Drugs

PEER-REVIEWED FEATURE

Adagrasib: Adis Evaluation

Key Points

- An orally available, potent, irreversible, small molecule KRAS G12C inhibitor being developed by Mirati Therapeutics for the treatment of solid tumours harbouring KRAS G12C mutation
- Received its first approval on 12 December 2022 in the USA
- Approved for the treatment of adults with KRAS G12C-mutated locally advanced or metastatic NSCLC who have received ≥ 1 prior systemic therapy

Summary

Adagrasib (KRAZATI™) is an orally available, potent, irreversible, small molecule inhibitor of KRAS G12C mutant isoform being developed by Mirati Therapeutics for the treatment of solid tumours harbouring KRAS G12C oncogenic driver mutation, including non-small cell lung cancer (NSCLC) and colorectal cancer (CRC).

Adagrasib covalently binds to the mutant cysteine in KRAS G12C and locks the mutant KRAS protein in its inactive state, thereby preventing downstream signalling without affecting wild-type KRAS protein.

In December 2022, adagrasib received its first approval in the USA for the treatment of adults with KRAS G12C-mutated locally advanced or metastatic NSCLC (as determined by an FDA approved test) who have received ≥ 1 prior systemic therapy. It was approved under accelerated approval based on objective response rate and duration of response, and its continued approval for this indication may be contingent upon verification and description of a clinical benefit in a confirmatory trial(s). The drug is under regulatory review for NSCLC in the European Union and is in development for CRC in the US. Clinical studies of adagrasib in solid tumours, including CRC, are underway in several countries.

Dhillon S. D. Drugs. 2023. https://doi.org/10.1007/s40265-023-01839-y