Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Okitask 25 mg Coated Granules in Sachet

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains 25 mg Ketoprofen (as lysine salt).

Excipients with known effect:
Aspartame (E951) 350 micrograms
Glucose 63 micrograms
Sucrose 6.13 milligrams
Sodium 6.9 micrograms

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Coated granules in sachet

White to ivory granules.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Okitask 25 mg Coated Granules in Sachet is recommended in the symptomatic treatment of acute mild to moderate pain such as rheumatic and muscular pain, headache, toothache, menstrual pain, and for pain and fever associated with common cold and flu symptoms.

Okitask 25 mg Coated Granules in Sachet is indicated in adults aged 18 years and over.

4.2 Posology and method of administration

Posology

Indication	Age group	Dose	Duration
Symptomatic relief of pain and fever	Adults aged 18 years and over	1 sachet as a single dose repeated 2 to 3 times a day as needed.*	The minimum effective dose should be used for the shortest time necessary to relieve symptoms (see section 4.4).

*Leave at least 4 hours between doses.

For short term use only.

Consult a doctor if symptoms persist or worsen, or if the product is required for more than 10 days.
Do not take more than 3 sachets in any 24-hour period.

Elderly
Ketoprofen Lysine Salt should be used with caution in the elderly.
For elderly patients, a dose of 1 sachet a day is recommended.

Paediatrics
Ketoprofen should not be used in children and adolescents under the age of 18 years.

Method of administration

The contents of the sachet must only be placed onto the tongue and swallowed. Okitask 25 mg Coated Granules in Sachet can be taken with or without water.

4.3 Contraindications

The medicinal product should not be used in the following cases:

- In patients with hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- In patients with a history of hypersensitivity reactions such as bronchospasm, asthma attacks, acute rhinitis, urticaria, rashes or other allergic reactions to substances with a similar mechanism of action (such as acetylsalicylic acid or other NSAIDs). (see section 4.8)

- During the third trimester of pregnancy (see section 4.6)
- In severe cardiac insufficiency (see section 4.4)
- In patients with gastric or duodenal ulcer, chronic dyspepsia, and gastritis, or any history of gastrointestinal bleeding, ulceration, or perforation
- In patients with leukocytopenia or thrombocytopenia, active bleeding, or bleeding diathesis on treatment with anticoagulants
- In patients with severe renal or hepatic insufficiency (see section 4.4).

4.4 Special warnings and precautions for use

General:
Undesirable effects may be minimised by using the minimum effective dose for the shortest duration necessary to control symptoms.

Masking of symptoms of underlying infections
As for other NSAIDs, Okitask can mask symptoms of infection such as fever, which may lead to delayed initiation of appropriate treatment and thereby worsening the outcome of the infection. This has been observed in bacterial community acquired pneumonia and bacterial complications to varicella. When Okitask is administered for fever or pain relief in relation to infection, monitoring of infection is advised. In nonhospital settings, the patient should consult a doctor if symptoms persist or worsen.
Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal (see section 4.2).

Respiratory:
Patients with asthma associated with chronic or allergic rhinitis, chronic sinusitis and/or nasal polyposis are more prone to allergies to acetylsalicylic acid and/or NSAIDs than the rest of the population. Administration of Ketoprofen Lysine Salt may cause attacks of asthma or bronchospasm in subjects who are allergic to acetylsalicylic acid or NSAIDs (see section 4.3). Consequently, in these subjects, and in cases of chronic obstructive pulmonary disease or kidney disease, the product should be used under medical supervision only.

Other NSAIDs:
The use of Ketoprofen Lysine Salt with concomitant NSAIDs, including cyclooxygenase-2 selective inhibitors, should be avoided.

SLE and mixed connective tissue disease:
Patients with systemic lupus erythematosus and mixed connective tissue have an increased risk of aseptic meningitis when taking NSAIDs.

Renal:
At the beginning of treatment, renal function should be closely monitored in patients with cardiac insufficiency, cirrhosis, and nephrosis, those on treatment with diuretics (see section 4.5) and patients with renal impairment, particularly when elderly. In these patients, use of ketoprofen may cause a reduction in renal blood supply, due to prostaglandin inhibition, leading to kidney failure.

Hepatic:
In patients with abnormal hepatic function values or a history of liver disease, transaminase values must be evaluated periodically, particularly during long-term treatment. Rare cases of jaundice and hepatitis have been reported associated with the use of ketoprofen.

Attention is required when the product is administered to patients with hepatic porphyria, as it could trigger an attack.

Cardiovascular and cerebrovascular effects
Clinical studies and epidemiological data suggest that the use of some NSAIDs (particularly at high doses and for long-term treatment) can be associated with an increase in the risk of arterial thrombotic events (for example myocardial infarction or stroke). Insufficient data is available to be able to exclude a similar risk for ketoprofen.

As with other NSAIDs, patients with uncontrolled hypertension, confirmed ischaemic cardiomyopathy, peripheral arterial disease and/or cerebrovascular disease may be treated with Ketoprofen Lysine Salt only after careful consideration.

Careful consideration should be exercised for patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, and smoking) for whom long-term treatment or high doses are not recommended.

Impaired female fertility:
In cases of pregnancy, fertility, or breastfeeding, see section 4.6.

Gastrointestinal:
GI bleeding, ulceration, or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious GI events.

Some epidemiological evidence suggests that ketoprofen may be associated with a high risk of serious gastrointestinal toxicity, relative to some other NSAIDs, especially at high doses (see also section 4.2 and 4.3).

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3), and in the elderly. These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk (see below and section 4.5). Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment. Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors, or anti-platelet agents such as aspirin (see section 4.5).

When GI bleeding or ulceration occurs in patients receiving Ketoprofen Lysine Salt, the treatment should be withdrawn. NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated (see section 4.8). Patients should be closely monitored, particularly for gastrointestinal bleeding.

Dermatological:
Very rare cases of severe, in some cases fatal, reactions, including exfoliative dermatitis, StevensJohnson syndrome and toxic epidermal necrolysis have been reported in association with use of NSAIDs (see section 4.8). Ketoprofen Lysine Salt should be suspended at the first signs of rash, mucosal lesions, or any other sign of hypersensitivity.

Vision:
Discontinue treatment in the event of sight problems, such as blurred vision.

Excipients:

Okitask 25 mg Coated Granules in Sachet contains aspartame artificial sweetener: patients with phenylketonuria should use this product with caution.

Okitask 25 mg Coated Granules in Sachet contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Okitask 25 mg Coated Granules in Sachet contains glucose. Patients with rare glucosegalactose malabsorption should not take this medicine.

Okitask 25 mg Coated Granules in Sachet contains less than 1 mmol sodium (23 mg) per sachet, that is to say essentially "sodium-free".

If symptoms persist or worsen, or if new symptoms occur, the patient should consult a doctor.

4.5 Interaction with other medicinal products and other forms of interactions

Combinations to be avoided

Alcohol: Alcohol consumed on its own can cause irritation of the gastrointestinal tract, therefore there is an increased risk of gastrointestinal bleeding and ulceration when NSAIDs are taken concomitantly with alcohol. Patients are advised to avoid this combination.

Anti-coagulants (such as heparin and warfarin): NSAIDs may enhance the effects of anti-coagulants (see section 4.4). Due to the increased risk of bleeding, patients must be closely monitored when co-administration is necessary.

Ciclosporin: Increased risk of nephrotoxicity when NSAIDs are given with Ciclosporin

Dabigatran: Possible increased risk of bleeding when NSAIDS are given with dabigatran.

Erlotinib: Increased risk of bleeding when NSAIDs are given with erlotinib

Lithium: Risk of plasma lithium concentration elevation, which may reach toxic levels, due to a reduction in the renal excretion of lithium. Where applicable, plasma levels of lithium should be closely monitored, and the dose of lithium adjusted during and after treatment with NSAIDs.

Methotrexate, at doses higher than 15 mg/week: Increased risk of methotrexate-related blood toxicity, particularly when administered at high doses (>15 mg/week), most probably associated with the displacement by methotrexate-bound proteins and reduced renal clearance. Therefore, patients on treatment with these medicinal products must seek medical advice before taking the product.

Other NSAIDs (including cyclooxygenase-2 selective inhibitors) and high-dose salicylates unless low-dose aspirin (not above 75mg daily) has been advised by a doctor, as this may increase the risk of adverse reactions such as: Increased risk of gastrointestinal ulceration and bleeding (see section 4.4).

Quinolones: Possible increased risk of convulsions when NSAIDs are given with quinolones

Venlafaxine: Increased risk of bleeding when NSAIDs given with venlafaxine.

Associations requiring caution

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding (see section 4.4).

Antihypertensive agents, ACE inhibitors and angiotensin II receptor antagonists: In patients with impaired renal function (for example, dehydrated and elderly patients), co-administration of an ACE-inhibitor or an angiotensin II receptor antagonist and cyclooxygenase inhibitors may cause a further deterioration in renal function, including potential acute renal insufficiency.
These combinations must therefore be administered with caution, particularly in elderly patients. Patients must be suitably hydrated and renal function monitoring should be considered after starting concomitant therapy. NSAIDs may antagonise the blood pressure lowering effects of antihypertensive therapy.

Baclofen: NSAIDs possibly reduce the excretion of baclofen (increased risk of toxicity).

Cardiac glycosides: NSAIDs possibly increase plasma concentration of cardiac glycosides, also possible exacerbation of heart failure and reduction of renal function.

Corticosteroids: Increased risk of gastrointestinal ulceration or bleeding (see section 4.4).

Coumarins: NSAIDs possibly enhance anticoagulant effect of coumarins

Diphenylhydantoin and Sulphonamides: since Sprintafen is highly protein-bound, it may be necessary to reduce the dose of diphenylhydantoin or sulphonamides administered during treatment.

Diuretics: Patients taking diuretics and those who are also severely dehydrated are at a greater risk of developing renal insufficiency secondary to the reduction in renal blood flow caused by prostaglandin inhibition. These patients must be rehydrated before starting co-administration and renal function should be closely monitored (see Section 4.4) after the start of treatment. NSAIDs may reduce the effect of diuretics.

Hypoglycaemic agents (sulfonylureas): NSAIDs possibly enhance the effects of sulfonylureas.

Methotrexate at doses lower than 15 mg/week:
Weekly complete blood count monitoring is required during the first few weeks of combined use. Monitoring should be conducted more frequently in the presence of an even slight deterioration in renal function and in elderly subjects.

Pentoxiphylline: Increased risk of bleeding. More frequent clinical check-ups and monitoring of bleeding time required.

Penicillamine: Possible increased risk of nephrotoxicity when NSAIDs are given with penicillamine.

Pemetrexed: NSAIDs possibly reduce renal excretion of pemetrexed.

Prasugrel: Possible increased risk of bleeding when NSAIDs are given with prasugrel.

Probenecid: Concomitant administration of probenicid may significantly reduce Sprintafen plasma clearance.

Tacrolimus: Increased risk of nephrotoxicity when NSAIDs given with tacrolimus.

Zidovudine: Increased risk of hematological toxicity when NSAIDs are given with zidovudine.

Ritonavir: Plasma concentrations of NSAIDs are possibly increased by ritonavir.

4.6 Fertility, pregnancy and lactation

Pregnancy
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5 %. The risk is believed to increase with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

During the first and second trimester of pregnancy, Sprintafen Lysine Salt should not be given unless clearly necessary. If Sprintafen Lysine Salt is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:

- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);

- renal dysfunction, which may progress to renal failure with oligo-hydroamniosis; the mother and the neonate, at the end of pregnancy, to:
- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses.
- inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently, Sprintafen Lysine Salt is contraindicated during the third trimester of pregnancy.

Breastfeeding
Insufficient data are available on excretion of Sprintafen in human milk. Sprintafen lysine salt is not recommended in nursing mothers.

Fertility
Long-term use of some NSAIDs is associated with reduced female fertility, which is reversible on stopping treatment. The use of Sprintafen, as with any drug known to inhibit cyclooxygenase/prostaglandin synthesis, might impair fertility and is not recommended in women attempting to conceive. In women who have difficulty conceiving or who are undergoing investigation of infertility, withdrawal of Sprintafen should be considered.

4.7 Effects on ability to drive and use machines

Sprintafen Lysine Salt has negligible influence on the ability to drive or use machines at the recommended dosage and treatment duration. Adverse reactions such as blurred vision, dizziness and drowsiness may occur (see section 4.8). If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

Gastrointestinal: the most commonly-observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation, or GI bleeding, sometimes fatal, particularly in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4) have been reported following administration. Less frequently, gastritis has been observed.

In very rare cases, hypersensitivity may present in the form of severe systemic reactions (laryngeal oedema, glottic oedema, dyspnoea, palpitations, Steven-Johnsons Syndrome) through to anaphylactic shock. Immediate medical assistance is required in such cases.

Each adverse event has been categorised according to the following frequency classification:

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1000 to <1/100)
Rare (≥1/10000 to <1/1000)
Very rare (<1/10000)
Not known (cannot be estimated from the available data)

System organ class	**Undesirable effect and Frequency**
Blood and lymphatic system disorders	**Rare:** Haemorrhagic anaemia **Not known:** Thrombocytopenia, agranulocytosis, medullary insufficiency, and hypoplasia
Immune disorders	**Not known:** Anaphylactic reactions (including shock), hypersensitivity
Psychiatric disorders	**Not known:** Mood altered
Nervous system disorders	**Uncommon:** Headache, vertigo, drowsiness **Rare:** Paraesthesia **Not known:** Seizures, dysgeusia.
Eye disorders	**Rare:** Blurred vision
Ear and labyrinth disorders	**Rare:** Tinnitus
Cardiac disorders	**Not known:** Cardiac failure
Vascular disorders	**Not known:** Hypertension, vasodilation
Respiratory, thoracic, and mediastinal disorders	**Rare:** Asthma **Not known:** Bronchospasm (particularly in patients with confirmed

	hypersensitivity to acetylsalicylic acid and other NSAIDs), rhinitis, dyspnoea, laryngeal oedema, glottic oedema.
Gastrointestinal disorders	**Common:** Dyspepsia, nausea, abdominal pain, vomiting **Uncommon:** Constipation, diarrhoea, flatulence, and gastritis **Rare:** Stomatitis, peptic ulcer **Not known:** Exacerbation of colitis and Crohn's disease, gastrointestinal bleeding and perforation, ulcerative stomatitis, melaena, haematemesis, duodenal perforation and ulcer
Hepato-biliary disorders	**Rare:** Hepatitis
Skin and subcutaneous tissue disorders	**Uncommon:** Rash, pruritus **Not known:** Photosensitivity reactions, alopecia, urticaria, angio-oedema, bullous skin reactions including Stevens-Johnson syndrome and toxic epidermal necrosis, oedema and exanthem.
Renal and urinary disorders	**Not known:** Acute renal failure, tubulointerstitial nephritis, nephritic syndrome.
General disorders and administration site conditions	**Uncommon:** Fatigue, oedema
Investigations	**Rare:** Weight gain, transaminase elevation and elevated serum bilirubin concentration due to hepatic disorders. **Not known:** renal function test alterations.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Symptoms
The UK National Poisons Information Service considers 10 mg/kg Sprintafen as a toxic dose. In most instances of overdose the symptoms observed are usually limited to lethargy, drowsiness, abdominal pain, nausea, vomiting, which are generally reversible with supportive care. Respiratory depression, coma or convulsions have occurred following large Sprintafen overdoses. GI bleeding, hypotension, hypertension, or acute renal failure may occur but are rare.

Treatment measures
There are no specific antidotes for Sprintafen lysine salt overdose. Management should occur at a specialised centre, with symptomatic and supportive treatment instituted. It should include maintenance of airway patency, monitoring of cardiac and vital signs, treatment to compensate for dehydration, monitoring of urinary excretion and correction of acidosis. Considered oral administration of active charcoal if the patient presents within 1 hour of ingestion of a potentially toxic amount. Frequent or prolonged convulsions should be treated with intravenous diazepam.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroids, propionic acid derivatives.

ATC code: M01AE03.

Sprintafen Lysine Salt has a higher solubility compared with Sprintafen acid.

Mechanism of action
The mechanism of action of NSAIDs is related to the reduction in prostaglandin synthesis caused by inhibition of the enzyme cyclooxygenase.
More specifically, NSAIDs inhibit the transformation of arachidonic acid into cyclic endoperoxides, PGG_2 and PGH_2, the precursors of prostaglandins PGE_1, PGE_2, PGF_2a and PGD_2, prostacyclin PGI_2 and thromboxanes (TxA_2 and TxB_2). Inhibition of prostaglandin synthesis may also interfere with other mediators such as quinines, causing an indirect action in addition to the direct action.

Sprintafen Lysine Salt has a potent analgesic effect, on account of both its anti-inflammatory and central effects. Painful inflammatory conditions are resolved or reduced, thereby favouring articular motility.

5.2 Pharmacokinetic properties

Absorption

Sprintafen lysine has a higher solubility compared to Sprintafen acid. Sprintafen lysine salt is absorbed rapidly and completely.

In a pharmacokinetic study on 69 subjects, peak plasma concentrations of 2.77 µg/ml (SD 0.82 µg/ml) were achieved 15 – 30 minutes after administration.

No accumulation has been observed following repeated administrations of Sprintafen.

When Sprintafen is administered with food, its total bioavailability (AUC) is not altered; however, the rate of absorption is slowed.

Distribution
95-100% of Sprintafen binds with plasma proteins (primarily albumin).
Plasma clearance values are between 0.06 and 0.08 L/kg/h and the distribution value is 0.1-0.4 L/kg.

Biotransformation
Sprintafen is extensively metabolised by the hepatic microsomal enzymes, primarily by conjugation and only marginally by means of hydroxylation. The resulting metabolites have no pharmacological activity.

Elimination
The product is eliminated rapidly and primarily via the kidneys. It has a plasma half-life of approximately 1.5 hours. 60-80% of a dose of Sprintafen 25 mg Granules is excreted in urine as a glucoronide metabolite within 24 hours.

5.3 Preclinical safety data

The LD_{50} of Sprintafen lysine salt following oral administration in rats and mice was 102 and 444 mg/kg, respectively, equal to 30-120 times the active anti-inflammatory and analgesic dose for the animal. For intraperitoneal administration, the LD_{50} of Sprintafen lysine salt is 104 and 610 mg/kg in rats and mice, respectively.

Prolonged treatment with oral Sprintafen lysine salt in rats, dogs, and monkeys, at doses equal to or higher than the therapeutic doses, did not cause any toxicity. Gastrointestinal and renal alterations were reported at high doses, in line with the known side effects of non-steroidal anti-inflammatory drugs in animals. In one prolonged toxicity study on oral or rectal administration in rabbits, Sprintafen was seen to be better tolerated when administered via the rectal route than via the oral route. In a tolerability study conducted in rabbits via the intramuscular route, Sprintafen lysine salt was seen to be well tolerated.
In teratogenesis, fertility, reproduction, and post-natal toxicity studies, Sprintafen was seen to have no teratogenic effect or negative effect on the reproductive function.
Sprintafen lysine salt was not reported as being mutagenic during *in vitro* and *in vivo* genotoxicity tests. Carcinogenesis studies on Sprintafen in mice and rats showed that it had no carcinogenic effect.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Povidone (E1201)
Silica, colloidal anhydrous (E551)
Hypromellose
Basic butylated methacrylate copolymer
Sodium laurilsulphate
Stearic acid (E570)
Magnesium stearate (E572)
Aspartame (E951)
Mannitol (E421)

Xylitol (E967)
Talc (E553B)

Flavour
Glucose
Sucrose
Maltodextrin
Maize starch (E1450)
Butylated hydroxyanisole (E320)
Arabic gum
Lime flavour
Lemon flavour
Mint flavour.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

No special storage conditions are required for this medicinal product.

6.5 Nature and contents of container

Opaque, PE/aluminium sachets containing 700 mg of coated granules in the following pack sizes:

8, 10, 15, 16, 20 sachets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Dompé Farmaceutici S.p.A.
Via San Martino 12-12/a
20122 Milano
Italy

8 MARKETING AUTHORISATION NUMBER

PA23072/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1st March 2019

10 DATE OF REVISION OF THE TEXT

February 2021