

## New Product Highlights

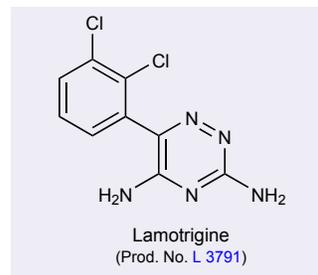
### Lamotrigine: An anticonvulsant that blocks both inhibitory and excitatory neurotransmission

Epilepsy is a devastating brain disorder characterized by the periodic and unpredictable occurrence of seizures. Several anti-epileptic drugs are currently available, although their use is symptomatic in that while these drugs inhibit seizures, neither effective prophylaxis nor cure is available. Examples include **carbamazepine** (Prod. No. [C 4024](#)), **phenytoin** (Prod. No. [D 4007](#)), **gabapentin** (Prod. No. [G-154](#)), **ethosuximide** (Prod. No. [E 7138](#)) and **sodium valproate** (Prod. No. [P 5443](#)).

Sigma-RBI is pleased to introduce **Lamotrigine** (GI 267119X, BW-430C, Prod. No. [L 3791](#)), a compound that is structurally unrelated to any known antiepileptic drugs. Although its mechanism of action is poorly understood, lamotrigine has been shown to block voltage-dependent sodium and calcium channels, thereby preventing the excessive release of the excitatory amino acid neurotransmitters **L-glutamic acid** (Prod. Nos. [G 1626](#), [G 1501](#)), and **L-aspartic acid** (Prod. No. [A 9256](#)) [1,2]. Thus, lamotrigine prevented release of these neurotransmitters from both rat cortical slices and

synaptosomes [3,4]. In addition to its effects on the release of excitatory neurotransmitters, lamotrigine has recently been shown to reduce both spontaneous and evoked GABA<sub>A</sub> receptor-mediated synaptic transmission in slices of rat amygdala [5].

Lamotrigine is therefore a unique anticonvulsant in that it reduces both excitatory and inhibitory synaptic events. It will be of interest to researchers studying the mechanisms underlying the generation of seizure activity in the brain and the mode of action of anti-epileptic drugs.



#### References

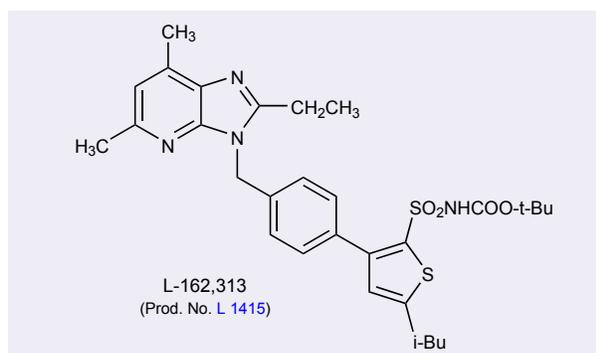
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### L-162,313: Non-peptide AT<sub>1</sub> angiotensin II receptor agonist

The AT<sub>1</sub> angiotensin receptor plays a major role in the regulation of blood pressure and electrolyte and fluid balance by mediating the effects of **angiotensin II** (Ang II, Prod. No. [A 9525](#)), an octapeptide hormone [1]. Blockade of the AT<sub>1</sub> angiotensin receptor has been the focus of significant research leading to the development of several non-peptide AT<sub>1</sub> receptor antagonists. Resulting compounds such as losartan, valsartan and eprosartan display therapeutic efficacy as antihypertensives.

In an effort to further elucidate the activities of these and related compounds, a series of compounds with agonist activity at the AT<sub>1</sub> angiotensin receptor were identified [2]. Administration of these compounds produced a dose-dependent increase in arterial blood pressure in rats. Additionally, these effects were inhibited by both peptide (**saralasin**, Prod. No. [A 2275](#)) and non-peptide (L-158,809) AT<sub>1</sub> angiotensin receptor antagonists. The prototype non-peptide AT<sub>1</sub> angiotensin receptor agonist **L-162,313** (Prod. No. [L 1415](#)) [2] is now available from Sigma-RBI. In addition to its ability to increase blood pressure in the rat, L-162,313 stimulated phosphoinositide hydrolysis in COS-7 cells transfected with the rat AT<sub>1</sub> angiotensin receptor, displaying an EC<sub>50</sub> of 33 ± 11 nM [3].

Much of the current angiotensin receptor research has focused on the structural basis of ligand-receptor interactions [4-6]. L-162,313 is widely used to characterize these relationships since its interaction with the AT<sub>1</sub> angiotensin receptor differs from those of Ang II and of structurally related non-peptide AT<sub>1</sub> angiotensin receptor antagonists. L-162,313 is therefore a useful tool for studying the structural intricacies of the AT<sub>1</sub> angiotensin receptor.



#### References

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