

The purpose of VA PBM Services drug monographs is to provide a focused drug review for making formulary decisions. Updates will be made if new clinical data warrant additional formulary discussion. The Product Information or other resources should be consulted for detailed and most current drug information.

Alpelisib (PIQRAY®)
Mini-Monograph
June 2023

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

FDA APPROVAL	Description/MOA	Select inhibitor of PI3K α -isoform
	Indication(s) Under Review	Advanced or metastatic, HR+, HER2- PIK3CA-mutated breast cancer
	Dosage Form(s)	Oral tablets

CLINICAL EVIDENCE	Study/Design	SOLAR-1; Randomized, double-blind, placebo-controlled
	Population	N=572; HR+, HER2- advanced or mBC; PD or recurred on/after AI-based treatment (with or w/o CDK4/6i) Excluded: inflammatory br ca, DM type 1 or uncontrolled type 2, pneumonitis
	Demographics	mAge 63 yrs; women (99.8%); white (66%); Asian (22%); ECOG PS 0 (68%)
	Intervention	Alpelisib 300mg + fulvestrant 500mg IM vs. placebo + fulvestrant 500mg IM
	Results	Cohort w/PIK3CA mutation: PFS 11 vs. 5.7 mos; HR 0.65 (0.50-0.85); p=0.0013; ORR 36 vs. 16% No significant difference in OS: 39 vs. 31 mos[HR 0.86; p1.15]; 25% discontinuation rate due to stomatitis, diarrhea, rash and hyperglycemia
	Summary	Significant PFS-benefit in those with PIK3CA mutation; no benefit in those without; no OS difference; \uparrow Gr 3/4 hyperglycemia, rash & diarrhea in alpelisib arm

SAFETY	Boxed warnings	None
	Contraindications	Severe hypersensitivity to alpelisib or any component of the formulation
	Warnings/Precautions	Dermatologic, GI and pulmonary toxicity, hyperglycemia, hypersensitivity,
	Adverse reactions	\geq 20%: \uparrow glucose, \uparrow SCr, diarrhea, rash, \uparrow GGT, \uparrow ALT, \uparrow lipase, \downarrow lymphocytes, nausea, fatigue, \downarrow hgb, \downarrow appetite, stomatitis, vomiting, \downarrow calcium, \downarrow glucose, aPTT prolonged
	Drug Interactions	Avoid CYP3A4 inducers, BRCP inhibitors, closely monitor with CYP2C9 substrates

Drug and Alternatives	Formulary status	Clinical Guidance	Other Considerations
Alpelisib	TBD	None	Oral formulation to be taken with food; caution and close monitoring in patients with diabetes; severe diarrhea may result in dehydration, AKI IM injection
+ fulvestrant	PA-F	None	
Fulvestrant alone	PA-F Restrict to H/O	None	

Projected Place in Therapy/Conclusions

- In postmenopausal women and men who are HR+, HER2-, PIK3CA-mutation+, who have progressed on AI-based therapy, addition of alpelisib to fulvestrant, as 2L resulted in improved PFS-outcomes and ORR compared to fulvestrant alone; The difference in OS was not different between alpelisib + fulvestrant vs. fulvestrant alone
- Close monitoring is essential for potential cutaneous reactions, severe diarrhea/colitis, pneumonitis and hyperglycemia as patient intolerance to AE profile led to discontinuation of 25% in SOLAR-1
- Review patient med profile for potential drug-drug interactions

References

- Andre F, Ciruelos E, Rubovszky G, et al. for SOLAR-1 Study Group. Alpelisib for PIK3CA-mutated, hormone receptor-positive advanced breast cancer. N Engl J Med 2019; 380: 20: 1929.
- Alpelisib (PIQRAY) prescribing information. Novartis pharmaceuticals Corp. East Hanover, New Jersey. May 2022