DRUG NAME: Iniparib

SYNONYM(S): BSI-201,[1] SAR240550,[1] MS-292

COMMON TRADE NAME(S):

CLASSIFICATION: miscellaneous (PARP1 inhibitor)

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

MECHANISM OF ACTION:

Iniparib is an inhibitor of PARP1 [Poly (ADP-ribose) polymerase 1]. PARP is a large collection of at least 18 isoforms, the most abundant being PARP1 which is DNA-dependant. Inhibition of PARP1, which is essential for the repair of DNA single-strand breaks (SSBs), prevents the recruitment of DNA repair enzymes, which leads to failure of SSB repair and accumulation of SSBs ultimately causing cell death. Iniparib is a highly lipophilic, soluble, small-molecule prodrug which is metabolized to an active C-nitroso intermediate, ultimately leading to inactivation of PARP1 activity.[2]

USES:

Primary uses:
Breast Cancer

Other uses:

*Health Canada approved indication

SPECIAL PRECAUTIONS:

- ***phototoxicity*** has been observed *in vitro*, therefore patients should be advised to avoid direct sunlight or wear long-sleeved clothing and/or use sunscreen with an SPF≥ 30 if exposure cannot be avoided.[1]
- ***drug interactions*** are possible. Iniparib may alter the metabolism of drugs predominantly metabolized by CYP 1A2, and drugs known to deplete glutathione concentrations may increase iniparib levels and increase the potency of iniparib.[1]
- ***CNS toxicity***, including convulsions, has been observed at higher dosage levels in animal toxicology studies and is considered as a possible risk.[1]

SIDE EFFECTS:

NOTE: The following table is based upon safety data from clinical trials where the treatment regimen may have included iniparib in combination with other chemotherapeutic agents. Although the potential safety risk as a single agent is unknown, the reported adverse events may be considered as possible with iniparib both as single agent or in combination with chemotherapy.[1]

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
blood and lymphatic system/ febrile neutropenia	***anemia*** (67%, severe 23%)
	bleeding
	febrile neutropenia
	leucopenia (28%, severe 12%)[3]
	neutropenia (81%, severe 67%)[3]
	pancytopenia
	thrombocytopenia (63%, severe 37%)[3]

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
gastrointestinal	*emetogenic potential: high-moderate*
	abdominal pain[3] (5%, severe 0%)
	constipation (42%, severe 2%)[3]
	diarrhea (19%, severe 2%)[3]
	dyspepsia[3] (11%, severe 0%)
	oropharyngeal pain[3] (>10%)
	nausea (67%, severe 0%)[3]
	stomatitis (19%, severe 0%)[3]
	vomiting (28%, severe 2%)[3]
general disorders and administration site conditions	*extravasation hazard: irritant*
	asthenia, fatigue (70%, severe 7%)
	chills
	general physical health deterioration
	peripheral edema (19%, severe 0%)[3]
	pyrexia (25%, severe 0%)[3]
immune system	drug hypersensitivity
infections and infestations	celulitis
	pneumonia
	sepsis
	urinary tract infection (>10%)[3]
investigations	ALT increase[3] (18%, severe 5%)
	AST increase (12%, severe 2%)
	hyperglycemia[3] (9%, severe 2%)
	weight decrease[3] (2%, severe 0%)
metabolism and nutrition	anorexia (14%, severe 0%)[3]
	dehydration (11%, severe 2%)[3]
musculoskeletal and connective tissue	arthralgia[3] (16%, severe 2%)
	back, neck, or extremity pain[3] (>10%)
	bone pain[3] (14%, severe 2%)
	musculoskeletal chest pain[3] (>10%)
nervous system	dizziness (14%, severe 0%)[3]
	dysgeusia (>10%)[3]
	headache (25%, severe 0%)[3]
	peripheral neuropathy (16%, severe 0%)
psychiatric	anxiety[3] (14%, severe 0%)
	depression[3] (11%, severe 0%)

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
	insomnia[3] (11%, severe 2%)
renal and urinary	***acute renal failure***
respiratory, thoracic and mediastinal	cough (18%, severe 2%)[3]
	dyspnea (28%, severe 4%)[3]
	exertional dyspnea (28%, severe 4%)[3]
	pulmonary embolism
skin and subcutaneous tissue	alopecia (16%, severe 0%)[3]
	erythema[3] (>10%)
	rash (9%, severe 0%)[3]
	urticaria
vascular	deep vein thrombosis
	thrombosis

Adapted from standard reference[1] unless specified otherwise.

SUPPLY AND STORAGE:

Injection: BiPar Sciences/sanofi-aventis supplies iniparib as 100mg single-use vials of liquid in a concentration of 10 mg/mL. Store in refrigerator.[1]

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

SOLUTION PREPARATION AND COMPATIBILITY:

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

Additional information:

Compatibility: consult detailed reference

PARENTERAL ADMINISTRATION:

BCCA administration guideline noted in ***bold***, ***italics***

Subcutaneous	no information found
Intramuscular	no information found
Direct intravenous	no information found
Intermittent infusion	over 1 hour[1]
Continuous infusion	no information found

BCCA administration guideline noted in ***bold***, ***italics***

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*:**

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

	Cycle Length:	
Intravenous[1]:	3 weeks:	5.6 mg/kg IV for one dose on days 1, 4, 8, and 11

REFERENCES:

1. sanofi-aventis Canada. Iniparib (BSI-201;SAR240550) Special Access Program Guidance for the Physician. Laval, Quebec; 15December2010.
2. Liang H, Tan AR. Iniparib, a PARP1 inhibitor for the potential treatment of cancer, including triple-negative breast cancer. IDrugs 2010;13(9):646-656.
3. O'Shaughnessy J, Osborne C, Pippen JE, et al. Iniparib plus chemotherapy in metastatic triple-negative breast cancer. NEJM 2011;January 5(NEJM.org):1-10.