

BCR-ABL Tyrosine Kinase Inhibitors (TKI) + Proton Pump Inhibitors (PPI) (Final)

BCR-ABL Tyrosine Kinase inhibitors bosutinib, dasatinib, imatinib, nilotinib, and ponatinib are indicated for Philadelphia chromosome-positive chronic myeloid leukemia. Ponatinib is only approved in T315I-positive patients. These TKIs demonstrate pH dependent absorption for oral administration which may result in decreased efficacy when given concomitantly with medications that increase gastric pH. Dasatinib area under the curve (AUC) is decreased when co-administered with antacids, H2 antagonists, and PPIs.¹ Bosutinib and nilotinib AUCs are decreased with concomitant PPIs but antacids and H2 antagonists may be considered if TKI is given 2 hours before the antacid/H2 antagonist.^{2,3} However, for nilotinib a retrospective study has shown no difference in cytogenetic response rates for patients taking PPIs.⁴ Imatinib and ponatinib AUCs are not appreciably decreased by PPI co-administration.^{5,6}

Type of BCR-ABL Tyrosine Kinase Inhibitors	Imatinib, ponatinib	nilotinib	bosutinib, dasatinib
Not likely to decrease AUC	○ ^{5,6}		
Possible decrease in AUC and efficacy		■ ^{3,4}	
Probable decrease in AUC and efficacy			◆ ^{1,2}

○ = No special precautions. ■ = Assess risk and take action if necessary. ◆ = Use only if benefit outweighs risk

Footnotes:

1. Sprycel [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2015
2. Bosulif [package insert]. New York, NY: Pfizer Labs; 2015.
3. Tasigna [package insert]. East Hanover, NJ: Novartis; 2015.
4. Yin OQ, Giles FJ, Bacarani M, et al. Concurrent use of proton pump inhibitors or H2 blockers did not adversely affect nilotinib efficacy in patients with chronic myeloid leukemia. *Cancer Chemother Pharmacol*. 2012;70(2):345-350.
5. Iclusig [package insert]. Cambridge, MA: ARIAD Pharmaceuticals, Inc. 2016.
6. Egorin MJ, Shah DD, Christner SM, et al. Effect of a proton pump inhibitor on the pharmacokinetics of imatinib. *Br J Clin Pharmacol*. 2009;68(3):370-374.