

BCCA usual dose noted in ***bold, italics***

Oral:[2,4,11]	Initial doses are titrated as follows: 0.025 mg PO once daily for 3 consecutive days starting on day one, followed by 0.05 mg PO once daily for 3 consecutive days starting on day four, and then, followed by 0.075 mg PO once daily starting on day seven. Maintenance: ***0.075 mg*** (range 0.075-0.15 mg) ***PO once daily***. If further titration is necessary, titrate upwards to optimal response at intervals not shorter than one week. Increments of 0.025 – 0.075 mg have been used.[12-15] One-third of patients require doses ≥ 0.3 mg daily. If further titration is necessary, titrate with dose increments of 0.075-0.15 mg at intervals not shorter than four weeks. Maximum dose = 0.9 mg/day. Administer with a snack at bedtime.
Concurrent radiation:	no information found
Dosage in myelosuppression:	modify according to protocol by which patient is being treated; if no guidelines available, refer to Appendix 6 "Dosage Modification for Myelosuppression"
Dosage in renal failure:	no information found
Dosage in hepatic failure:	no information found
Dosage in dialysis:	no information found

Children: no information found

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