

Abstract

Background: Levofloxacin inhalation solution (LIS) is approved for managing chronic *Pseudomonas aeruginosa* infections in adult patients with cystic fibrosis (CF). The European Medicines Agency made a provisional marketing authorisation of LIS conditional on its long-term safety evaluation in clinical practice.

Methods: The safety of LIS was evaluated using data from the UK (2017-2021) and German CF Registries (2019-2021). Propensity score models were used to compare the LIS cohorts (patients treated with LIS at any time during observation) with the non-LIS cohorts (treated with other inhaled antibiotics). Primary endpoints included haemoptysis, liver disease, tendon rupture, antimicrobial resistance and treatment discontinuation.

Results: In the UK Registry, 103 and 511 adult patients were included in the LIS and non-LIS cohorts, respectively. In the German Registry, equivalent numbers were 524 and 1893. In the UK, no significant difference in haemoptysis rates was observed between the LIS and non-LIS cohorts (17.5% vs 19.6%, adjusted relative risk [aRR]: 0.88, 95%CI 0.56–1.39, $P=0.583$). In the German Registry, a higher risk of haemoptysis was observed in the LIS cohort (17% vs 12%; aRR: 1.30, 95%CI 1.06–1.59, $P=0.012$). There was no increased risk of liver disease associated with LIS treatment, and tendon ruptures were rare. Antimicrobial resistance patterns were similar in LIS and non-LIS cohorts, and treatment discontinuation due to adverse events was low in both registries.

Conclusions: LIS was generally safe although may be associated with a higher risk of haemoptysis. No difference in liver disease, tendon rupture or treatment discontinuation compared to other inhaled antibiotics was observed.

Keywords: Levofloxacin Inhalation Solution, Cystic Fibrosis, Inhaled Antibiotics, Haemoptysis, liver disease