ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼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. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Brinsupri 25 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 25 mg of brensocatib (as monohydrate).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet (tablet)
Grey, approximately 9 mm diameter round tablet debossed with “25” on one side and “BRE” on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Brinsupri is indicated for the treatment of non-cystic fibrosis bronchiectasis (NCFB) in patients 12 years of age and older with two or more exacerbations in the prior 12 months.

4.2 Posology and method of administration

Posology

The recommended dose is 25 mg orally once daily with or without food.

Missed dose
Patients who miss a dose should take the next dose at their regular time the next day. Patients should not double the dose to make up for the missed dose.

Special populations

Elderly
No dose adjustment is required for elderly patients (see section 5.2).

Renal and hepatic impairment
No dose adjustment is required for patients with renal or hepatic impairment (see section 5.2).

Paediatric population
The safety and efficacy of Brinsupri in children younger than 12 years of age have not yet been established. No data are available.

Method of administration

For oral use.

This medicinal product should be taken once daily with or without food.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Fungal infections

In clinical studies, fungal infections, mainly candida-related, indicative of immunosuppression (i.e., oral candidiasis, oesophageal candidiasis, oropharyngeal candidiasis, fungal bronchitis) and isolated cases of Aspergillus infections, were more frequent with brensocatib 25 mg (1.5%) compared to placebo (1.1%).

Immunocompromised patients

The safety of brensocatib has not been established in immunocompromised patients. Caution is advised when using brensocatib in patients with moderate to severe neutropenia (absolute neutrophil count [ANC] < 1,000/mm^3).

Vaccinations

The concomitant use of brensocatib and live attenuated vaccines has not been evaluated. The use of live attenuated vaccines should be avoided in patients receiving brensocatib.

Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

In vitro studies are inconclusive regarding the potential of brensocatib to induce CYP2B6 and CYP3A4 (see section 5.2). *In vivo* induction cannot be excluded. Co-administration with CYP3A4 substrates used in bronchiectasis (e.g. inhaled corticosteroids, macrolide antibiotics or inhaled bronchodilators such as salmeterol or vilanterol) may result in decreased plasma concentrations and reduced therapeutic effect. Adjustment of the concomitant treatment may be considered if efficacy is reduced.

Paediatric population

Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data on the use of brensocatib in pregnant women. Animal studies have shown reproductive toxicity (see section 5.3).

Brinsupri is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breast-feeding

It is unknown whether brensocatib or its metabolites are excreted in human milk. Available data in animals have suggested excretion of brensocatib in milk (see section 5.3).

A risk to the newborns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from brensocatib therapy, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

There are no fertility data in humans. Animal studies indicate no impact on male or female fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Brinsupri has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse reactions are headache (9.2%), hyperkeratosis (5.9%), dermatitis (4.2%), rash (4.1%), upper respiratory tract infections (3.9%), and dry skin (3.0%).

Tabulated list of adverse reactions

The safety of brensocatib was evaluated on the pooled safety population from two placebo-controlled clinical trials, ASPEN and WILLOW, which consisted of 1 326 adult and 41 adolescent patients 12 years of age and older with NCFB who received at least one dose of brensocatib for up to 52 weeks.

The frequency of adverse reactions is defined using the following convention: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1 000 to < 1/100), rare (≥ 1/10 000 to < 1/1 000), very rare (< 1/10 000), not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1: Adverse reactions

System organ class	Frequency	Adverse reaction
Infections and infestations	Common	Upper respiratory tract infection Gastroenteritis
Nervous system disorders	Common	Headache
Gastrointestinal disorders	Common	Gingival disorder Periodontal disease
Skin and subcutaneous tissue disorders	Common	Hyperkeratosis* Rash Dry skin Dermatitis Skin exfoliation Alopecia

* See ‘Description of selected adverse reactions’ below.

Description of selected adverse reactions

Hyperkeratosis
In the pooled safety population, hyperkeratosis (including skin lesion, keratosis pilaris, exfoliative rash and seborrheic keratosis) was reported more frequently with brensocatib 25 mg than placebo (5.9% vs 3.1%). All events were of mild or moderate severity.

Paediatric population

The safety assessment in adolescents aged 12 to 17 with NCFB is based on 41 subjects exposed to brensocatib in the 52-week Phase 3 ASPEN trial (see section 5.1). The safety profile in these adolescents was similar to that observed in adults.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Doses of up to 120 mg, given as a single dose, did not have evidence of dose-related toxicities.

There is no specific treatment for an overdose with brensocatib. If an overdose occurs, the patient should be treated supportively with appropriate monitoring as necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: not yet assigned, ATC code: not yet assigned

Mechanism of action

Brensocatib is a competitive and reversible inhibitor of dipeptidyl peptidase 1 (DPP1). DPP1 activates pro-inflammatory neutrophil serine proteases (NSPs) during neutrophil maturation in the bone marrow. Brensocatib reduces the activity of NSPs implicated in the pathogenesis of bronchiectasis, including neutrophil elastase, cathepsin G and proteinase 3.

Pharmacodynamic effects

At 5 times the maximum recommended daily dose of brensocatib, there was no effect on QTc prolongation.

Clinical efficacy

The efficacy of brensocatib was assessed in a Phase 3, randomised, double-blind, placebo-controlled, parallel-group, multicentre, multinational trial (ASPEN) with a total of 1 721 patients 12 years of age and older with NCFB (1 680 adults and 41 adolescents).

All patients were randomised to one of two doses of brensocatib (25 mg: n = 575; 10 mg: n = 583) or placebo (n = 563), administered once daily for 52 weeks.

All adult patients enrolled had a history of confirmed NCFB by chest computed tomography with at least 2 documented pulmonary exacerbations prior screening in the past 12 months. Adolescent

patients had at least one pulmonary exacerbation in the prior 12 months. A qualifying exacerbation was defined by the need for a physician-prescribed course of systemic antibiotics for signs and symptoms of respiratory infection.

Demographics and baseline characteristics of ASPEN are provided in Table 2.

Table 2: Demographics and baseline characteristics of patients in ASPEN

	ASPEN (N = 1 721)
Age (years), mean (SD)	60 (16)
Female n (%)	1 107 (64)
White n (%)	1 266 (74)
Black or African American n (%)	10 (1)
Asian n (%)	191 (11)
Hispanic or Latino n (%)	511 (30)
≥ 3 PEx in prior 12 months n (%)	502 (29)
Former smoker n (%)	510 (30)
ppFEV_1 post-bronchodilator, mean (SD)	74 (23)
Sputum positive for *Pseudomonas aeruginosa* n (%)	607 (35)
Chronic macrolide therapy n (%)	329 (19)

N = number of patients in the intent-to-treat analysis set; n = number of patients; PEx = pulmonary exacerbations; pp = percent predicted; FEV_1 = forced expiratory volume in 1 second; SD = standard deviation

Exacerbations
The primary efficacy endpoint in ASPEN was the annualised rate of pulmonary exacerbations (PEx) over the 52-week treatment period.

Pulmonary exacerbations were defined as worsening of 3 or more major symptoms over 48 hours with increase in cough, sputum volume, sputum purulence or increased breathlessness or decreased exercise tolerance and fatigue and/or malaise and, haemoptysis, resulting in a healthcare provider's decision to prescribe systemic antibiotics. Pulmonary exacerbations were considered as severe if requiring treatment with intravenous antibiotics and/or resulted in hospitalisation.

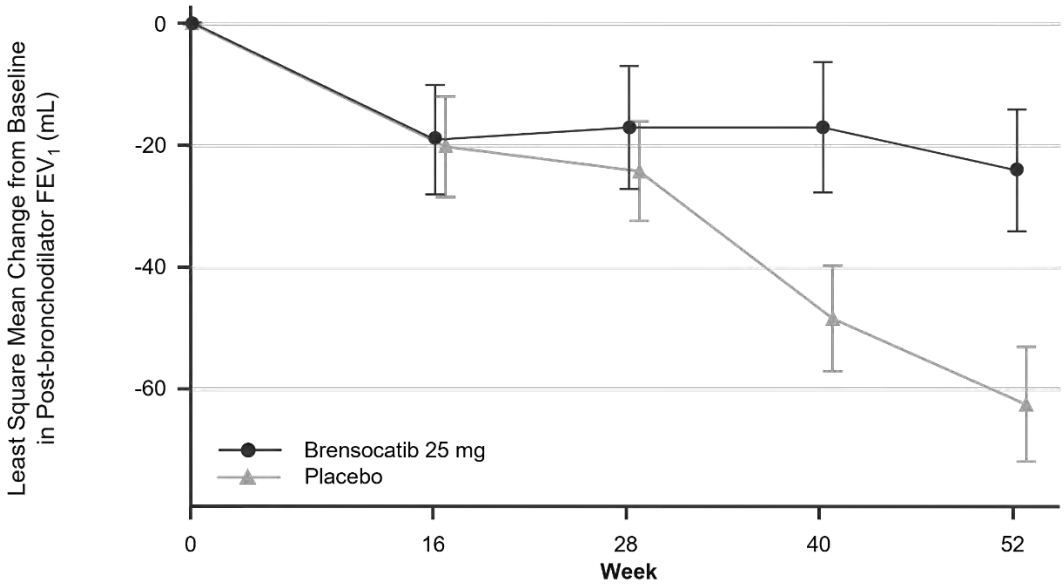
In ASPEN, treatment with 25 mg of brensocatib in patients with NCFB demonstrated significant reductions in the annualised rate of pulmonary exacerbations compared with placebo. Key results are shown in Table 3.

Table 3: Exacerbations endpoints over 52 weeks in ASPEN

	Brensocatib 25 mg (N = 575)	**Placebo (N = 563)**	
Annualised rate of PEx	1.04	1.29	Rate ratio (95% CI): 0.81 (0.69, 0.94)
Median time to first PEx (weeks)	50.71	36.71	Hazard ratio (95% CI): 0.83 (0.70, 0.97)
Proportion of patients that were exacerbation free at week 52 (%)	48.5	40.3	Odds ratio (95% CI): 1.40 (1.10, 1.79)

Lung function
Change from baseline in post-bronchodilator FEV_1 was assessed as a secondary endpoint. A dose of brensocatib 25 mg significantly reduced FEV_1 decline in comparison to placebo at week 52 (Least Squares mean difference 38; 95% CI: 11, 65) (Figure 1).

Figure 1: LS mean change (SE) from baseline in post-bronchodilator FEV_1 (mL) over time



Paediatric population (adolescents)

In the pivotal 52-week study, 41 adolescents (12 to < 18 years) were randomised to brensocatib 25 mg once daily, brensocatib 10 mg once daily or placebo. The adolescent subgroup was small and the study was not powered for efficacy in adolescents; confidence intervals were wide and results are inconclusive. Trends towards fewer pulmonary exacerbations and positive changes in post-bronchodilator FEV_1 were observed with 25 mg brensocatib versus placebo. Safety and pharmacokinetic data in adolescents were generally consistent with adults (see sections 4.8 and 5.2).

The European Medicines Agency has deferred the obligation to submit the results of studies with Brinsupri in one or more subsets of the paediatric population in NCFB (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

The absolute oral bioavailability of brensocatib has not been studied in humans. Brensocatib is rapidly absorbed after oral administration. T_{max} for tablets is approximately 1 hour in patients. Brensocatib oral absorption is not affected by food intake. Co-administration with a high fat meal delayed the time to reach peak concentration by 0.75 hours, however, the extent of brensocatib absorption remained the same.

Distribution

After oral administration, the volume of distribution at steady state was 126-138 L (CV: 22.4-23.3%) in adult patients and 71.3-83.6 L (CV: 19.9-26.3%) in adolescents with NCFB. The protein binding of brensocatib to human plasma was 82.2%-87.2%.

Biotransformation

Brensocatib undergoes metabolism primarily by CYP3A. Brensocatib accounted for 16.2% of the total radioactivity in plasma. Only one major circulating metabolite, thiocyanate, was detected in plasma. Thiocyanate is an endogenous compound, and clinical data showed that thiocyanate plasma concentrations were not affected and remained in the normal range on brensocatib treatment.

Interactions

In vitro studies

CYP450 enzymes
Brensocatib is a substrate of CYP3A.
Brensocatib does not inhibit CYP1A2, CYP2C8, CYP2C9, CYP2C19, or CYP2D6. *In vitro* studies are inconclusive regarding the potential of brensocatib to induce CYP2B6 and CYP3A4. *In vivo* induction cannot be excluded.

Transporter systems
Brensocatib is a substrate of P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP).
Brensocatib is not a substrate of MATE1, MATE2-K, OAT1, OAT3, OATP1B1, OATP1B3, OCT1 and OCT2.
Brensocatib is not an inhibitor of P-gp, BCRP, OATP1B1, OATP1B3, OAT1, OAT3, OCT2, MATE1, and MATE2-K.

Effect of brensocatib on other medicinal products
In vitro data and population pharmacokinetic analyses indicate that brensocatib is unlikely to inhibit or significantly induce the activity of CYP isozymes or drug transporters at clinically relevant dose levels. However, *in vitro* studies were inconclusive regarding the potential of brensocatib to induce CYP2B6 and CYP3A4, and *in vivo* induction cannot be excluded.

Effect of other medicinal products on brensocatib
Brensocatib AUC and C_{max} increased by 55% and 68% with a strong CYP3A inhibitor (e.g. clarithromycin) and by 32% and 53% with a strong P-gp inhibitor (e.g. verapamil) but decreased by 33% and 15% with a strong CYP3A inducer (e.g. rifampicin). C_{max} and AUC remained unchanged with a potent proton-pump inhibitor (e.g. esomeprazole). The interaction effect on brensocatib systemic exposure is not clinically meaningful.

Elimination

Following a single oral dose of radiolabelled brensocatib, 54.2% of dose was excreted in urine and 28.3% in faeces with most radioactivity excreted within 72 hours. The unchanged brensocatib in urine and faeces were 22.8% and 2.41% of dose, respectively.

Terminal half-life was 32.6-39.6 hours (CV: 26.6-33.0%) in adult patients and 26.9-27.8 hours (CV: 26.8-37.3%) in adolescent patients.

Linearity/non-linearity

Brensocatib exhibits linear and time-independent pharmacokinetics with low to moderate intra- and inter-subject variability over a dose range of 5-120 mg following single administration and a dose range of 10-40 mg following once-daily administration. Population pharmacokinetics analysis using pooled data from 11 clinical studies in healthy subjects (n = 291) and patients with NCFB (n = 783) showed that brensocatib pharmacokinetics can be adequately described by a 2-disposition compartments with first-order oral absorption.

Pharmacokinetic/pharmacodynamic relationships

Exposure-response relationships were observed between brensocatib exposure (AUC) and clinical efficacy (i.e. decline of lung function measured as FEV_1). At 25 mg, > 99% NCFB patients in the ASPEN trial achieved an AUC threshold that was associated with clinically meaningful improvement in FEV_1. No exposure-response relationships were detected for the occurrence of periodontal disease or pneumonia. A relationship between brensocatib exposure (AUC) and hyperkeratosis (mild and

moderate) was observed. However, the predicted probability of mild or moderate hyperkeratosis was low at brensocatib 25 mg (3.01% in adults and 3.36% in adolescents).

Special populations

Population pharmacokinetic analysis showed no evidence of a clinically significant effect of age (range: 12 to 85 years), sex, race/ethnicity or body weight (range: 32 to 155 kg) on the pharmacokinetics of brensocatib.

Paediatric population
Based on the population pharmacokinetic analysis, there was no clinically meaningful age-related difference in the pharmacokinetics of brensocatib between adults and adolescents aged 12 to 17 years. Brensocatib has not been studied in children under 12 years of age (see section 4.2).

Hepatic impairment
In subjects with mild, moderate or severe hepatic impairment (Child-Pugh scores 5 to 12), brensocatib clearance following a single dose was comparable to that in healthy subjects. No dose adjustments are recommended for patients with mild, moderate or severe hepatic impairment (see section 4.2).

Renal impairment
In subjects with mild, moderate or severe renal impairment, (creatinine clearance $\geq$ 15 mL/min/1.73 m^2 and not requiring dialysis), brensocatib clearance following a single dose was comparable to that in healthy subjects. No dose adjustments are recommended for patients with mild, moderate or severe renal impairment (see section 4.2).

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, genotoxicity and carcinogenic potential. Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

General toxicity

In a 6-month rat study microscopic changes in the kidney (basophilic tubules in the outer medulla) and the lung (perivascular neutrophil infiltration and vacuolated macrophage accumulation consistent with phospholipids) were observed at 50 mg/kg/day. The no-observed-adverse-effect-level was considered to be 9 mg/kg/day (AUC 20 times the maximum recommended human dose [MRHD]).

In a 9-month dog study no adverse findings were observed at any dose (AUC 5 times the MRHD). In a preceding 6-month dog study, administration of brensocatib at 50 mg/kg/day caused periodontal disease resulting in early termination of the group. At $\geq$ 8 mg/kg/day, dose-dependent microscopic findings were noted in the testis (seminiferous tubule degeneration and atrophy), in the epididymis (decreased number of spermatozoa and cellular debris), and in the lung (accumulations of vacuolated macrophages consistent with phospholipids). At 50 mg/kg/day, additional microscopic findings were noted in the kidney (tubular regeneration) and in the lymphoid tissues (axillary, mandibular and mesenteric lymph nodes, gut associated lymphoid tissue and spleen) as indicated by the accumulations of vacuolated macrophages.

Reproductive and developmental toxicity

In a rat fertility and embryo-foetal development study, following treatment with brensocatib from 2 weeks prior to mating, during mating and up to the end of major embryonic organogenesis, recoverable minor malformations of bent scapula and wavy ribs were noted at plasma exposure (AUC) 128-times the human exposure at the MRHD. There was an increased incidence of skeletal variations (malpositioned pelvic girdle and vestigial supernumerary full and/or short ribs in both cervical and thoracolumbar regions) and differences in ossification at AUC $\geq$ 42-times the human exposure at the

MRHD. The no effect dose for developmental toxicity was at AUC of 3-times the human exposure at the MRHD. In a rabbit embryo-foetal development study, treatment with brensocatib during implantation and major organogenesis induced maternal toxicity (reductions in body weight gain and food consumption) at AUC ≥ 5-times the human exposure at the MRHD. There were no adverse developmental effects at AUC 20-times the human exposure at the MRHD.

In a pre- and post-natal development study in rats treated from gestation day 6 through lactation day 20, no adverse findings were observed at any dose (up to AUC 17-times the human exposure at the MRHD). Brensocatib was detected in pups, suggesting that male and female pups were likely exposed via maternal milk during lactation.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Cellulose, microcrystalline
Calcium hydrogen phosphate dihydrate
Sodium starch glycolate
Silica, colloidal hydrated
Glycerol dibehenate

Film-coating

Poly(vinyl alcohol)
Titanium dioxide (E 171)
Macrogol 4000 (MW 3350)
Talc
Black iron oxide (E 172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

18 months

6.4 Special precautions for storage

Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

PVC/PCTFE aluminium foil blister card containing 14 film-coated tablets.
Pack size of 28 tablets (2 blister cards of 14 tablets each) in a carton.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Insmed Netherlands B.V.
Stadsplateau 7
3521 AZ Utrecht
Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1995/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Patheon France
40 Boulevard De Champaret
38300 Bourgoin Jallieu
France

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

- **Obligation to conduct post-authorisation measures**

The MAH shall complete, within the stated timeframe, the below measures:

Description	**Due date**
Non-interventional post-authorisation safety study (PASS): Evaluation of the long-term safety in patients treated with Brinsupri in the real world setting.	Q4 2034

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON – 28 TABLETS (2 BLISTERS OF 14 TABLETS)

1. NAME OF THE MEDICINAL PRODUCT

Brinsupri 25 mg film-coated tablets
brensocatib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 25 mg of brensocatib (as monohydrate).

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

28 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Insmed Netherlands B.V.
Stadsplateau 7
3521 AZ Utrecht
Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1995/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Brinsupri

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER OF 14 TABLETS

1. NAME OF THE MEDICINAL PRODUCT

Brinsupri 25 mg tablets
brensocatib

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Insmed Netherlands B.V.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Brinsupri 25 mg film-coated tablets
brensocatib

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Brinsupri is and what it is used for

What Brinsupri is
Brinsupri contains the active substance brensocatib, which belongs to the class of medicines called dipeptidyl peptidase 1 (DPP1) inhibitors.

What Brinsupri is used for
Brinsupri is used to treat patients 12 years and older with non-cystic fibrosis bronchiectasis (NCFB) who have experienced two or more flare-ups or worsening of symptoms (also known as exacerbations) in the past 12 months. NCFB is a long-term (chronic) condition where the airways of the lungs are damaged, causing a cough with mucus production.

How Brinsupri works
Brinsupri targets a protein called DPP1, which is involved in the process that causes inflammation in the lungs. By blocking the activity of this protein, the medicine prevents flare-ups in the lungs and may improve some symptoms of NCFB.

2. What you need to know before you take Brinsupri

Do not take Brinsupri if you are allergic to brensocatib or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or pharmacist before taking Brinsupri if you have recently had or plan to have a vaccination.

Children and adolescents
Do not give this medicine to children under 12 years of age because its safety and benefits are not known in children in this age group.

Other medicines and Brinsupri
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.
It is not known if Brinsupri can harm your unborn baby. If you are pregnant, you should not take Brinsupri. If you can become pregnant, you should use adequate contraception during treatment with Brinsupri.
There is not enough information to say whether the medicine passes into human breast milk. A decision must be made whether to stop breast-feeding or to stop using Brinsupri, based on the benefit of breast-feeding for the child and the benefit of treatment for the mother. Your doctor will discuss this with you.

Driving and using machines
Brinsupri is unlikely to affect your ability to drive and use machines.

Brinsupri contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. How to take Brinsupri

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose for adults and adolescents aged 12 years and older is one 25 mg tablet taken by mouth once daily with or without food.

If you take more Brinsupri than you should
If you take more Brinsupri than you should, seek urgent medical attention, taking the medicine packaging with you.

If you forget to take Brinsupri
Take your next dose at the usual time the next day. Do not take a double dose to make up for a forgotten tablet.

If you stop taking Brinsupri
You should not stop taking Brinsupri without discussing this with your doctor.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Common (may affect up to 1 in 10 people)
- nose and throat infection (upper respiratory tract infection)
- diarrhoea and vomiting (gastroenteritis)
- headache

- problems affecting the gums, including red, swollen and bleeding gums (gingival disorder)
- inflammation and infection of the gum and bone surrounding the teeth (periodontal disease)
- small areas of skin thickening (hyperkeratosis)
- rash
- dry skin
- inflammation of the skin (dermatitis)
- shedding dead cells from the skin's outer layer (skin exfoliation)
- hair loss (alopecia).

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Brinsupri

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton after 'EXP'. The expiry date refers to the last day of that month.

Store in the original package in order to protect from moisture.

Do not use this medicine if you notice the tablets are damaged or if there are signs of tampering with the medicine packaging.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Brinsupri contains
- The active substance is brensocatib. Each film-coated tablet contains 25 mg of brensocatib (as monohydrate).
- The other ingredients are:
  Tablet core: cellulose, microcrystalline; calcium hydrogen phosphate dihydrate; sodium starch glycolate; silica, colloidal hydrated and glycerol dibehenate. See section 2 'Brinsupri contains sodium' for further information.
  Film-coating: poly(vinyl alcohol); titanium dioxide (E 171); macrogol 4000 (MW 3350); talc and black iron oxide (E 172).

What Brinsupri looks like and contents of the pack
Brinsupri 25 mg film-coated tablets (tablets) are round, grey tablets approximately 9 mm in diameter, with "25" on one side and "BRE" on the other side.

The film-coated tablets are provided in aluminium foil blister cards containing 14 film-coated tablets. Each pack contains 28 film-coated tablets.

Marketing Authorisation Holder
Insmed Netherlands B.V.
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3521 AZ Utrecht
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Manufacturer
Patheon France
40 Boulevard De Champaret
38300 Bourgoin Jallieu
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This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.