DRUG NAME: AGS-16C3F

SYNONYM(S):

COMMON TRADE NAME(S):

CLASSIFICATION: miscellaneous

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

MECHANISM OF ACTION:

AGS-16C3F is an antibody-drug conjugate comprised of a fully human monoclonal antibody (AGS-16M7.8) conjugated with a microtubule disrupting agent (monomethyl auristatin F) via a noncleavable maleimidocaproyl linker. Following cell surface binding, the conjugate travels to the cell lysosomes where it is degraded, thereby releasing monomethyl auristatin F (MMAF). MMAF is a potent antitubulin agent which induces cell death by inhibiting the polymerization of tubulin and blocking mitosis. AGS-16C3F is derived from a Chinese hamster ovary (CHO) cell line.[1]

USES:

Primary uses:

Renal cell cancer

*Health Canada approved indication

Other uses:

SPECIAL PRECAUTIONS:

Contraindications:

- history of hypersensitivity reaction to AGS-16C3F or Chinese hamster ovary cell proteins[1]

Caution:

- to prevent ***corneal toxicity***, prophylactic use of prednisolone acetate 1% ophthalmic suspension is recommended for each cycle of treatment, beginning one day prior to AGS-16C3F administration and continuing for two weeks[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. When placebo-controlled trials are available, adverse events will generally be included if the incidence is ≥5% higher in the treatment group.

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
blood and lymphatic system/ febrile neutropenia	***anemia*** (11-18%)
	febrile neutropenia (0%)
	neutropenia (3%)
	thrombocytopenia (3-35%); usual onset day 7 to 8

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
cardiac	right ventricular failure (3%)
ear and labyrinth	ear discomfort (3%)
	tinnitus (3%)
eye (see paragraph following **Side Effects** table)	***blurry vision*** (44%)
	corneal deposits (15%)
	dry eye (50%)
	eye pain (9%)
	eye pruritus (6%)
	keratitis (32%)
	reduced visual acuity (6%)
gastrointestinal	*emetogenic potential:* low[3]
	constipation (9%)
	nausea (38%)
	stomatitis (9%)
	vomiting (29%)
general disorders and administration site conditions	*extravasation hazard:* none[4]
	chills (15%)
	fatigue (59%)
	infusion-related reactions (6-24%); see paragraph following **Side Effects** table
	pyrexia (15%)
immune system	hypersensitivity (3%)
investigations	ALT (6%)
	AST (3%)
	creatinine increase (6%)
	hypoalbuminemia (3%)
	hypomagnesemia (6%)
	hypophosphatemia (3%)
	weight loss (6%)
metabolism and nutrition	***appetite decrease*** (32%)
	dehydration (3%)
musculoskeletal and connective tissue	arthralgia (6%)
	muscle stiffness (3%)
	myalgia (6%)
nervous system	***headache*** (21%)
	paresthesias (3%)
	peripheral neuropathy (3%)

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
	peripheral sensory neuropathy (3%)
	syncope (3%)
respiratory, thoracic and mediastinal	epistaxis (9%)
skin and subcutaneous tissue	alopecia (3%)
	photosensitivity reaction (3%)

Adapted from standard reference[1] unless specified otherwise.

Infusion-related reactions are reported in up to 24% of patients. Reactions are mainly grade one to two in severity and include pruritus, flushing, upper body rash or fever. Following a reaction, subsequent doses are well tolerated with suitable premedication prior to each infusion.[1]

Visual and ***ocular disorders*** are reported in approximately 85% of patients. The most frequently reported events are dry eye, blurry vision, and keratitis, but other reported toxicities include reduced acuity, diplopia, eye pain/irritation, photophobia, foreign body sensation, eye swelling, increased lacrimation, and keratopathy. Ophthalmological exams in affected patients frequently reveal corneal lesions, deposits, or ulcers. Prophylactic use of prednisolone acetate 1% ophthalmic drops is recommended in all patients to prevent corneal toxicity. For each cycle, steroid drops are to be applied to both eyes starting one day prior to the administration of AGS-16C3F, and continued for a total of 14 days. AGS-16C3F dose reduction or treatment delay/discontinuation may be required to manage reported symptoms.[1,2]

SUPPLY AND STORAGE:

Injection: Astellas supplies AGS-16C3F as 30 mg single-use (preservative free) vials of lyophilized powder. Refrigerate. Protect from light in original packaging. Do not shake.[2]

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

Additional information: During preparation, unopened vials may be kept at room temperature for up to 4 h prior to use if protected from light.[2]

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	no information found
Intramuscular	no information found

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

Direct intravenous	do NOT use[2]
Intermittent infusion	***over 60 minutes***[2,5,6]
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

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:	
Intravenous:	3 weeks[2]:	***1.8 mg/kg IV for one dose on day 1*** (total dose per cycle 1.8 mg/kg)

REFERENCES:

1. Astellas. AGS-16C3F Investigator's brochure. 19 July 2018 (version 6.0).
2. Agensys. Pharmacy Guide Protocol AGS-16C3F-15-3: A multi-center, open label, randomized phase 2 study of AGS-16C3F vs. axitinib in metastatic renal cell carcinoma. Santa Monica, California; 8 June 2016 - version 2.0.
3. BC Cancer. (SCNAUSEA) Guidelines for Prevention and Treatment of Chemotherapy-induced Nausea and Vomiting in Adults. Vancouver, British Columbia: BC Cancer; 1 Dec 2018.
4. BC Cancer Provincial Systemic Therapy Program. Provincial Systemic Therapy Program Policy III-20: Prevention and Management of Extravasation of Chemotherapy. Vancouver, British Columbia: BC Cancer; January 2016.
5. BC Cancer. (Study Code GUT16C3F) Clinical Trial Dispensing Instructions for: A multi-center, open label, randomized phase 2 study of AGS-16C3F vs. aXitinib in metastatic renal cell carcinoma. Vancouver, British Columbia: BC Cancer; 18 April 2018.
6. Laura Standley. Personal communication. Lead Clinical Study Manager, Astellas Pharma Global Development Inc.; 23 January 2019.