

Sanofi	HMR1766 (ataciguat)
<b>Mechanism of Action</b>	Soluble guanylate cyclase (sGC) activator <a href="http://www.ncbi.nlm.nih.gov/gene/2981">http://www.ncbi.nlm.nih.gov/gene/2981</a>
<b>Overview</b>	HMR1766 is a nitric oxide (NO) independent activator of soluble guanylate cyclase (sGC) preferentially activating the oxidized sGC form; pathological conditions (diabetes or atherosclerosis) increase the level of the oxidized form, which is insensitive to NO. HMR1766 reduced tactile and cold allodynia in the spared nerve injury induced mouse model of neuropathic pain and thermal hyperalgesia in the Carrageenan-induced mouse model of inflammatory pain. In a unilateral hind limb ischemia peripheral artery disease (PAD) model in diabetic rats, HMR1766 reduced muscle fatigue and increased perfusion pressure in the ischemic leg. In ApoE knockout mice on high fat diet, HMR1766 prevented endothelial dysfunction and reduced atherosclerotic plaques. In various models, HMR1766 positively affected markers of coronary function and thrombosis, and myocardial function.
<b>Safety/Tolerability</b>	Toxicity studies (6/12-month), embryotoxicology, and fertility studies did not raise concerns. None of the studies conducted in humans have revealed any safety findings of clinical relevance. HMR1766 was well tolerated in healthy subjects and coronary artery disease (CAD) patients, patients with PAD, or neuropathic pain, with placebo like safety profile.
<b>Additional Information</b>	Four clinical trials had been conducted, 2 in stable angina pectoris, 1 in PAD, and 1 in neuropathic pain, but none demonstrated sufficient efficacy.
<b>Suitable for and Exclusions</b>	HMR1766 is a moderate inhibitor of CYP2C9 and weak inhibitor of CYP3A. No data are available as yet to support use in pediatrics.
<b>Clinical Trials</b>	<a href="http://clinicaltrials.gov/ct2/results?term=HMR1766">http://clinicaltrials.gov/ct2/results?term=HMR1766</a>
<b>Publications</b>	<a href="http://www.ncbi.nlm.nih.gov/pubmed?term=HMR1766%20">http://www.ncbi.nlm.nih.gov/pubmed?term=HMR1766%20</a>