SUMMARY OF PRODUCT CHARACTERISTIC

1. NAME OF THE PHARMACEUTICAL PRODUCT

DEKSIT 25 mg/4 mg Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredients:

Each tablet contains 36,90 mg dexketoprofen trometamol equivalent to 25 mg dexketoprofen and 4 mg thiocolchicoside.

Excipients:

Sodium starch glycolate Type A 10.4 mg

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Tablet

It has the appearance of a yellowish, round, flat notched tablet.

4. CLINICAL PROPERTIES

4.1 Therapeutic indications

DEKSIT is indicated for symptomatic treatment of osteoarthritis, painful syndromes of the vertebral column, extra-articular rheumatism, painful muscle spasms, post-traumatic and postoperative pain.

4.2. Posology and method of application

Posology / application frequency and duration

Unless otherwise recommended by the doctor;

The treatment dose is one tablet 3 times a day.

DEKSIT should not be considered for long-term use and treatment should be limited to the symptomatic period. The treatment period is 5-7 days.

Method of Application:

For oral use only.

Tablets should be taken on a full stomach with a glass of water (150 mL).

If diarrhea occurs following oral administration, treatment should be discontinued.

Additional information on special populations:

Kidney / Liver failure:

Dexketoprofen

In patients with mild renal dysfunction (creatinine clearance 50-80 ml/min) the initial dose should be reduced to a total daily dose of 50 mg. Dexketoprofen should not be used in patients with moderate to severe renal dysfunction (creatinine clearance <50 ml/min).

Patients with mild or moderate liver dysfunction should start treatment at low doses (50 mg total daily dose) and be closely monitored. Dexketoprofen should not be used in patients with severe liver dysfunction.

Thiocolchicoside

The safety and effectiveness of thiocolchicoside in patients with renal/liver impairment have not been studied.

Pediatric population:

There are no studies of DEKSIT in children and adolescents. Therefore, its reliability and effectiveness have not been proven. It should not be used in people under 18 years of age.

Geriatric population:

Dexketoprofen

It is recommended to start dexketoprofen treatment at the lowest of the dosage range (50 mg total daily dose) in elderly patients. Once good tolerance is confirmed, dosage can be increased to amounts recommended for the general population.

Thiocolchicoside

The safety and effectiveness of thiocolchicoside in elderly patients have not been studied.

During treatment with drugs containing non-steroidal anti-inflammatory drugs (NSAIDs) Gastrointestinal

4.3 Contraindications

DEKSIT is contraindicated in the following cases:

- Dexketoprofen, thiocolchicoside, other NSAIDs or the content of DEKSIT patients with hypersensitivity to any excipients,
- In flaccid paralysis, muscle hypotonia,
- In patients with bleeding problems and using anticoagulant drugs,
- Gastrointestinal bleeding or other active bleeding or bleeding disorders in patients,
- Like other non-steroidal anti-inflammatory drugs (NSAIDs), DEKSIT should not be used in patients whose asthma attacks, urticaria and acute colds are exacerbated by the use of acetylsalicylic acid or other NSAIDs that inhibit the prostaglandin synthetase enzyme. Severe, rarely fatal, anaphylaxis-like reactions have been reported to occur with the use of NSAIDs in these patients (see Section 4.4 Special warnings and precautions for use - Anaphylactoid reactions and Pre-existing asthma).
- In patients with active or suspected peptic ulcer/bleeding or a history of recurrent peptic ulcer/bleeding (two or more distinct episodes of proven ulceration or bleeding) or chronic dyspepsia.
- In patients with a history of gastrointestinal bleeding or perforation related to previous NSAID therapy,
- In patients with Crohn's disease or ulcerative colitis,
- In patients with a history of bronchial asthma,
- In patients with severe heart failure,
- In patients with moderate or severe renal dysfunction,
- In patients with severe liver dysfunction,
- In patients with hemorrhagic diathesis or other coagulation disorders,
- In the treatment of perioperative pain in case of coronary artery bypass graft (CABG) surgery (see section 4.4 Special warnings and precautions for use),
- Throughout pregnancy and lactation,
- Contraindicated in women of childbearing potential who are not using effective contraception (see section 4.6).
- In patients aged 18 and under,

- It should not be used by patients with a history of asthma, urticaria or allergic-type reactions as a result of taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylaxis-like reactions due to NSAIDs have been reported in such patients (see section 4.4).

4.4. Special use warnings and precautions

Dexketoprofen

Cardiovascular (CV) risks:
-NSAIDs may increase the risk of potentially fatal CV thrombotic events, myocardial infarction and stroke. This risk may increase depending on duration of use. The risk may be higher in patients with CV disease or risk factors for CV disease.
DEKSIT TABLET is contraindicated in the treatment of preoperative pain in coronary artery bypass surgery**.**
Gastrointestinal (GI) risks:
NSAIDs cause serious GI adverse effects, such as bleeding, ulceration, and stomach or intestinal perforation, which can be fatal. These adverse events can occur at any time, with or without warning symptoms.
Elderly patients are at higher risk for serious GI effects.

Warnings:

The safety of use of dexketoprofen in children and adolescents has not been established.

Caution should be exercised when used in patients with a history of allergic conditions.

The incidence of adverse effects with NSAIDs is high in the elderly. In these patients, treatment should be started at low doses.

Concomitant use of DEKSIT with other NSAIDs, including selective cyclooxygenase-2 (COX-2) inhibitors, should be avoided.

Undesirable effects can be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2 and gastrointestinal and cardiovascular risks below).

Gastrointestinal (GI) effects - risk of GI ulceration, bleeding or perforation:

NSAIDs, including dexketoprofen, may cause serious GI adverse effects, including inflammation, bleeding, ulceration, or perforation of the stomach, small intestine, or large intestine, which can be fatal. These serious adverse effects can be experienced by patients treated with NSAIDs at any time during treatment, with or without warning signs. Only one in five patients who develop a serious GI adverse event during treatment with an NSAID is symptomatic. Upper GI ulcers, major bleeding, or perforations due to NSAIDs appear to occur in approximately 1% of patients treated

for 3 to 6 months and in approximately 2% to 4% of patients treated for one year. Persistence of these trends over time increases the likelihood that the patient will develop a serious GI event at some stage of treatment. However, even short-term treatment is not without risks.

Extreme caution should be exercised when prescribing NSAIDs to patients with a prior history of ulcer disease or GI bleeding. Studies have shown that patients who use NSAIDs and have a prior history of peptic ulcers and/or GI bleeding have a 10-fold increased risk of developing GI bleeding compared to patients without these risk factors. In addition to a history of ulcers, studies have identified many concomitant treatments and conditions that may lead to comorbidities that may increase the risk of GI bleeding, such as: treatment with oral corticosteroids, treatment with anticoagulants (warfarin) or antiplatelet agents (aspirin), treatment with selective serotonin reuptake inhibitors, prolonged treatment with NSAIDs, smoking, alcohol use, advanced age and poor general health status. Most spontaneous reports of fatal GI events have been reported by elderly and frail patients; therefore, it is necessary to be especially careful when administering treatment in this population.

To minimize the potential risk of an adverse GI event, patients should be treated for the shortest possible duration and with the lowest effective dose of the NSAID. Patients and physicians should be alert for signs and symptoms of GI ulceration and bleeding during NSAID therapy, and if serious GI events are suspected, additional evaluation and additional treatment should be initiated immediately. If the serious adverse event persists, NSAID therapy should be discontinued. In high-risk patients, alternative treatments that do not include NSAIDs should be considered.

GI bleeding, ulceration, or perforation, which can be fatal, has been reported with all NSAIDs at any stage of treatment, with or without warning symptoms or a history of serious GI events. If GI bleeding or ulceration occurs in patients receiving DEKSIT, treatment should be discontinued.

The risk of gastrointestinal bleeding, ulceration or perforation increases as the NSAID dose increases, especially in patients with a history of ulcers complicated by bleeding or perforation (see section 4.3) and in the elderly.

Elderly: There is an increased frequency of adverse reactions to NSAIDs in the elderly, particularly gastrointestinal bleeding and perforation, which can be fatal (see section 4.2). These patients should start treatment at the lowest possible dose.

As with all NSAIDs, any history of oesophagitis, gastritis and/or peptic ulcer should be investigated to ensure complete recovery before initiating dexketoprofen trometamol treatment. Patients with gastrointestinal symptoms or a history of gastrointestinal disease should be monitored for digestive disorders, especially gastrointestinal bleeding.

NSAIDs can be used with caution in people with a history of gastrointestinal diseases (ulcerative colitis, Crohn's disease) as they may increase the risk of disease (see section 4.8, undesirable effects).

Concomitant treatment with protective agents (e.g. misoprostol or proton pump inhibitor) should be considered in these patients, as well as in patients requiring concomitant use of low-dose acetylsalicylic acid or the use of other drugs likely to increase gastrointestinal risk (see below and section 4.5).

Patients with a history of gastrointestinal toxicity, especially the elderly, should report abnormal abdominal symptoms (especially gastrointestinal bleeding), especially during the initial phase of treatment.

Caution is advised in patients taking concomitant oral corticosteroids, anticoagulants such as warfarin, selective serotonin reuptake inhibitors, or antiplatelet drugs such as acetylsalicylic acid, which may increase the risk of ulceration or bleeding (see section 4.5).

All non-selective NSAIDs can inhibit platelet aggregation and prolong bleeding time through inhibition of prostaglandin synthesis. Therefore, the use of dexketoprofen trometamol is not recommended in patients treated with warfarin or other coumarins or heparins that affect hemostasis.

Renal effects:

As with all NSAIDs, it may increase plasma urea nitrogen and creatinine.

Detailed note is below.

Long-term use of NSAIDs causes renal papillary necrosis and other renal damage. Additionally, patients have also experienced renal toxicity, as renal prostaglandins play a compensatory role in the maintenance of renal perfusion. In such patients, NSAID administration may cause a dose-dependent decrease in prostaglandin formation and, secondarily, renal blood flow, which may precipitate overt renal decompensation. Patients at highest risk of causing such a reaction are those with impaired kidney function, heart failure, liver dysfunction, those using diuretics and angiotensin-converting enzyme (ACE) inhibitors, and the elderly. After stopping NSAID therapy, there is usually a return to pre-treatment status.

Like all NSAIDs, DEKSIT may increase plasma urea nitrogen and creatinine. Like other prostaglandin synthesis inhibitors, it may be associated with undesirable effects on the renal system, which may lead to glomerular nephritis, interstitial nephritis, renal papillary necrosis, nephrotin syndrome and acute renal failure.

Advanced kidney diseases:

There is no information from controlled studies regarding the use of dexketoprofen trometamol in patients with advanced renal disease. Therefore, DEKSIT treatment is not recommended in patients with advanced kidney disease. If DEKSIT treatment is initiated, it is recommended that the patient's renal functions be closely monitored.

Cardiovascular thrombotic events:

Clinical studies of up to 3 years with many selective COX-2 and non-selective COX inhibitors have shown an increased risk of serious cardiovascular (CV) thrombotic events, myocardial infarction and stroke, which can be fatal. COX-2 selective and non-selective all NSAIDs may carry similar risks. Patients known to have cardiovascular disease or to be at risk for cardiovascular disease may be at a higher risk. To reduce the risk of adverse cardiovascular events in patients receiving NSAID therapy, the lowest effective dose should be used for the shortest possible duration. Even if there are no previous cardiovascular symptoms, the physician and the patient should be alert to such events. The patient should be informed about the symptoms and/or signs of serious cardiovascular events and what to do if they occur.

There is no consistent evidence that concomitant use of aspirin reduces the increased risk of serious cardiovascular thrombotic events associated with NSAID use. Concomitant use of NSAIDs with aspirin increases the risk of serious GI events (see Section 4.4 Special warnings and precautions for use).

An increased incidence of myocardial infarction and stroke was observed in two large, controlled clinical studies of a COX-2 selective NSAID given for pain management in the first 10 to 14 days following coronary artery bypass graft (CABG) surgery (see section 4.3 Contraindications).

Hypertension:

As with all other NSAIDs, dexketoprofen trometamol may cause hypertension or worsening of pre-existing hypertension, both of which may increase the risk of cardiovascular events. Diuretic treatment responses of patients treated with thiazide diuretics or loop diuretics may be impaired when using NSAIDs. NSAIDs, including dexketoprofen trometamol, should be used with caution in patients with hypertension. Blood pressure should be closely monitored at the beginning of dexketoprofen trometamol treatment and throughout the course of treatment.

Congestive heart failure and edema:

Fluid retention and edema have been observed in some patients treated with NSAIDs, including dexketoprofen trometamol. Therefore, DEKSIT should be used with caution in patients with fluid retention or heart failure.

Appropriate monitoring and recommendations are necessary as fluid retention and edema have been reported in association with NSAID therapy in patients with a history of hypertension and/or mild-to-moderate congestive heart failure.

Elderly patients are more likely to experience renal, cardiovascular or liver dysfunction (see section 4.2).

Clinical studies and epidemiological data suggest that the use of some NSAIDs (especially at high doses and long-term treatment) may be associated with a small increased risk of arterial thrombotic events (especially myocardial infarction or stroke). There are insufficient data for dexketoprofen trometamol to exclude such a risk.

Patients with uncontrolled hypertension, congestive heart failure, diagnosed ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease should be treated with dexketoprofen trometamol after careful evaluation. The same caution should be exercised before initiating long-term treatment in patients with cardiovascular risk factors (e.g. hypertension, hyperlipidemia, diabetes mellitus, smoking).

Systemic lupus erythematosus (SLE) disease and mixed connective tissue disease:

In patients with SLE and mixed connective tissue disorders, there may be an increased risk of aseptic meningitis (see section 4.8).

Dexketoprofen should be used with caution in patients with hematopoietic disorders, systemic lupus erythematosus, or mixed connective tissue disease.

Like all other NSAIDs, it may cause small transient increases in some liver parameters and significant increases in AST and ALT. When there are drug-related increases in such parameters, treatment should be discontinued.

Anaphylactoid reactions:

As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, may occur in rare cases with dexketoprofen trometamol, without previous exposure to the drug. DEXIT should not be given to patients with aspirin triad. This symptom complex typically occurs in asthmatic patients who have rhinitis with or without nasal polyps or who exhibit severe and potentially fatal bronchospasm following the use of aspirin or NSAIDs.

(see Section 4.3 Contraindications and Section 4.4 Special warnings and precautions for use – Pre-existing asthma). If an anaphylactoid reaction occurs, immediate help should be given.

Dexketoprofen, like other NSAIDs, may mask the symptoms of infectious diseases.

Skin reactions:

Serious skin reactions, some fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported very rarely in association with the use of

NSAIDs, including dexketoprofen trometamol. These serious events can occur without warning. Patients should be informed of the signs and symptoms of serious skin reactions and use of dexketoprofen trometamol should be discontinued at the first occurrence of skin rash, skin itching, mucosal lesions, or any signs of hypersensitivity.

Pregnancy:

Dexketoprofen trometamol, like other NSAIDs, should not be used in late pregnancy because it may cause premature closure of the ductus arteriosus (the opening between the two large arteries coming out of the heart [aorta and pulmonary artery], which are open in the womb and must close following birth).

Fertility:

As with other NSAIDs, the use of dexketoprofen trometamol may affect fertility and is not recommended in women trying to become pregnant. In women who have difficulty conceiving or are being investigated for infertility, discontinuation of dexketoprofen trometamol should be considered. Dexketoprofen trometamol should not be used during the first and second trimesters of pregnancy unless clearly necessary.

Precautions:

General:

Dexketoprofen trometamol should not be expected to replace corticosteroids or treat corticosteroid deficiency. Stopping corticosteroid suddenly may cause a flare-up of the disease. Patients on long-term corticosteroid therapy should reduce their treatment slowly and gradually if the decision is made to discontinue corticosteroid therapy.

The pharmacological activity of dexketoprofen trometamol, contained in DEKSIT, in reducing [fever and] inflammation may reduce the usefulness of these diagnostic signs used in diagnosing complications of painful conditions that are thought to be non-infectious.

DEXIT should be used with caution in patients with hematopoietic disorders, systemic lupus erythematosus or mixed connective tissue disease.

Hepatic effects:

Borderline elevations of one or more liver tests may occur in up to 15% of patients taking NSAIDs, including dexketoprofen trometamol. These laboratory abnormalities may progress, remain unchanged, or resolve spontaneously with continued treatment. Significant increases in ALT and AST levels (three times the upper limit of normal or more) have been reported in approximately 1% of patients in clinical studies with NSAIDs. Rare cases of severe hepatic reactions, including jaundice and fatal fulminant hepatitis, liver necrosis and liver failure, some

with fatal outcome, have also been reported.

During long-term treatment with dexketoprofen trometamol, regular monitoring of liver function is necessary as a precautionary measure. If abnormal liver function tests persist or worsen, if clinical signs or symptoms consistent with liver disease develop, or if other symptoms (e.g. eosinophilia, skin rashes, etc.) occur, treatment with DEKSIT should be discontinued.

Hematological effects:

Anemia sometimes occurs in patients taking NSAIDs, including dexketoprofen trometamol. This may be due to fluid retention, GI blood loss, or an unspecified effect on erythropoiesis. Patients receiving long-term treatment with NSAIDs, including DEKSIT, should have their hemoglobin and hematocrit levels checked regularly, even if they do not show any signs or symptoms of anemia.

NSAIDs have been shown to prolong bleeding time in some patients by inhibiting platelet aggregation. In contrast to aspirin, their effects on platelet function are qualitatively less severe, shorter lasting and reversible. Patients with pre-existing coagulation disorders or those using anticoagulants who may be adversely affected by changes in platelet function should be carefully monitored during the use of DEKSIT.

Pre-existing asthma:

Patients with asthma may have aspirin-sensitive asthma. Aspirin use in aspirin-sensitive asthmatic patients has been associated with severe bronchospasm that can result in death. Since cross-reactivity, including bronchospasm, between aspirin and other NSAIDs has been reported in these patients with aspirin sensitivity, DEKSIT should not be given to patients with this form of aspirin sensitivity and should be used with caution in patients with pre-existing asthma.

Laboratory tests:

Because serious GI tract ulcerations and bleeding can occur without warning symptoms, physicians should monitor patients for signs or symptoms of GI bleeding. Complete blood count and biochemistry profiles of patients receiving long-term NSAID therapy should be checked periodically. If clinical signs and symptoms consistent with liver or renal disease develop, or if systemic symptoms (e.g. eosinophilia, rash, etc.) occur, or if liver test results are abnormal or worsen, DEKSIT intake should be stopped.

Thiocolchicoside

Preclinical studies have shown that one of the thiocolchicoside metabolites (SL59.0955) induces aneuploidy (i.e. unequal number of chromosomes in dividing cells) at concentrations close to the human exposure observed at doses of 8 mg twice daily oral administration (see section 5.3). Aneuploidy appears to be a risk factor for teratogenicity, embryo fetotoxicity/spontaneous

abortion and impaired male fertility, and a potential risk factor for canker. As a precaution, product use in doses exceeding the recommended dose or long-term use should be avoided (See Section 4.2).

In postmarketing experience, cytolytic and cholestatic hepatitis have been reported with thiocolchicoside. Severe cases (e.g. fulminant hepatitis) have been reported in patients using concomitant NSAIDs or paracetamol. Patients should be cautioned to immediately report symptoms that may be related to liver toxicity (see section 4.8).

The use of thiocolchicoside in children is not recommended.

Thiocolchicoside may precipitate seizures, especially in patients with epilepsy or in patients at risk of seizures (see section 4.8).

Patients should be carefully informed about the potential risk of pregnancy and the effective contraceptive measures to be followed.

If diarrhea occurs following oral administration, thiocolchicoside treatment should be discontinued.

This product contains less than 1 mmol (23 mg) sodium per tablet; so it's essentially "sodium-free".

4.5. Interactions with other medicinal products and other forms of interaction

Dexketoprofen

The following interactions generally apply to all non-steroidal anti-inflammatory drugs (NSAIDs):

Not recommended combinations:

- Concomitant use of two or more NSAIDs (including acetylsalicylic acid) should be avoided as it may increase the risk of adverse events (see section 4.4).
- Aspirin: When dexketoprofen is given together with aspirin, protein binding decreases although the clearance of free dexketoprofen does not change. Although the clinical significance of this interaction is unknown, as with other NSAIDs, concomitant administration of dexketoprofen and aspirin is generally not recommended because it increases the likelihood of adverse effects.
- Anticoagulants: NSAIDs may potentiate the effects of anticoagulants such as warfarin (see section 4.4) due to increased plasma protein binding of dexketoprofen, inhibition of platelet function and gastroduodenal mucosal damage. If this combination cannot be avoided, close clinical observation and laboratory values should be monitored. Warfarin: The effect of

warfarin and NSAIDs on GI bleeding is synergistic; That is, patients using these two drugs together have a higher risk of serious GI bleeding than patients using these two drugs alone.
Heparins: Increased risk of haemorrhage (due to platelet function inhibition and gastroduodenal mucosa damage). If the combination cannot be avoided, close clinical observation and laboratory values should be monitored.

- Corticosteroids: There is an increased risk of gastrointestinal ulceration or bleeding (see section 4.4).
- Lithium (identified with many NSAIDs): NSAIDs cause increases in plasma lithium levels and decreases in renal lithium clearance. The mean minimum lithium concentration increased by 15% and renal clearance decreased by approximately 20%. These effects are attributed to the inhibition of renal prostaglandin synthesis by NSAIDs. Therefore, when NSAIDs and lithium are administered simultaneously, the patient should be carefully monitored for lithium toxicity.
- Use of methotrexate at doses of 15 mg/week or higher: In general, an increase in hematological toxicity is observed due to the decrease in renal clearance of methotrexate with anti-inflammatory agents. NSAIDs have been reported to competitively inhibit methotrexate accumulation in rabbit kidney sections. This indicates that NSAIDs may increase methotrexate toxicity. Caution should be exercised if NSAIDs are administered simultaneously with methotrexate.
- Hydantoins and sulfonamides: The toxic effects of these compounds may be increased.

Combinations requiring attention:

- Diuretics, ACE inhibitors and angiotensin II receptor antagonists: Dexketoprofen may reduce the effect of diuretics and antihypertensive products. Available reports indicate that NSAIDs may reduce the antihypertensive effect of ACE-inhibitors. This interaction should be considered in patients taking NSAIDs concomitantly with ACE-inhibitors. In some patients with compromised renal function (e.g., dehydrated patients or elderly patients with compromised renal function), concomitant use of cyclooxygenase-inhibiting agents and ACE inhibitors or angiotensin II receptor antagonists may result in further deterioration of renal function, which is usually reversible. In cases where dexketoprofen and a diuretic are prescribed together, patients should be ensured to be adequately hydrated and renal functions should be monitored at the beginning of treatment, as diuretics may increase the risk of nephrotoxicity of NSAIDs.
- Furosemide: Clinical studies and postmarketing observations indicate that the use of dexketoprofen may reduce the natriuretic effect of furosemide and thiazides in some patients.

This response is attributed to inhibition of renal prostaglandin synthesis. When treated concomitantly with NSAIDs, the patient should be closely monitored for signs of renal insufficiency (see Section 4.4 Special warnings and precautions for use - Renal effects) and to ensure diuretic effectiveness.

- Use of methotrexate in doses lower than 15 mg/week: The hematological toxicity of methotrexate increases, generally due to the reduction of its renal clearance by anti inflammatory compounds. Blood counts should be monitored weekly during the first weeks of the combination. Monitoring should be increased in cases with slightly impaired renal function and also in the elderly.
- Pentoxifylline: Increases the risk of bleeding. Clinical monitoring should be increased and bleeding time should be checked more frequently.
- Zidovudine: Risk of increased red cell toxicity due to the effect on reticulocytes, with severe anemia occurring one week after starting NSAID intake. Complete blood count and reticulocyte count should be checked one to two weeks after starting treatment with NSAIDs.
- Sulfonylureas: NSAIDs may increase the hypoglycemic effects of sulfonylureas by displacing them from their plasma protein binding sites.

Combinations to consider:

- Beta blockers: Treatment with an NSAID may reduce their antihypertensive effects by inhibition of prostaglandin synthesis.
- Cyclosporine and tacrolimus: Nephrotoxicity may increase due to the renal prostaglandin synthesis inhibition-mediated effects of NSAIDs. Renal functions should be evaluated during combination therapy.
- Thrombolytics: Increases the risk of bleeding.
- Antiplatelet agents and selective serotonin reuptake inhibitors (SSRIs): Increase the risk of gastrointestinal bleeding (see section 4.4).
- Probenecid: Plasma concentrations of dexketoprofen may increase; This interaction may be due to an inhibitory mechanism and glucuronide conjugation at the site of renal tubular secretion and requires adjustment of the dexketoprofen dose.
- Cardiac glycosides: NSAIDs may worsen heart failure, decrease glomerular filtration rate (GFR), and increase plasma glycoside levels.
- Mifepristone: Since prostaglandin synthetase inhibitors carry a theoretical risk of altering the effectiveness of mifepristone, NSAIDs should not be used within 8-12 days after taking mifepristone.

- Quinolone antibiotics: Data obtained from animal studies indicate that taking high doses of quinolones together with NSAIDs may increase the risk of developing convulsions.

Thiocolchicoside

Considering recent clinical experience, thiocolchicoside, non-steroidal anti-inflammatory agents, phenylbutazone, analgesics and preparations used in the treatment of neuritis are successfully and safely administered together with anabolic steroids, sedatives, barbiturates and succinylcholine.

It is not recommended to take thiocolchicoside with other drugs that have a muscle relaxant effect on the musculoskeletal system, as they may increase the effects of each other. For the same reason, if it is used together with another drug that acts on smooth muscles, more caution should be exercised and the patient should be observed in case the frequency of undesirable effects increases.

Additional information regarding special populations:

No interaction studies have been conducted in special populations.

Pediatric population:

No interaction studies of the combination of dexketoprofen and thiocolchicoside have been conducted. Additionally, there are no studies conducted in children and adolescents. Therefore, its reliability and effectiveness have not been proven. It should not be used in people under 18 years of age.

4.6. Pregnancy and lactation

General advice

Pregnancy category: X.

DEKSIT is contraindicated during pregnancy (see section 4.3)

Women with childbearing potential/Birth control (Contraception)

Dexketoprofen

Inhibition of prostaglandin synthesis may adversely affect pregnancy and/or embryo/fetal development. Data from epidemiological studies have raised concerns about an increased risk of miscarriage and cardiac malformations and gastroschisis after prostaglandin synthesis inhibitor use in early pregnancy. The absolute risk for cardiovascular malformations increased from less than 1% to approximately 1.5%. The risk is believed to increase with dose and duration of treatment. In animals, prostaglandin synthesis inhibitor administration has been shown to cause increased pre- and post-implantation loss and embryo-fetal death. Additionally, an increased

incidence of various malformations, including cardiovascular, has been reported in animals given prostaglandin synthesis inhibitors during the organogenetic period. However, animal studies with dexketoprofen trometamol did not show reproductive toxicity (see section 5.3).

Thiocolchicoside

Women of childbearing potential must use effective birth control during treatment.

Pregnancy period

Dexketoprofen

Dexketoprofen is contraindicated in the third trimester of pregnancy.

During the first and second trimester of pregnancy, dexketoprofen trometamol should not be given unless clearly necessary. If dexketoprofen trometamol is used by a woman who is trying to become pregnant or is in the first and second trimesters of pregnancy, the dose should be kept as low as possible and the duration of treatment should be as short as possible.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may have the following effects on the fetus:

- Cardiopulmonary toxicity (premature closure of the ductus arteriosus and pulmonary hypertension);
- Kidney dysfunction, which can lead to kidney failure with oligohydramnios;

At the end of pregnancy, mother and newborn:

- Possibility of prolongation of bleeding time, an antiplatelet effect that may occur even at very low doses;
- Uterine contraction, which can cause delayed or prolonged labor inhibition.

Thiocolchicoside

There is limited data on the use of thiocolchicoside in pregnant women. Therefore, potential hazards to the embryo and fetus are unknown.

Animal studies have shown teratogenic effects (see section 5.3). DEKSIT 25 mg/4 mg Tablet is contraindicated during pregnancy and in women with pregnancy potential who do not use contraception.

Lactation period

Although NSAIDs can be seen in very low concentrations in breast milk in the limited studies conducted to date, it is not known whether dexketoprofen passes into breast milk. Due to its excretion in breast milk, thiocolchicoside use is contraindicated during breastfeeding (see section

4.3).

Reproductive ability/Fertility

Use of dexketoprofen trometamol together with other NSAIDs may affect fertility and is not recommended in women trying to become pregnant. Discontinuation of dexketoprofen trometamol should be considered in women who have difficulty conceiving or are being investigated for infertility. Dexketoprofen trometamol should not be used during the first and second trimesters of pregnancy unless clearly necessary.

A fertility study in rats showed no impairment of fertility at doses up to 12 mg/kg – dose levels that did not induce any clinical effects. Thiocolchicoside and its metabolites show aneugenic activity at different concentration levels; this is a risk factor for impairment of human fertility (see section 5.3).

4.7. Effects on ability to drive and use machines

After taking DEKSIT, there may be undesirable effects such as drowsiness, somnolence, dizziness, weakness and visual disturbances. If affected, patients should not drive or operate machinery.

4.8. Undesirable effects

Adverse effects reported with the separate use of dexketoprofen trometamol and thiocolchicoside are listed below:

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); unknown (cannot be estimated from the available data).

Dexketoprofen

Undesirable effects reported to be at least possibly related to dexketoprofen trometamol in clinical studies and undesirable effects reported after the marketing of dexketoprofen trometamol are listed below, classified by system organ class and frequency of occurrence.

Blood and lymph system diseases

Very rare: Neutropenia, thrombocytopenia

Immune system diseases

Rare: Larynx edema

Very rare: Anaphylactic reaction including anaphylactic shock.

Metabolism and nutritional diseases

Rare: Anorexia

Psychiatric diseases

Uncommon: Insomnia, anxiety

Nervous system diseases

Uncommon: Headache, dizziness, somnolence

Rare: Paresthesia, syncope

Eye diseases

Very rare: Blurred vision

Ear and inner ear diseases

Uncommon: Vertigo

Very rare: Tinnitus

Cardiac diseases

Uncommon: Palpitations

Very rare: Tachycardia

Vascular diseases

Uncommon: facial flushing

Rare: Hypertension

Very rare: Hypotension

Respiratory, thoracic disorders and mediastinal diseases

Rare: Bradypnea

Very rare: Bronchospasm, dyspnea

Gastrointestinal diseases

Common: Nausea and/or vomiting, abdominal pain, diarrhoea, dyspepsia

Uncommon: Gastritis, constipation, dry mouth, flatulence

Rare: Peptic ulcer, peptic ulcer bleeding or perforation (see section 4.4)

Very rare: Pancreatitis

Hepatobiliary diseases

Very rare: Hepatocellular damage

Skin and subcutaneous tissue diseases

Uncommon: Skin rash

Rare: Urticaria, acne, increased sweating.

Very rare: Stevens Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome)

angioneurotic edema, facial edema, photosensitivity reactions, pruritus

Musculoskeletal disorders, connective tissue and bone diseases

Rare: Back pain

Kidney and urinary tract diseases

Rare: Polyuria, acute renal failure

Very rare: Nephritis or nephrotic syndrome

Reproductive system and breast diseases

Rare: Menstrual disorders, prostatic disorders

General disorders and administration site conditions

Uncommon: Fatigue, pain, asthenia, rigor, malaise Rare: Peripheral edema

Research

Rare: Liver function test abnormality

Gastrointestinal: The most commonly observed adverse events were gastrointestinal. Sometimes fatal peptic ulcer, perforation or gastrointestinal bleeding may occur, especially in the elderly (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melena, hematemesis, ulcerative stomatitis, colitis and exacerbation of Crohn's disease (see section 4.4 Special warnings and precautions for use) have been reported following administration. Less frequently, gastritis has been observed. Pancreatitis has been reported very rarely.

Hypersensitivity reactions have been reported following treatment with NSAIDs. These include (a) non-specific allergic reaction and anaphylaxis, (b) respiratory tract reactivity including asthma, severe asthma, bronchospasm or dyspnea, or (c) various types of rashes, urticaria, purpura, facial edema and, less commonly, exfoliative bullous dermatosis (It can include a variety of skin disorders, including epidermal necrolysis and erythema multiforme.

Edema, hypertension, and heart failure have been reported in association with NSAID therapy.

As with other NSAIDs, the following undesirable effects may occur: aseptic meningitis, which may be more common in patients with systemic lupus erythematosus or mixed connective tissue disease; haematological reactions (purpura, aplastic and hemolytic anemia and rarely agranulocytosis and medullary hypoplasia).

Bullous reactions including Steven Johnson Syndrome and Toxic Epidermal Necrolysis (very rare). Photosensitivity.

Clinical study and epidemiological data suggest that the use of some NSAIDs (especially at high doses and with long-term treatment) may be associated with a small increased risk of arterial

thrombotic events (especially myocardial infarction or stroke) (see section4.4).

Other less commonly reported adverse reactions include:

Renal: Various forms of nephrotoxicity such as interstitial nephritis, nephrotic syndrome, and renal failure.

Liver: Abnormal liver function, hepatitis and jaundice.

Neurology and sensory organs: Visual disturbances, optic neuritis, headaches, paresthesias, symptoms of aseptic meningitis (especially in patients with existing autoimmune disorders such as systemic lupus erythematosus, mixed connective tissue disease), neck stiffness, headache, nausea, vomiting, fever or also disorientation (see section 4.4), depression, confusion, hallucinations, tinnitus, vertigo, drowsiness, malaise, weakness and dizziness.

Hematological events: Thrombocytopenia, neutropenia, agranulocytosis, aplastic anemia and hemolytic anemia.

Dermatological events: Bullous reactions including Steven Johnson Syndrome and Toxic Epidermal Necrolysis (very rare). Photosensitivity.

Thiocolchicoside

Adverse effects observed in clinical studies and related to the intake of thiocolchicoside are listed below:

Immune system disorders

Uncommon: Pruritus Rare: Urticaria,

Unknown: Angioneurotic edema, i.m. anaphylactic shock following administration

Nervous system diseases

Common: Somnolence

Not known: Vasovagal syncope (usually occurs within minutes following i.m. administration), transient confusion and excitation, convulsions.

Cardiac diseases

Rare: Hypotension

Gastrointestinal diseases

Common: Diarrhea (see section 4.4), gastralgia

Uncommon: Nausea, vomiting

Hepatobiliary disease

Not known: Cystolytic and cholestatic hepatitis (see section 4.4)

Skin and subcutaneous tissue diseases

Uncommon: Allergic skin reaction

4.9. Overdose and treatment

Dexketoprofen

Symptoms of dexketoprofen trometamol overdose are unknown.

The following have been observed in association with NSAIDs:

a) Symptoms

Headache, nausea, vomiting, epigastric pain, gastrointestinal bleeding, rarely diarrhea, disorientation, excitation, coma, dizziness, dizziness, tinnitus, fainting, occasionally convulsions. In cases of significant poisoning, acute renal failure and liver damage are possible.

b) Therapeutic measures

In case of accidental ingestion or overuse, symptomatic treatment should be administered immediately according to the clinical condition of the patient. If more than 5 mg/kg is taken by an adult or a child within one hour, administration of activated charcoal should be considered.

Alternatively, in adults, gastric lavage should be considered within one hour of a potentially life-threatening overdose. Good urine output should be ensured.

Renal and liver function should be closely monitored.

Patients should be observed for at least four hours after ingestion of potentially toxic amounts. Frequent or prolonged convulsions should be treated with intravenous diazepam.

Depending on the patient's clinical condition, other measures may need to be taken. Dexketoprofen trometamol can be removed from the body by dialysis.

Thiocolchicoside

No specific symptoms of overdose have been reported in patients treated with thiocolchicoside.

Treatment:

In case of overdose, medical observation and symptomatic measures are recommended (see section 5.3).

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamics properties

Pharmacotherapeutic group: Propionic acid derivatives and centrally acting myorelaxants

ATC Code: M03BX55 (Combination of Dexketoprofen and Thiocolchicoside)

Dexketoprofen

Dexketoprofen trometamol the tromethamine salt of S-(+)-2-(3-benzoylphenyl) propionic acid is an analgesic, anti-inflammatory and antipyretic drug belonging to the non-steroidal anti-inflammatory drug group (M01A).

The mechanism of action of non-steroidal anti-inflammatory drugs is related to the reduction of prostaglandin synthesis by inhibition of the cyclooxygenase pathway. In particular, there is inhibition of the transformation of arachidonic acid into cyclic endoperoxides, PGG2 and PGH2, which forms the prostaglandins PGE1, PGE2, PGF2α, and PGD2, as well as the prostacyclin PGI2 and thromboxanes (TxA2 and TxB2). Additionally, inhibition of prostaglandin synthesis also affects other mediators of inflammation, such as kinin, causing an indirect effect in addition to the direct effect.

Dexketoprofen has been shown to be an inhibitor of COX-1 and COX-2 activities in animal and human experiments.

Clinical studies in various pain models have shown that dexketoprofen trometamol has an effective analgesic effect. The onset of analgesic effect was achieved within 30 minutes after application in some studies. The analgesic effect lasts 4-6 hours.

Thiocolchicoside

Thiocolchicoside is a semi-synthetic sulfurized colchicoside derivative with muscle relaxant pharmacological activity.

Thiocolchicoside binds only to GABAergic and strychnine-sensitive glycinergic receptors in vitro. Thiocolchicoside, which acts as a GABAergic receptor antagonist, may exert its muscle relaxant effects through complex regulatory mechanisms at the supraspinal level; however, a glycinergic mechanism of action cannot be excluded. The interaction properties of thiocolchicoside with GABAergic receptors are qualitatively and quantitatively shared with its main circulating metabolite, the glucuronide derivative (see Section 5.2).

The muscle relaxant properties of thiocolchicoside and its main metabolite have been demonstrated in vivo in various predictive models performed in rats and rabbits. The lack of muscle relaxant effect of thiocolchicoside in spinalized rats indicates the predominant supraspinal effect of this compound. Additionally, electroencephalographic (EEG) studies have shown that thiocolchicoside and its main metabolite have no sedative effects.

5.2. Pharmacokinetic properties

General properties

Absorption:

Dexketoprofen

Dexketoprofen reaches Cmax within 30 minutes (range 15-60 minutes) after oral administration of trometamol to humans. When administered with food, the AUC (area under the curve) does not change, whereas the Cmax of dexketoprofen trometamol decreases and the rate of absorption is delayed (increased tmax).

Thiocolchicoside

- After IM administration, thiocolchicoside maximum plasma concentration (Cmax) occurs within 30 minutes and reaches 113 ng/mL after the 4 mg dose and 175 ng/mL after the 8 mg dose. The relevant AUC values are 283 and 417 ng.h/mL, respectively. Additionally, the pharmacologically active metabolite SL18.0740 is observed at low concentrations, with Cmax values of 11.7 ng/mL and AUC values of 83 ng.h/mL occurring within 5 hours post-dose.

No data are available for the inactive metabolite SL59.0955.

- After oral administration, no thiocolchicoside is detected in plasma. Only two metabolites are observed:

The pharmacologically active metabolite is SL18.0740 and the inactive metabolite is SL59.0955. Maximum plasma concentrations for both metabolites occur 1 hour after thiocolchicoside administration. After a single 8 mg oral dose of thiocolchicoside, Cmax and AUC values for SL18.0740 are approximately 60 ng/mL and 130 ng.h/mL, respectively. For SL59.0955 these values are much lower: Cmax is approximately 13 ng/mL; AUC varies between 15.5 ng.hour/mL (up to 3 hours) - 39.7 ng.hour/mL (up to 24 hours).

Distribution:

Dexketoprofen

The distribution half-life of dexketoprofen trometamol is 0.35 hours. As with other drugs that show

high binding to plasma proteins (99%), the average value of the volume of distribution is less than 0.25 L/kg. In multiple-dose pharmacokinetic studies, the observation that the AUC after the last administration did not differ from that obtained after a single dose administration is an indication that drug accumulation does not occur. Dexketoprofen does not take part in the accumulation of xenobiotics in fatty tissues.

Thiocolchicoside

The apparent volume of distribution of thiocolchicoside is estimated to be approximately 42.7 L after 8 mg IM administration. No data are available for either metabolite.

Biotransformation:

Dexketoprofen

Obtaining only the S-(+) enantiomer in the urine after administration of dexketoprofen trometamol indicates that there is no conversion to the R-(-) enantiomer in humans. In multiple-dose pharmacokinetic studies, the observation that the AUC after the last administration did not differ from that obtained after a single dose administration indicates that drug accumulation does not occur.

Thiocolchicoside

After oral administration, thiocolchicoside is first metabolized to the aglycone 3-demethylthiocolchicosine or SL59.0955. This step occurs mainly by intestinal metabolism, which explains the absence of unchanged thiocolchicoside in the circulation when administered orally.

SL59.0955 is then metabolized to SL18.074, which has pharmacological activity equivalent to thiocolchicoside, thus supporting the pharmacological activity of thiocolchicoside after its oral administration. Additionally, SL59.0955 is demethylated to didemethyl-thiocolchicine.

Elimination:

Dexketoprofen

The elimination half-life of dexketoprofen trometamol is 1.65 hours. The primary elimination route of dexketoprofen is renal excretion following glucuronide conjugation.

Thiocolchicoside

- After IM administration, the apparent thiocolchicoside t1/2 value is 1.5 hours and plasma clearance is 19.2 L/hour.

- After oral administration, total radioactivity is excreted primarily in the feces (79%), while urinary

excretion is only 20%. Unchanged thiocolchicoside is not excreted through urine or feces.

SL18.0740 and SL59.0955 are found in urine and feces, while didemethyl-thiocolchicine appears only in feces.

After oral administration of thiocolchicoside, the SL18.0740 metabolite is eliminated with an apparent t1/2 in the range of 3.2 to 7 hours and the SL59.0955 metabolite with an average t1/2 of 0.8 hours.

Linearity / Nonlinear state:

Dexketoprofen

Dexketoprofen trometamol exhibits linear pharmacokinetics with a dose-dependent increase during systemic exposure following oral dosing.

Thiocolchicoside

Data not available.

Characteristic properties in patients

Dexketoprofen

Kidney failure:

In volunteers with mild to moderate renal impairment, following a single dose of 12.5 mg dexketoprofen trometamol, increases in Cmax of only 22% and 37%, respectively, were observed compared to healthy volunteers. In general, dose adjustments for dexketoprofen are recommended in patients with renal impairment (see section 4.2).

Liver failure:

Following single and repeated doses in patients with mild to moderate hepatic impairment, no statistically significant differences in pharmacokinetic parameters were observed compared to healthy volunteers. In general, dose adjustment is recommended in patients with hepatic impairment (see section 4.2).

Elderly:

Following oral administration of 25 mg dexketoprofen trometamol, elderly volunteers showed an approximately 50% increase in AUC and half-life compared to young volunteers, and a 40% decrease in clearance was seen after single or repeated dosing; There was no change in Tmax and Cmax. Although significant drug accumulation in plasma is not observed following repeated dosing, in elderly patients with renal impairment, careful dose adjustment is required for this population (see section 4.2).

Thiocolchicoside

Data not available.

5.3. Pre-clinical safety data

Dexketoprofen

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, toxicity to reproduction and immunopharmacology. In chronic toxicity studies conducted on mice and monkeys, the No Observed Adverse Effect Level (NOAEL) was determined as 3 mg/kg/day. The main undesirable effects observed at high doses are dose-dependent gastrointestinal erosions and ulcers.

Thiocolchicoside

Acute toxicity:

At high doses, thiocolchicoside caused severe vomiting in dogs, diarrhea in rats, and convulsions in both rodents and non-rodents following acute oral administration.

Chronic toxicity:

The thiocolchicoside profile was evaluated in vitro and in vivo following parenteral and oral administration.

With thiocolchicoside administered orally for periods of up to 6 months, both at repeated doses of ≤2 mg/kg/day in rats and at repeated doses of ≤2.5 mg/kg/day in non-human primates, and at repeated doses of up to 0.5 mg/kg/day for 4 weeks in primates. Thiocolchicoside administered intramuscularly was well tolerated.

At high doses, after acute oral administration, thiocolchicoside induced vomiting in dogs, diarrhea in rats, and convulsions in both rodents and nonrodents.

After repeated administration, thiocolchicoside orally may cause gastro-intestinal disorders. (enteritis, vomiting) and induced vomiting by intramuscular route.

Carcinogeniciy:

Carcinogenic potential has not been evaluated.

Genotoxicity:

Thiocolchicoside itself did not induce gene mutation in bacteria (Ames test), chromosomal damage

in vitro (chromosomal aberration test in human lymphocytes) and chromosomal damage in vivo (in vivo intraperitoneal micronucleus test in mouse bone marrow).

The major glucuroconjugated metabolite SL18.0740 did not induce gene mutation (Ames test) in bacteria; however, it induced chromosomal damage in vitro (in vitro micronucleus assay on human lymphocytes) and chromosomal damage in vivo (in vivo intraperitoneal micronucleus assay in mouse bone marrow administered orally). The formation of micronuclei, mostly as a result of chromosome loss (centromere-positive micronuclei after FISH centromere staining), is an indicator of aneugenic properties. The aneugenic effect of SL18.0740 was observed at concentrations in in vitro testing and at plasma exposures of EAA in in vitro testing that were higher than those observed in therapeutic human plasma (10-fold higher than AUC). The aglycone metabolite (3-demethylthiocolchicine - SL59.0955), formed mainly after anal administration, induced in vitro chromosomal damage (in vitro micronucleus test on human lymphocytes) and in vivo chromosomal damage (in vivo oral micronucleus test in rat bone marrow after orally administered). The formation of micronuclei mostly as a result of chromosome loss (centromere-positive micronuclei after FISH or CREST centromere staining) is an indicator of their aneugenic properties. The aneugenic effect of SL59.0955 was observed at exposures in in vivo testing, at concentrations tested orally, and in in vitro testing that approximated that observed in human plasma at therapeutic doses of 8 mg twice daily. The anogenic effect may cause aneuploid cell formation in dividing cells. Aneuploidy is an alteration in chromosome number and loss of heterozygosity that is known as a risk factor for teratogenicity, embryotoxicity/spontaneous abortion, impaired male fertility when it affects germ cells, and as a potential risk factor for cancer when it affects somatic cells. The presence of the aglycone metabolite (3-demethylthiocolchicine-SL59.0955) has not been evaluated after intramuscular administration. Therefore, the formation of metabolites formed through this application cannot be ignored.

In rats, an oral dose of 12 mg/kg/day thiocolchicoside caused major malformations (growth retardation, embryo death, disruption of sex distribution ratio) along with fetotoxicity. The non-toxic dose is 3 mg/kg/day.

In rabbits, thiocolchicoside showed maternotoxicity starting at 24 mg/kg/day. Additionally, minor abnormalities were observed (supernumerary teeth, ossification retardation).

Teratogenicity:

In rats, thiocolchicoside at a dose of 12 mg caused major malformations along with fetotoxicity (growth retardation, embryo death, deterioration in sex distribution). The non-toxic dose is 3

mg/kg/day.

In rabbits, thiocolchicoside showed maternotoxicity starting from 24 mg/kg/day. Additionally, minor abnormalities (supernumerary teeth, ossification retardation) were observed.

Fertility disorders:

In a fertility study in rats, no impairment of fertility was observed at doses up to 12 mg/kg/day, i.e., dose levels that produced no clinical effect. Thiocolchicoside and its metabolites show aneugenic activity at different concentration levels; This condition is known as a risk factor for impaired human fertility.

6. PHARMACEUTIC PROPERTIES

6.1. List of Excipients

Partial pregelatinized corn starch
Sodium starch glycollate Type A
Microcrystalline cellulose PH 102
Microcrystalline cellulose PH 101
Magnesium stearate
Pure water

6.2. Incompatibilities

It is invalid.

6.3. Shelf life

24 months.

6.4. Special precautions for storage

Store at room temperature below 25ºC, protected from moisture and light.

6.5. The nature and content of the packaging

It is presented in a PVC/PVD/Aluminum blister pack of 14 tablets and a cardboard box with instructions for use.

6.6. Disposal of residual substances from the medicinal product and other special precautions

Unused products or waste materials should be disposed of in accordance with the "Medical Waste

Control Regulation" and "Packaging and Packaging Waste Control Regulations".

7. MARKETING AUTHORIZATION NUMBER

Drogsan İlaçları San. ve Tic. A.Ş.
Oğuzlar Mah. 1370. Sok. No: 7/3
06520 Balgat / Ankara – Türkiye
Tel: 0312 287 74 10
Faks: 0312 287 61 15

8. MARKETING AUTHORIZATION CERTIFICATE NUMBER(S)

9. FIRST MARKETING AUTHORIZATION CERTIFICATE DATE / MARKETING AUTHORIZATION CERTIFICATE RENEWAL DATE

First license date:
License renewal date:

10. DATE OF RENEWAL OF SPC

20.03.2023