colobreathe®

Colistimethate Sodium 1,662,500 IU
inhalation powder, hard capsules

Effective *Pseudomonas aeruginosa* treatment for patients with cystic fibrosis[1,2]

Essential Pharma acquired the European rights to Colobreathe® from Teva Laboratories UK Limited in January 2024.[3]

Colobreathe® is the first rare disease medicine to be added to the Essential Pharma product portfolio. The acquisition will help ensure that cystic fibrosis patients in Europe have continued access to an important medicine.[3]

Colobreathe® (colistimethate sodium) is indicated for the management of chronic pulmonary infections due to *Pseudomonas aeruginosa* in patients with cystic fibrosis (CF) aged 6 years and older.[2]

Prescribing Information is available at the end of this document.

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Essential Pharma on 01784 477167 or at EssentialpharmaUK@EU.ProPharmaGroup.com

CF, cystic fibrosis.

MAT-COL-GB-0002-0724
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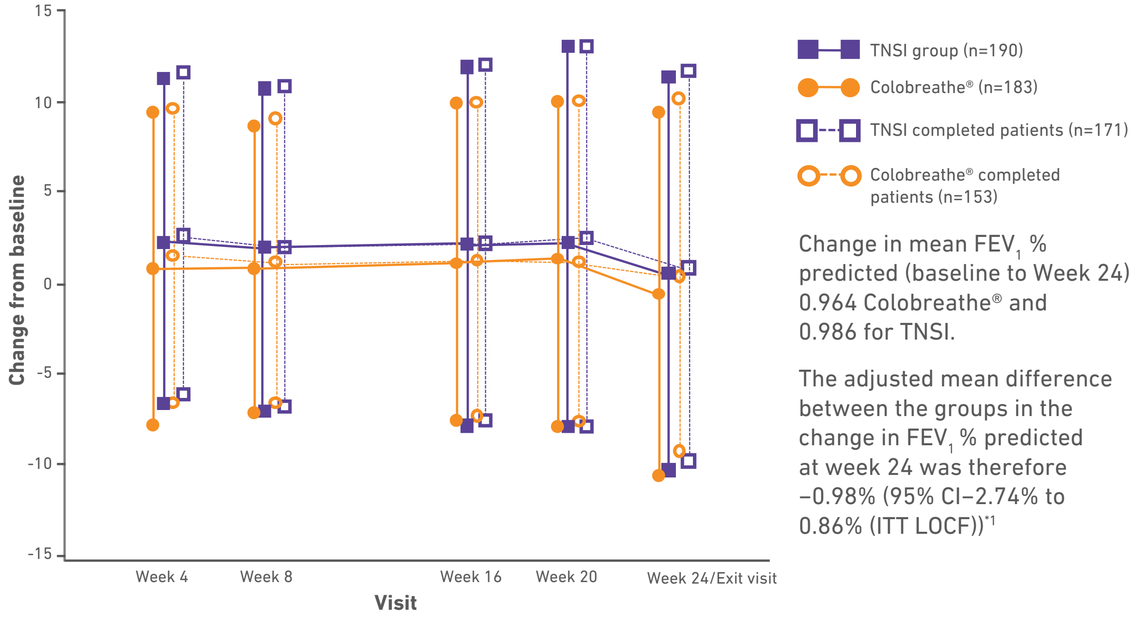
Colobreathe® shows **comparable efficacy to nebulised tobramycin**[1]

Primary endpoint: Colobreathe® has demonstrated non-inferiority vs. inhaled tobramycin at 24 weeks in maintenance of lung function[1]

FEV_1 % change from baseline to Week 24 (ITT)[1]



Change in mean FEV_1 % predicted (baseline to Week 24) 0.964 Colobreathe® and 0.986 for TNSI.

The adjusted mean difference between the groups in the change in FEV_1 % predicted at week 24 was therefore −0.98% (95% CI−2.74% to 0.86% (ITT LOCF))*[1]

Figure adapted from Schuster et al. 2013[1]

Study design

- A prospective, randomised, Phase III, open-label study of patients with CF aged ⩾6 years with chronic *P. aeruginosa* lung infection and FEV_1 % predicted between 25–75%[1]
- Prior to randomisation all patients received at least two 28-day TNSI on-off cycles followed by either:[1]
  - Continuous treatment over a 24-week period with Colobreathe® DPI (one capsule containing colistimethate sodium 1,662,500 IU, twice daily), or
  - Three 28-day, on-off courses of TNSI using a PARI LC Plus nebuliser (twice-daily 300 mg/5 ml tobramycin inhaler solution)

Primary endpoint:

- Change in mean FEV_1 % predicted from baseline at week 24[1]

*The lower limit of the 95% CI (−2.71%, for patients who completed the study) was within the predefined 3% margin for treatment difference.[1]

CF, cystic fibrosis; CDPI, Colobreathe® dry powder inhaler; FEV_1, forced expiratory volume in 1 second; ITT, intention to treat; ITT LOCF, intention-to-treat last observation carried forward; TNSI, tobramycin nebuliser solution for inhalation.

Colobreathe® demonstrates **low levels of microbial resistance**[1,2,4-8]

- *P. aeruginosa* resistance to colistin is low[1]
- Despite 20 years of use, colistin demonstrates low levels of microbial resistance[4,5,7]
- Treatment with Colobreathe® may be continued for as long as the physician considers that the patient is obtaining clinical benefits[2]
- Colistin's mode of action may be a key contributing factor for low levels of microbial resistance[2,7,8]

Susceptibility of *P. aeruginosa* isolated from CF patients to commonly used antimicrobial agents in two studies[5,6]

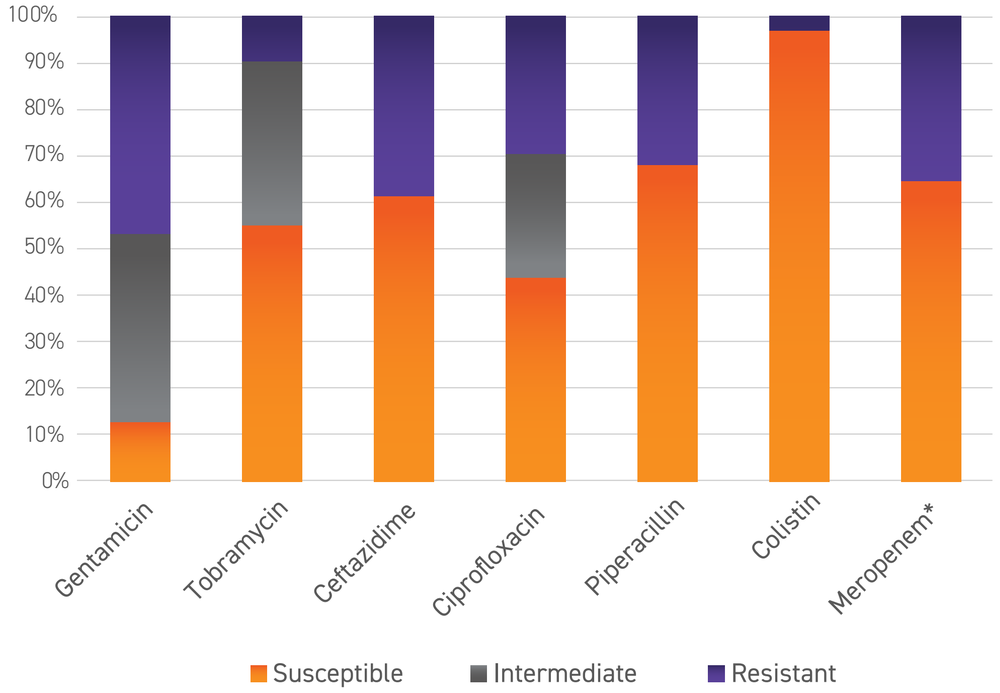


Figure adapted from Pitt et al 2003[5] and Unal et al 2005[6]

Antibiotics were prepared at a concentration defining the border between susceptibility and resistance to an antibiotic, as recommended by the British Society of Antimicrobial Chemotherapy (BSAC). Concentrations of isolates in µg/ml: gentamicin ≤1; ≥8, tobramycin ≤1; ≥8, ceftazidime ≤8; ≥16, ciprofloxacin ≤1; ≥8, piperacillin ≤16; ≥32, Colomycin® ≤4; ≥8 (i.e., bacteria susceptible to a minimum inhibitory concentration [MIC]), of Colomycin® ≤4 µg/ml were considered susceptible, and bacteria for which the MIC of Colomycin® was ≥8 µg/ml were considered resistant [Pitt 2003].

*Data presented from the MYSTIC program. Interpretations of susceptibility were based on Clinical and Laboratory Standards Institute (CLSI). The following CLSI breakpoint was used in order to determine the percentages of susceptible isolates: meropenem 4 µg/ml [Unal 2005].

BSAC, British Society of Antimicrobial Chemotherapy; CLSI, Clinical and Laboratory Standards Institute; CF, cystic fibrosis; MIC, minimum inhibitory concentration.

Overall, Colobreathe® was **well tolerated in the Freedom study**[1]

Most frequent AEs (≥5% of total number of events)[1]

	Colobreathe® (n=186)*	TNSI (n=193)	Total (n=379)
Total number of adverse events	1232	1194	2426
Cough	193 (15.7)	123 (10.3)	316 (13.0)
Dysgeusia	132 (10.7)	62 (5.2)	194 (8.0)
Dyspnoea	81 (6.6)	98 (8.2)	179 (7.4)
Lower respiratory tract infection	79 (6.4)	85 (7.1)	164 (6.8)
Throat irritation	94 (7.6)	63 (5.3)	157 (6.5)
Productive cough	62 (5.0)	76 (6.4)	138 (5.7)

Data presented as n (%), safety population.[1]

Table adapted from Schuster et al 2013[1]

- The number of AEs was similar for both groups[1]
- There was a higher incidence of **cough, throat irritation** and **dysgeusia** in the Colobreathe® group compared with the TNSI group[1]
  - The incidence of treatment-related AEs was higher in the Colobreathe® group vs the TNSI group (153/186 patients, 82.3% compared with 90/193, 46.6%), and discontinuations where the primary cause was an AE were also higher in the Colobreathe® group (18/186 patients, 9.7%, compared with 3/193, 1.6%).
- Most **AEs were mild to moderate** in intensity and diminished as patients continued with treatment[1]
- SAEs were higher in the TNSI group (6.2% of patients vs 4.3% for Colobreathe®)[1]

*One patient was randomised but received no treatment.[1]

AEs, adverse events; CF, cystic fibrosis; SAEs, serious adverse events; TNSI, tobramycin nebuliser solution for inhalation.

Colobreathe®

Effective *Pseudomonas aeruginosa* treatment for patients with CF[1]

- Comparable efficacy to nebulised tobramycin[1]
- Portable, easy to use[1,2]
- One capsule, inhaled twice daily[2]
- Simple regimen – treatment may be continued for as long as the physician considers that the patient is obtaining clinical benefit[2]
- Minimal cleaning and maintenance; new device required every month[1,2]
- Lower antimicrobial resistance vs tobramycin[1,2]
- Colobreathe® is well tolerated - most adverse events were rated mild to moderate in intensity and tended to diminish as patients continued with treatment in the Freedom study[1]
- For a step-by-step guide on how your patient should use Colobreathe® with the turbospin inhaler, please refer to the Patient Information Leaflet available here and Risk Materials available here.

Packaging may vary.

CF, cystic fibrosis.

Colobreathe® Prescribing Information

Colobreathe® (colistimethate sodium) 1,662,500 IU inhalation powder, hard capsule
Prescribing Information
Please consult the Summary of Product Characteristics (SmPC) before prescribing

Presentation: Inhalation powder, hard transparent capsule containing 1,662,500 IU (equal to 125 mg) of colistimethate sodium. **Indications:** Management of chronic pulmonary infections due to *Pseudomonas aeruginosa* in patients with cystic fibrosis aged 6 years and older. Consideration should be given to official guidance on the appropriate use of antibacterial active substances. **Dosage and administration:** First dose should be administered under medical supervision to ensure proper administration. For inhalation use only using the Turbospin® powder inhaler. *Adults and children aged 6 years and older*: One capsule to be inhaled twice daily, 12 hours apart. *Children <6 years*: Not recommended. *Renal and Hepatic Impairment:* No dose adjustment necessary. If other treatments are being taken, recommended order: inhaled bronchodilators; chest physiotherapy; other inhaled medicines; Colobreathe. **Contraindications:** Hypersensitivity to active substance, colistin sulphate or polymyxin B. **Special warnings and precautions for use:** *Bronchospasm or coughing* may occur on inhalation. These reactions may diminish with continued use or be ameliorated by treatment with beta$_2$-agonists. If bronchospasm or coughing remains problematic, consider discontinuation of treatment. The use of colistimethate sodium in patients with clinically significant *haemoptysis* should be undertaken or continued only if the benefits of treatment are considered to outweigh the risks of inducing further haemorrhage. If *acute respiratory exacerbations* develop additional intravenous or oral antibacterial agent therapy should be considered. After each inhalation of Colobreathe, the mouth should be rinsed with water to reduce the risk of *oral fungal super-infection* and to reduce any unpleasant taste. There is very low transpulmonary absorption of colistimethate after inhalation of Colobreathe. Care should be taken in administering Colobreathe to patients who are known to have a propensity for *nephrotoxic or neurotoxic events*. Caution should be taken with concomitant use of Colobreathe and parenteral or nebulised colistimethate sodium. Caution should be taken with *concomitant use* of colistimethate sodium and potential nephrotoxic or neurotoxic medicinal products, including non-depolarising muscle relaxants. Use with extreme caution in patients with *myasthenia gravis or porphyria*. **Interactions:** *In-vivo* interaction studies have not been performed. No data available for use with other inhaled antibacterial agents. Use with caution with concomitant use of other formulations of colistimethate sodium due to possibility of summative toxicity. Concomitant use of inhaled colistimethate sodium with other medications that are potentially nephrotoxic or neurotoxic, such as aminoglycosides, or neuromuscular blocking products, such as curariform agents should be undertaken with caution. Co-treatment with colistimethate sodium and macrolides such as azithromycin and clarithromycin, or fluoroquinolones such as norfloxacin and ciprofloxacin should be undertaken with caution in patients with myasthenia gravis. **Pregnancy and lactation:** Not recommended during pregnancy or in women of childbearing potential not using contraception. Risk/benefit assessment for woman and child should be made when woman is breastfeeding. **Effects on ability to drive and use machines:** Patients should be warned not to drive or operate machinery if symptoms of neurotoxicity occur such as dizziness, confusion or visual disturbances. **Undesirable effects:** *Very* Common (⩾ 1/10): Dyspnoea, cough, dysphonia, throat irritation, dysgeusia. *Common (⩾ 1/100 to <1/10)*: Balance disorder, headache, tinnitus, haemoptysis, bronchospasm, asthma, wheezing, chest discomfort, lower respiratory tract infection, productive cough, crackles lung, vomiting, nausea, arthralgia, pyrexia, asthenia, fatigue, forced expiratory volume decreased. **For further information on adverse events please consult the SmPC. Legal category:** POM. **Presentation & cost:** 56 capsule pack and one Turbospin inhaler device £968.80. **Marketing authorisation numbers:** (56 [7 blisters of 8 capsules]); PLGB 41871/0023. For further information contact Essential Pharma Limited, 8a Crabtree Road, Egham, Surrey, TW20 8RN. **Date of last revision:** August 2024.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Essential Pharma Limited on 01784 477167

1. Schuster A et al. Thorax. 2013;68:344–350. **2.** Colobreathe® Summary of Product Characteristics. **3.** Essential Pharma. Essential Pharma acquires European rights to Colobreathe® (colistimethate sodium) from Teva. Available from: https://essentialpharmagroup.com/essential-pharma-acquires-european-rights-to-colobreathe-from-teva/. Accessed September 2024. **4.** Littlewood JM et al. Respir Med. 2000;94:632–640. **5.** Pitt TL et al. Thorax. 2003; 58: 794–796. **6.** Unal S, Garcia-Rodriguez JA. Diagn Microbio Infect Dis. 2005;53:267-271. **7.** Li J et al. Int J Antimicrob Agents. 2005; 25(1):11–25. **8.** Li J et al. Lancet Infect Dis. 2006;6:589–601.

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