

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

GRANUPAS 4 g gastro-resistant granules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains 4 g of para-aminosalicylic acid.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gastro-resistant granules

The granules are small off white/ light brown coloured approximately 1.5mm diameter.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

GRANUPAS is indicated for use as part of an appropriate combination regimen for multi-drug resistant tuberculosis in adults and paediatric patients from 28 days of age and older when an effective treatment regimen cannot otherwise be composed for reasons of resistance or tolerability (see section 4.4).

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Posology

Adults

4 g (one sachet) three times per day.

The recommended schedule is 4 g every 8 hours. GRANUPAS can be taken with food.

Maximum daily dose is 12 g. Usual duration of treatment is 24 months.

Paediatric population

The optimal dose regimen in children is uncertain. Limited pharmacokinetic data suggest no substantial difference between adults and children.

For infants, children and adolescents the dosage will be adapted to the patient's weight at 150 mg/kg per day, divided in two intakes. A dosing spoon is provided to measure small doses below 4g for young children.

The safety and efficacy of GRANUPAS in neonates have not been established.No data are available.

Desensitization

Desensitization can be accomplished by starting with 10 mg para-aminosalicylic acid given as a single dose. The dosage is doubled every 2 days until reaching a total of 1 gram after which the dosage is divided to follow the regular schedule of administration. If a mild temperature rise or skin reaction develops, the increment is to be dropped back one level or the progression held for one cycle. Reactions are rare after a total dosage of 1.5 g.

Method of administration

Oral use.

The contents of the sachet should be added to a glass of orange or tomato juice. They will not dissolve, but swirling the juice in the glass will help re-suspend the granules if they sink. It should be drunk at once ensuring that the granules are not left in the glass. Any granules left-over at the bottom of the glass should be swallowed immediately by adding a small quantity of liquid. Smaller doses in children should be measured using the dosing spoon and given by sprinkling on apple sauce or yogurt.

The medicinal product should be swallowed immediately after mixing with orange juice, tomato juice, apple sauce and yogurt whilst the granules are intact.

The granules should not be crushed or chewed.

4.3 Contraindications

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

Severe renal disease. Patients with severe renal impairment should not receive GRANUPAS. Patients with severe renal disease will accumulate the inactive acetyl metabolite of para-aminosalicylic acid.

4.4 Special warnings and precautions for use

Mild to moderate renal impairment

Given that the metabolites of para-aminosalicylic acid are largely excreted via glomerular filtration, caution is warranted in patients with mild to moderate renal impairment (see also section 4.3).

Gastric ulcer

GRANUPAS should be used with caution in patients with peptic ulcer.

Hepatic impairment

GRANUPAS should be used with caution in patients with hepatic impairment.

Hepatic toxicity

Para-aminosalicylic acid may cause hepatitis. The first symptoms usually appear within three months of the start of therapy with a rash as the most common adverse reaction followed by fever and much less frequently by gastrointestinal disturbances of anorexia, nausea or diarrhoea. Treatment should be stopped immediately in this case.

Hypersensitivity

The patient must be monitored carefully during the first three months of therapy and treatment must be discontinued immediately at the first sign of a rash, fever or other premonitory signs of intolerance. See section 4.2 for posology adjustments for desensitization.

Patients should be advised that the skeletons of the granules may be seen in the stools.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed with GRANUPAS.

Results from literature suggest the following:

Vitamin B12

Vitamin B12 absorption may be reduced by para-aminosalicylic acid with clinically significant erythrocyte abnormalities developing after depletion; patients on therapy of more than one month should be considered for maintenance of vitamin B12.

Malabsorption syndrome

A malabsorption syndrome can develop in patients on para-aminosalicylic acid, but is usually not complete. The complete syndrome includes steatorrhoea, an abnormal small bowel pattern on x-ray, villus atrophy, depressed cholesterol, reduced D-xylose and iron absorption. Triglyceride absorption is always normal.

Digoxin

Para-aminosalicylic acid may decrease the gastrointestinal absorption of digoxin, by inhibiting the absorption function of intestinal cells. Serum digoxin levels should be monitored in patients on concomitant therapy.

Ethionamide

Co-administration of para-aminosalicylic acid and ethionamide may intensify adverse reactions of para-aminosalicylic acid, mainly the gastrointestinal effects, including jaundice, hepatitis, nausea, vomiting, diarrhoea, abdominal pain or anorexia. Ethionamide should be withdrawn if these effects are significant.

Diphenylhydramine

This medicinal product decreases the gastrointestinal absorption of para-aminosalicylic acid, and should not be administered concomitantly.

Antiretrovirals

No drug interaction studies have been conducted in patients with HIV infection taking antiretroviral agents and para-aminosalicylic acid. Given the metabolic pathway of GRANUPAS no significant drug interaction is anticipated.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited data from the use of para-aminosalicylic acid in pregnant women. Studies in animals have shown some embryologic toxicity (see section 5.3).

Literature reports on para-aminosalicylic acid in pregnant women always report co-administration of other medicinal products. As there are no adequate and well controlled studies of para-aminosalicylic acid in humans, GRANUPAS should be given to a pregnant woman only if clearly needed.

Breastfeeding

Para-aminosalicylic acid is excreted into breast milk, therefore breastfeeding mothers should not breastfeed during treatment.

Fertility

There is no evidence available on the effect of para-aminosalicylic acid on fertility.

4.7 Effects on ability to drive and use machines

Para-aminosalicylic acid has negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

Most frequent adverse reactions were related to the gastrointestinal system. Cutaneous hypersensitivity reactions were also frequent as well as adverse reactions related to the nervous system.

Tabulated list of adverse reactions

In the table below all adverse reactions are listed by system organ class and by frequency. Frequency is defined as very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ 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.

System Organ Class	Frequency	Adverse reaction
<i>Blood and lymphatic system disorders</i>	Very rare	Thrombocytopenia, purpura, leukopenia, anemia, methemoglobinemia, agranulocytosis
<i>Metabolism and nutrition disorders</i>	Rare	hypothyroidism
	Very rare	Hypoglycemia
<i>Nervous system disorders</i>	Very rare	Tendon pain, headache, visual abnormalities, peripheral neuropathy, dizziness
	Common	Giddiness, vestibular syndrome
<i>Gastrointestinal disorders</i>	Common	abdominal pain, vomiting, nausea, bloating, diarrhea, soft stools,
	Uncommon	anorexia,
	Rare	Malabsorption syndrome, peptic ulcer, gastrointestinal bleeding, jaundice, metallic taste
<i>Skin and subcutaneous tissue disorders</i>	Common	Cutaneous hypersensitivity, skin rash
	Rare	urticaria
<i>Renal and urinary disorders</i>	Very rare	crystalluria
<i>Investigations</i>	Very rare	Decreased prothrombine level, hepatocytolysis. Increased blood alkaline phosphatase, transaminases. weight loss

Paediatric population

Frequency, type and severity of adverse reactions in children are expected to be the same as 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

No case of overdose in adults or paediatrics has been reported. Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antimycobacterials, drugs for treatment of tuberculosis ATC code: J04AA01

Mechanism of action

Aminosalicic acid is bacteriostatic against *Mycobacterium tuberculosis*. It inhibits the onset of bacterial resistance to streptomycin and isoniazid.

The mechanism of action of para-aminosalicylic acid resembles the sulfonamides, competing with paraminobenzoic acid (PABA) for dihydropteroate synthetase (DHP), a key enzyme in the biosynthesis of folates. However, para-aminosalicylic acid appears to be a weak inhibitor of DHP in

vitro, raising the possibility that it may have a different target. Para-aminosalicylic acid is acetylated in the liver and converted into the inactive metabolite, N-acetyl-para-aminosalicylic acid which is devoid of bacteriostatic activity. The plasma half-life of this agent is about 1 hour, the concentration is not substantially altered in hepatic dysfunction. The concentration of the metabolite may be increased in cases of renal failure.

5.2 Pharmacokinetic properties

Absorption

GRANUPAS is a gastro-resistant preparation and, therefore, the acid-resistant coating of the granules protects against degradation in the stomach therefore preventing the formation of meta-aminophenol (a known hepatotoxin). The small granules are designed to escape the restriction on gastric emptying of large particles. Under neutral conditions as are found in the small intestine or in neutral foods, the acid-resistant coating is dissolved within one minute.

Care must be taken in the administration of these granules to protect the acid-resistant coating by maintaining the granules in an acidic food during dosage administration.

Because the granules are protected by an enteric coating, absorption does not commence until they leave the stomach. The soft skeletons of the granules remain and may be seen in the stools.

In a single dose (4 grams) pharmacokinetic study in healthy adult volunteers ($N=11$) the initial time to a 2 µg/mL serum level of aminosalicylic acid was 2 hours with a range of 45 minutes to 24 hours; the median time to peak was 6 hours with a range of 1.5 to 24 hours; the mean peak level was 20 µg/mL with a range of 9 to 35µg/mL: a level of 2µg/mL was maintained for an average of 8 hours with a range of 5 to 9.5 a level of 1 µg/mL was maintained for an average of 8.8 hours with a range of 6 to 11.5 hours.

Distribution

Para-aminosalicylic acid is distributed in various tissues and fluids including the lungs, kidneys, liver and peritoneal fluid. Pleural or synovial fluid concentrations are approximately equal to plasma. The drug does not cross the blood brain barrier in patients unless the meninges are inflamed, when the concentration of para-aminosalicylic acid in cerebrospinal fluid is about 10 to 50% of the plasma. It is unknown whether it passes through the placental barrier. Small amounts of this agent are distributed in the milk and bile.

Plasma protein binding is about 50 to 60%, the kinetic distribution has a half-life of 0.94 hours and a volume of distribution of 1.001 L/kg.

Biotransformation

The major metabolites of PAS are produced by conjugation to glycine in para-aminosalicylic acid (PASU) for up to 25% of the dose and to N-acetyl in N-acetyl para-aminosalicylic acid (Ac-PAS) for up to 70% of the dose. Together they constitute more than 90% of the total metabolites of PAS found in urine.

Elimination

In a single dose study the plasma half-life of para-aminosalicylic acid administered as GRANUPAS was 1.62 ± 0.85 h.

Para-aminosalicylic acid and its metabolites are excreted by glomerular filtration and tubular secretion. The cumulative excretion of para-aminosalicylic after 24 hours is 84% of an oral dose of 4 g, 21% as para-aminosalicylic acid and 63% as the acetylated form. The acetylation process is not genetically determined as is the case for isoniazid.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology and repeated dose toxicity.

The data available from a rat embryofetal development study, where animals were given sodium aminosalicylate (3.85 to 385 mg/kg) were limited. Bone defects were observed at 77 mg/kg only and increased fetal weight was noted at the other doses. Other malformations were observed; however, the exact nature of these findings is unknown. The lack of a dose-response relationship suggests that the findings are not of clinical relevance, but it is noted that the findings were observed at doses below those proposed clinically. In the rabbit, sodium aminosalicylate had no effects on embryofetal development; however, the doses evaluated were below those proposed clinically.

Sodium aminosalicylic acid was not mutagenic in Ames test strain TA 100. In human lymphocyte cultures in-vitro clastogenic effects of achromatic, chromatid, isochromatic breaks or chromatid translocations were not seen at 153 or 600 µg /mL but at 1500 and 3000 µg/mL there was a dose related increase in chromatid aberrations. No *in vivo* genotoxicity study has been conducted with GRANUPAS.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal silicon dioxide
Dibutyl sebacate
Methacrylic acid – Ethyl acrylate Copolymer (1:1) Dispersion 30%
Hypromellose
Microcrystalline cellulose
Talc

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).
The sachets can be stored below 25°C up to 24 hours after first opening.

6.5 Nature and contents of container

Sachets consisting of paper/low density polyethylene/aluminium foil/primer/low density polyethylene.

Pack size of 30 sachets. A calibrated measuring spoon is provided.

6.6 Special precautions for disposal and other handling

The granules should not be crushed or chewed.
DO NOT USE if sachet is swollen or if the granules have lost their light brown colour, and are turning dark brown or purple.

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

7. MARKETING AUTHORISATION HOLDER

Lucane Pharma,
172 rue de Charonne
75011 Paris
France

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/896/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 07 April 2014.

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency: <http://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

Lucane Pharma,
172 rue de Charonne
75011 Paris
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

The marketing authorisation holder shall submit the first periodic safety update report for this product within 6 months following authorisation. Subsequently, the marketing authorisation holder shall submit periodic safety update reports for this product in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and 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 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.

If the submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time.

• Additional risk minimisation measures

None

• Obligation to conduct post-authorisation measures

None

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON BOX

1. NAME OF THE MEDICINAL PRODUCT

GRANUPAS 4 g gastro-resistant granules
Para-aminosalicylic acid

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each sachet contains 4 g of para-aminosalicylic acid

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Gastro-resistant granules
30 sachets
Calibrated measuring spoon

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.
Do not chew or crush.
Warning: Do not use if sachet is swollen or the granules have lost their light brown color and are dark brown or purple

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 a refrigerator.

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

Lucane Pharma
172 rue de Charonne
75011 Paris
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/896/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

GRANUPAS 4g

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SACHET

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

GRANUPAS 4g gastro-resistant granules
Para aminosalicylic acid
Oral use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

4 g

6. OTHER

Warning: Do not use if sachet is swollen or the granules have lost their light brown color and are dark brown or purple.
Do not chew or crush.
Read the package leaflet before use.

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

GRANUPAS 4 g gastro-resistant granules Para-aminosalicylic acid

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 or pharmacist.
- 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 GRANUPAS is and what it is used for
2. What you need to know before you take GRANUPAS
3. How to take GRANUPAS
4. Possible side effects
5. How to store GRANUPAS
6. Contents of the pack and other information

1. What GRANUPAS is and what it is used for

GRANUPAS contains para-aminosalicylic acid which is used in adults and children aged 28 days and older to treat resistant tuberculosis in combination with other medicines, in cases of resistance or intolerability with other treatments.

2. What you need to know before you take GRANUPAS

Do not take GRANUPAS if

- you are allergic to para-aminosalicylic acid or any of the other ingredients of this medicine (listed in section 6)
- you have severe kidney disease.

If you are not sure, talk to your doctor or pharmacist before taking GRANUPAS.

Warnings and precautions

Talk to your doctor or pharmacist before taking GRANUPAS

- if you have liver problems or mild or moderate kidney disease
- if you have a stomach ulcer

Children

Use of GRANUPAS is not recommended in newborn babies (under 28 days of age).

Other medicines and GRANUPAS

Tell your doctor or pharmacist if you are taking, have recently taken or are planning to take any other medicines.

It is especially important to tell your doctor if you are taking any of the following:

- Antituberculosis medicines or ethionamide (other treatments against tuberculosis)
- Vitamin B12
- Digoxin (for heart disease)

- Diphenylhydramine (for allergic reactions)

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 or pharmacist for advice before taking this medicine.

- GRANUPAS should only be used during pregnancy if advised by your physician
- Do not breastfeed whilst taking GRANUPAS. This is because small amounts of the medicine can pass into mother's milk.

Driving and using machines

GRANUPAS is unlikely to affect your ability to drive and use machines.

3. How to take GRANUPAS

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

Adults

The recommended dose for adults is 1 sachet three times a day, with a schedule of 1 sachet every 8 hours. Your physician may need to start with a lower dose to prevent possible side effects.

Do not take more than 3 sachets per day. Treatment is usually given for two years (24 months).

- Add the contents of the sachet to a drink of tomato or orange juice.
- Drink straight away
- If some granules are left in the glass, add some more juice and drink straight away.

Infants, children and adolescents

The dose in infants, children and adolescents will be calculated by your doctor based on the patient's body weight. The recommended total dose per day is 150 mg for each kg of body weight. This daily amount is divided into two doses spread out through the day.

- Use the spoon that comes with the medicine to measure the dose.
- To measure the dose:
 - Lines on the spoon indicate the amount (in milligrams of para-aminosalicylic acid). Take the correct amount as prescribed by your doctor.
 - Put granules directly into the spoon.
 - Tap the spoon once on a table to give a horizontal level of granules and continue filling if necessary.
- Sprinkle the granules onto apple sauce or yogurt.
- Make your child eat it straight away.

Taking this medicine

- Do not crush or chew the granules.
- Do not use the sachet if it is swollen or the granules have lost their light brown colour.
- You may notice granules appearing in your stools; this is normal.

If you take more GRANUPAS than you should

Speak to a doctor or pharmacist.

If you forget to take a dose of GRANUPAS

Do not take a double dose to make up for a forgotten dose. Wait until the next dose is due, then take your normal dose.

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.

During the first 3 months of your treatment with GRANUPAS, you must be attentive to any sign of allergic reaction or hepatitis, like skin eruption and/or fever. If you experience any of these symptoms, you must talk to your doctor immediately.

Common side effects (may affect more than 1 in 100 people): giddiness, stomach ache (abdominal pain), vomiting, nausea, bloating, diarrhoea, soft stools, skin redness or rash, disturbance of gait and equilibrium.

Uncommon side effects (may affect more than 1 in 1,000 people): loss of appetite (anorexia)

Rare side effects (may affect more than 1 in 10,000 people): thyroid gland problems, reduced ability to absorb nutrients from food ulcer, bleeding in the gut, yellowing of skin or eyes (jaundice), metallic taste, itchy rash.

Very rare side effects (may affect less than 1 in 10,000 people): reduction in numbers of red or white blood cells, reduction in blood platelets, red spots on the skin, low levels of blood sugar, tendon pain, headache, visual abnormalities, nerve damage in the hands and feet, dizziness, prolonged bleeding time, elevated liver enzymes, weight loss, crystals in urine.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. 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 GRANUPAS

Keep out of the sight and reach of children.

Do not use after the expiry date which is stated on the carton and sachet after EXP. The expiry date refers to the last day of the month.

Store in a refrigerator (2°C – 8°C). The sachets can be stored below 25°C up to 24 hours after opening.

Do not use GRANUPAS if you notice the sachets are swollen or if the granules are dark brown or purple.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What GRANUPAS contains

The active substance is para-aminosalicylic acid.

Each sachet of gastroresistant granules contains 4 g of para-aminosalicylic acid.

The other ingredients are colloidal silicon dioxide, dibutyl sebacate, methacrylic acid – ethyl acrylate copolymer (1:1) dispersion 30%, hypromellose, microcrystalline cellulose, talc.

What GRANUPAS looks like and contents of the pack

This medicine is presented as light brown gastro-resistant granules in sachets.
Each box contains 30 sachets. A calibrated measuring spoon is provided.

Marketing Authorisation Holder

Lucane Pharma
172 rue de Charonne
75011 Paris - France

Manufacturer

Lucane Pharma,
172 rue de Charonne
75011 Paris
France

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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

There are also links to other websites about rare diseases and treatments.