

**Supplementary Table 1: Anti-infectives for lower respiratory tract topical use.\***

| Drug name                  | Formulation                               | Specifications                   | Matching drug delivery device | Approved indications  | Remarks   |
|----------------------------|---|----------------------------------|-------------------------------|---|---|
| Tobramycin                 | Injection                                 | 2 ml: 80 mg (880,000 units)/tube | –                             | Nebulization for adjuvant treatment of bronchial and pulmonary infections as indicated in package insert.     | The blood concentration is extremely low when tobramycin is used as nebulized inhalation.   |
|                            | Inhalation solution                       | 5 ml: 300 mg/tube                | Air 360 mini nebulizer        | Bronchiectasis with PA infection in adults  | Inhalation formulation contains no preservative, and the pH value is adjusted to 6.0, so the irritation to airway is reduced compared with injection. |
|                            | Inhalation solution (TOBI)                | 5 ml: 300 mg/tube                | PARI LC Plus nebulizer        | CF with PA infection aged 6 years and over.   |   |
|                            | Concentrated inhalation solution          | 4 ml: 300 mg/tube                | –                             |   |   |
|                            | Concentrated atomized liquid              | 1.7 ml: 170 mg/tube              | Tolero nebulizer              |   |   |
| DPI                        | 28 mg/capsule (TOBI)                      | Podhaler                         |                               | DPI has higher deposition in lung than nebulized inhalation solution, and it is faster and easier to operate. |   |
| Amikacin                   | Liposome inhalation suspension            | 10ml: 590mg/tube (LAI)           | Lamira nebulizer              | Refractory MAC lung disease.  | Compared with amikacin injection, LAI has longer retention and release time in lung and less systemic absorption after inhalation.                    |
| Colistin methane sulfonate | Injection                                 | 1 MIU/tube, 2 MIU/tube           | –                             | CF with PA infection.   | It should be freshly prepared and used.   |
|                            | DPI                                       | 1.6625 MIU (125 mg)/capsule      | Turbospin inhaler             | CF with PA infection aged 6 years and over. (unlisted in China)   |   |
| Aztreonam                  | Aztreonam lysine inhalant                 | 75 mg/tube                       | Altera nebulizer              | CF with PA colonization aged 7 years and over.  | It is prepared with lysine, thus avoiding arginine-related airway inflammatory reaction. It should be reconstituted before use.                       |
| Levofloxacin               | Inhalation solution                       | 2.4 ml: 240 mg/tube              | Zirela nebulizer              | CF with chronic PA infection.   |   |
| Isoniazid                  | Injection                                 | 2 ml: 100 mg/tube                | –                             | Atomization inhalation for the treatment of pulmonary tuberculosis as indicated by package insert.            |   |
| Zanamivir                  | DPI                                       | 5 mg/bubble                      | Diskhaler                     | Treatment of non-severe influenza in adults and adolescents over 12 years old.                                | Patients who are allergic to milk should avoid using it. Not recommended for patients with chronic airway diseases.                                   |
| Amphotericin B             | Deoxycholate amphotericin B for injection | 5 mg/tube, 25 mg/tube            | –                             | Treatment of pulmonary mycosis by atomization inhalation or local injection as indicated by package inserts.  |   |
| Pentamidine                | Injection                                 | 0.2 g/tube, 0.3 g/tube           | –                             | Prevention of PJP in high-risk population who are not tolerable to sulfonamides.                              |   |

\*This table lists the drugs that have been approved for topical airway use at home or abroad as of December 2019, or the drugs with relevant usage listed in the package inserts. CF: Cystic fibrosis; DPI: Dry powder inhaler; LAI: Liposomal Amikacin for Inhalation; MAC: *Mycobacterium avium* complex; MIU: Million international units; PA: *Pseudomonas aeruginosa*; PJP: *Pneumocystis Jirovecii* Pneumonia; TOBI: Tobramycin solution for inhalation.

**Supplementary Table 2: Inhalation and topical anti-infective therapy of common refractory lower respiratory tract infections.**

| Disease   | Recommended drugs and their dosage*   | Remarks  |
|---|---|--|
| VAP   | Nebulized inhalation of tobramycin, 300 mg bid;<br>Nebulized inhalation of amikacin, 400 mg bid or 25 mg/kg qd;<br>Nebulized inhalation of colistin methane sulfonate, 1–2 MIU/time, bid-tid;<br>Nebulized inhalation of polymyxin B sulfate, 2.0–2.5 mg•kg <sup>-1</sup> •d <sup>-1</sup> , administered by 2–4 times.<br>The duration of therapy is 14 days.  | Authoritative guidelines at home and abroad recommend inhalation combined with intravenous systemic antibiotic treatment for lower respiratory tract infection caused by XDR GNB, but the best dosages and course of treatment are still inconclusive. Nebulized inhalation of polymyxin B sulfate injection has only observational research data, which can be used as appropriate when necessary. Appropriate atomization device should be used, and appropriate oxygen concentration and ventilation mode should be set according to the pathophysiological characteristics of patients. The ventilation circuit tube needs to be optimized for antibiotics nebulization.   |
| CF bronchiectasis                                 | Nebulized inhalation of tobramycin solution, 300 mg bid, 3–7 cycles;<br>Nebulized inhalation of tobramycin concentrated solution, 170 mg/time, bid;<br>Tobramycin DPI, 4 capsules bid;<br>Nebulized inhalation of colistin methane sulfonate, 1–2 MIU bid;<br>Methane sulfonate polymyxin E DPI 1.6625 MIU bid;<br>Nebulized inhalation of aztreonam lysine inhalant, 75 mg tid;<br>Nebulized inhalation of levofloxacin inhalation solution, 240 mg bid. | These medications are recommended to use as 28-day cycles (i.e., 28 days of on and off-treatment), and the total course of treatment is according to the recommended number of cycles or until there is no obvious benefit.  |
| Non-CF bronchiectasis                             | Nebulized inhalation of tobramycin, 300 mg bid, and the course of treatment is 28 days, which can be extended to 6 months.<br>Nebulized inhalation of colistin methane sulfonate, 1 MIU bid, and the course of treatment is 6 months.   | International authoritative guidelines recommended inhaled antibiotics for stable moderate to severe bronchiectasis patients with positive sputum culture of PA. Intermittent administration is recommended for long-term inhalation therapy.  |
| Bronchopulmonary mycosis                          | Invasive bronchopulmonary mycosis: Nebulized inhalation of amphotericin B deoxycholate which is dissolved into 0.2%–0.3% solution with sterilized water for injection, 5–10 mg, bid-tid.<br><br>CPA: Inject amphotericin B deoxycholate into cavity colonized by <i>Aspergillus</i> via bronchoscope. Dissolve 50 mg of amphotericin B in 20 ml of 5% glucose solution, and the injection volume depends on the cavity size.                              | For IPA, there are only case reports suggesting that aerosol inhalation of amphotericin B might be effective for patients with poor response to systemic antifungal treatment, treatment failure or intolerance. There is no prophylactic indication in China, and authoritative guidelines abroad recommend that amphotericin B 25 mg/day be inhaled with combination of azole drugs for preventing pulmonary mycosis in patients with delayed recovery of neutropenia after lung transplantation, hematopoietic stem cell transplantation or other solid organ transplantation.<br><br>Intracavitary injection of amphotericin B combined with systemic treatment can be considered for CPA patients with poor systemic antifungal effect, treatment failure or intolerance. |
| Tracheobronchial tuberculosis                     | Nebulized inhalation: Dilute 200 mg of isoniazid and 200 mg amikacin for injection into 20 ml normal saline, qd–bid, and the course of treatment is 1–2 months.<br>Intratracheal administration via bronchoscope: Amikacin 200–400 mg and isoniazid 200–300 mg, once a week, usually 4–8 times; if the lesion heals slowly, the course of treatment can be extended to over 8 weeks.  | The curative effect of systemic combined local chemotherapy on tracheobronchial tuberculosis is validated. It is recommended by the consensus of domestic experts that type I–III and VI can be treated by nebulized inhalation or intratracheal administration during interventional therapy under bronchoscope.  |
| Cavitary or drug-resistant pulmonary tuberculosis | Intrabronchial administration: Isoniazid for injection 200 mg–300 mg combined with amikacin for injection 200 mg–400 mg, once a week, and the course of treatment is 4–8 weeks; or local infusion of rifampicin gel for interventional therapy, 5–7 ml gel per cavity, 1–2 times a week, and the course of treatment is 4–8 weeks.  | It is recommended by the consensus of domestic experts that local chemotherapy via bronchoscope can be considered based on systemic treatment in patients with cavitary pulmonary tuberculosis having poor response to systemic treatment, or tuberculosis cavity is not closed for a prolonged time due to drug-resistant tuberculosis. Rifampicin powder injection is not recommended for local treatment, and gel preparation (off-label) can be used when necessary.   |
| NTM pulmonary disease                             | Nebulized inhalation of amikacin for injection: The dosage is initially 200 mg once a day and increased to 400 mg/day after 2 weeks. If it is well tolerated, increase the dosage to 300–400 mg twice daily after another 2 weeks.<br>Nebulized inhalation of amikacin lipid suspension, 590 mg, qd.  | Inhaled amikacin is used to treat NTM patients who have difficulty in systemic administration, e.g. aminoglycosides contraindicated due to side effects or require long-term treatment. The goal of treatment is to improve clinical symptoms rather than cure diseases.   |
| Influenza   | Zanamivir DPI for the treatment of influenza: 10 mg/time, bid, for 5 consecutive days; for prophylactic use, 5 mg bid.  | Recommended for the treatment of non-severe influenza, and there is no indication for prophylaxis in China.  |
| PJP   | Nebulized inhalation of pentamidine, 60–150 mg, once every 2 weeks; or 120–300 mg, once a month.  | Inhaled pentamidine is used for the prevention of PJP in high-risk population with sulfanilamide intolerance and having no indication for treatment.   |

\*For drugs that are off label for inhalation or respiratory topical therapy, the advantages and disadvantages should be weighed, and the informed consent should be fully obtained before use. Bid: Twice a day; CF: Cystic fibrosis; CPA: Chronic pulmonary aspergillosis; DPI: Dry powder inhalation; GNB: Gram-negative bacilli; IPA: Invasive pulmonary aspergillosis; MAC: *Mycobacterium avium* complex; MIU: Million international units; NTM: Nontuberculous mycobacteria; PA: *Pseudomonas aeruginosa*; PJP: *Pneumocystis Jirovecii* Pneumonia; qd: Once a day; tid: Three times a day; VAP: Ventilator-associated pneumonia; XDR: Extensive drug resistance.