

5-HT1 Antagonists-Pipeline Insights – 2018 Size, Share, Industry, Forecast and outlook (2024-2031) Market -

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Contents

5-HT1 ANTAGONISTS-PIPELINE INSIGHTS

- As a group of G protein-coupled receptors (GPCRs), ligand-gated ion channels (LGICs), and the serotonin (5-HT) receptors are found in the central and peripheral nervous systems.
- After activated by the neurotransmitter serotonin, its natural ligand, 5-HT receptors mediate both excitatory and inhibitory neurotransmission by modulating the release of many neurotransmitters as well as many hormones.
- 5-HT receptors influence various biological and neurological processes including aggression, appetite, cognition, anxiety, learning, memory, nausea, mood, sleep, and thermoregulation.
- Thus, 5-HT receptors are the target of various pharmaceutical drugs, such as antidepressants, anorectics, antiemetics, antipsychotics, gastroprokinetic agents, hallucinogens, antimigraine agents, and entactogens. Numerous 5-HT receptor families and subtypes have evolved.
- 5-HT1A receptor is a subtype of serotonin (5-HT) receptor located in presynaptic and postsynaptic regions. Activation of this receptor was involved in the mechanism of action of drugs like anxiolytic, antidepressant and antipsychotic drugs. WAY 100635, BMY 7378, Cyanopindolol, Lecozotan has often been used as selective 5-HT1A receptor antagonists.
- There are a couple of drugs on the market that hit 5-HT1A receptors (such as buspirone and vilazodone). These are not only 5-HT1A drugs alone but are also having many other effects. Clinically active Anti-depressant treatments modify the response of 5-HT1A receptors in a number of brain regions.
- It has been postulated that desensitization of 5-HT1A autoreceptors after chronic

treatment with antidepressant drugs, which is a key factor in antidepressant efficacy and can cause the delay between the commencement of treatment and the alleviation of depressive symptoms.

- Some of the 5-HT_{1A} receptor antagonists currently under studies include NRX-101 by NeuroRx to treat suicidal Bipolar Depression, Latuda by Sunovion pharmaceuticals to treat Major Depressive Disorder.
- The human 5-HT_{1B} and 5-HT_{1D} receptors have been pharmacologically differentiated using nonselective 5-HT_{1B/D} receptor antagonists such as ketanserin, ritanserin, and methiothepin.
- A novel series of benzanilides have been reported recently, as the first selective 5-HT_{1B/D} receptor antagonists. GR 127935, a representative compound of this series, is displaying mixed agonist-antagonist properties.
- The clinical pipeline of 5-HT₁ antagonists is found to have less number of studies. The drugs included in phase III trials of drug development are Vortioxetine and Fluoxetine developing by H.Lundbeck A/S and Takeda, Morphine sulphate, and Granisetron.
- Drugs that inhibit the re-uptake of 5-HT, such as fluoxetine, have been used clinically for many years. Minerva Neurosciences are developing MIN-117, antidepressant drug candidate, targeting 5-HT_{1A} receptors to address unmet medical needs in patients suffering from Major Depressive Disorder and presenting with anxio-depressive symptoms.
- Physiological functions of these drugs –receptor type interactions will be the future area of research. The precise function of these receptors remains undefined, and progress toward this has been hampered by the lack of selective ligands.
- The interest of the major pharmaceutical companies in 5-HT₁ antagonists increased by the discovery of selective and potent tools, along with the fact that the blockade of terminal 5-HT₁ receptors by selective antagonists has been proposed as a new approach for more efficient fast-acting antidepressant drugs, as the acute blockade of these 5-HT autoreceptors will, in theory, immediately mimic their desensitization.
- The limitations of existing therapies, such as the slow onset of action and poor safety and tolerability, with many of the typical side effects are challenging for developing new therapeutics.

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