

## Mode of Action

Neuravena® (EFLA® 955) is an extract prepared from a proprietary variety of wild green oat herb. It improves overall mental fitness, concentration and cognitive performance in stressful situations.

Neuravena® combines two different mechanisms improving mental health:

- Monoamine oxidase B (MAOB) inhibition
- Phosphodiesterase 4 (PDE4) inhibition

### Monoamine oxidase B inhibition

- Monoamine oxidase B (MAOB) is a mitochondrial enzyme involved in the degradation of biogenic amines, preferentially phenylethylamine, dopamine and benzylamine.
- Lack in biogenic amines is well correlated with several CNS dysfunctions.
- Selective MAOB inhibitors, such as selegiline or Neuravena®, bind to and inhibit MAOB, preventing in this case dopamine degradation. This results in greater stores of dopamine available for release.
- MAOB inhibitors are used and/or investigated for the improvement of mental alertness and mental state performance as well as treatment of depression, Alzheimer's disease and Parkinson's disease.
- Components of Neuravena® mediates MAOB-inhibition with an IC50 value of ca. 80 µg/ml.

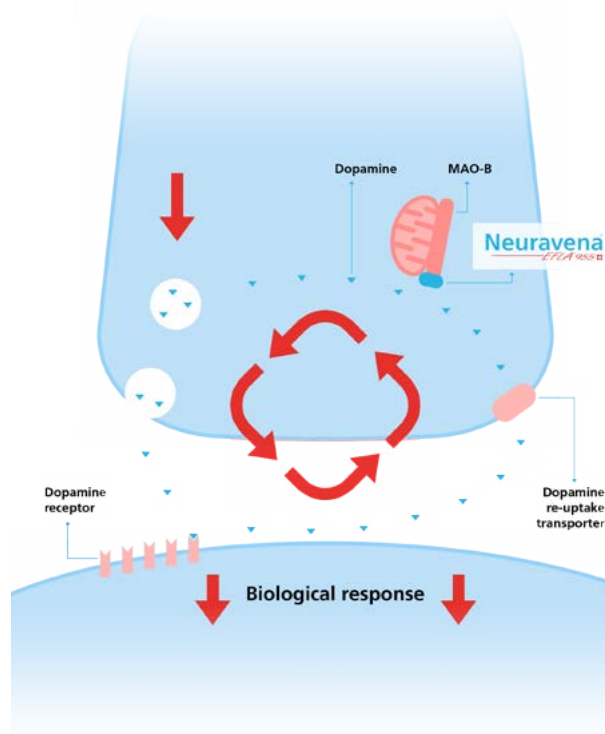


Fig. 1: Inhibition of MAOB by Neuravena®

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## Phosphodiesterase 4 inhibition

- **Phosphodiesterases (PDE)** are ubiquitous enzymes which hydrolyzes the cyclic nucleotides; cyclic adenosine-3,5-monophosphate (cAMP) and cyclic guanosine -3,5- monophosphate (cGMP), to their inactive 5'nucleotide monophosphate, 5' AMP and 5' GMP respectively.
- **PDE4** is a cAMP specific phosphodiesterase and encoded by 4 genes PDE4A, PDE4B, PDE4C, and PDE4D with at least 25 splice variants, each of which has unique cellular distribution and function.
- PDEs are important regulators of signal transduction mediated by these second messenger molecules.
- Physiologically, a low cellular dose of cyclic nucleotides is correlated with many disorders in humans' inclusive CNS dysfunctions. PDE4 inhibitors bind to and inhibit PDE4, preventing in this case cAMP degradation. This results in greater stores of cAMP to maintain physiological brain functions.
- A well-known PDE4 inhibitor is Rolipram. Beneficial effects of Rolipram include improved long term memory, increased wakefulness and increased neuroprotection.
- Components (preferentially the flavonoids) of Neuravena® mediate PDE4-inhibition with an IC<sub>50</sub> value of ca. 75 µg/ml.
- Beside MAOB and PDE4 inhibition probably other mechanisms also involved in improving mental alertness by Neuravena®.

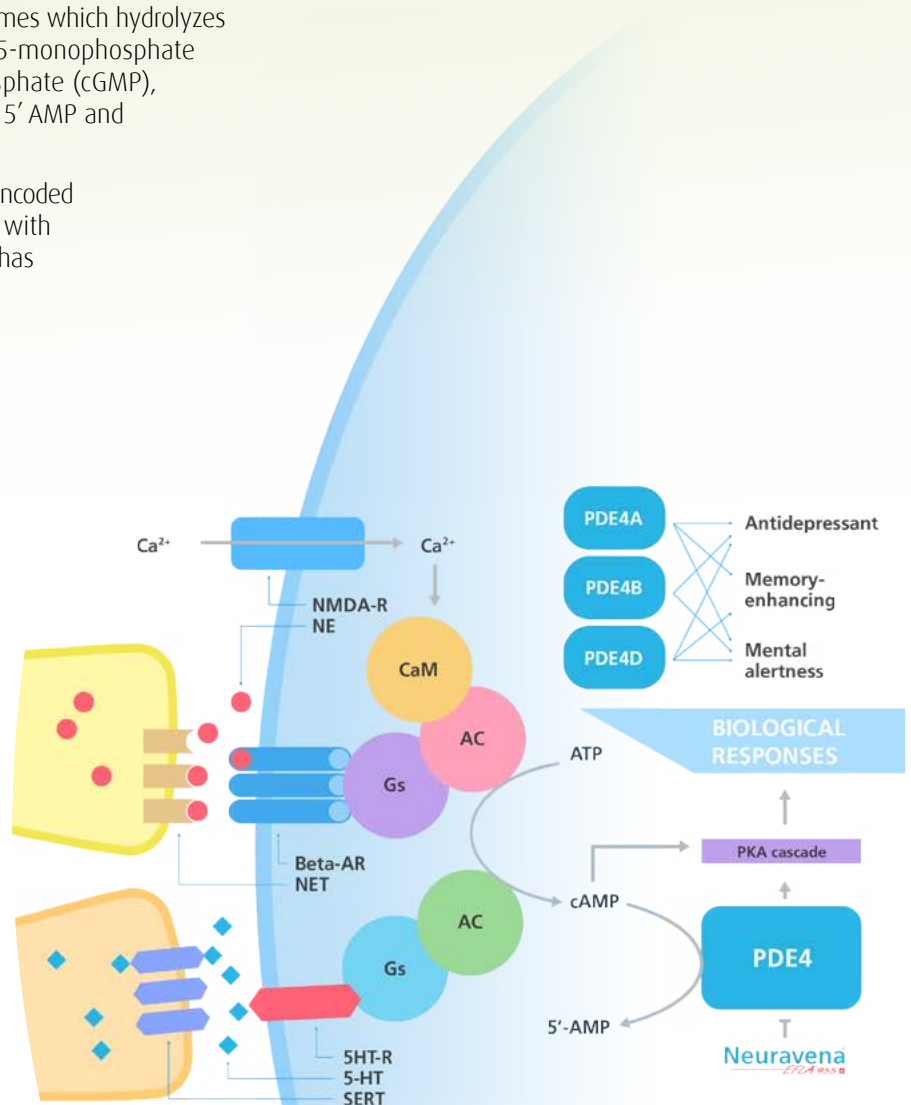
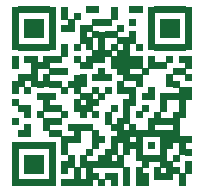


Fig. 2: Inhibition of PDE4 by Neuravena®

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