ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Sibnayal 8 mEq prolonged-release granules
Sibnayal 24 mEq prolonged-release granules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sibnayal 8 mEq prolonged-release granules

One sachet contains 282 mg of potassium citrate and 527 mg of potassium hydrogen carbonate.
This corresponds to 7.9 mEq of alkali (i.e. 2.6 mEq of citrate and 5.3 mEq of hydrogen carbonate) and to 7.9 mEq of potassium (i.e. 308 mg of potassium).

Sibnayal 24 mEq prolonged-release granules

One sachet contains 847 mg of potassium citrate and 1,582 mg of potassium hydrogen carbonate.
This corresponds to 23.6 mEq of alkali (i.e. 7.8 mEq of citrate and 15.8 mEq of hydrogen carbonate) and to 23.6 mEq of potassium (i.e. 924 mg of potassium).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Prolonged-release granule

Green (potassium citrate) and white (potassium hydrogen carbonate), biconvex, 2 mm diameter.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Sibnayal is indicated for the treatment of distal renal tubular acidosis (dRTA) in adults, adolescents and children aged one year and older.

4.2 Posology and method of administration

Posology

Dosing is based on age and weight.
When initiating alkalising therapy, the target starting daily dose indicated below for each age group should be used and incrementally titrated to obtain the optimal dose that provides adequate metabolic acidosis control based on plasma bicarbonate levels.

- Adults: initiation at 1 mEq/kg/day, with a maximal incremental increase/decrease of 0.5 mEq/kg/day to optimal dose
- Adolescents from 12 years: initiation at 1 mEq/kg/day, with a maximal incremental increase/decrease of 1.0 mEq/kg/day to optimal dose
- Children from 4 to 11 year inclusive: initiation at 2 mEq/kg/day, with a maximal incremental increase/decrease of 1.5 mEq/kg/day to optimal dose
- Children from 1 to 3 years inclusive: initiation at 4 mEq/kg/day, with a maximal incremental increase/decrease of 1.5 mEq/kg/day to optimal dose

When switching from another alkalising therapy to Sibnayal, treatment should be initiated at the target dose used with the previous therapy (in mEq/kg/day) and titrated where necessary as described above.

The maximum dose, regardless of the age group, is either 10 mEq/kg/day or a total daily dose of 336 mEq, whichever is lower.

The total daily dose should be administered in two intakes. For each individual patient, the nearest dose to the target dose should be fixed by combining whole sachets of the two available strengths.

In case of vomiting within two hours after intake, the patient should take another dose.
The use of this medicine requires medical supervision.

Special populations

Elderly
No dose adjustment is required.

Renal impairment
Sibnayal should only be used in individuals with glomerular filtration rate (GFR) > 44 mL/min/1.73m². For individuals with GFR between 45 and 59 mL/min/1.73m² Sibnayal should only be used if the potential benefits are considered to outweigh the potential risks (see Table 1).

Table 1: Dosing recommendations in individuals with renal impairment

GFR mL/min/1.73m²	**Treatment of dRTA**
45-59	• Plasma potassium levels in the normal ranges: A regular monitoring of renal function parameters and blood potassium levels is necessary at starting dose and after new dose increase or if any decrease of GFR. Then frequency is according to physicians´s criteria, but at least twice a year (see section 4.4).
	• Elevated plasma potassium: Contraindicated
≤ 44	Contraindicated

Hepatic impairment
There is no need for specific target starting daily dose adjustment in patients with hepatic impairment.

Paediatric population
The safety and efficacy of Sibnayal in children below one year of age have not been established. No data are available.

Method of administration

For oral use.

The total daily dose is administered twice daily, typically twelve hours apart.

Sibnayal must be taken orally, swallowed with a large glass of water.
The full dose of granules per intake can be swallowed in several smaller portions if necessary, but the content of each sachet must be entirely taken.
Doses should be taken preferably during meals.

For patients who are unable to swallow granules as described above, the granules may be mixed (without crushing) with small amounts of soft food (e.g., fruit puree, yoghurt). The Sibnayal soft food mixture must be used immediately and cannot be stored. The mixture should be swallowed without chewing. Care should be taken to ensure that Sibnayal is not retained in the mouth.

In no instance granules must be mixed with hot food, hot liquid or alcohol or chewed or crushed as this can disrupt their prolonged release properties and may lead to large sudden release of alkalising agent that could affect product efficacy and safety (see section 5.2).

Sibnayal granules are not suitable for administration via feeding tubes due to high risk of obstructing the tubes.

4.3 Contraindications

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

Renal impairment with GFR ≤ 44 mL/min/1.73m².

Hyperkalaemia.

4.4 Special warnings and precautions for use

Hyperkalaemia and cardiotoxicity

Sibnayal should be used with caution in patients who have conditions pre-disposing them to hyperkalaemia, such as renal impairment, or crush syndrome, as a further rise in plasma potassium may lead to cardiac arrest. Close monitoring of plasma potassium in patients at risk is required at starting dose and after new dose increase or in case of worsening of pre-existing disease. Then frequency is according to physicians´s criteria, but at least twice a year.

Sibnayal should be used with caution in case of combination with other products increasing plasma potassium or predisposing to cardiac dysrhythmia (see section 4.5).

Gastrointestinal disorders

Sibnayal should be used with caution in patients having gastro-intestinal disorders as they could affect efficacy and safety, such as malabsorption, delayed gastric emptying, diarrhoea, nausea, vomiting. In such cases the blood bicarbonate levels should be regularly monitored and dose adjusted to maintain within normal ranges.

The matrix of the granules can be found in the stools, which does not affect the efficacy or safety of Sibnayal.

Renal insufficiency

Sibnayal should only be used in individuals with glomerular filtration rate (GFR) > 44 mL/min/1.73m². For individuals with GFR between 45 and 59 mL/min/1.73m² Sibnayal should only be used if the potential benefits are considered to outweigh the potential risks. For these patients doses should be adjusted by regular monitoring of plasma bicarbonate and potassium (see section 4.2). Special care should be taken in elderly people in whom renal function can be decreased.

Potassium contents

Sibnayal 8 mEq contains 308 mg of potassium per sachet. This is to be taken into consideration if the patient has a reduced kidney function or if the patient is on a controlled potassium diet.

Sibnayal 24 mEq contains 924 mg of potassium per sachet. This is to be taken into consideration if the patient has a reduced kidney function or if the patient is on a controlled potassium diet.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

Medicinal products that may increase plasma potassium or induce hyperkalaemia

Concomitant use of Sibnayal with medicinal products that may increase potassium levels or induce hyperkalaemia (e.g. ACE inhibitors, potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium, ciclosporin or other medicinal products such as heparin sodium or nonsteroidal anti-inflammatory medicinal products) necessitates monitoring of potassium plasma levels (see section 4.4).

Medicinal products affected by plasma potassium disturbances

Periodic monitoring of plasma potassium and ECG is recommended when Sibnayal is administered with medicinal products affected by plasma potassium disturbances due to the potential risk for a pro-arrhythmic effect (e.g. digitalis glycosides, corticosteroids, anti-arrhythmics such as quinidine, amiodarone, chlorpromazine, cisapride or sparfloxacine).

Medicinal products affected by increased urine pH

Patients with dRTA have alkaline urine due to their proton secretion defect. This may impact the excretion of the medicinal product into the urine (such as an increase of the elimination of salicylates, tetracyclines, and barbiturates and a decrease in the elimination of quinidine) or reduce the effectiveness of methenamine. As Sibnayal may further increase urine pH to a small extent, the interaction of alkaline urine with these medications may be enhanced.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data from the use of Sibnayal in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development (see section 5.3).
Sibnayal should only be used during pregnancy if the expected benefits outweigh the potential risks. Although during pregnancy and more so during labour, there is more risk associated to a potentially severe acidosis and hypokalaemia in dRTA patients than to alkali treatment, in women with problem pregnancies there might be an increased risk to develop hyperkalemia when potassium intake is high.

Breast-feeding

Potassium is excreted in human milk, but at therapeutic doses of Sibnayal no effects on the breastfed newborns/infants are anticipated.
Sibnayal can be used during breast-feeding.

Fertility

Potassium citrate and potassium hydrogen carbonate are not known to affect fertility.

4.7 Effects on ability to drive and use machines

Sibnayal 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 abdominal pain (14%, very common), upper abdominal pain (8%, common) and gastro-intestinal pain (2%, common).
Nausea (2%, common) can be experienced at initiation of therapy.

Tabulated list of adverse reactions

The list of adverse reactions is based on the experience in clinical trials.
The frequency of adverse reactions is defined using the following convention: very common (≥1/10) ; common (≥1/100 to <1/10) ; uncommon (≥1/1000 to <1/100) ; rare (≥1/10000 to <1/1000) and very rare (<1/10000).

Gastrointestinal disorders:

- abdominal pain as very common
- abdominal pain upper, diarrhoea, dyspepsia, gastrointestinal disorder, gastrointestinal pain, nausea and vomiting as common.

Description of selected adverse reactions

Gastrointestinal disorders
Gastro-intestinal pain, abdominal pain and upper abdominal pain were generally of mild or moderate intensity and resolved within 24 hours without the need to modify or stop the treatment. All other gastro-intestinal adverse reactions (dyspepsia, vomiting, diarrhoea) were also of mild or moderate intensity, and resolved within 1 to 3 days, without modification or interruption of treatment.

Paediatric population

In clinical trials, although numbers were small, the safety profile was comparable in treated patients for adults (N= 16 healthy subjects and 7 dRTA patients) and paediatric population (N=27, including 10 adolescents (12-17 years old inclusive), 14 children (4-11 years old inclusive) and 3 infants (6 months – 3 years inclusive)).

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

Reports of a laxative effect after excessive oral doses of individual alkalising salts have occurred.
An acute massive intake of potassium can cause hyperkalaemia resulting in nausea, vomiting, and diarrhoea and in severe cases paraesthesia, muscular weakness, mental confusion, electrocardiographic abnormalities (large and symmetric T waves), arrhythmia, atrioventricular block and heart failure.
Hyperkalaemia is a particular concern in patients with underlying renal insufficiency.
In case of severe hyperkalaemia, patients should be monitored (mostly plasma potassium level and ECG) and the appropriate symptomatic and supportive therapy instituted in specialised care units, where emergency treatments leading to rapid elimination of potassium such as ion exchange resin, combination of insulin-dextrose or β2 mimetics (salbutamol) or haemodialysis will be implemented.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: mineral supplements, potassium, ATC code: A12BA30.

Mechanism of action

Sibnayal is a fixed-dose combination of potassium citrate and potassium hydrogen carbonate (also known as potassium bicarbonate) as prolonged release granules.
The pharmacological properties are directly linked to the capacity of potassium citrate and potassium hydrogen carbonate to maintain electrolyte balance. Both act as alkalising agents and buffer the metabolic acidosis. Sibnayal provides a source of potassium to correct hypokalaemia. In addition, citrate acts also as a calcium chelating agent.

Pharmacodynamic effects

In a randomised, double blind, placebo-controlled, two-period, incomplete crossover study in healthy adults, Sibnayal at doses ranging from 1.0 to 2.9 mEq/kg/day during 5 days was shown to increase urine pH (marker of alkalinising effect in healthy subjects) with a dose-proportional effect as compared to placebo. The effect was maintained over 12 hours at all the doses evaluated.

Clinical efficacy and safety

The efficacy and safety of Sibnayal for the treatment of dRTA was evaluated in a multi-centre, open-label, sequential study that included 37 patients with an established diagnosis of dRTA (7 adults, 10 adolescents (12-17 years), 15 children (4-11 years), 5 infants (1-4 years)) who were being treated with their standard-of-care (SoC) short-acting alkalising agents in repeated daily intakes . Patients continued on their SoC for 5 days (n=35) and then received Sibnayal twice daily, initially during a titration period to establish the optimal dose (up to 30 days duration) and then for 5 days at this optimal dose (n=32).

With Sibnayal, the primary endpoint showed that the mean (SD) plasma bicarbonate pre-dose level during 3 days of treatment at steady state was 23.1 (1.62) mmol/L with 90% (26/29) of the patients achieving 3-day mean normal bicarbonate levels. This effect was generally maintained during 24 months of therapy, although some variability was observed with a responder rate of 56-92%. Mean achieved plasma potassium level was 4.0 (0.44) mmol/L with 83% (24/29) of the patients at normal levels.

With SoC, the mean (SD) plasma bicarbonate pre-dose level during 3 days of treatment at steady state was 21.7 (3.06) mmol/L with 45% (13/29) of the patients at normal levels. The mean achieved plasma potassium level was 3.8 (0.44) mmol/L with 82% at normal levels.

5.2 Pharmacokinetic properties

Sibnayal is a prolonged-release granules formulation to cover a 12-hour treatment period after administration.
Pharmacokinetic features of citrate, bicarbonate and potassium are based on the literature.

Absorption

Oral citrate is absorbed at a pH between 4.8 and 6.4 along the upper portion of the small intestine (duodenum, early part of jejunum). Under these conditions, the intestinal absorption of citrate is rapid and almost complete.

Oral bicarbonate is absorbed throughout the gastrointestinal tract. Bicarbonate neutralises gastric acid with the production of CO_2 eliminated by the respiratory route. Bicarbonate not involved in that reaction is rapidly absorbed by the intestinal mucosa.

The potassium ions are fully absorbed, irrespective of the amount consumed. The majority of potassium absorption occurs in the small intestine, mainly through passive diffusion.

Distribution and biotransformation

Most of the citrate in the blood circulates unbound and the remaining quota is complexed to calcium, potassium or sodium. The citrate ion from oral alkali citrates undergoes oxidative metabolic breakdown to carbon dioxide (CO_2) or bicarbonate. Consequently, a basifying effect is associated with its metabolism. Ingestion of 36 mmol of citrate (i.e. 108 mEq) is equivalent to less than 2% of the daily turnover of citrate involved in energy metabolism within the body.

The absorbed bicarbonate is distributed like the endogenous bicarbonate in the intracellular and extracellular compartments of the organism. Bicarbonate is not really metabolised. However, bicarbonate is in equilibrium with hydrogen ions and carbon dioxide and, through its concentration, regulates the acid-base balance.

Potassium is carried from extracellular fluids to the intracellular fluids, and its distribution between cells is tightly controlled, with only 1.5–2.5% of total body potassium found in the extracellular fluid. A large proportion of the body burden of potassium (98%) is found in muscle and the skeleton, and it is also present in high concentrations in the blood, central nervous system, intestine, liver, lung and skin. An active ion transport system maintains the gradient across the plasma membrane.

Elimination

Citrate is mainly eliminated by the renal route. In its trivalent form, it is filtered freely through the renal glomerulus. Dietary alkali absorption increases citrate excretion by inhibiting its reabsorption at the mitochondrial level and by increasing its secretion by the nephron.
Bicarbonate provides an alkali load and therefore stimulates an increase in urinary excretion of citrate. Increased excretion of bicarbonate in the urine also occurs. Bicarbonate can also be partially eliminated by the respiratory route (in the form of CO_2). The major excretory route of potassium is via the kidneys (90%). The rest is eliminated in the faeces and small amounts may also be excreted in sweat.

Special population

Pharmacokinetics of potassium can be modified in patients with renal impairment for whom glomerular filtration of potassium is less active, in cardiac patients who present a susceptibility to hyperkalaemia and in adrenocortical patients for whom the risk of hyperkalaemia is accentuated.
Pharmacokinetics of citrate, bicarbonate and/or potassium can be modified in patients with gastro-intestinal issues (e.g. malabsorption, delayed gastric emptying, oesophageal compression, intestinal obstruction or other chronic gastro-intestinal disease) that could modify absorption.
Pharmacokinetics should not be modified in patients with hepatic impairment, or in patients with overweight or obesity.

Interaction with alcohol

When Sibnayal is mixed with alcohol *in vitro*, the rate of dissolution of the granules increases and can occur rapidly leading to a loss of the prolonged-effect (see section 4.2).

5.3 Preclinical safety data

Non-clinical data reveals no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core granules

Hypromellose (E464)
Microcrystalline cellulose (E460(i))
Glycerol dibehenate
Magnesium stearate (E470b)
Silica colloidal anhydrous
Magnesium oxide, heavy (E530)

Coating

Ethylcellulose (E462)
Chlorophyllin (E140 (ii))

Technological agent (on coated granules)

Talc

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years.

6.4 Special precautions for storage

Do not store above 25 °C.

6.5 Nature and contents of container

Three-layered foil (polyethylene terephthalate polyester/aluminium/low density polyethylene) sealed sachet for single use.

Sibnayal 8 mEq prolonged-release granules

Packs of 60 sachets.
Multipacks containing 120 (2 packs of 60) sachets.
Multipacks containing 180 (3 packs of 60) sachets.
Multipacks containing 240 (4 packs of 60) sachets.
Multipacks containing 300 (5 packs of 60) sachets.
Multipacks containing 360 (6 packs of 60) sachets.

Sibnayal 24 mEq prolonged-release granules

Packs of 60 sachets.
Multipacks containing 120 (2 packs of 60) sachets.
Multipacks containing 180 (3 packs of 60) sachets.
Multipacks containing 240 (4 packs of 60) sachets.
Multipacks containing 300 (5 packs of 60) sachets.
Multipacks containing 360 (6 packs of 60) sachets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

After opening the sachet, discard any unused content.

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

7. MARKETING AUTHORISATION HOLDER

ADVICENNE
262 rue du Faubourg Saint Honoré
75008 Paris
France

8. MARKETING AUTHORISATION NUMBER(S)

Sibnayal 8 mEq prolonged-release granules

EU/1/20/1517/001
EU/1/20/1517/002
EU/1/20/1517/003
EU/1/20/1517/004
EU/1/20/1517/005
EU/1/20/1517/006

Sibnayal 24 mEq prolonged-release granules

EU/1/20/1517/007
EU/1/20/1517/008
EU/1/20/1517/009
EU/1/20/1517/010
EU/1/20/1517/011
EU/1/20/1517/012

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 30 April 2021

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(s) responsible for batch release

ELAIAPHARM
2881 route des Crêtes
ZI les Bouillides Sophia Antipolis
06560 Valbonne
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.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

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
BOX OF 60 SACHETS

1. NAME OF THE MEDICINAL PRODUCT

Sibnayal 8 mEq prolonged-release granules
potassium citrate / potassium hydrogen carbonate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each sachet contains 282 mg of potassium citrate and 527 mg of potassium hydrogen carbonate

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Prolonged-release granules.
60 sachets.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use. Do not chew.

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

Do not store above 25°C.

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

ADVICENNE, 262 rue du Faubourg Saint Honoré, 75008 Paris, France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1517/001 60 sachets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Sibnayal 8 mEq

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 OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (WITH BLUEBOX)

1. NAME OF THE MEDICINAL PRODUCT

Sibnayal 8 mEq prolonged-release granules
potassium citrate / potassium hydrogen carbonate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each sachet contains 282 mg of potassium citrate and 527 mg of potassium hydrogen carbonate

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Prolonged-release granules.
Multipack: 120 (2 packs of 60) sachets
Multipack: 180 (3 packs of 60) sachets
Multipack: 240 (4 packs of 60) sachets
Multipack: 300 (5 packs of 60) sachets
Multipack: 360 (6 packs of 60) sachets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.
Do not chew.

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

Do not store above 25°C.

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

ADVICENNE, 262 rue du Faubourg Saint Honoré, 75008 Paris, France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1517/002 120 sachets (2 packs of 60)
EU/1/20/1517/003 180 sachets (3 packs of 60)
EU/1/20/1517/004 240 sachets (4 packs of 60)
EU/1/20/1517/005 300 sachets (5 packs of 60)
EU/1/20/1517/006 360 sachets (6 packs of 60)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Sibnayal 8 mEq

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 OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUEBOX)

1. NAME OF THE MEDICINAL PRODUCT

Sibnayal 8 mEq prolonged-release granules
potassium citrate / potassium hydrogen carbonate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each sachet contains 282 mg of potassium citrate and 527 mg of potassium hydrogen carbonate

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Prolonged-release granules.
60 sachets. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.
Do not chew.

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

Do not store above 25°C.

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

ADVICENNE, 262 rue du Faubourg Saint Honoré, 75008 Paris, France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1517/002 120 sachets (2 packs of 60)
EU/1/20/1517/003 180 sachets (3 packs of 60)
EU/1/20/1517/004 240 sachets (4 packs of 60)
EU/1/20/1517/005 300 sachets (5 packs of 60)
EU/1/20/1517/006 360 sachets (6 packs of 60)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Sibnayal 8 mEq

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SACHET

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

Sibnayal 8 mEq prolonged-release granules
potassium citrate / potassium hydrogen carbonate
kalii citras / kalii hydrogenocarbonas
Oral use

2. METHOD OF ADMINISTRATION

Do not chew.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON
BOX OF 60 SACHETS

1. NAME OF THE MEDICINAL PRODUCT

Sibnayal 24 mEq prolonged-release granules
potassium citrate / potassium hydrogen carbonate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each sachet contains 847 mg of potassium citrate and 1582 mg of potassium hydrogen carbonate

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Prolonged-release granules.
60 sachets.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use. Do not chew.

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

Do not store above 25°C.

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

ADVICENNE, 262 rue du Faubourg Saint Honoré, 75008 Paris, France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1517/007 60 sachets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Sibnayal 24 mEq

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 OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (WITH BLUEBOX)

1. NAME OF THE MEDICINAL PRODUCT

Sibnayal 24 mEq prolonged-release granules
potassium citrate / potassium hydrogen carbonate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each sachet contains 847 mg of potassium citrate and 1582 mg of potassium hydrogen carbonate

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Prolonged-release granules.
Multipack: 120 (2 packs of 60) sachets
Multipack: 180 (3 packs of 60) sachets
Multipack: 240 (4 packs of 60) sachets
Multipack: 300 (5 packs of 60) sachets
Multipack: 360 (6 packs of 60) sachets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.
Do not chew.

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

Do not store above 25°C.

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

ADVICENNE, 262 rue du Faubourg Saint Honoré, 75008 Paris, France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1517/008 120 sachets (2 packs of 60)
EU/1/20/1517/009 180 sachets (3 packs of 60)
EU/1/20/1517/010 240 sachets (4 packs of 60)
EU/1/20/1517/011 300 sachets (5 packs of 60)
EU/1/20/1517/012 360 sachets (6 packs of 60)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Sibnayal 24 mEq

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 OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUEBOX)

1. NAME OF THE MEDICINAL PRODUCT

Sibnayal 24 mEq prolonged-release granules
potassium citrate / potassium hydrogen carbonate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each sachet contains 847 mg of potassium citrate and 1582 mg of potassium hydrogen carbonate

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Prolonged-release granules.
60 sachets. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.
Do not chew.

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

Do not store above 25°C.

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

ADVICENNE, 262 rue du Faubourg Saint Honoré, 75008 Paris, France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1517/008 120 sachets (2 packs of 60)
EU/1/20/1517/009 180 sachets (3 packs of 60)
EU/1/20/1517/010 240 sachets (4 packs of 60)
EU/1/20/1517/011 300 sachets (5 packs of 60)
EU/1/20/1517/012 360 sachets (6 packs of 60)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Sibnayal 24 mEq

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SACHET

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

Sibnayal 24 mEq prolonged-release granules
potassium citrate / potassium hydrogen carbonate
kalii citras / kalii hydrogenocarbonas
Oral use

2. METHOD OF ADMINISTRATION

Do not chew.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Sibnayal 8 mEq prolonged-release granules
Sibnayal 24 mEq prolonged-release granules
potassium citrate/potassium hydrogen carbonate

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 Sibnayal is and what it is used for

Sibnayal contains two active substances, potassium citrate and potassium hydrogen carbonate (also known as potassium bicarbonate).

Sibnayal is an alkalising medicine that is used to control blood acidity caused by a kidney disease called distal renal tubular acidosis (dRTA).

Sibnayal will help reduce the effect of dRTA on your everyday life.

Sibnayal is used in adults, adolescents and children above 1 year.

2. What you need to know before you take Sibnayal

Do not take Sibnayal if:

- you are allergic to potassium citrate or potassium bicarbonate or any of the other ingredients of this medicine (listed in section 6),
- you have a severe kidney disease or kidney failure,
- you have a high level of potassium in your blood (hyperkalaemia).

Warnings and precautions

Talk to your doctor before taking Sibnayal if:
- you have a disease or you take a medicine that can increase your blood potassium (see below “Other medicines and Sibnayal”),
- you frequently have gastro-intestinal symptoms such as bloating, diarrhoea, nausea, vomiting,
- you have chronic kidney disease.

Sibnayal prolonged-release granules are designed to release the active substances slowly after taking the granules. You may see remains of the granules in your stools. This is normal and does not reduce the effectiveness of the medicine.

If you vomit within two hours after intake, you should take another dose.

You will need regular appointments with your doctor. From time to time, your doctor may need to do blood, urine or heart tests, to adjust the dose of Sibnayal. Your doctor will regularly check your kidney function if you are elderly and/or have worsening kidney function.

Children

Do not give this medicine to children below 1 year of age because of the risk of choking.

Other medicines and Sibnayal

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Some medicines may affect how Sibnayal works or make side effects more likely. These include:
- any medicine that increases the level of potassium in your blood such as:
  - angiotensin-converting enzyme (ACE) inhibitors (used to treat high blood pressure, heart disease and kidney disease in patients suffering from type 1 diabetes),
  - potassium-sparing diuretics (used to treat high blood pressure, fluid build-up in tissue (oedema) and heart conditions),
  - potassium supplements (used to prevent or treat low potassium levels in the blood),
  - ciclosporin (used to prevent or treat transplant rejection),
  - heparin sodium (used to prevent or delay blood clotting),
  - nonsteroidal anti-inflammatory drugs (NSAIDs) (used to reduce fever, pain and inflammation),
- any medicine that may be affected by a disturbance in the level of potassium in your blood such as:
  - digitalis glycosides (such as digoxin, used to treat heart failure and certain heart rhythm disorders),
  - corticosteroids (used to treat inflammation),
- any other medicine that could cause heart rhythm disorders such as:
  - amiodarone and quinidine (used to control cardiac rhythm),
  - chlorpromazine (used to treat certain mental illnesses),
  - cisapride (used to treat heartburn),
  - sparfloxacin (used to treat certain bacterial infections).

Some medicines may be affected by increased urine pH in relation with Sibnayal treatment such as :
- salicylates (used to treat pain and inflammation – aspirin-like medicines),
- tetracyclines (used to treat certain bacterial infections),
- barbiturates (sleep inducing medicines).

Sibnayal with food, drink and alcohol

Do not mix Sibnayal with hot food or hot liquids.
Do not drink alcohol while you are taking Sibnayal.

Pregnancy, breast-feeding and fertility

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.

Driving and using machines

Sibnayal is not likely to affect your ability to drive or use machines.

Sibnayal contains potassium

Sibnayal 8 mEq contains 308 mg of potassium per sachet. This is to be taken into consideration if you have a reduced kidney function or if you are on a controlled potassium diet.

Sibnayal 24 mEq contains 924 mg of potassium per sachet. This is to be taken into consideration if you have a reduced kidney function or if you are on a controlled potassium diet.

3. How to take Sibnayal

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

The amount of Sibnayal that people have to take depends on their age, weight and condition. Your doctor will tell you exactly the dose of Sibnayal to take. This will always be one or more whole sachets.

Your doctor may need to adjust your dose of Sibnayal.

The use of this medicine requires medical supervision.

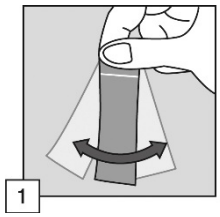
Dosage

The dose is adjusted by the doctor according to the level of bicarbonate in your blood.

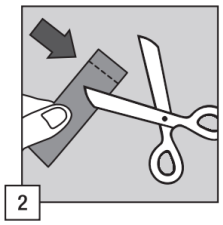
How to use

Sibnayal is for oral use (to be taken by mouth).
If you are not sure of how to use Sibnayal, contact your doctor or pharmacist.

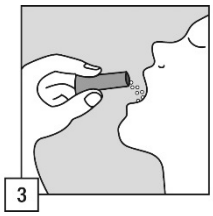
1. Hold the sachet vertically with your fingers above the dotted line. Shake it from side to side to ensure the contents move to the bottom of the sachet.



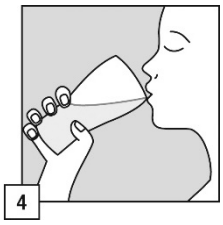
2. Cut the sachet along the dotted line, using scissors if necessary.



3. Place all or part of the sachet contents directly into your mouth on your tongue.



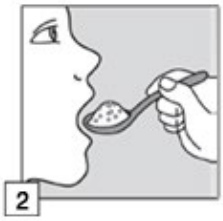
4. Swallow the granules immediately with a large glass of water. Do not chew or crush the granules. **Repeat steps 1 to 4** as required until you have taken the full dose.



For patients who are unable to swallow granules

1. Mix Sibnayal with small amounts of soft and cold food (e.g. fruit puree or yoghurt) directly on the spoon. You must swallow the soft food mixture immediately. Do not store the mixture for use later.

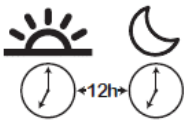
2. Place the mixture directly into the mouth and swallow it without chewing. Make sure that Sibnayal does not remain in the mouth. **Repeat steps 1 and 2** as required until the full dose has been taken.



Do not mix the granules with liquid before taking them.

When to take Sibnayal

Take Sibnayal in the morning and in the evening, during a meal. You must leave an interval of about 12 hours in between each dose to cover the whole night-and-day period.



Dose adjustment

Dose increases/decreases should be gradual, taking place over a few weeks. Your doctor will adjust the dose according to your condition. The usual recommended dose is 4 to 6 whole sachets of 24 mEq each day.

Please consult your doctor in the event of any side effects, as he / she may have to adjust the dose of this medicine.

Switch from another alkalising medicine

If you are switching from another alkalising medicines to Sibnayal, your doctor should closely supervise the switchover.

If you take more Sibnayal than you should

Talk to your doctor or pharmacist if you have taken more Sibnayal than you should have.
You may feel nauseous, need to vomit and have diarrhoea.
If you have taken a large amount of Sibnayal, you may feel weak or get unexplained tightness of the muscles, spasms (muscular contraction), abnormal tingling or burning sensations, pins and needles or numbness, mental confusion or an abnormal heart rate.

If you forget to take Sibnayal

Do not take a double dose to make up for a forgotten dose. Take it as soon as you remember. However, if your next dose is in less than six hours, skip the missed dose. Do not take more than two doses a day.

Talk to your doctor if you forget to take one or more doses.

If you stop taking Sibnayal

This medicine is for long-term use. It will only be effective as long as you are using it.
Do not stop unless your doctor tells you to, even if you feel better, as your disease may get worse. If you want to stop treatment, first talk to your doctor.

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

4. Possible side effects

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

Very common side effects (which may affect more than 1 in 10 people)
- abdominal pain (belly pain)

Common side effects (which may affect up to 1 in 10 people)
- upper abdominal pain (upper belly pain),
- gastrointestinal pain and disorders (stomach and intestinal pain and disorders),
- dyspepsia (poor digestion),
- vomiting,
- diarrhoea
- feeling sick (nausea) when starting treatment.

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 Sibnayal

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

Do not store above 25°C.

After opening a sachet, discard any unused content.

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 Sibnayal contains

The active substances are potassium citrate and potassium hydrogen carbonate (also known as potassium bicarbonate).

Each sachet of Sibnayal 8 mEq contains 282 mg of potassium citrate and 527 mg of potassium hydrogen carbonate.

Each sachet of Sibnayal 24 mEq contains 847 mg of potassium citrate and 1,582 mg of potassium hydrogen carbonate.

The other ingredients are hypromellose (E464), microcrystalline cellulose (E460 (i)), glycerol dibehenate, magnesium stearate (E470b), silica colloidal anhydrous, magnesium oxide heavy (E530), ethylcellulose (E462), chlorophyllin (E140 (ii)), talc.

What Sibnayal looks like and contents of the pack

Sibnayal is a mixture of green and white prolonged-released granules supplied in sachets.
Cartons contain 60 sachets.

Sibnayal is available in multipacks comprising 2, 3, 4, 5 and 6 cartons, each containing 60 sachets.
Not all pack sizes may be marketed.

Marketing Authorisation Holder

ADVICENNE
262 rue du Faubourg Saint Honoré
75008 Paris
France

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

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Manufacturer

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06560 Valbonne
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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: http://www.ema.europa.eu.