

## Acid-Reducing Agents

Kinase inhibitor	Tmax (hour)	PPI	Time of intake of kinase inhibitor and PPI	Effect on kinase inhibitor exposure - AUC	Effect on kinase inhibitor exposure - C <sub>max</sub>	(FDA/EMA) recommendations	Refs.
Afatinib	2-5	N.A.	N.A.	N.A.	N.A.	PPIs can be used concomitantly*	[1, 2]
Axitinib	2-4	Rabeprazole 20mg q.d.	Concomitantly	15%↓	42%↓	PPIs can be used concomitantly	[1, 2]
Bosutinib	6	Lansoprazole 60mg q.d.,	Concomitantly	26%↓	46%↓	Avoid combination	[3]
Cabozantinib	2-5	Omeprazole 40 mg q.d.	PPI 1 hour before cabozantinib	7%↓	10%↓	PPIs can be used concomitantly	[1,2]
Crizotinib	4-6	Esomeprazole 40 mg	Concomitantly	10%↓	--	PPIs can be used concomitantly	[1,2]
Dabrafenib	2	N.a.	N.A.	N.A.	N.A.	Avoid combination*	[1,2]
Dasatinib	0,5-3	Omeprazole 40mg q.d.	Concomitantly	43%↓	42%↓	Avoid combination	[1, 2, 4]
Erlotinib	4	Omeprazole 40mg q.d.	Concomitantly	46%↓	61%↓	Avoid combination	[1,2]
Gefitinib	3-7	N.A.	N.A.	N.A.	N.A.	Avoid combination**	[1,2]
Ibrutinib	1-2	N.A.	N.A.	N.A.	N.A.	Avoid combination*	[1,2]
Imatinib	2-4	Omeprazole 40mg q.d.	Concomitantly	--	--	PPIs can be used concomitantly	[1,2]
Lapatinib	3-4	Esomeprazole 40mg q.d.	PPI 12 hours before Lapatinib	27%↓	--	Avoid combination	[1,2]
Nilotinib	3	Esomeprazole 40mg q.d.	Concomitantly	34%↓	27%↓	PPIs can be used concomitantly	[5-7]
Nintedanib	2-4	N.A.	N.A.	N.A.	N.A.	PPIs can be used concomitantly*	[1,2]
Pazopanib	3,5	Esomeprazole 40 mg q.d.	Concomitantly***	40%↓	42%↓	PPIs can be used concomitantly	[1,2]
Ponatinib	4	Lansoprazole 60mg q.d.	Concomitantly	--	25%↓	PPIs can be used concomitantly	[8]
Regorafenib	3-4	N.A.	N.A.	N.A.	N.A.	Avoid combination	[1,2]
Ruxolitinib	1	N.A.	N.A.	N.A.	N.A.	PPIs can be used concomitantly*	[1,2]
Sorafenib	3	Esomeprazole 40 mg q.d.	Concomitantly	--	--	PPIs can be used concomitantly	[1,2]
Sunitinib	6-12	N.A.	N.A.	N.A.	N.A.	PPIs can be used concomitantly*	[1,2]
Trametinib	1,5	N.A.	N.A.	N.A.	N.A.	PPIs can be used concomitantly*	[1,2]
Vandetanib	6	Omeprazole 40 mg q.d.	Concomitantly	--	15%↓	PPIs can be used concomitantly	[9]
Vemurafenib	4	N.A.	N.A.	N.A.	N.A.	PPIs can be used concomitantly*	[1,2]

\* Based only on "in vitro" and basic chemical data; \*\* Based on a study with ranitidine 450mg b.i.d., 13 hours and 1 hour before gefitinib (AUC 47%↓; C<sub>max</sub> 71%↓);

\*\*\* Esomeprazole (evening) concomitantly with pazopanib (in the morning).

EMA, European Medicines Agency; FDA, Food and Drug Administration; PPI, proton pump inhibitor; N.A., not available