In 2016 Pitolisant as first histamine H3 receptor (H3R) inverse agonist/antagonist has received market approval by the European Medicine Agency for the orphan disease narcolepsy with and without cataplexy and is marketed by Bioprojet in whole Europe. Their contract in 2017 with Harmony Bioscience should open the U.S. market for Pitolisant. Several clinical trials on different therapeutic indications with different H3R antagonists have been described. Alzheimer's disease, schizophrenia, multiple sclerosis, alcohol abuse, and obstructive sleep apnea are only a selection of potential indications of clinical trials, mostly without the report on the exact outcome. Actually, the most prominent therapeutic application for Pitolisant and related H3R antagonists could be excessive daytime sleepiness. This somnolence frequently occur with Parkinson patients on dopaminergic medication.

Very recently, we have been able to follow an off-label use of Pitolisant as case study on a small number of children having Prader-Willi syndrome (PWS), a very rare genetic disease with hypotonia, hyperphagia, and cognitive impairments. The preliminary outcome hints on remarkable cognitive and social improvements connected to higher wakefulness and alertness during daytime. For the H3R-related influence on sleep periods during daytime on children with PWS, it is not possible to draw any conclusion so far due to the small and heterogeneous cohort with three patient reports only.