SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

BIODALGIC 50 mg, effervescent tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Tramadol (hydrochloride)..... 50.00 mg
For one effervescent tablet.
Excipients with known effects : aspartame (source of phenylalanine), lactose, sodium.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Effervescent tablet.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Treatment of moderate to severe pain in adults.

4.2. Posology and method of administration

Posology

As with all pain medications, the dosage of tramadol should be tailored to the intensity of the pain and the clinical response of each patient.
Acute pain:
The loading dose is 100 mg (2 tablets) followed by 50 or 100 mg (1 or 2 tablets) every 4-6 hours without exceeding 400 mg/24 h (8 tablets).
Chronic pain:
The loading dose is 50 or 100 mg (1 or 2 tablets) followed by 50 or 100 mg (1 or 2 tablets) every 4-6 hours without exceeding 400 mg/24 h (8 tablets).

- From age 75, it is recommended to increase the interval between doses (every 9 hours).

- In case of liver failure: reduce the unit dose by half or increase the interval between doses by 2 times (every 12 hours).

- In case of renal insufficiency: increase the interval between doses by 2 times (every 12 hours for a creatinine clearance < 30 ml/min).

Avoid using tramadol if creatinine clearance is < 10 ml/min .

Method of administration

Oral route.
Drink immediately after the tablet has completely dissolved in a little water.

4.3. Contraindications

- Hypersensitivity to the active substance, to opiates or to any of the excipients listed in section 6.1.

- Acute poisoning or overdose with central nervous system depressants (alcohol, hypnotics, other analgesics...).

- Concurrent or recent treatment (stopped less than 15 days ago) with MAOIs.

- Severe respiratory failure.
- Severe hepatocellular insufficiency.
- Child under 15 years old.
- Breastfeeding, if long-term treatment is necessary (see section 4.6).
- Epilepsy not controlled by treatment (see section 4.4).
- Combination with buprenorphine, nalbuphine and pentazocine (see section 4.5).
- Due to the presence of aspartame, this medication is contraindicated in cases of phenylketonuria.

This medication should generally not be used:

- During pregnancy,
- In combination with carbamazepine.

4.4. Special warnings and precautions for use

Special warnings

Sleep-related breathing disorders: Opioids can cause sleep-related breathing disorders, including central sleep apnea (CSA) and sleep-related hypoxemia. The risk of CSA increases with the dose of opioids used. In patients with CSA, a reduction in the total opioid dose should be considered.
Adrenal insufficiency: Opioid analgesics can occasionally cause reversible adrenal insufficiency requiring monitoring and glucocorticoid replacement therapy. Symptoms of acute or chronic adrenal insufficiency may include, for example, severe abdominal pain, nausea and vomiting, low blood pressure, extreme fatigue, decreased appetite, and weight loss.
Tolerance, as well as physical and psychological dependence, may develop, particularly after prolonged use. In predisposed patients, treatment should be carried out under strict medical supervision.
Tramadol is not suitable for withdrawal or substitution treatment in patients with opioid dependence. Although an opioid agonist, tramadol cannot alleviate morphine withdrawal symptoms.
The use of tramadol in patients taking vitamin K antagonists is not recommended (see section 4.5).
Tramadol should be used with caution in diabetic patients due to the risk of hypoglycemia.
Seizures have been reported in patients receiving tramadol at the recommended doses. The risk of seizures is increased if tramadol doses exceed the upper limit of the recommended daily dose (400 mg). Tramadol may also increase the risk of seizures in patients taking other products that lower the seizure threshold (see section 4.5).
Patients with controlled epilepsy or patients at risk of seizures should only be treated with tramadol if absolutely necessary.
Drinking alcohol during treatment is not recommended.
Due to the presence of lactose, this medicine is contraindicated in cases of congenital galactosemia, glucose-galactose malabsorption syndrome, or lactase deficiency.
Metabolism via CYP2D6
Tramadol is metabolized by a liver enzyme, CYP2D6. If a patient has a deficiency or complete absence of this enzyme, the expected analgesic effect may not be achieved. It is estimated that up to 7% of the Caucasian population may have this deficiency. However, if the patient is an ultrarapid metabolizer, there is a risk, even at the recommended dose, of experiencing adverse effects related to opiate toxicity.
General symptoms of opiate toxicity include mental confusion, drowsiness, shallow breathing, constricted pupils, nausea, vomiting, constipation, and loss of appetite. In severe cases, patients may experience symptoms of circulatory and respiratory failure, which can be life-threatening and, in very rare cases, fatal.
The estimated prevalences of ultra-rapid metabolizers in different populations are summarized below:
Population % prevalence
African/Ethiopian 29%
African American: 3.4% to 6.5%
Asian: 1.2% to 2%
Caucasian, 3.6% to 6.5%
Greek 6.0%
Hungarian 1.9%

Northern Europeans: 1% to 2%
Post-operative use in children
The literature reports cases of tramadol administered to children postoperatively after tonsillectomy and/or adenoidectomy for the treatment of obstructive sleep apnea, leading to rare but potentially life-threatening adverse events. The administration of tramadol to children for postoperative pain relief should be approached with extreme caution and accompanied by close monitoring for symptoms related to opioid toxicity, particularly respiratory depression.
Children with impaired respiratory function
The use of tramadol is not recommended in children with impaired respiratory function, particularly in cases of neuromuscular deficit, severe cardiac or respiratory conditions, upper respiratory tract or lung infections, multiple trauma, or major surgery. These factors may worsen the symptoms of opioid toxicity.
Serotonin syndrome
Serotonin syndrome, a potentially fatal condition, has been reported in patients treated with tramadol in combination with other serotonergic agents or with tramadol alone (see sections 4.5, 4.8 and 4.9).
If concomitant treatment with other serotonergic agents is clinically justified, careful observation of the patient is advised, particularly during treatment initiation and dose increases.
Symptoms of serotonin syndrome may include changes in mental state, autonomic instability, neuromuscular abnormalities, and/or gastrointestinal symptoms.
If serotonin syndrome is suspected, a dose reduction or discontinuation of treatment should be considered depending on the severity of the symptoms. Withdrawal of serotonergic medications generally leads to rapid improvement.

Precautions for use

Tramadol should only be used after careful assessment of the benefit-risk ratio, depending on the origin of the pain and the patient's profile (see section 5.3).
If treatment with tramadol is discontinued, it is advisable to gradually reduce the dose to avoid withdrawal symptoms.
Tramadol should be used with caution in patients with intracranial hypertension, head trauma, altered consciousness without obvious cause, or disorders of the respiratory center or function.
Tramadol should be used with caution in the elderly, due to the risk of falls and loss of consciousness.
This medicine contains 214 mg of sodium per tablet, which is equivalent to 10.7% of the WHO's maximum recommended daily intake of 2 g of sodium for an adult.
This medicine contains lactose. Patients with galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption (rare hereditary disorders) should not take this medicine.
This medicine contains aspartame. It should be noted that there are no clinical or non-clinical data regarding the use of aspartame in children under 12 weeks of age.

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

Pharmacokinetic studies to date have shown that concomitant or prior administration of cimetidine (enzyme inhibitor) is unlikely to cause clinically relevant interactions.

Medications that cause serotonin syndrome

Tramadol can cause seizures and increase the epileptogenic potential of selective serotonin reuptake inhibitors (SSRIs), serotonin and adrenaline reuptake inhibitors (SARIs), tricyclic antidepressants, antipsychotics and other drugs that lower the seizure threshold (such as bupropion, mirtazapine, tetrahydrocannabinol).
The concomitant therapeutic use of tramadol and serotonergic drugs, such as selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), MAO inhibitors (see section 4.3), tricyclic antidepressants and mirtazapine, may cause serotonin syndrome, a potentially fatal condition (see sections 4.4 and 4.8).
Discontinuing serotonergic agents generally leads to rapid improvement. Treatment depends on the type and severity of symptoms.
Other drugs known to inhibit CYP3A4, such as ketoconazole and erythromycin, could inhibit the metabolism of tramadol (N-demethylation) and probably also the metabolism of the -active demethylated O metabolite. The clinical significance of such an interaction has not been studied (see section 4.8).

Medications that lower the seizure threshold

The combined use of proconvulsant drugs, or drugs that lower the seizure threshold, must be carefully considered due to the severity of the risk involved. These drugs include, in particular, most antidepressants (tricyclic antidepressants, selective serotonin reuptake inhibitors), neuroleptics (phenothiazines and butyrophenones), mefloquine, chloroquine, bupropion, tramadol, and fluoroquinolones.

Sedative medications

It is important to consider that many medications or substances can have additive depressant effects on the central nervous system and contribute to decreased alertness. These include morphine derivatives (analgesics, antitussives, and substitution treatments), neuroleptics, barbiturates, benzodiazepines, anxiolytics other than benzodiazepines (e.g., meprobamate), hypnotics, sedative antidepressants (amitriptyline, doxepin, mianserin, mirtazapine, trimipramine), sedative H1 antihistamines, centrally acting antihypertensives, baclofen, and thalidomide.

Contraindicated combinations (see section 4.3)

+ Irreversible MAOIs (iproniazid)
Risk of developing serotonin syndrome: diarrhea, tachycardia, sweating, tremors, confusion or even coma.
A period of two weeks should be observed between stopping the MAOI and starting treatment with tramadol, and at least one week between stopping treatment with tramadol and starting the MAOI.

Associations not recommended

+ Morphine agonist-antagonists (buprenorphine, nalbuphine, pentazocine)
Reduced analgesic effect due to competitive receptor blockade, with a risk of developing a withdrawal syndrome.
+ Alcohol (beverage or excipient)
Increased sedative effect of morphine analgesics when combined with alcohol.
Impaired alertness can make driving vehicles and operating machinery dangerous.
Avoid consuming alcoholic beverages and medications containing alcohol.
+ Carbamazepine
Risk of decreased plasma concentrations of tramadol.
Simultaneous or prior administration of carbamazepine (an enzyme inducer) may reduce the analgesic effects and shorten the duration of action of tramadol.
+ Reversible MAOIs including linezolid and methylene blue
Risk of developing serotonin syndrome: diarrhea, tachycardia, sweating, tremors, confusion or even coma.
If the combination cannot be avoided, very close clinical monitoring is required. Initiate the combination at the minimum recommended doses.
+ Partial opioid antagonists
Risk of reduced analgesic effect.
+ Naltrexone
Risk of reduced analgesic effect.
+ Sodium oxybate
Increase in central depression.
Impaired alertness can make driving vehicles and operating machinery dangerous.

Associations requiring precautions for use

+ Vitamin K antagonist
Risk of increased effect of the vitamin K antagonist and increased risk of bleeding. More frequent INR monitoring.
Possible adjustment of the vitamin K antagonist dosage during and after tramadol treatment.

Associations to consider

+ Other morphine agonist analgesics, morphine-like antitussives (dextromethorphan, noscapine, pholcodine), true morphine antitussives (codeine, ethylmorphine)
Increased risk of respiratory depression which can be fatal in case of overdose.
+ Other medications that lower the seizure threshold
Increased risk of seizures.
+ Other sedative medications
Increase in central depression.
Impaired alertness can make driving vehicles and operating machinery dangerous.
+ Benzodiazepines and related drugs
Increased risk of respiratory depression which can be fatal in case of overdose.
+ Barbiturates
Increased risk of respiratory depression which can be fatal in case of overdose.
+ MAOI-B
Risk of developing serotonin syndrome.

+ Selective serotonin reuptake inhibitors (citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline)
Risk of seizures and/or serotonin syndrome.
+ Venlafaxine
Risk of seizures and/or serotonin syndrome.
+ Bupropion
Increased plasma concentrations of tramadol due to decreased hepatic metabolism by bupropion. Furthermore, there is a risk of seizures due to the additive effects of the two drugs.
+ Ondansetron
Decreased intensity and duration of the analgesic effect of tramadol and risk of decreased antiemetic effect of ondansetron.

4.6. Fertility, pregnancy and breastfeeding

Pregnancy

Animal studies using tramadol have shown effects on organ development, ossification, and neonatal mortality at very high doses. Teratogenic effects have not been observed. Tramadol crosses the placental barrier. There is insufficient evidence regarding the safety of tramadol use during pregnancy in humans. Therefore, BIODALGIC 50 mg capsules should not be used by pregnant women.
Administered before or during childbirth, tramadol does not alter uterine contractility. Tramadol may cause changes in respiratory rate in newborns, which are generally without adverse clinical consequences. Prolonged use during pregnancy may lead to withdrawal symptoms in the newborn.

Breastfeeding

Approximately 0.1% of the tramadol dose administered to the mother is excreted in breast milk. During the immediate postpartum period, a daily oral intake of up to 400 mg of tramadol by the mother corresponds to an average amount of tramadol ingested by the breastfed infant of 3% of the mother's body-weight-adjusted dose. Therefore, tramadol should either not be used during lactation or breastfeeding should be discontinued during tramadol treatment. Discontinuation of breastfeeding is generally not necessary following a single dose of tramadol.

Fertility

Post-marketing studies have not shown any effect of tramadol on fertility. Animal studies have not shown any effect of tramadol on fertility.

4.7. Effects on the ability to drive vehicles and use machinery

Impaired alertness can make driving and operating machinery dangerous, especially when combined with the consumption of alcoholic beverages or central nervous system depressants.

4.8. Undesirable effects

System - Organ	Very common (1 in 10 patients)	Frequent (1 to 10 patients out of 100)	Rare (1 to 10 patients out of 1000)	Very rarely (1 to 10 patients out of 10,000)	Frequency not known (Frequency cannot be estimated from the available data)
Immune system disorders				Allergic reactions (such as hives, angioedema, bronchospasm, and exceptional cases of anaphylactic shock which can be fatal)	
Central nervous system disorders	Drowsiness, headaches, dizziness,		Syncope, involuntary		Serotonin syndrome

System - Organ	Very common (1 in 10 patients)	Frequent (1 to 10 patients out of 100)	Rare (1 to 10 patients out of 1000)	Very rarely (1 to 10 patients out of 10,000)	Frequency not known (Frequency cannot be estimated from the available data)
	excessive sweating, feeling unwell		muscle contractions		
Heart conditions		Tachycardia, hypotension, palpitations, elevated blood pressure			
Gastrointestinal disorders	Nausea, vomiting, dry mouth, constipation	Abdominal pain			
Skin and subcutaneous tissue disorders		Rash			
Urinary and kidney disorders				Urinary problems such as dysuria and/or urinary retention	
Visual disorders		Minor vision problems			
Hepatobiliary disorders					Cholestasis (tramadol alone) Hepatic cytolysis (especially in combination with paracetamol) Elevated liver enzymes
Respiratory, thoracic and mediastinal disorders				Respiratory rate disorders. Respiratory depression may occur if the administered doses greatly exceed the recommended doses or if other central nervous system depressant drugs are administered concomitantly .	hiccups
General conditions and anomalies at the administration site		Asthenia, euphoria.			
Psychiatric disorders				Withdrawal symptoms (panic attacks, severe anxiety, hallucinations, paresthesia, tinnitus, other CNS disorders)	neuropsychiatric disorders (depending on individual reactivity and mainly in the elderly) such as confusion and exceptionally such as hallucinations and/or delirium; convulsions mainly after administration of high doses or after concomitant

System - Organ	Very common (1 in 10 patients)	Frequent (1 to 10 patients out of 100)	Rare (1 to 10 patients out of 1000)	Very rarely (1 to 10 patients out of 10,000)	Frequency not known (Frequency cannot be estimated from the available data)
					treatment with drugs that can lower the seizure threshold or that themselves trigger convulsions (see section 4.4).
Metabolism and nutrition disorders					Hypoglycemia Hyponatremia

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals report any suspected adverse reactions via the national reporting system: French National Agency for Medicines and Health Products Safety (ANSM) and the network of Regional Pharmacovigilance Centers - Website: https://signalement.social-sante.gouv.fr/ .

4.9. Overdose

Signs of overdose include: miosis, vomiting, cardiovascular collapse, respiratory depression which can lead to respiratory arrest, coma and convulsions.
Serotonin syndrome has also been reported.
The first therapeutic steps will be to maintain respiratory and cardiovascular functions and to transfer urgently to a hospital setting.
Naloxone can be used in cases of respiratory depression, provided that respiratory functions are monitored.
Diazepam can be used in cases of seizures.
Tramadol is poorly or not at all hemodialyzable.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Tramadol is a central analgesic whose effectiveness is due to synergy at therapeutic doses:

- An opioid effect due to binding to μ-type opioid receptors,

- From a central monoaminergic effect due to an inhibition of the reuptake of noradrenaline and serotonin, a mechanism involved in the control of central nociceptive transmission.

Like other drugs in this class, tramadol has antitussive properties. Its effects on the gastrointestinal tract are minimal at therapeutic doses. Tramadol's respiratory depressant effects are less pronounced than those of morphine. Animal studies have shown a lower potential for dependence compared to morphine, and a very low potential for tolerance.

5.2. Pharmacokinetic properties

Following a single oral administration of a dose of 50 to 100 mg, bioavailability is between 70 and 90%.
After repeated oral administration every 6 hours of 50 to 100 mg, steady state is rapidly reached in about 36 hours and bioavailability increases, exceeding 90%.
The peak serum concentration after oral administration of 100 mg of tramadol is approximately 300 ng/ml (Cmax) and is reached after approximately 2 hours (tmax).
Plasma protein binding is 20%, and the volume of distribution is large (3 to 4 l/kg).
Tramadol crosses the placental barrier and passes in very small quantities into breast milk (approximately 0.1% of the administered maternal dose).
The elimination half-life is between 5 and 7 hours in healthy volunteers; 90% of tramadol is metabolized, mainly in the liver; one of the demethylated metabolites has an analgesic effect; its half-life is of the same order as that of tramadol.

Tramadol and its metabolites are almost entirely excreted via the kidneys (95%). The remainder is eliminated in the feces.
The pharmacokinetics of tramadol are only very slightly modified by the age of the patient; in subjects over 75 years of age, the half-life is slightly increased.
In patients with renal insufficiency, tramadol clearance is reduced in parallel with creatinine clearance; the half-life is on average 12 hours.
In patients with hepatic insufficiency, tramadol clearance is reduced, depending on the severity of the hepatic insufficiency.
Inhibition of one or both cytochromes CYP3A4 and CYP2D6 involved in the biotransformation of tramadol may alter the plasma concentration of tramadol or its active metabolites.

5.3. Preclinical safety data

In animals, signs of intoxication that appear after repeated administration of high doses are consistent with morphine intoxication.
Some of the in vitro mutagenicity tests conducted with tramadol proved positive.
However, in vivo tests in mice, rats and Chinese hamsters on bone marrow and germ cells have ruled out an in vivo mutagenic potential of tramadol.
Reproductive studies have shown an increase in neonatal mortality rates and a delay in the development of certain organs at doses far exceeding those used clinically.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Anhydrous citric acid, sodium bicarbonate, anhydrous sodium sulfate, lactose monohydrate, macrogol 6000, anhydrous sodium carbonate, sodium cyclamate, povidone K25, aspartame, orange flavour*, simethicone.
Composition of the orange flavor : orange oil, orange essential oil, citric acid monohydrate, butylhydroxyanisole, dextrin, gum arabic.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

3 years

6.4. Special precautions for storage

Store below 25°C.

6.5. Nature and contents of container

15 tablets, 1 polypropylene tube of 15 with desiccant
30 tablets, 2 polypropylene tubes of 15 tablets with desiccant.
90 tablets, 6 polypropylene tubes of 15 with desiccant.
Not all presentations may be commercially available.

6.6. Special precautions for disposal and handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

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75013 PARIS
FRANCE

8. OPERATOR

FRILAB SA
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1207 GENEVA
SWISS

9. MANUFACTURER

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1 NUNGESSER STREET
59121 PROUVY
FRANCE

10. DATE OF REVISION OF THE TEXT

July 2025

11. DOSIMETRY

Not applicable.

11. INSTRUCTIONS FOR THE PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.

CONDITIONS FOR PRESCRIPTION AND DISPENSING

List I.
Prescription limited to 12 weeks.