ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Cystadane 1 g oral powder

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 g of powder contains 1 g of betaine anhydrous.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral powder.
White crystalline free flowing powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Adjunctive treatment of homocystinuria, involving deficiencies or defects in:
- cystathionine beta-synthase (CBS),
- 5,10-methylene-tetrahydrofolate reductase (MTHFR),
- cobalamin cofactor metabolism (cbl).

Cystadane should be used as supplement to other therapies such as vitamin B6 (pyridoxine), vitamin B12 (cobalamin), folate and a specific diet.

4.2 Posology and method of administration

Cystadane treatment should be supervised by a physician experienced in the treatment of patients with homocystinuria.

Posology
Children and Adult
The recommended total daily dose is 100 mg/kg/day given in 2 doses daily. However, the dose should be individually titrated according to plasma levels of homocysteine and methionine. In some patients doses above 200 mg/ kg/day were needed to reach therapeutic goals. Caution should be exercised with up-titrating doses for patients with CBS deficiency due to the risk for hypermethioninaemia. Methionine levels should be closely monitored in these patients.

Special populations
Hepatic or renal impairment
Experience with betaine anhydrous therapy in patients with renal insufficiency or non-alcoholic hepatic steatosis has demonstrated no need to adapt the dose regimen of Cystadane.

Method of administration
The bottle should be lightly shaken before opening. Three measuring spoons are provided which dispense either 100 mg, 150 mg or 1 g of betaine anhydrous. It is recommended that a heaped measuring spoon is removed from the bottle and a flat surface e.g. base of a knife is drawn across the top of the measure. This will give the following doses: small measure 100 mg, middle size measure 150 mg and large measure 1 g of betaine anhydrous.

The powder should be mixed with water, juice, milk, formula or food until completely dissolved and ingested immediately after mixing.

Therapeutic monitoring
The aim of treatment is to keep plasma levels of total homocysteine below 15 µM or as low as possible. The steady-state response usually occurs within a month.

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

Uncommon cases of severe cerebral oedema associated with hypermethioninemia were reported with betaine anhydrous therapy in patients with CBS deficiency (see section 4.8). Complete recovery was seen after treatment discontinuation:

- *The plasma methionine concentrations should be kept below 1000 µM. It is recommended to measure plasma methionine level at start of treatment and about annually or biannually thereafter. If methionine increases particularly above the first safety threshold of 700 µmol/L, patient should be monitored more frequently and compliance with diet should be checked. In order to reduce methionine levels, modification of diet as well as dose reduction of Cystadane or temporal interruption of Cystadane treatment should be considered.*
- If any symptoms of cerebral oedema like morning headaches with vomiting and/or visual changes appear, plasma methionine level and compliance to the diet should be checked and treatment with Cystadane interrupted.
- If symptoms of cerebral oedema recur after re-introduction of treatment then betaine anhydrous therapy should be discontinued indefinitely.

To minimise the risk of potential drug interactions, it is advisable to leave 30 minutes between the intake of betaine anhydrous and amino acids mixtures and/or medicinal products containing vigabatrin and GABA analogues (see section 4.5).

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.
Based on *in vitro* data, betaine anhydrous might interact with amino acids mixtures and medicinal products containing vigabatrin and GABA analogues.

4.6 Fertility, pregnancy and lactation

Pregnancy
Data on a limited number of exposed pregnancies indicate no adverse event of betaine anhydrous on pregnancy or on the health of the foetus/newborn child. To date, no other relevant epidemiologic data are available. Animal reproduction studies have not been conducted. During pregnancy, administering betaine anhydrous in addition to pyridoxine, folate, anticoagulant and diet under close monitoring of plasma homocysteine would be compatible with good maternal and foetal outcomes. However, Cystadane should not be used during pregnancy unless clearly necessary.

Breast-feeding
It is not known whether betaine anhydrous is excreted in human milk (although its metabolic precursor, choline, occurs at high levels in human milk). Because of lack of data, caution should be exercised when prescribing Cystadane to breast-feeding women.

Fertility
No data is available.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Summary of the safety profile
In general, adverse reactions seen with betaine anhydrous therapy appeared to be not serious and are mainly related to the gastrointestinal system. Gastrointestinal disorders like diarrhoea, glossitis, nausea, stomach discomfort, vomiting and dental disorders may occur uncommonly.
The most commonly reported adverse reaction during treatment is blood methionine increased. Complete recovery was seen after treatment discontinuation (see section 4.4).

Tabulated list of adverse reactions
Reported adverse reactions are listed below, by system organ class and by frequency.
Frequencies are defined as: 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). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Metabolism and nutrition disorders	Uncommon: anorexia
Psychiatric disorders	Uncommon: agitation, irritability
Nervous system disorders	Uncommon: brain oedema*
Gastrointestinal disorders	Uncommon: diarrhoea, glossitis, nausea, stomach discomfort, vomiting
Skin and subcutaneous tissue disorders	Uncommon: hair loss, hives, skin odour abnormal
Renal and urinary disorders	Uncommon: urinary incontinence
Investigations	Very common: blood methionine increased*

Description of selected adverse reactions
*Uncommon cases of severe cerebral oedema and hypermethioninemia were reported within 2 weeks to 6 months of starting betaine anhydrous therapy in patients with CBS deficiency, with complete recovery after treatment discontinuation.
Symptoms of cerebral oedema include morning headaches with vomiting and/or visual changes
High increases in plasma methionine levels in a range from 1,000 to 3,000 µM were noted in these patients. As cerebral oedema has also been reported in patients with hypermethioninemia, secondary hypermethioninemia due to betaine anhydrous therapy has been postulated as a possible mechanism of action.
For specific recommendations, see section 4.4.

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 has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other alimentary tract and metabolism products, ATC code: A16AA06.

Mechanism of action
Betaine anhydrous was shown to lower plasma homocysteine levels in the three types of homocystinuria, i.e. CBS deficiency; MTHFR deficiency and cbl defect. The extent of this effect was dependent on the absolute degree of hyperhomocysteinemia, being higher in severe hyperhomocysteinemia.

Pharmacodynamic effects
Betaine anhydrous acts as a methyl group donor in the remethylation of homocysteine to methionine in patients with homocystinuria. As a result, plasma levels of homocysteine should decrease in these patients, to 20-30 % of pre-treatment levels.
Betaine anhydrous has also been shown to increase plasma methionine and S-adenosyl methionine (SAM) levels in patients with MTHFR deficiency and cbl defects. In CBS-deficient patients without dietary restriction of methionine, excessive accumulation of methionine has been observed.
Betaine anhydrous supplementation was shown to improve the metabolic abnormalities in the cerebrospinal fluid of patients with homocystinuria.

Clinical efficacy and safety
Elevated homocysteine plasma levels are associated with cardiovascular events (such as thrombosis), osteoporosis, skeletal abnormalities, and optic lens dislocation. In observational studies, clinical improvement (cardiovascular and neurodevelopmental) was reported by the treating physician in about 75% of patients taking betaine anhydrous. Most of these patients were also receiving other treatments such as vitamin B6 (pyridoxine), vitamin B12 (cobalamin) and folate with variable biochemical responses. In most cases, adding betaine anhydrous resulted in a further reduction in plasma homocysteine level. It is likely that due to the multiple nature of therapy (dietary, pharmaceutical, supportive) in these patients, there may be an element of overestimation in the clinical effects of betaine anhydrous treatment. Late detection of homocystinuria in symptomatic state is responsible for residual morbidity due to irreversible damage to connective tissue (ophtalmological, skeletal) that cannot be corrected by further therapy. The available clinical data do not allow correlating posology and clinical efficacy. There is no evidence of development of tolerance.

In a few cases, increased plasma methionine levels were associated with cerebral oedema (see sections 4.4 and 4.8).

Monitoring plasma homocysteine levels has demonstrated that the onset of action of betaine anhydrous occurred within several days and that a steady-state response was achieved within one month.

Paediatric population
In paediatric patients less than 10 years of age, the usual effective dose regimen is 100 mg/kg/day given in 2 doses daily; increasing the frequency above twice daily and/or the dose above 150 mg/kg/day does not improve the homocysteine-lowering effect.

Monitoring betaine plasma concentrations does not help to define the efficacy of treatment, since these concentrations do not directly correspond to the flux through the cytosolic betaine homocysteine methyl transferase pathway.

5.2 Pharmacokinetic properties

The pharmacokinetic data of homocystinuric patients on long-term betaine anhydrous supplementation are very similar to those of healthy volunteers. This demonstrates that differences in betaine anhydrous kinetics are most probably due to betaine anhydrous depletion in untreated homocystinuria and are only meaningful for the initial treatment.

Absorption
The absolute bioavailability of betaine anhydrous has not been determined. In healthy adult volunteers (age between 21 to 49 years), after a single oral dose of betaine anhydrous (50 mg/kg), absorption was rapid (t_{max} = 0.9 ± 0.3 hours and a C_{max} = 0.9 ± 0.2 mM).
After a repeated dose regimen of 100 mg/kg/day for 5 days, the absorption kinetics did not change.

Distribution
Betaine anhydrous was rapidly distributed into a relatively large volume (V/F = 1.3 l/kg).
After a repeated dose regiment of 100 mg/kg/day for 5 days, the distribution half life was prolonged significantly (up to 36 h), indicating saturable transport and redistribution processes.

Biotransformation
Betaine anhydrous is a methyl group donor

Elimination
With a slow elimination rate (mean half life = 14 h, mean total body clearance, CL/F, = 84 ml/h/kg), renal clearance is negligible (5% of total body clearance), assuming 100% bioavailability.

5.3 Preclinical safety data

At high doses, a CNS depressant effect and irritation of the gastrointestinal tract was seen in rats. Long-term carcinogenicity and reproductive toxicity studies have not been conducted on betaine anhydrous. A standard battery of genotoxicity test reveals no specific hazard for humans.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Unopened bottle: 3 years
After the first opening: 3 months.

6.4 Special precautions for storage

Do not store above 25°C.
Keep the bottle tightly closed in order to protect from moisture.
For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

HDPE bottles with a child resistant closure.
Each pack contains 1 bottle with 180 g of powder and three measuring spoons.

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

Recordati Rare Diseases
Tour Hekla
52 avenue du Général de Gaulle
F-92 800 Puteaux
France

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/06/379/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15 February 2007
Date of latest renewal: 21 November 2016

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. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Recordati Rare Diseases
Tour Hekla
52 avenue du Général de Gaulle
F-92800 Puteaux
France

or

Recordati Rare Diseases
Eco River Parc
30, rue des Peupliers
F-92000 Nanterre
France

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see annex I: Summary of Product Characteristics, section 4.2)

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.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Cystadane 1 g oral powder
Betaine anhydrous

2. STATEMENT OF ACTIVE SUBSTANCE

1 g of powder contains 1 g of betaine anhydrous.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

180 g of oral powder and three measuring spoons.
Three measuring spoons (green, blue, pink) dispense 100mg, 150mg or 1g of betaine anhydrous.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Lightly shake the bottle before opening.
Read the package leaflet before use.
Oral 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
Shelf life after the first opening: 3 months.

9. SPECIAL STORAGE CONDITIONS

Do not store above 25°C.
Keep the bottle tightly closed 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

Recordati Rare Diseases
Tour Hekla
52 avenue du Général de Gaulle
F-92 800 Puteaux
France

12. MARKETING AUTHORISATION NUMBER

EU/1/06/379/001

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cystadane 1 g oral powder

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

BOTTLE LABEL

1. NAME OF THE MEDICINAL PRODUCT

Cystadane 1 g oral powder
Betaine anhydrous

2. STATEMENT OF ACTIVE SUBSTANCE

1 g of powder contains 1 g of betaine anhydrous.
Three measuring spoons (green, blue, pink) dispense 100mg, 150mg or 1g of betaine anhydrous.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

180 g of oral powder.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Lightly shake the bottle before opening.
Read the package leaflet before use
Oral 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
Shelf life after the first opening: 3 months.
Opened:

9. SPECIAL STORAGE CONDITIONS

Do not store above 25°C.
Keep the bottle tightly closed 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

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France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/06/379/001

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cystadane 1 g oral powder

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Cystadane 1 g oral powder
Betaine anhydrous

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 Cystadane is and what it is used for

Cystadane contains betaine anhydrous which is intended to be an adjunctive treatment of homocystinuria, an inherited (genetic) disease where the amino acid methionine cannot be broken down completely by the body.

Methionine is present in regular food protein (e.g. meat, fish, milk, cheese, eggs). It is converted into homocysteine which is then normally converted into cysteine during digestion. Homocystinuria is a disease caused by the accumulation of homocysteine which is not converted to cysteine and is characterised by formation of clots in the veins, bone weakness, and skeletal and crystalline lens abnormalities. The use of Cystadane together with other treatments such as vitamin B6, vitamin B12, folate and a specific diet aims to reduce the elevated homocysteine levels in your body.

2. What you need to know before you take Cystadane

Do not take Cystadane
- if you are allergic to betaine anhydrous or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or pharmacist before taking Cystadane.
If you notice side effects like headaches, vomiting or a change in your vision and you are of the homocystinuria subtype called CBS (cystathionine beta-synthase deficiency), please contact your doctor immediately, they could be signs of a swelling in the brain (cerebral oedema). In that case your doctor will monitor your methionine level in your body and may review your diet. Your treatment with Cystadane may need to be interrupted.
If you are treated with Cystadane and with an amino-acid mixture and if you need to take other medicines at the same time, leave 30 minutes between the intake (see “section “Other medicines and Cystadane”).

Other medicines and Cystadane
Tell your doctor if you are taking, have recently taken or might take any other medicines.
If you are taking amino-acid mixture or medicines such as vigabatrin or Gaba analogues (medicine used to treat epilepsy), please tell your doctor as they might interact with your treatment with Cystadane.

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. Your doctor will decide if you can use this medicine during pregnancy and breast-feeding.

Driving and using machines
Cystadane has no or negligible influence on the ability to drive and use machines.

3. How to take Cystadane

The use of this medicine will be supervised by a doctor experienced in the treatment of patients with homocystinuria.
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 in children and adults is 100mg/kg/day divided in 2 dosesper day. In some patients doses above 200 mg/ kg/day were needed to reach therapeutic goals. Your doctor may adapt the dose depending on your laboratory values.

You will therefore need regular blood tests to determine the correct daily dose.

You should take Cystadane orally (by mouth).
To measure the dose:
- shake the bottle lightly before opening
- take the correct measuring spoon:
  - the small green spoon measures 100 mg of betaine anhydrous powder;
  - the middle size blue spoon measures 150 mg of betaine anhydrous powder ;
  - the large pink spoon measures 1 g of betaine anhydrous powder.
- take a heaped spoonful of powder out of the bottle
- pass the flat back of a knife over the top of the spoon
- the powder left in the spoon is one spoonful
- take the correct number of spoonfuls of powder from the bottle

Mix the measured dose of powder with water, juice, milk, formula or food until completely dissolved and ingest immediately after mixing.

If you take more Cystadane than you should
If you accidentally take too much Cystadane, talk to a doctor or pharmacist immediately.

If you forget to take Cystadane
Do not take a double dose to make up for forgotten doses. If you forget to take a dose take it as soon as you remember it and continue the next dose as planned.
If you stop taking Cystadane
Do not stop the treatment without consulting your doctor. Contact your doctor or pharmacist before stopping.

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.

The most commonly side effect when taking Cystadane which may affect more than 1 in 10 people (frequency very common) is elevated levels of methionine in the blood.
Methionine level can be related to swelling in the brain (cerebral swelling), which may affect up to 1 in 100 people (frequency uncommon). If you experience morning headaches with vomiting and/or visual changes, contact immediately your doctor (they could be signs of a swelling in the brain).

Gastrointestinal disorders like diarrhoea, nausea, vomiting, stomach discomfort and inflammation of the tongue may occur uncommonly (may affect up to 1 in 100 people).
Other uncommon side effects (may affect up to 1 in 100 people) may include decreased appetite (anorexia), agitation, irritability, hair loss, hives, skin odour abnormal, lack of control over passing urine (urinary incontinence).

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 Cystadane

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 bottle label and the carton after EXP. The expiry date refers to the last day of that month.

Do not store above 25°C.
Keep the bottle tightly closed in order to protect from moisture.
After the first opening of the bottle, the medicine should be used within 3 months.

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 Cystadane contains
- The active substance is betaine anhydrous. 1 g of oral powder contains 1 g of betaine anhydrous.
- There is no other ingredient.

What Cystadane looks like and contents of the pack
Cystadane is a white crystalline free flowing powder. It is presented in bottles with child resistant closures. Each bottle contains 180 g of powder. Each carton contains one bottle and three measuring spoons.

Marketing Authorisation Holder
Recordati Rare Diseases

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Manufacturer
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or

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

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This leaflet was last revised in

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.