

# Apathy in Alzheimer's Disease A Regulatory Viewpoint

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# Apathy

- No drug approved for apathy in any therapeutic context
- In order for a medicine to be approved in a symptom cluster/dimension for a novel indication:
  - The Applicant should provide the scientific rationale for targeting a specific domain (biological basis) and its relationship with the product intended for development (mechanism of action)
  - Justification for the choice of endpoint should be included (validation plan)



# Definition of Apathy

- The definition should be uncontroversial, while apathy is often confused with amotivation (lack of motivation) or anhedonia (inability to feel pleasure)
- The definition and “diagnostic criteria” often encompass 3 different domains: behaviour, cognition and emotions
- If the definition of apathy is confusing , the population for clinical trials cannot be reliably identified.



# Endpoints

- The overlapping with anhedonia has brought additional confusion to the field from the definition of the biomarkers to the scales for outcome measure/endpoints and the mechanism of action to claim for an indication (reward/pleasure neurocircuits?)
- These attempts should be discussed early on with regulatory agencies through scientific advices and with the academic community through white papers



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