# DOGMATIL®
# SULPIRIDE

## 1. QUALITATIVE AND QUANTITATIVE COMPOSITION

**DOGMATIL Capsule**:
Each capsule contains Sulpiride 50 mg

**DOGMATIL Forte Tablet**:
Each tablet contains Sulpiride 200 mg

For the full list of excipients, see section 5.1 List of excipients.

## 2. PHARMACEUTICAL FORM

**DOGMATIL**
**Capsule**
Capsule with cap and body capsule colour is white opaque, contains: white powder, cap capsule : DOGMATIL (black printing colour), body capsule: DOGMATIL (black printing colour).

**DOGMATIL Forte**
**Tablet**
A white tablet, top side: plus line, bottom side: embossed Dogmatil. The tablet should not be divided.

## 3. CLINICAL PARTICULARS

### 3.1. Therapeutic indications

The treatment of digestive ulcers, psychofunctional disorders, major psychiatric conditions, and vertigo of various origins.

### 3.2. Posology and method of administration

| | |
|---|---|
| **Digestive ulcers** | Maintenance treatment :<br>3 capsules @ 50 mg per day for 3 weeks<br><br>After treatment :<br>1 - 3 capsules per day for 3 - 4 weeks |
| **Psychofunctional Disorders**<br>• Minor behaviour disorder.<br>• Reactional depressive conditions.<br>• Neurosis with psychomotor inhibition.<br>• Post-concussion syndrome.<br>• Depressive conditions in geriatry. | Adult :<br>2 to 4 capsules @ 50 mg per day, divided in several doses.<br><br>Children :<br>5 to 10 mg/kg per day, divided in several doses. |
| **Major psychiatric conditions**<br>• Acute, delusional, hallucinatory, confusional psychosis.<br>• Depressive states of various origins, melancholia.<br>• Acute schizophrenia, chronic delusions.<br>• Severe behaviour disorders.<br>• Childhood and adolescence psychosis and pre-psychotic states. | Maintenance treatment by oral route :<br>2 to 4 tablets @ 200 mg per day, divided in several doses.<br><br>Children:<br>10 mg/kg per day, divided in several doses. |
| **Vertigo of various origins** | 3 to 6 capsules per day. |

**Tolerance:**

- Long term or repeated treatments without addiction.
- Keeping of vigilance, which is frequently improved.
- No effect on the neurovegetative system.

### 3.3. Contraindications

This medicine should never be used in the following situations:

- Hypersensitivity to the active substance or to any of the excipients mentioned in section 5.1. List of excipients
- Prolactin-dependent tumors (e.g. pituitary adenoma and breast cancer)
- Pheochromocytoma, known or suspected.
- Contraindicated combinations:
  - Non-Parkinson's dopaminergics (Cabergoline, Quinagolide)
  - Citalopram, Escitalopram, Hydroxyzine, Domperidone, Piperaquine
- Acute porphyria
- Taking tablets or capsules is contraindicated in children under 6 years of age because it can cause choking.

### 3.4. Special warnings and precautions for use

**Warnings:**

Stroke

The mechanism of this increased risk is unknown. This medicine should be used with caution in patients with risk factors for stroke.

Elderly patients with dementia

The risk of mortality is increased in elderly patients with psychosis associated with dementia and treated with antipsychotics. The respective role of the antipsychotic and patient characteristics in the increase in mortality in epidemiological studies is unclear.

Breast cancer

Sulpiride may increase prolactin levels and should therefore be used with caution. Regardless of gender, patients with a personal or family history of breast cancer should be closely monitored during sulpiride treatment.

Decreased intestinal peristalsis

Cases of intestinal obstruction have been reported in patients treated with antipsychotics. Rare cases of ischemic colitis and intestinal necrosis, sometimes fatal, have also been reported. The majority of these patients were treated concomitantly with one or more drugs inducing a decrease in intestinal motility (especially drugs with anticholinergic properties). The onset of abdominal pain with vomiting and/or diarrhea should attract attention. It is imperative that constipation is recognized and actively treated. The occurrence of an ileus/intestinal obstruction must require emergency treatment.

Taking this medication is not recommended in combination with alcohol, levodopa, dopaminergic antiparkinson drugs, antiparasitic drugs that may cause torsades de pointes, methadone, other neuroleptics and drug that may cause torsades de pointes (see section 3.5 Interaction with other drugs and other forms of interactions).

It is necessary to take into account the risk of the onset of tardive dyskinesia, even with low doses, particularly in the elderly.

In children, as the effectiveness and safety have not been fully studied, caution should be exercised when using sulpiride. Due to the cognitive impairment, an annual clinical examination to assess learning abilities is recommended. The dosage should be regularly adjusted according to the child's clinical condition.

Taking tablets or capsules is contraindicated in children under 6 years of age because it can cause choking.

This medicine contains lactose. Its use is not recommended in patients with galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption syndrome (rare hereditary diseases).

**Precautions:**

Diabetic patients and patients with risk factors for diabetes who are starting treatment with sulpiride should have their blood glucose levels monitored appropriately.
Apart from exceptional situations, this medicine should not be used in cases of Parkinson's disease.
In case of renal insufficiency, reduce the dosage and increase monitoring; in case of severe renal insufficiency, it is recommended to prescribe discontinuous courses.
Monitoring of sulpiride treatment should be strengthened:

- In epileptic patients due to the possibility of lowering the epileptogenic threshold, cases of convulsions have been reported in patients treated with sulpiride (see section 3.8. Undesirable effects)
- In elderly patients with greater sensitivity to orthostatic hypotension, sedation, and extrapyramidal effects

Cases of leukopenia, neutropenia and agranulocytosis have been reported with antipsychotics including DOGMATIL. Unexplained infections or unexplained fever may indicate leukopenia (see section 3.8. Undesirable effects) and require immediate blood tests.
DOGMATIL should be used with caution in patients with a history of glaucoma, ileus, congenital digestive stenosis, urinary retention or prostatic hyperplasia.
DOGMATIL should be used with caution in hypertensive patients, and more particularly in the elderly, due to the risk of hypertensive crisis. Appropriate monitoring should be implemented in these patients.

### 3.5. Interaction with other drugs and other forms of interactions

Sedative medications

It should be taken into account that many medications or substances can add to their central nervous system depressanteffects and contribute to decreased alertness. These include morphine derivatives (analgesics, cough suppressants andsubstitution treatments), neuroleptics, barbiturates, benzodiazepines, anxiolytics other than benzodiazepines (e.g., meprobamate), hypnotics, sedative antidepressants (amitriptyline, doxepin, mianserin, mirtazapine, trimipramine), sedative H1antihistamines, central antihypertensives, baclofen and thalidomide.

Medications that may cause torsades de pointes

This serious heart rhythm disorder can be caused by a number of medications, whether antiarrhythmic or not. Hypokalemia (see hypokalemic medications) is a contributing factor, as is bradycardia (see bradycardic medications) or a pre-existingprolongation of the QT interval, whether congenital or acquired.
Drugs that cause this adverse effect include class Ia and III antiarrhythmics and certain neuroleptics. Other drugs not belongingto these classes are also involved.
For dolasetron, erythromycin, spiramycin and vincamine, only the intravenously administered forms are affected by thisinteraction.
The use of one torsadogenic drug with another torsadogenic drug is generally contraindicated.
However, some of them, due to their essential nature, are exceptions to the rule, being only not recommended with othertorsadogenics. These are methadone, antiparasitic drugs (chloroquine, halofantrine, lumefantrine, pentamidine) andneuroleptics.
However, citalopram, domperidone, and escitalopram do not follow this relaxation, and are contraindicated with all torsadogens.

Contraindicated combinations

- Citalopram, escitalopram
  Increased risk of ventricular rhythm disorders, particularly torsades de pointes.
- Non-Parkinson's Dopaminergics (Cabergoline, quinagolide)
  Reciprocal antagonism of dopamine agonist and neuroleptics.

- Domperidone
  Increased risk of ventricular rhythm disorders, particularly torsades de pointes.
- Hydroxyzine
  Increased risk of ventricular rhythm disorders, particularly torsades de pointes.
- Piperaquine
  Increased risk of ventricular rhythm disorders, particularly torsades de pointes.

Associations not recommended

- Antiparasitics likely to cause torsades de pointes (chloroquine, halofantrine, lumefantrine, pentamidine)
  Increased risk of ventricular rhythm disorders, particularly torsades de pointes.
  If possible, discontinue one of the two treatments.
  If the association cannot be avoided, prior QT control and monitored ECG monitoring.
- Dopaminergic antiparkinsonian drugs (amantadine, apomorphine, bromocriptine, entacapone, lisuride, pergolide, piribedil, pramiprexole, rasagiline, ropinirole, rotigotine, selegiline)
  Reciprocal antagonism of dopaminergic and neuroleptic drugs.
  Dopaminergics can cause or worsen psychotic disorders. If neuroleptic treatment is necessary in Parkinson's patients treatedwith dopaminergics, these should be gradually reduced until they are stopped (abruptly stopping them exposes them to the riskof "neuroleptic malignant syndrome").
- Other drugs that may cause torsades de pointes: class Ia (quinidine, hydroquinidine, disopyramide) and class III (amiodarone, dronedarone, sotalol, dofetilide, ibutilide) antiarrhythmics, and other drugs such as arsenious, diphemanil, dolasetron IV, domperidone, erythromycin IV, hydroxychloroquine, levofloxacin, mequitazine, mizolastine, prucalopride, vincamine IV, moxifloxacin, spiramycin IV, toremifene, vandetanib.
  Increased risk of ventricular rhythm disorders, particularly torsades de pointes.
- Other neuroleptics that may cause torsades de pointes (amisulpride, chlorpromazine, cyamemazine, droperidol, flupenthixol, fluphenazine, haloperidol, levomepromazine, pimozide, pipamperone, pipotiazine, sultopride, tiapride, zuclopenthicol)
  Increased risk of ventricular rhythm disorders, particularly torsades de pointes.
- Alcohol (beverage or excipient)
  Increased sedative effect of these substances by alcohol.
  Impaired alertness can make driving vehicles and operating machinery dangerous.
  Avoid taking alcoholic beverages and medications containing alcohol.
- Levodopa
  Reciprocal antagonism of levodopa and neuroleptics.
  In Parkinson's patients, use the minimum effective doses of each of the two drugs.
- Methadone
  Increased risk of ventricular rhythm disorders, particularly torsades de pointes.

Combinations requiring precautions for use

- Anagrelide
  Increased risk of ventricular rhythm disorders, particularly torsades de pointes.
  Clinical and electrocardiographic monitoring during the association.
- Azithromycin
  Increased risk of ventricular rhythm disorders, particularly torsades de pointes.
  Clinical and electrocardiographic monitoring during the association.
- Beta-blockers in heart failure (bisoprolol, carvedilol, metoprolol, nebivolol)
  Increased risk of ventricular rhythm disorders, particularly torsades de pointes.
  Clinical monitoring and ECG.
- Bradycardics (including class Ia antiarrhythmics, beta-blockers, certain class III antiarrhythmics, certain calciumantagonists, crizotinib, digitalis, pasireotide, pilocarpine, anticholinesterases)
  Increased risk of ventricular rhythm disorders, particularly torsades de pointes.
  Clinical monitoring and ECG.
- Ciprofloxacin, levofloxacin, norfloxacin
  Increased risk of ventricular rhythm disorders, particularly torsades de pointes.
  Clinical and electrocardiographic monitoring during the association.

- Clarithromycin
  Increased risk of ventricular rhythm disorders, particularly torsades de pointes.
  Clinical and electrocardiographic monitoring during the association.
- Hypokalemic agents (hypokalemic diuretics, alone or in combination, stimulant laxatives, glucocorticoids, tetracosactide and amphotericin B by IV route).
  Increased risk of ventricular rhythm disorders, particularly torsades de pointes.
  Correct any hypokalemia before administering the product and perform clinical, electrolyte and ECG monitoring.
- Lithium
  Risk of the appearance of neuropsychiatric signs suggestive of neuroleptic malignant syndrome or lithium intoxication.
  Regular clinical and biological monitoring, particularly at the start of the association.
  Discontinuation of one of the two treatments at the first signs of neurotoxicity.
- Ondansetron
  Increased risk of ventricular rhythm disorders, particularly torsades de pointes.
  Clinical and electrocardiographic monitoring during the association.
- Roxithromycin
  Increased risk of ventricular rhythm disorders, particularly torsades de pointes.
  Clinical and electrocardiographic monitoring during the association.
- Sucralfate
  Decreased digestive absorption of sulpiride.
  Take sucralfate away from sulpiride (more than 2 hours, if possible).
- Gastrointestinal, antacid and charcoal topicals
  Decreased digestive absorption of sulpiride.
  Take gastrointestinal and antacid topicals away from sulpiride (more than 2 hours, if possible).

Associations to consider
- Other sedative medications
  Increase in central depression. Impaired alertness can make driving vehicles and using machines dangerous.
- Beta-blockers in heart failure (bisoprolol, carvedilol, metoprolol, nebivolol)
  (For beta-blockers used in heart failure, see also “Combinations requiring precautions for use”).
  Vasodilatory effect and risks of hypotension, particularly orthostatic (additive effect).
- Dapoxetine
  Risk of increased adverse effects, particularly dizziness or syncope.
- Orlistat
  Risk of therapeutic failure in case of concomitant treatment with orlistat.
- Blood pressure lowering medications
  Risk of increased risk of hypotension, particularly orthostatic.

### 3.6. Fertility, pregnancy, and breastfeeding

Pregnancy

Data on the use of sulpiride in pregnant women are very limited. The safety of sulpiride during pregnancy has not been established.

Sulpiride crosses the placenta. Animal studies have shown reproductive toxicity.
The use of sulpiride is not recommended during pregnancy and in women of childbearing potential not using effective contraception, unless the expected benefits justify the potential risks.

Neonates exposed to antipsychotic drugs (including amisulpride) during the third trimester of pregnancy are at risk of experiencing extrapyramidial neurological disturbances and/or withdrawal symptoms following delivery. There have been post-market reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, and feeding disorder in these neonates. These complications have varied in severity; while in some cases symptoms have been self-limited, in other cases neonates have required additional medical treatment or monitoring. All newborns should be carefully monitored to assess the severity of adverse effects.

Breastfeeding
Sulpiride is excreted into breast milk and its use should be avoided in mothers wishing to breast feed.

Fertility
A decrease in fertility linked to the pharmacological effects of the drug (prolactin-dependent effect) was observed in treated animals.

**3.7. Effects on the ability of drive and use machines**

The medicine may cause drowsiness, dizziness, visual disturbances, and impair the mental and/or physical abilities required for the performance of hazardous tasks such as operating machinery or driving a vehicle. Caution should be used while driving or operating machinery, especially because the particular sensitivity of each patient to the medicine has not been established.

**3.8. Undesirable effects**

The following frequency rating is used, when applicable:

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); not known (cannot be estimated from the available data).

Blood and lymphatic system disorders (see section 3.4. Special warnings and precautions for use):

| | |
|---|---|
| Uncommon | : Leukopenia |
| Not known | : Neutropenia, agranulocytosis |

Immune system disorders:

| | |
|---|---|
| Not known | : Anaphylactic reactions including urticaria, dyspnoea, hypotension and anaphylactic shock |

Endocrine disorders:

| | |
|---|---|
| Common | : Hyperprolactinaemia |

Psychiatric disorders:

| | |
|---|---|
| Common | : Insomnia |
| Not known | : Confusion |

Nervous system disorders:

| | |
|---|---|
| Common | : Sedation or drowsiness, extrapyramidal disorder (these symptoms are generally reversible upon administration of antiparkinsonian medication), Parkinsonism, tremor, akathisia |
| Uncommon | : Hypertonia, dyskinesia, and dystonia |
| Rare | : Oculogyric crisis |
| Not known | : Neuroleptic malignant syndrome, hypokinesia, tardive dyskinesia (have been reported, as with all neuroleptics, after a neuroleptic administration of more than three months. Antiparkinsonian medication is ineffective or may induce aggravation of the symptoms), convulsion |

Metabolism and nutrition disorders:

| | |
|---|---|
| Not known | : Hyponatraemia, syndrome of inappropriate antidiuretic hormone secretion (SIADH) |

Cardiac disorders:

| | |
|---|---|
| Rare | : Ventricular arrhythmia, ventricular fibrillation, ventricular tachycardia. |

Not known : Electrocardiogram QT prolonged, cardiac arrest, torsades de pointes, sudden death (see section 3.4. Special warnings and precautions for use)

Vascular disorders:
Uncommon : Orthostatic hypotension
Not known : Venous embolism, pulmonary embolism, deep vein thrombosis (see section 3.4. Special warnings and precautions for use)

Respiratory, thoracic and mediastinal disorders:
Not known : Pneumonia aspiration (mainly in association with other CNS depressants)

Gastrointestinal disorders:
Common : Constipation
Uncommon : Salivary hypersecretion

Hepatobiliary disorders:
Common : Hepatic enzyme increased

Skin and subcutaneous tissue disorders:
Common : Maculo-papular rash

Musculoskeletal and connective tissue disorders:
Not known : Torticollis, trismus

Pregnancy, puerperium and perinatal conditions:
Not known : Extrapyramidal symptoms, drug withdrawal syndrome neonatal (see section 3.6. Fertility, pregnancy and breastfeeding)

Reproductive system and breast disorders:
Common : Breast pain, galactorrhoea
Uncommon : Breast enlargement, amenorrhoea, orgasm abnormal, erectile dysfunction
Not known : Gynaecomastia

General disorders and administration site conditions:
Common : Weight gain

**Reporting of suspected adverse reactions**
Reporting of 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:
Pusat Farmakovigilans/MESO Nasional Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif
Badan Pengawas Obat dan Makanan
Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560
Email: pv-center@pom.go.id
Phone: +62-21-4244691 Ext.1079
Website: https://e-meso.pom.go.id/ADR

For adverse event and product quality complaint, please contact pv.soho@sohoglobalhealth.com or (021) 460-5550.

### 3.9. Overdose

Experience with sulpiride in overdose is limited.

Symptoms

Dyskinesia with spasmodic torticollis, tongue protrusion, and trismus may occur. Some patients may develop a life-threatening Parkinson's syndrome or even coma. Cases of fatal outcomes have been reported mainly in combinations with other psychotropic substances.

Treatment

Sulpiride is partially eliminated by hemodialysis.

There is no specific antidote to sulpiride. Symptomatic treatment, resuscitation under close continuous respiratory and cardiac monitoring (risk of prolongation of the QT interval and ventricular arrhythmia) which will be continued until the patient recovers.

If severe extrapyramidal syndrome occurs, administer an anticholinergic.

## 4. PHARMACOLOGICAL PROPERTIES

### 4.1. Pharmacodynamic Properties

Pharmacotherapeutic group: ANTIPSYCHOTIC NEUROLEPTIC BENZAMIDE, ATC code: N05AL01
Sulpiride interferes with cerebral dopaminergic nerve transmissions and, at low doses, exerts an activating action simulating a dopaminomimetic effect. At higher doses, sulpiride also has an antiproductive action.

### 4.2. Pharmacokinetic Properties

*Absorption*

Administered orally, the peak plasma level of sulpiride is reachedin 3 to 6 hours. It is 0.25 mg/l after administration of a 50 mg capsule and is 0.73 mg/l after administration of a 200 mg tablet.
The bioavailability of oral forms is 25 to 35%, with high inter-individual variability.
The kinetics of sulpiride remain linear after administration at doses ranging from 50 to 300 mg.

*Distribution*

The average volume of distribution of sulpiride is 2.72 ± 0.66 l/kg.
The protein binding rate is approximately 40%.

*Metabolism*

Sulpiride is poorly metabolized in humans.

*Elimination*

Sulpiride is primarily excreted renally, by glomerular filtration. Total systemic clearance of sulpiride is 415 ml/min and renal clearance is 310 ml/min. The average half-life of sulpiride is 7 hours.

### 4.3. Preclinical safety data

In long-term animal studies with neuroleptic drugs, including sulpiride, an increased incidence of various endocrine tumours (some of which have occasionally been malignant) has been seen in some but not all strains of rats and mice studied. The significance of these findings to man is not known; there is no current evidence of any association between neuroleptic use and tumour risk in man.

## 5. PHARMACEUTICAL PARTICULARS

### 5.1. List of excipients

**DOGMATIL**:
Magnesium Stearate, Talc, Copovidone, Lactose.

**DOGMATIL Forte:**

Magnesium Stearate, Talc, Microcrystalline Cellulose, Lactose, Povidone, Corn Starch, Colloidal Silicon Dioxide.

**5.2. Incompatibilities**

None known

**5.3. Storage**

Store below 30°C, protect from light

**5.4. Availability**

**DOGMATIL 50 mg**

Box, 10 strip @ 10 capsules (DKL7624229901A1)

**DOGMATIL FORTE 200 mg** (for psychiatric use only)

Box, 2 strip @ 10 tablets (DKL7824230010A1)

**ON MEDICAL PRESCRIPTION ONLY**

**Manufactured by :**
**PT. SOHO Industri Pharmasi**
a SOHO Global Health Company
Jakarta - Indonesia