To view prescribing information for Chiesi CF products please scroll down through this document or alternatively click the appropriate button below.

For UK and Ireland Healthcare Professionals

Quinsair®

levofloxacin nebuliser solution

Prescribing information UK

Prescribing information Ireland

BRAMITOB®

TOBRAMYCIN

Prescribing information UK

Prescribing information Ireland

bronchitol®

MANNITOL

Prescribing information UK

Prescribing information Ireland

Chiesi

IE-CF-2000165 Date of Preparation: November 2020

Quinsair▼ Prescribing Information - UK

Quinsair ▼ 240 mg Nebuliser Solution Prescribing Information
Please refer to Summary of Product Characteristics (SPC) before prescribing.

Presentation: Each mL of nebuliser solution contains levofloxacin hemihydrate equivalent to 100mg of levofloxacin. Each ampoule (amp) contains 240mg of levofloxacin. **Indication:** Management of chronic pulmonary infections due to *Pseudomonas aeruginosa* in adult patients with cystic fibrosis (CF). **Dosage and administration:** 240mg (one amp) by inhalation twice daily. Doses should be as close as possible to 12 hours apart. Alternating cycles of 28 days on then 28 days off treatment. Cyclical therapy may be continued as long as clinical benefit seen. Missed doses should be taken as soon as the patient remembers, providing there is at least an 8 hour interval before the next dose. The contents of more than one amp should not be inhaled to compensate for the missed dose. If acute symptomatic bronchospasm occurs, the use of a short-acting inhaled bronchodilator may be beneficial prior to subsequent doses. *Elderly (≥65 years) and Paediatric (<18 years)*: Safety and efficacy have not been established. *Renal impairment*: Not recommended in severe renal impairment. *Recommended treatment order if on multiple inhaled therapies*: 1. Bronchodilators, 2. dornase alfa, 3. airway clearance techniques, 4. Quinsair, 5. inhaled steroids. Quinsair should only be used with the Zirela® Nebuliser Handset (including a Zirela Aerosol Head) connected to an eBase Controller or an eFlow rapid Control Unit. Please review Zirela Nebuliser System Manufacturers Instructions prior to the first use. **Contraindications:** Hypersensitivity to active substance, other quinolones or any excipient; history of tendon disorders related to fluoroquinolone administration; epilepsy; pregnancy; breast-feeding. **Warnings and precautions:** Avoid in patients with history of serious adverse reactions when using quinolone/fluoroquinolones. Treatment should only be initiated in the absence of alternative treatment options and after a benefit/risk assessment. Serious, potentially fatal hypersensitivity reactions, severe bullous skin reactions and hepatobiliary disorders. Stop treatment if hepatic disease signs and symptoms develop, e.g. anorexia, jaundice, dark urine, pruritus or tender abdomen. Caution with known risk factors for prolongation of the QT interval, e.g. congenital long QT syndrome, uncorrected electrolyte imbalance, cardiac disease (e.g. heart failure, myocardial infarction and bradycardia) and concomitant use of QTc-prolonging drugs (e.g. Class IA and III antiarrhythmics, tricyclic antidepressants, macrolides, antipsychotics) particularly with the elderly and women. Predisposal to seizures: Quinolones may lower the seizure threshold and may trigger seizures. Use with extreme caution in patients predisposed to seizures or on concomitant treatment with active substances that lower the cerebral seizure threshold, e.g. theophylline. Psychotic reactions: Psychotic reactions reported. In very rare cases, these have progressed to suicidal thoughts and self-endangering behaviour, sometimes after a single dose. Caution in psychotic patients or a history of psychiatric disease. Peripheral neuropathy: Sensory/sensorimotor polyneuropathy have been reported. Patients should inform their doctor if pain, burning, tingling, numbness, or weakness develop to prevent the development of an irreversible condition. Exacerbation of myasthenia gravis: Not recommended in patients with history of myasthenia gravis as may exacerbate muscle weakness and cause the requirement for respiratory support or death. Tendinitis and tendon rupture: May occur as early as within 48 hours of starting treatment and up to several months after treatment discontinuation. Increased risk in older patients, renal impairment, solid organ transplants, patients receiving 1000mg daily, and those using corticosteroids. Avoid concomitant use of corticosteroids. If signs of tendinitis, discontinue levofloxacin treatment and consider alternative. Bronchospasm: Bronchospasm is associated with inhaled therapies. For acute symptomatic bronchospasm, use a short-acting bronchodilator prior to subsequent doses. Haemoptysis: May induce a cough reflex. Administration to patients with clinically significant haemoptysis should be undertaken only if the benefits outweigh the risks of inducing further haemorrhage. Glucose-6-phosphate dehydrogenase (G6PD) deficiency: If Quinsair has to be used in patients with latent or actual defects in G6PD activity, they should be monitored as they may be prone to haemolytic reactions. Vitamin K antagonists: Coagulation tests should be monitored due to possible increases (PT/INR) and/or bleeding in patients treated concomitantly with a vitamin K antagonist (e.g. warfarin). Dysglycaemia: Blood glucose monitoring recommended as disturbances in blood glucose (both hypo- and hyperglycaemia) have been reported, usually in patients with diabetes receiving concomitant treatment with an oral hypoglycaemic medicinal product (e.g. glibenclamide) or with insulin. *Clostridium difficile*-associated disease (CDAD): Diarrhoea, particularly if severe, persistent and/or bloody, during or after treatment (including several weeks. after treatment), may be symptomatic of CDAD. Can range in severity from mild to life-threatening, e.g. pseudomembranous colitis. Resistance to levofloxacin, other antibacterial medicinal products and treatment-emergent microorganisms: Potential risk of fluoroquinolone-resistant *P. aeruginosa* and superinfection with fluoroquinolone-insusceptible microorganisms. Vision disorders: Consult an eye specialist immediately if vision becomes impaired or any effects on the eyes are experienced. Prevention of photosensitisation: Photosensitisation has been reported. Patients should not expose themselves to strong sunlight or to artificial UV rays during treatment and for 48 hours following treatment discontinuation. Interference with laboratory tests: In patients treated with levofloxacin, determination of opiates in urine may give false-positive results. Levofloxacin may inhibit the growth of *Mycobacterium tuberculosis* and may give false-negative results in bacteriological diagnosis of tuberculosis. Aortic aneurysm and dissection and heart valve regurgitation/incompetence: Increased risk particularly in elderly, sometimes complicated by rapture (including fatal rapture). Care should be taken in patients with positive family history of aneurysm disease, or congenital heart valve disease, or in patients diagnosed with pre-existing or predisposing conditions for aortic aneurysm and/or aortic dissection or heart valve regurgitation/incompetence (e.g. Marfan syndrome, Ehlers-Danlos syndrome, Turner syndrome, Behcet's disease, hypertension, rheumatoid arthritis, or aortic aneurysm and dissection (vascular disorders such as Takayasu arteritis or giant cell arteritis or known atherosclerosis or Sjögren's syndrome) or for heart valve regurgitation/incompetence (e.g. infective endocarditis). Risk may also be increased in patients treated concurrently with systemic corticosteroids. In case of sudden abdominal, chest or back pain, acute dyspnoea, new onset of heart palpitations, or development of oedema of the abdomen or lower extremities, patients should be advised to immediately seek medical advice. Very rare cases of prolonged, disabling and potentially irreversible serious adverse drug reactions: Affecting body systems (musculoskeletal, nervous, psychiatric and senses) have been reported. Discontinue levofloxacin immediately at the first signs or symptoms and advise patients to contact their prescriber. **Interactions:** A pronounced lowering of the cerebral seizure threshold may occur when quinolones are given concurrently with theophylline, non-steroidal anti-inflammatory drugs, or other substances which lower the seizure threshold. The renal clearance of levofloxacin was reduced with probenecid and cimetidine. The half-life of ciclosporin was increased by 33% when co-administered with levofloxacin. Increased coagulation tests (PT/INR) and/or bleeding with levofloxacin and vitamin K antagonist combination (e.g. warfarin). Use with caution in patients receiving active substances known to prolong the QT interval (e.g. Class IA and III antiarrhythmics, tricyclic antidepressants, macrolides, antipsychotics). **Fertility, pregnancy and lactation:** No clinical data on fertility or lactation in humans, contraindicated in breast-feeding women. Contraindicated in pregnancy. **Effects on driving and operating machinery:** Minor influence on the ability to drive and use machines. Some adverse reactions (e.g. fatigue, asthenia, visual disturbances, and dizziness) may impair ability to concentrate and react, advice should be given not to drive or use machines if these symptoms occur. **Side effects:** *Very common*: anorexia*, dysgeusia, cough/productive cough, dyspnoea, changes in bronchial secretions*, haemoptysis*, fatigue/asthenia, exercise tolerance decreased, forced expiratory volume decreased*. *Common*: vulvovaginal mycotic infection, insomnia*, headache, dizziness*, tinnitus*, dysphonia, nausea, vomiting, abdominal pain*, diarrhoea*, constipation*, rash, arthralgia, myalgia*, pyrexia, ALT increased, AST increased, pulmonary function test decreased*, blood glucose increased and decreased*, blood creatinine increased*, breath sounds abnormal*. *Uncommon*: Oral fungal infection, anaemia*, neutropenia*, hypersensitivity*, anxiety*, depression*, hyposmia*, somnolence*, peripheral neuropathy, visual disturbance*, hearing loss*, tachycardia, bronchospasm, bronchial hyper-reactivity, obstructive airways disorder, retching, dyspepsia*, flatulence*, hepatitis*, hyperbilirubinaemia*, urticaria*, pruritus*, tendinitis, costochondritis, joint stiffness, renal failure*, liver function test abnormal, ALP increased*, ECG QT prolonged*, eosinophil count increased*, platelet count decreased*. (Refer to SPC for full list of side effects). *Adverse events with uncertain relatedness to Quinsair but which are known to be associated with systemic administration of levofloxacin and/or are plausibly associated with Quinsair and were reported more frequently than with placebo in clinical studies. **Legal category:** POM. **Price and pack:** £2,181.53 (56 amp per 28-day pack). **Marketing authorisation (MA) no:** EU/1/14/973/001. **UK Distributor:** Chiesi Limited, 333 Styal Road, Manchester, M22 5LG, United Kingdom**. Date of Preparation:** Nov 2020.

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 Chiesi Limited on 0800 0092329 or PV.UK@Chiesi.com.
▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Quinsair® ▼
levofloxacin nebuliser solution

Chiesi

Quinsair▼ Prescribing Information - Ireland

Quinsair ▼ 240 mg Nebuliser Solution Prescribing Information
Please refer to the Summary of Product Characteristics (SPC) before prescribing.

Presentation: Each mL of nebuliser solution contains levofloxacin hemihydrate equivalent to 100mg of levofloxacin. Each ampoule (amp) contains 240mg of levofloxacin. **Indication:** Management of chronic pulmonary infections due to *Pseudomonas aeruginosa* in adult patients with cystic fibrosis (CF). **Dosage and administration:** 240mg (one amp) by inhalation twice daily. Doses should be as close as possible to 12 hours apart. Alternating cycles of 28 days on then 28 days off treatment. Cyclical therapy may be continued as long as clinical benefit seen. Missed doses should be taken as soon as the patient remembers, providing there is at least an 8 hour interval before the next dose. The contents of more than one amp should not be inhaled to compensate for the missed dose. If acute symptomatic bronchospasm occurs, the use of a short-acting inhaled bronchodilator may be beneficial prior to subsequent doses. *Elderly (≥65 years) and Paediatric (<18 years)*: Safety and efficacy have not been established. *Renal impairment*: Not recommended in severe renal impairment. *Recommended treatment order if on multiple inhaled therapies*: 1. Bronchodilators, 2. dornase alfa, 3. airway clearance techniques, 4. Quinsair, 5. inhaled steroids. Quinsair should only be used with the Zirela® Nebuliser Handset (including a Zirela Aerosol Head) connected to an eBase Controller or an eFlow rapid Control Unit. Please review Zirela Nebuliser System Manufacturers Instructions prior to the first use. **Contraindications:** Hypersensitivity to active substance, other quinolones or any excipient; history of tendon disorders related to fluoroquinolone administration; epilepsy; pregnancy; breast-feeding. **Warnings and precautions:** Avoid in patients with history of serious adverse reactions when using quinolone/fluoroquinolones. Treatment should only be initiated in the absence of alternative treatment options and after a benefit/risk assessment. Serious, potentially fatal hypersensitivity reactions, severe bullous skin reactions and hepatobiliary disorders. Stop treatment if hepatic disease signs and symptoms develop, e.g. anorexia, jaundice, dark urine, pruritus or tender abdomen. Caution with known risk factors for prolongation of the QT interval, e.g. congenital long QT syndrome, uncorrected electrolyte imbalance, cardiac disease (e.g. heart failure, myocardial infarction and bradycardia) and concomitant use of QTc-prolonging drugs (e.g. Class IA and III antiarrhythmics, tricyclic antidepressants, macrolides, antipsychotics) particularly with the elderly and women. Predisposal to seizures: Quinolones may lower the seizure threshold and may trigger seizures. Use with extreme caution in patients predisposed to seizures or on concomitant treatment with active substances that lower the cerebral seizure threshold, e.g. theophylline. Psychotic reactions: Psychotic reactions reported. In very rare cases, these have progressed to suicidal thoughts and self-endangering behaviour, sometimes after a single dose. Caution in psychotic patients or a history of psychiatric disease. Peripheral neuropathy: Sensory/sensorimotor polyneuropathy have been reported. Patients should inform their doctor if pain, burning, tingling, numbness, or weakness develop to prevent the development of an irreversible condition. Exacerbation of myasthenia gravis: Not recommended in patients with history of myasthenia gravis as may exacerbate muscle weakness and cause the requirement for respiratory support or death. Tendinitis and tendon rupture: May occur as early as within 48 hours of starting treatment and up to several months after treatment discontinuation. Increased risk in older patients, renal impairment, solid organ transplants, patients receiving 1000mg daily, and those using corticosteroids. Avoid concomitant use of corticosteroids. If signs of tendinitis, discontinue levofloxacin treatment and consider alternative. Bronchospasm: Bronchospasm is associated with inhaled therapies. For acute symptomatic bronchospasm, use a short-acting bronchodilator prior to subsequent doses. Haemoptysis: May induce a cough reflex. Administration to patients with clinically significant haemoptysis should be undertaken only if the benefits outweigh the risks of inducing further haemorrhage. Glucose-6-phosphate dehydrogenase (G6PD) deficiency: If Quinsair has to be used in patients with latent or actual defects in G6PD activity, they should be monitored as they may be prone to haemolytic reactions. Vitamin K antagonists: Coagulation tests should be monitored due to possible increases (PT/INR) and/or bleeding in patients treated concomitantly with a vitamin K antagonist (e.g. warfarin). Dysglycaemia: Blood glucose monitoring recommended as disturbances in blood glucose (both hypo- and hyperglycaemia) have been reported, usually in patients with diabetes receiving concomitant treatment with an oral hypoglycaemic medicinal product(e.g. glibenclamide) or with insulin. *Clostridium difficile*-associated disease (CDAD): Diarrhoea, particularly if severe, persistent and/or bloody, during or after treatment (including several weeks. after treatment), may be symptomatic of CDAD. Can range in severity from mild to life-threatening, e.g. pseudomembranous colitis. Resistance to levofloxacin, other antibacterial medicinal products and treatment-emergent microorganisms: Potential risk of fluoroquinolone-resistant *P. aeruginosa* and superinfection with fluoroquinolone-insusceptible microorganisms. Vision disorders: Consult an eye specialist immediately if vision becomes impaired or any effects on the eyes are experienced. Prevention of photosensitisation: Photosensitisation has been reported. Patients should not expose themselves to strong sunlight or to artificial UV rays during treatment and for 48 hours following treatment discontinuation. Interference with laboratory tests: In patients treated with levofloxacin, determination of opiates in urine may give false-positive results. Levofloxacin may inhibit the growth of *Mycobacterium tuberculosis* and may give false-negative results in bacteriological diagnosis of tuberculosis. Aortic aneurysm and dissection and heart valve regurgitation/incompetence: Increased risk particularly in elderly, sometimes complicated by rapture (including fatal rapture): care should be taken in patients with positive family history of aneurysm disease, or congenital heart valve disease, or in patients diagnosed with pre-existing or predisposing conditions for aortic aneurysm and/or aortic dissection or heart valve regurgitation/incompetence (e.g. Marfan syndrome, Ehlers-Danlos syndrome, Turner syndrome, Behcet's disease, hypertension, rheumatoid arthritis, or aortic aneurysm and dissection (vascular disorders such as Takayasu arteritis or giant cell arteritis or known atherosclerosis or Sjögren's syndrome) or for heart valve regurgitation/incompetence (e.g. infective endocarditis)). Risk may also be increased in patients treated concurrently with systemic corticosteroids. In case of sudden abdominal, chest or back pain, acute dyspnoea, new onset of heart palpitations, or development of oedema of the abdomen or lower extremities, patients should be advised to immediately seek medical advice. Very rare cases of prolonged, disabling and potentially irreversible serious adverse drug reactions: Affecting body systems (musculoskeletal, nervous, psychiatric and senses) have been reported. Discontinue levofloxacin immediately at the first signs or symptoms and advise patients to contact their prescriber. **Interactions:** A pronounced lowering of the cerebral seizure threshold may occur when quinolones are given concurrently with theophylline, non-steroidal anti-inflammatory drugs, or other substances which lower the seizure threshold. The renal clearance of levofloxacin was reduced with probenecid and cimetidine. The half-life of ciclosporin was increased by 33% when co-administered with levofloxacin. Increased coagulation tests (PT/INR) and/or bleeding with levofloxacin and vitamin K antagonist combination (e.g. warfarin). Use with caution in patients receiving active substances known to prolong the QT interval (e.g. Class IA and III antiarrhythmics, tricyclic antidepressants, macrolides, antipsychotics). **Fertility, pregnancy and lactation:** No clinical data on fertility or lactation in humans, contraindicated in breast-feeding women. Contraindicated in pregnancy. **Effects on driving and operating machinery:** Minor influence on the ability to drive and use machines. Some adverse reactions (e.g. fatigue, asthenia, visual disturbances, and dizziness) may impair ability to concentrate and react, advice should be given not to drive or use machines if these symptoms occur. **Side effects:** *Very common*: anorexia*, dysgeusia, cough/productive cough, dyspnoea, changes in bronchial secretions*, haemoptysis*, fatigue/asthenia, exercise tolerance decreased, forced expiratory volume decreased*. *Common*: vulvovaginal mycotic infection, insomnia*, headache, dizziness*, tinnitus*, dysphonia, nausea, vomiting, abdominal pain*, diarrhoea*, constipation*, rash, arthralgia, myalgia*, pyrexia, ALT increased, AST increased, pulmonary function test decreased*, blood glucose increased and decreased*, blood creatinine increased*, breath sounds abnormal*. *Uncommon*: Oral fungal infection, anaemia*, neutropenia*, hypersensitivity*, anxiety*, depression*, hyposmia*, somnolence*, peripheral neuropathy, visual disturbance*, hearing loss*, tachycardia*, bronchospasm, bronchial hyper-reactivity, obstructive airways disorder, retching, dyspepsia*, flatulence*, hepatitis*, hyperbilirubinaemia*, urticaria*, pruritus*, tendinitis, costochondritis, joint stiffness, renal failure*, liver function test abnormal, ALP increased*, ECG QT prolonged*, eosinophil count increased*, platelet count decreased* (Refer to SPC for full list of side effects). *Adverse events with uncertain relatedness to Quinsair but which are known to be associated with systemic administration of levofloxacin and/or are plausibly associated with Quinsair and were reported more frequently than with placebo in clinical studies. Additional information is available on request. **Legal category:** POM. **Pack:** 56 amp per 28-day pack. **Marketing authorisation (MA) no:** EU/1/14/973/001. **Ireland Distributor:** Chiesi Limited, 333 Styal Road, Manchester, M22 5LG, United Kingdom**. Date of Preparation:** Nov 2020.

Adverse events should be reported to HPRA Pharmacovigilance, Website: www.hpra.ie Adverse events should also be reported to Chiesi Limited on 1800 817459 or PV.UK@Chiesi.com. ▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Quinsair® ▼
levofloxacin nebuliser solution

Chiesi

Bramitob Prescribing Information - UK

Bramitob® 300mg/4ml Nebuliser Solution Prescribing Information
Please refer to Summary of Product Characteristics (SPC) before prescribing.

Presentation: Each Bramitob 4ml single-dose container contains tobramycin 300mg. **Indication:** Management of chronic pulmonary infection due to *Pseudomonas aeruginosa* in patients with cystic fibrosis aged 6 years and older. **Dosage and administration:** For inhalation use only. Consideration should be given to official guidance on appropriate use of antibacterial agents. Therapy should be initiated by physicians experienced in management of cystic fibrosis. Recommended dose for adults and children above 6 years is one single-dose container (300mg) twice daily (morning and evening) for 28 days. Dose interval should be as close as possible to 12 hours. After 28 days of therapy, patients should stop treatment for next 28 days. Alternate cycles of 28 days of active therapy followed by 28 days without treatment should be maintained. The efficacy and safety of Bramitob have not been demonstrated in patients less than 6 years of age. Tobramycin should be used with caution in elderly patients who may have reduced renal function. Tobramycin should be used with caution in patients with known or suspected renal dysfunction. Bramitob should be discontinued in the case of nephrotoxicity until serum concentration of tobramycin fall below 2 mcg/ml. No changes in Bramitob dose are required in hepatic insufficiency. Dosage is not adjusted for body weight. All patients should be administered one single-dose container of Bramitob twice daily. The contents of one single-dose container (300mg) emptied into the nebuliser should be administered by inhalation over approximately 15 minutes using a PARI LC PLUS reusable nebuliser equipped with PARI TURBO BOY compressor or PARI LC SPRINT equipped with compressor PARI BOY Sx. Patients receiving different respiratory therapies, it is recommended that they are taken in the following order: bronchodilator, respiratory physiotherapy, other inhaled medicinal products, and finally Bramitob. Bramitob should not be mixed with other inhalation medicinal products. **Contraindications:** Hypersensitivity to tobramycin, any other aminoglycosides or any excipients. Contraindicated in patients receiving potent diuretics such as furosemide and ethacrynic acid which have proved to be ototoxic. **Warnings and precautions:** Use with caution in patients with known or suspected renal, auditory, vestibular or neuromuscular dysfunction, or with severe active haemoptysis. Renal and eighth cranial nerve function should be closely monitored in patients with known or suspected renal impairment. Bronchospasm in presence of bronchodilator therapy may indicate allergic reaction. The first dose of Bramitob should be given under medical supervision, using a pre-nebulisation bronchodilator if this is already part of the current treatment regimen for the patient. Use with great caution in patients with neuromuscular disorders including Parkinsonism and other conditions characterised by myasthenia. Monitor serum tobramycin concentrations in patients with known or suspected renal dysfunction after two to three doses to allow dose adjustment if necessary and also at three to four day intervals during therapy. Renal function should be assessed at baseline and thereafter periodically reassessed. If evidence of nephrotoxicity, therapy should be discontinued until drug minimum serum concentrations fall below 2mcg/ml. Monitor renal function in elderly patients and patients receiving parenteral aminoglycoside therapy. Patients should be monitored for ototoxicity throughout treatment period and have auditory function assessed. Use in patients with active, severe haemoptysis should only be undertaken if benefits outweigh risks. There is a theoretical risk that patients being treated with nebulised tobramycin may develop *P. aeruginosa* isolates resistant to intravenous tobramycin. **Interactions:** Concurrent and/or sequential use with other potentially nephrotoxic or ototoxic medicinal products should be avoided. Should not be administered concurrently with ethacrynic acid, furosemide, urea or intravenous and oral mannitol. **Fertility, pregnancy and lactation:** Not to be used during pregnancy or lactation unless benefits to the mother outweigh risks to the foetus or baby. If used during pregnancy, or if patient becomes pregnant during therapy, patient should be informed of potential hazard to the foetus. It is unknown whether inhaled tobramycin is detectable in breast milk. Due to potential risk for ototoxicity and nephrotoxicity with tobramycin in infants, decision should be made whether to terminate nursing or discontinue Bramitob. **Effects on driving and operating machinery:** On basis of reported adverse drug reactions, presumed to be unlikely to affect the ability to drive and use machinery. Nevertheless, patients should be alerted that dizziness and/or vertigo may occur. **Side effects:** *Common:* cough, dysphonia. Uncommon: fungal infection, oral candidiasis, headache, vertigo, hypoacusis, deafness neurosensory, forced expiratory volume decreased, dyspnoea, rales, haemoptysis, oropharyngeal pain, productive cough, salivary hypersecretion, glossitis, abdominal pain upper, nausea, rash, asthenia, chest discomfort, mucosal dryness, transaminases increased, pharyngitis. *Rare:* laryngitis, anorexia, dizziness, aphonia, tinnitus, hearing loss, bronchospasm, chest discomfort, lung disorder, epistaxis, rhinitis, asthma, dysgeusia, mouth ulceration, vomiting, rash, pyrexia, chest pain, pain, pulmonary function test decreased. *Very Rare:* lymphadenopathy, hypersensitivity, somnolence, ear disorders, ear pain, hyperventilation, hypoxia, sinusitis, diarrhoea, abdominal pain, urticaria, pruritis, back pain, malaise (Refer to SPC for full list of side effects). **Legal category:** POM. **Price and Pack:** £1187.00 (1 x 56 single dose containers.) **Marketing authorisation (MA) no:** PL 8829/0155. **MA holder:** Chiesi Limited, 333 Styal Road, Manchester, M22 5LG. **Date of Preparation:** April 2019

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 Chiesi Limited on 0800 0092329 or PV.UK@Chiesi.com.

BRAMITOB®
TOBRAMYCIN

Chiesi

BACK

Bramitob Prescribing Information - Ireland

Bramitob® 300mg/4ml Nebuliser Solution Prescribing Information
Please refer to Summary of Product Characteristics (SPC) before prescribing.

Presentation: Each Bramitob 4ml single-dose container contains tobramycin 300mg. **Indication:** Management of chronic pulmonary infection due to *Pseudomonas aeruginosa* in patients with cystic fibrosis aged 6 years and older. **Dosage and administration:** For inhalation use only. Consideration should be given to official guidance on appropriate use of antibacterial agents. Therapy should be initiated by physicians experienced in management of cystic fibrosis. Recommended dose for adults and children above 6 years is one single-dose container (300mg) twice daily (morning and evening) for 28 days. Dose interval should be as close as possible to 12 hours. After 28 days of therapy, patients should stop treatment for next 28 days. Alternate cycles of 28 days of active therapy followed by 28 days without treatment should be maintained. The efficacy and safety of Bramitob have not been demonstrated in patients less than 6 years of age. Tobramycin should be used with caution in elderly patients who may have reduced renal function. Tobramycin should be used with caution in patients with known or suspected renal dysfunction. Bramitob should be discontinued in the case of nephrotoxicity until serum concentration of tobramycin fall below 2 mcg/ml. No changes in Bramitob dose are required in hepatic insufficiency. Dosage is not adjusted for body weight. All patients should be administered one single-dose container of Bramitob twice daily. The contents of one single-dose container (300mg) emptied into the nebuliser should be administered by inhalation over approximately 15 minutes using a PARI LC PLUS reusable nebuliser equipped with PARI TURBO BOY compressor or PARI LC SPRINT equipped with compressor PARI BOY Sx. Patients receiving different respiratory therapies, it is recommended that they are taken in the following order: bronchodilator, respiratory physiotherapy, other inhaled medicinal products, and finally Bramitob. Bramitob should not be mixed with other inhalation medicinal products. **Contraindications:** Hypersensitivity to tobramycin, any other aminoglycosides or any excipients. Contraindicated in patients receiving potent diuretics such as furosemide and ethacrynic acid which have proved to be ototoxic. **Warnings and precautions:** Use with caution in patients with known or suspected renal, auditory, vestibular or neuromuscular dysfunction, or with severe active haemoptysis. Renal and eighth cranial nerve function should be closely monitored in patients with known or suspected renal impairment. Bronchospasm in presence of bronchodilator therapy may indicate allergic reaction. The first dose of Bramitob should be given under medical supervision, using a pre-nebulisation bronchodilator if this is already part of the current treatment regimen for the patient. Use with great caution in patients with neuromuscular disorders including Parkinsonism and other conditions characterised by myasthenia. Monitor serum tobramycin concentrations in patients with known or suspected renal dysfunction after two to three doses to allow dose adjustment if necessary and also at three to four day intervals during therapy. Renal function should be assessed at baseline and thereafter periodically reassessed. If evidence of nephrotoxicity, therapy should be discontinued until drug minimum serum concentrations fall below 2mcg/ml. Monitor renal function in elderly patients and patients receiving parenteral aminoglycoside therapy. Patients should be monitored for ototoxicity throughout treatment period and have auditory function assessed. Use in patients with active, severe haemoptysis should only be undertaken if benefits outweigh risks. There is a theoretical risk that patients being treated with nebulised tobramycin may develop *P. aeruginosa* isolates resistant to intravenous tobramycin. **Interactions:** Concurrent and/or sequential use with other potentially nephrotoxic or ototoxic medicinal products should be avoided. Should not be administered concurrently with ethacrynic acid, furosemide, urea or intravenous and oral mannitol. **Fertility, pregnancy and lactation:** Not to be used during pregnancy or lactation unless benefits to the mother outweigh risks to the foetus or baby. If used during pregnancy, or if patient becomes pregnant during therapy, patient should be informed of potential hazard to the foetus. It is unknown whether inhaled tobramycin is detectable in breast milk. Due to potential risk for ototoxicity and nephrotoxicity with tobramycin in infants, decision should be made whether to terminate nursing or discontinue Bramitob. **Effects on driving and operating machinery:** On basis of reported adverse drug reactions, presumed to be unlikely to affect the ability to drive and use machinery. Nevertheless, patients should be alerted that dizziness and/or vertigo may occur. **Side effects:** *Common:* cough, dysphonia. *Uncommon:* fungal infection, oral candidiasis, headache, vertigo, hypoacusis, deafness neurosensory, forced expiratory volume decreased, dyspnoea, rales, haemoptysis, oropharyngeal pain, productive cough, salivary hypersecretion, glossitis, abdominal pain upper, nausea, rash, asthenia, chest discomfort, mucosal dryness, transaminases increased, pharyngitis *Rare:* laryngitis, anorexia, dizziness, aphonia, tinnitus, hearing loss, bronchospasm, chest discomfort, lung disorder, epistaxis, rhinitis, asthma, dysgeusia, mouth ulceration, vomiting, rash, pyrexia, chest pain, pain, pulmonary function test decreased. *Very Rare:* lymphadenopathy, hypersensitivity, somnolence, ear disorders, ear pain, hyperventilation, hypoxia, sinusitis, diarrhoea, abdominal pain, urticaria, pruritis, back pain, malaise (Refer to SPC for full list of side effects). Additional information is available on request. **Legal category:** POM. Pack: 1 x 56 single dose containers. **Marketing authorisation (MA) No:** PA 743/17/1. **MA holder:** Chiesi Limited, 333 Styal Road, Manchester, M22 5LG. **Date of Preparation:** April 2019.

Adverse events should be reported to HPRA Pharmacovigilance, Earlsfort Terrace, IRL, Dublin 2, Tel: +353 1 6764971, Fax: +353 1 6762517, Website: www.hpra.ie, e-mail: medsafety@hpra.ie. Adverse events should also be reported to Chiesi Limited on 1800 817459 or PV.UK@Chiesi.com.

BRAMITOB®
TOBRAMYCIN

Chiesi

Bronchitol Prescribing Information - UK

Bronchitol® 40mg Capsules Prescribing Information
Please refer to the full Summary of Product Characteristics before prescribing.

Presentation: Each Bronchitol hard capsule contains 40mg of mannitol inhalation powder. Capsules presented in double aluminium blisters in cartons of 10 (initiation dose assessment) and 280 (treatment). **Indication:** Treatment of cystic fibrosis (CF) in adults ≥ 18 years as add-on therapy to best standard of care. **Dosage and administration:** Recommended dose 400mg twice a day (10 capsules via inhaler BD). Before commencing treatment, patients should be assessed for bronchial hyperresponsiveness to inhaled mannitol during their initiation dose (see sections 4.4 and 5.1 of the SPC). The patient must complete and pass the initiation dose assessment before starting treatment with Bronchitol. The initiation dose assessment involves the measurement of baseline FEV_1/SpO_2, administration of a bronchodilator, a 5-15 minute pause, administration of escalating doses of Bronchitol. All FEV_1 measurements and SpO_2 monitoring should be performed 60 seconds after each dose. Patients' FEV_1 should also be monitored 15 minutes post initiation dose (see section 4.2 of the SPC). A bronchodilator must be administered 5-15 minutes before each dose of Bronchitol. For patients receiving several respiratory therapies, the recommended order is: 1. Bronchodilator, 2. Bronchitol, 3. Physiotherapy/exercise, 4. Dornase alfa (if applicable), 5. Inhaled antibiotics (if applicable). Detailed instructions on how to use the inhaler can be found in the patient information leaflet**.** Patients should be advised to carefully read them. Bronchitol is for inhalation use. The capsules must not be swallowed. **Contraindications:** Hypersensitivity to the active substance. Bronchial hyperresponsiveness to inhaled mannitol. **Warnings and precautions:** Hyperresponsiveness to mannitol: Patients must be monitored for bronchial hyperresponsiveness to inhaled mannitol during their initiation dose assessment before commencing the therapeutic dose regimen of Bronchitol. If the patient is unable to perform spirometry or complete the initiation dose assessment, they must not be prescribed Bronchitol. Patients should be monitored until FEV_1 has returned to baseline levels. If a hyperresponsive reaction is suspected during treatment, Bronchitol should be discontinued. Bronchospasm: Bronchospasm can occur with inhalation of medicinal product and has been reported with Bronchitol in clinical studies, even in patients who were not hyperresponsive to the initiation dose of inhaled mannitol. Review patients at 6 weeks of treatment to assess for bronchospasm. Bronchospasm should be treated with a bronchodilator or as medically appropriate. Asthma: Monitor patients with co-existing asthma for worsening signs and symptoms. Advise patients to report worsening of asthma. Haemoptysis: Patients with a history of significant episodes of haemoptysis (>60ml) should be carefully monitored for haemoptysis and Bronchitol should be withheld in the event of massive haemoptysis. Cough: Train patient on inhaler technique. Advise patient to report persistent cough. Impaired Lung Function: Not recommended in patients with a FEV_1 of less than 30% of predicted. Non-CF Bronchiectasis: Not recommended. **Interactions:** No formal interaction studies. Bronchitol has been used in trials involving concomitant treatment with other drugs used routinely in CF. There are no data on concomitant use of hypertonic saline with Bronchitol as it was excluded from studies. **Fertility, pregnancy and lactation:** Limited data in pregnancy: avoid use if pregnant. No data on lactation: A decision whether to discontinue breast feeding or discontinue Bronchitol should be made. No clinical data on fertility effects. **Effects on driving and operating machinery:** No or negligible influence. **Side effects:** *Common:* headache, cough, haemoptysis, oropharyngeal pain, wheezing, post-tussive vomiting, vomiting, condition aggravated, chest discomfort. *Uncommon:* bacterial disease carrier, bronchitis, bronchopneumonia, lung infection, oral candidiasis, pharyngitis, Staphylococcal infection, upper respiratory tract infection, decreased appetite, CF related diabetes, dehydration, initial insomnia, morbid thoughts, dizziness, ear pain, productive cough, throat irritation, asthma, bronchospasm, forced expiratory volume decreased, rhinorrhoea, dyspnoea, dysphonia, hyperventilation, obstructive airways disorder, respiratory tract congestion, sputum discoloured, hypoxia, nausea, diarrhoea, eructation, flatulence, gastrooesophageal reflux disease, glossodynia, retching, stomatitis, abdominal pain upper, aphthous stomatitis, odynophagia, acne, cold sweat, pruritus, rash, rash pruritic, musculoskeletal chest pain, arthralgia, back pain, joint stiffness, musculoskeletal pain, urinary incontinence, pyrexia, fatigue, influenza like illness, hernia pain, malaise, chest pain, blood alkaline phosphatase increased, bacteria or fungus sputum test positive. (Refer to SPC for full list of side effects). **Legal category:** POM. **Price and Pack:** £8.27 (10 capsules + 1 inhaler) £231.66 (280 capsules + 2 inhalers). **Marketing authorisation (MA) No:** EU/1/12/760/001-002. **MA holder:** Pharmaxis Europe Limited, 108 Q House, Furze Road, Sandyford, Dublin 18, D18 AY29, Ireland. **UK Distributor:** Chiesi Limited, 333 Styal Road, Manchester, M22 5LG, United Kingdom. **Date of Preparation:** March 2019.

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 Chiesi Limited on 0800 0092329 (UK) or PV.UK@Chiesi.com.

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Bronchitol Prescribing Information - Ireland

Bronchitol® 40mg Capsules Prescribing Information
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