PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

T/C DIASTAT®

Diazepam gel
Rectal Delivery System
5 mg/mL, 10 mg/2 mL and 15 mg/3 mL

Benzodiazepine Anticonvulsant

Bausch Health, Canada Inc.
2150 St-Elzear Blvd. West
Laval, Quebec
H7L 4A8

Date of Initial Authorization:
May 18, 2005

Date of Revision:
August 16, 2021

Submission Control Number: 216009

RECENT MAJOR LABEL CHANGES

1 INDICATIONS, 1.2 Geriatrics	05/2021
3 SERIOUS WARNINGS AND PRECAUTIONS BOX	05/2021
4 DOSAGE AND ADMINISTRATION, 4.2 Dosing Considerations	05/2021
7 WARNINGS AND PRECAUTIONS, Concomitant use with Opioids	05/2021
7 WARNINGS AND PRECAUTIONS, Dependence/Tolerance	05/2021
7 WARNINGS AND PRECAUTIONS, Falls and Fractures	05/2021
7 WARNINGS AND PRECAUTIONS, 7.1.4 Geriatrics	05/2021

TABLE OF CONTENTS

Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

DIASTAT (diazepam gel) is indicated for the management of selected, refractory, patients with epilepsy, on stable regimens of anti-epileptic drugs (AEDs), who require intermittent use of diazepam to control bouts of increased seizure activity.

These bouts are defined as a form of severe seizures variously referred to as recurrent, serial, cluster or crescendo seizures. These clusters are a predictable component of the patient's seizure disorder that are historically distinct from the patient's other seizures in either type, frequency, severity or duration and have an onset that is easily recognized by the family and physician. The clusters have a consistent component, such as an aura, prodrome or characteristic single or multiple seizures, that is predictably and temporally linked to subsequent seizures. Patients typically demonstrate recovery between these seizures. As is the case with all seizure classifications, there is a common pattern of seizure presentation and there are clearly different features for every individual.

DIASTAT is intended for use by caregivers to treat patients in the home setting, as well as in hospitals, emergency and urgent care units and residential institutions.

1.1 Pediatrics

Pediatrics (< 2 years of age): Health Canada has not authorized an indication for pediatric patients < 2 years of age as the safety and efficacy of DIASTAT has not been established, based on the data submitted and reviewed by Health Canada. Evidence from clinical experience suggests that use in the infant pediatric population is associated with differences in safety. A brief discussion can be found in the appropriate sections (see 14 CLINICAL TRIALS, 4 DOSAGE AND ADMINISTRATION, 10 CLINICAL PHARMACOLOGY, 7.1.3 Pediatrics).

1.2 Geriatrics

Geriatrics (> 60 years of age): Long-term use of DIASTAT should be avoided in patients > 60 years of age. Enhanced monitoring is recommended (see 7 WARNINGS AND PRECAUTIONS, Falls and fractures; 4.1 Dosing considerations).

2 CONTRAINDICATIONS

- Patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container. For a complete listing, see the 6 DOSAGE FORMS, COMPOSITION AND PACKAGING section of the Product Monograph.
- DIASTAT is contraindicated in patients with a known hypersensitivity to diazepam.
- DIASTAT (diazepam gel) may be used in patients with open angle glaucoma who are receiving appropriate therapy but is contraindicated in acute narrow angle glaucoma.

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions

Addiction, Abuse and Misuse

The use of benzodiazepines, including DIASTAT, can lead to abuse, misuse, addiction, physical dependence and withdrawal reactions. Abuse and misuse can result in overdose or death, especially when benzodiazepines are combined with other medicines, such as opioids, alcohol or illicit drugs.

Assess each patient's risk prior to prescribing DIASTAT

Monitor all patients regularly for the development of these behaviours or conditions.

DIASTAT should be stored securely to avoid theft or misuse.

Withdrawal

Benzodiazepines, like DIASTAT, can produce severe or life-threatening withdrawal symptoms.

- Avoid abrupt discontinuation or rapid dose reduction of DIASTAT.
- Terminate treatment with DIASTAT by gradually tapering the dosage schedule under close monitoring.

(see 7 WARNINGS AND PRECAUTIONS, Dependence/Tolerance)

Risks from Concomitant use with Opioids

Concomitant use of DIASTAT and opioids may result in profound sedation, respiratory depression, coma and death (see 7 WARNINGS AND PRECAUTIONS, General, Concomitant use with opioids; 9.1 Serious Drug Interactions).

- Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are not possible.
- Limit dosages and durations to the minimum required.
- Follow patients for signs and symptoms of respiratory depression and sedation.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- DIASTAT should always be prescribed at the lowest effective dose for the shortest duration possible.
- DIASTAT can produce withdrawal signs and symptoms or rebound phenomena following abrupt discontinuation or rapid dose reduction (see 3 SERIOUS WARNINGS AND

PRECAUTIONS BOX, Withdrawal; 7 WARNINGS AND PRECAUTIONS, Dependence/Tolerance). Abrupt discontinuation should be avoided and treatment – even if only of short duration - should be terminated by gradually tapering the dosage schedule under close monitoring.

- Tapering should be tailored to the specific patient. Special attention should be given to patients with a history of seizure.
- If a patient experiences withdrawal signs and symptoms, consider postponing the taper or raising the benzodiazepine to the previous dosage prior to proceeding with a gradual taper.
- Elderly and debilitated patients in particular may be more sensitive to benzodiazepines (see 7 WARNINGS AND PRECAUTIONS, Falls and Fractures). In these patients, it is recommended that the dosage be adjusted downward to reduce the likelihood of ataxia or oversedation.
- Long-term use of DIASTAT should be avoided in elderly patients. Enhanced monitoring is recommended.
- The prescribed dose of study medication should be adjusted by the physician periodically to reflect changes in the patient's age or weight. It is recommended that dosage be reviewed at 6-month intervals.

4.2 Recommended Dose and Dosage Adjustment

Calculating Prescribed Dose

The DIASTAT (diazepam gel) dose should be individualized for maximum beneficial effect. The target dose of DIASTAT is 0.2 - 0.5 mg/kg depending on age. See the dosing table for specific recommendations.

Table 1: Specific Recommendations (Dosing Table)

Age (years)	Target Dose
2 through 5	0.5 mg/kg
6 through 11	0.3 mg/kg
12 and older	0.2 mg/kg

DIASTAT is provided in fixed, unit-doses of 5 and 10 and 15 mg. The prescribed dose is obtained by rounding upward to the next available dose. The following table provides acceptable doses for each age category and weight range, such that patients will receive between 90% and 180% of the calculated target dose. The safety of this strategy has been established in clinical trials.

Table 2: Acceptable Weight Ranges for Each Dose and Age Category

2-5 Years 0.5 mg/kg		6-11 Years 0.3 mg/kg		12+ Years 0.2 mg/kg	
Weight (kg)	**Dose (mg)**	**Weight (kg)**	**Dose (mg)**	**Weight (kg)**	**Dose (mg)**
6 to 11	5	10 to 18	5	14 to 27	5
12 to 22	10	19 to 37	10	28 to 50	10
23 to 33	15	38 to 55	15	51 to 75	15
34 to 44	20*	56 to 74	20*	76 to 111	20*

*Not currently commercialized.

Additional Dose

If a single dose does not adequately treat the episode, the physician may wish to prescribe 2 doses of DIASTAT. The second dose may be given 4-12 hours after the first dose if seizures persist, are known to reoccur, or if the patient is known to have especially refractory seizures.

Treatment Frequency

It is recommended that patients be treated with DIASTAT no more frequently than every five days and no more than five times per month. If a patient requires more frequent administration of DIASTAT for seizure control, the patient's treatment regimen may require re-evaluation by the physician.

4.4 Administration

See 7 WARNINGS AND PRECAUTIONS, General section for general considerations.

5 OVERDOSAGE

In the DIASTAT (diazepam gel) clinical trials, the practice was to dose patients up to twice the target dose (see 4 DOSAGE AND ADMINISTRATION). Two patients received more than twice the target dose and reported no adverse events (AEs).

Previous reports of diazepam overdosage have shown that manifestations of diazepam overdosage include somnolence, confusion, coma, and diminished reflexes. Respiration, pulse and blood pressure should be monitored, as in all cases of drug overdosage, although, in general, these effects have been minimal. General supportive measures should be employed, along with intravenous fluids, and an adequate airway maintained. Hypotension may be combated by the use of levarterenol or metaraminol. Dialysis is of limited value.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 3: Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Rectal	Gel 5 mg/mL	Propylene Glycol, Ethyl Alcohol (10%), Hydroxypropyl Methylcellulose, Sodium Benzoate, Benzyl Alcohol (1.5%), Benzoic Acid, and Water

DIASTAT (diazepam gel) rectal delivery system is a non-sterile diazepam gel provided in a prefilled, unit-dose, rectal delivery system. The rectal delivery system includes a plastic applicator with a flexible, molded tip available in 2 lengths, designated for convenience as Pediatric, Universal or Adult. DIASTAT is available in the following 3 presentations:

Table 4: Doses of Diazepam with Respective Rectal Tip Sizes

Dose of Diazepam (mg)	Rectal Tip Size
5.0	Pediatric (4.4 cm)
10.0	Universal (4.4 cm)
15.0	Adult (6.0 cm)

Each package contains 2 DIASTAT rectal delivery systems, 2 packets of lubricating jelly, and Instructions for Use.

DIASTAT contains 5 mg/mL Diazepam, Propylene Glycol, Ethyl Alcohol (10%), Hydroxypropyl Methylcellulose, Sodium Benzoate, Benzyl Alcohol (1.5%), Benzoic Acid, and Water.

DIASTAT is clear to slightly yellow and has a pH between 6.5 and 7.2.

7 WARNINGS AND PRECAUTIONS

Please see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX

General

DIASTAT should only be administered by caregivers who in the opinion of the prescribing

physician: 1) are able to distinguish the distinct cluster of seizures (and/or the events presumed to herald their onset) from the patient's ordinary seizure activity, 2) have been instructed and judged to be competent to administer the treatment rectally, 3) understand explicitly which seizure manifestations may or may not be treated with DIASTAT, and 4) are able to monitor the clinical response and recognize when that response is such that immediate professional medical evaluation is required.

Concomitant use with Opioids

Concomitant use of benzodiazepines, including DIASTAT, and opioids may result in profound sedation, respiratory depression, coma, and death. Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are not possible (see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX, Risks from Concomitant use with Opioids; 9.1 Serious Drug Interactions).

Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioid analgesics alone. Because of similar pharmacological properties, it is reasonable to expect similar risk with the concomitant use of other CNS depressant drugs with benzodiazepines.

If a decision is made to prescribe DIASTAT concomitantly with opioids, prescribe the lowest effective dosages and minimum durations of concomitant use. In patients already receiving an opioid analgesic, prescribe a lower initial dose of DIASTAT than indicated, and titrate based on clinical response. If an opioid analgesic is initiated in a patient already taking DIASTAT, prescribe a lower initial dose of the opioid analgesic and titrate based on clinical response. Follow patients closely for signs and symptoms of respiratory depression and sedation (see 5 OVERDOSAGE).

Advise both patients and caregivers about the risks of respiratory depression and sedation when DIASTAT is used with opioids.

Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the opioid have been determined.

Carcinogenesis and Mutagenesis

Only animal data are available (see 16 NON-CLINICAL TOXICOLOGY, Carcinogenicity).

The data currently available are inadequate to determine the mutagenic potential of diazepam.

Dependence/Tolerance

Use of benzodiazepines, such as DIASTAT, can lead to abuse, misuse, addiction, physical dependence (including tolerance) and withdrawal reactions. Abuse and misuse can result in overdose or death, especially when benzodiazepines are combined with other medicines, such as opioids, alcohol, or illicit drugs.

The risk of dependence increases with higher doses and longer-term use but can occur with

short-term use at recommended therapeutic doses. The risk of dependence is greater in patients with a history of psychiatric disorders and/or substance (including alcohol) use disorder.

- Discuss the risks of treatment with DIASTAT with the patient, considering alternative (including non-drug) treatment options.
- Carefully evaluate each patient's risk of abuse, misuse and addiction, considering their medical condition and concomitant drug use, prior to prescribing DIASTAT. In individuals prone to substance use disorder, DIASTAT should only be administered if deemed medically necessary, employing extreme caution and close supervision.
- DIASTAT should always be prescribed at the lowest effective dose for the shortest duration possible. It is recommended that patients be treated with DIASTAT no more frequently than every five days and no more than five times per month.
- All patients receiving benzodiazepines should be routinely monitored for signs and symptoms of misuse and abuse. If a substance use disorder is suspected, evaluate the patient and refer them for substance abuse treatment, as appropriate.

DIASTAT is not recommended for chronic, daily use as an anticonvulsant because of the potential for development of tolerance to diazepam. Chronic daily use of diazepam may increase the frequency and/or severity of grand mal seizures, requiring an increase in the dosage of standard anticonvulsant medication. In such cases, abrupt withdrawal of chronic diazepam may also be associated with a temporary increase in the frequency and/or severity of seizures.

Withdrawal

Benzodiazepines, such as DIASTAT, can produce withdrawal signs and symptoms, ranging from mild to severe and even life threatening, following abrupt discontinuation or rapid dose reduction. Other factors that may precipitate withdrawal are switching from a long-acting to a short-acting benzodiazepine, decreasing blood levels of the drug or administration of an antagonist. The risk of withdrawal is higher with higher dosages and/or prolonged use but can occur with short-term use at recommended therapeutic doses.

The onset of withdrawal signs and symptoms can range from hours to weeks following drug cessation and occur even with tapered dosage. Some symptoms can persist for months. Since symptoms are often similar to those for which the patient is being treated, it may difficult to distinguish from a relapse of the patient's condition.

Severe or life-threatening signs and symptoms of withdrawal include catatonia, delirium tremens, depression, dissociative effects (e.g. hallucinations), mania, psychosis, seizures (including status epilepticus) and suicidal ideation and behavior.

Other withdrawal signs and symptoms include abdominal cramps, cognitive impairment, diarrhea, dysphoria, extreme anxiety or panic attacks, headache, hypersensitivity to light, noise and physical contact, insomnia, irritability, muscle pain or stiffness, paresthesia, restlessness, sweating, tension, tremors and vomiting. There is also a possibility of rebound anxiety or rebound insomnia.

- Abrupt discontinuation should be avoided and treatment - even if only of short duration - should be terminated by gradually tapering the dosage schedule under close monitoring.
- Tapering should be tailored to the specific patient. Special attention should be given to

patients with a history of seizure.
- If a patient experiences withdrawal symptom, consider postponing the taper or raising the benzodiazepine to the previous dosage prior to proceeding with a gradual taper.
- Inform patients of risk of discontinuing abruptly, reducing dosage rapidly or switching medications.
- Stress the importance of consulting with their health care professional in order to discontinue safely.
- Patients experiencing withdrawal symptoms should seek immediate medical attention.

(see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX, Addiction, Abuse and Misuse, Withdrawal; 4.1 Dosing Considerations).

Driving and Operating Machinery

As is true of most preparations containing central nervous system (CNS)-acting drugs, patients should be cautioned against engaging in hazardous occupations requiring complete mental alertness, such as operating machinery, driving a motor vehicle or riding a bicycle following use of DIASTAT.

Falls and fractures

There have been reports of falls and fractures among benzodiazepine users due to adverse reactions such as sedation, dizziness and ataxia. The risk is increased in those taking concomitant sedatives (including alcoholic beverages), the elderly or debilitated patients.

Hepatic/Biliary/Pancreatic

Precautions in treating patients with impaired hepatic function should be observed because patients with severely impaired hepatic function may be unable to biotransform diazepam to inactive metabolites.

Neurologic

CNS Depression

Concomitant Use of Other CNS Depressants: Since diazepam has a CNS-depressant effect, patients should be advised against the simultaneous use of alcohol or other CNS-depressants during DIASTAT therapy.

Use in Patients with Petit Mal Status: Tonic status epilepticus has been precipitated in patients treated with intravenous diazepam for petit mal status or petit mal variant status.

Use in Patients with Neurologic Damage: DIASTAT should be used with caution in patients with neurologic damage.

Renal

Metabolites of diazepam are excreted by the kidney; to avoid their excess accumulation, caution should be exercised in the administration to patients with compromised kidney function.

Respiratory

DIASTAT should be used with caution in patients with compromised respiratory function related to a concurrent disease process (e.g., asthma, pneumonia).

7.1 Special Populations

7.1.1 Pregnant Women

In humans, measurable amounts of diazepam have been found in maternal and cord blood, indicating placental transfer of the drug. Diazepam has been shown to be teratogenic in mice and hamsters when given orally in doses that are more than 140 times the highest DIASTAT treatment dose. Cleft palates and resorptions are the most common and consistently reported form of developmental toxicity produced in laboratory animals by high doses (>100 mg/kg) of diazepam during gestation. There are no adequate and well-controlled studies of diazepam in pregnant women. However, benzodiazepines have been associated with an increased risk of congenital malformations after first trimester exposure. Hypotonia, lethargy, hypothermia, respiratory and suckling difficulties have been reported in infants whose mothers received benzodiazepines during labor. Children born to mothers receiving benzodiazepines on a regular basis late in pregnancy may be at some risk of experiencing withdrawal symptoms during the postnatal period. DIASTAT should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

It is important to note that anticonvulsant drugs should not be discontinued in patients in whom the drug is administered to prevent seizures because of the strong possibility of precipitating status epilepticus with attendant hypoxia and threat to life. In individual cases where the severity and frequency of the seizure disorder are such that the removal of medication does not pose a serious threat to the patient, discontinuation of the drug may be considered prior to and during pregnancy, although it cannot be said with any confidence that even mild seizures do not pose some hazards to the developing embryo or fetus.

Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy with DIASTAT.

7.1.2 Breast-feeding

Diazepam is excreted in human milk; therefore, DIASTAT should not be administered to nursing women.

7.1.3 Pediatrics

Pediatrics (< 2 years of age)

Clinical studies have not been conducted to establish the efficacy and safety of DIASTAT in children under 2 years of age. Prolonged CNS depression has been observed in neonates

treated with diazepam, apparently due to an inability to biotransform diazepam into inactive metabolites. Therefore, Health Canada has not authorized an indication for pediatric use (<2 years of age) (see 1.1 Pediatrics).

7.1.4 Geriatrics

Geriatrics (> 60 years of age)

The effects of DIASTAT in patients over 60 years of age have not been well characterized. In elderly patients, DIASTAT should be used with caution due to an increase in half-life with a corresponding decrease in the clearance of free diazepam. It is also recommended that the dosage be adjusted downward to reduce the likelihood of ataxia or oversedation.

Long-term use of DIASTAT should be avoided in elderly or debilitated patients who may be more sensitive to benzodiazepines. There is an increased risk of cognitive impairment, delirium, falls, fractures, hospitalizations and motor vehicle accidents in these users. Enhanced monitoring is recommended in this population (see 4.1 Dosing Considerations).

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The most frequent adverse event (AE) reported to be related to DIASTAT (diazepam gel) in the 2 double-blind, placebo-controlled studies was somnolence (23%). Less frequent AEs were dizziness, headache, pain, diarrhea, euphoria, incoordination and nervousness, which occurred in approximately 2-5% of patients. In addition, ataxia (8%), asthenia (4%), hiccup (2%) and vertigo (2%) were reported in open-label studies. There were no differences in the pattern of AEs in children and adults.

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

DIASTAT AE data were collected from double-blind, placebo-controlled studies and open-label studies. The majority of AEs were mild to moderate in severity and transient in nature.

Table 5 : Number and Percent of Patients with Adverse Events for Combined Data from the Controlled Studies (AN094-001, AN094-003)
(Adverse events with a frequency of ≥ 1%)
Intent-to-Treat Population

	DIASTAT n= 101		Placebo n= 104	
	All n (%)	**Related* n (%)**	**All n (%)**	**Related* n (%)**
General	**12 (12)**	**7 (7)**	**14 (13)**	**9 (9)**
Abdominal Pain	2 (2)	1 (<1)	2 (2)	1 (<1)
Fever	0 (0)	0 (0)	4 (4)	2 (2)
Headache	5 (5)	2 (2)	4 (4)	3 (3)
Pain+	3 (3)	3 (3)	4 (4)	3 (3)
Cardiovascular	**2 (2)**	**2 (2)**	**1 (<1)**	**1 (<1)**
Vasodilatation	2 (2)	2 (2)	0 (0)	0 (0)
Digestive	**6 (6)**	**4 (4)**	**8 (8)**	**6 (6)**
Anorexia	1 (<1)	1 (<1)	2 (2)	2 (2)
Diarrhea	4 (4)	2 (2)	1 (<1)	0 (0)
Vomiting	1 (<1)	1 (<1)	2 (2)	2 (2)
Hemic and Lymphatic†	**2 (2)**	**0 (0)**	**3 (3)**	**1 (<1)**
Metabolic and Nutritional†	**0 (0)**	**0 (0)**	**3 (3)**	**1 (<1)**
Nervous	**32 (32)**	**29 (29)**	**16 (15)**	**13 (13)**
Ataxia	3 (3)	1 (<1)	1 (<1)	1 (<1)
Convulsion	1 (<1)	1 (<1)	3 (3)	0 (0)
Dizziness	3 (3)	3 (3)	2 (2)	2 (2)
Euphoria	3 (3)	3 (3)	0 (0)	0 (0)
Incoordination	3 (3)	3 (3)	0 (0)	0 (0)
Nervousness	2 (2)	2 (2)	2 (2)	2 (2)
Somnolence	23 (23)	23 (23)	8 (8)	8 (8)
Other Body System	**1 (<1)**	**1 (<1)**	**2 (2)**	**2 (2)**
Other	1 (<1)	1 (<1)	2 (2)	2 (2)
Respiratory	**4 (4)**	**0 (0)**	**3 (3)**	**2 (2)**
Asthma	2 (2)	0 (0)	0 (0)	0 (0)
Rhinitis	2 (2)	0 (0)	2 (2)	2 (2)
Skin and Appendages	**5 (5)**	**3 (3)**	**1 (<1)**	**0 (0)**
Rash	3 (3)	2 (2)	0 (0)	0 (0)
Special Senses	**1 (<1)**	**1 (<1)**	**2 (2)**	**0 (0)**
Otitis Media	0 (0)	0 (0)	2 (2)	0 (0)

Table 5 : Number and Percent of Patients with Adverse Events for Combined Data from the Controlled Studies (AN094-001, AN094-003)
(Adverse events with a frequency of ≥ 1%)
Intent-to-Treat Population

	DIASTAT n= 101		Placebo n= 104	
	All n (%)	Related* n (%)	All n (%)	Related* n (%)
Urogenital†	**1 (<1)**	**0 (0)**	**2 (2)**	**0 (0)**

*Related means the adverse event was definitely, probably, or possibly related to the study drug.
+ Pain includes rectal symptoms such as rectal burning, discomfort, that code to "pain".
† Individual adverse events in these categories were less than 1% and therefore are not included in this table.

8.3 Less Common Clinical Trial Adverse Reactions

General: Asthenia, infection.

Cardiovascular: Palpitation.

Digestive: Dyspepsia, dysphagia, fecal incontinence, nausea.
Hemic and Lymphatic: Anemia, cyanosis, ecchymosis, lymphadenopathy, thromboplastin decreased.
Metabolic and Nutritional: Acidosis, dehydration, peripheral edema.

Nervous: Agitation, grand mal convulsion, hyperkinesia, increased salivation, stupor, tremor, twitching.

Respiratory: Cough increased, pneumonia, sinusitis.

Skin and Appendages: Pruritus, skin discoloration, sweating.

Special senses: Mydriasis.

Urogenital: Kidney failure, urinary incontinence, urinary tract infection.

Other AEs occurring less frequently (< 2%) and reported to be related to DIASTAT in clinical studies

General: Abdominal pain, accidental injury, accidental overdose, back pain, chills, fever, infection.

Cardiovascular: Hypotension, pallor, postural hypotension, vasodilation.

Digestive: Abnormal stools, anorexia, diarrhea, dysphagia, increased salivation, nausea, nausea and vomiting, rectal disorder, rectal hemorrhage, tenesmus, thirst, vomiting.

Hemic and Lymphatic: Prothrombin time increased.

Musculoskeletal: Myasthenia, back pain.

Nervous: Agitation, amnesia, confusion, convulsion, dysarthria, emotional lability, euphoria, hyperkinesia, hypokinesia, hypotonia, incoordination, increased salivation, insomnia, movement disorder, nervousness, speech disorder, stupor, thinking abnormal, tremor, twitching.

Respiratory: Cough increased, hypoventilation, hypoxia.

Skin and Appendages: Pruritis, rash.

Special senses: Abnormal vision, amblyopia, diplopia, mydriasis, taste perversion.

Urogenital: Urinary incontinence.

8.5 Post-Market Adverse Reactions

Injury, Poisoning and Procedural Complications

There have been reports of falls and fractures in benzodiazepine users due to adverse reactions such as sedation, dizziness and ataxia. The risk is increased in those taking concomitant sedatives (including alcoholic beverages), the elderly and debilitated patients (see 7 WARNINGS AND PRECAUTIONS, Falls and Fracture).

Dependence/Withdrawal

Development of physical dependence and withdrawal following discontinuation of therapy has been observed with benzodiazepines such as DIASTAT. Severe and life-threatening symptoms have been reported. (see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX, Addiction, Abuse and Misuse; 7 WARNINGS AND PRECAUTIONS, Dependence/Tolerance).

9 DRUG INTERACTIONS

9.1 Serious Drug Interactions

Serious Drug Interactions

Concomitant use of DIASTAT and opioids may result in profound sedation, respiratory depression, coma and death.

- Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are not possible.
- Limit dosages and durations to the minimum required.
- Follow patients for signs and symptoms of respiratory depression and sedation.

(see 7 WARNINGS AND PRECAUTIONS, General, Risks from Concomitant use with Opioids)

9.2 Drug Interactions Overview

Potential drug-drug interactions may occur when diazepam is given concurrently with agents:

- that affect CYP2C19 (e.g., cimetidine, quinidine, tranylcypromine, rifampicin, omeprazole, propranolol, and imipramine) activity.
- that affect CYP3A4 (e.g., ketoconazole, clotrimazole, carbamazepine, phenytoin, dexamethasone and phenobarbital, cyclosporine, paclitaxel, terfenadine, theophylline and warfarine) activity.
- psychotropic agents or other CNS depressants (ex: phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants.)
- alcohol
- Valproate

9.3 Drug-Behavioral Interactions

Potential drug-behavioral Interactions may occur when diazepam is given (see 7 WARNINGS AND PRECAUTIONS, Neurologic, Concomitant Use of Other CNS Depressants).

9.4 Drug-Drug Interactions

Effects of Other Drugs on the Metabolism of Diazepam

There have been no clinical studies or reports in the literature to evaluate the interaction of rectally administered diazepam with other drugs. As with all drugs, the potential for interaction by a variety of mechanisms is a possibility.

In vitro studies using human liver preparations suggest that CYP2C19 and CYP3A4 are the principal isozymes involved in the initial oxidative metabolism of diazepam. Therefore, potential drug-drug interactions may occur when diazepam is given concurrently with agents that affect CYP2C19 (e.g., cimetidine, quinidine, tranylcypromine, rifampicin) or CYP3A4 (e.g., ketoconazole, clotrimazole, carbamazepine, phenytoin, dexamethasone and phenobarbital) activity.

The clearance of diazepam and certain other benzodiazepines can be delayed in association

with cimetidine administration. The clinical significance of this is unclear.

If DIASTAT is to be combined with other psychotropic agents or other CNS depressants, careful consideration should be given to the pharmacology of the agents to be employed - particularly with known compounds which may potentiate the action of diazepam, such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants.

When diazepam is used simultaneously with alcohol or other CNS depressants, the potential for a synergistic CNS-depressant effect must be considered. Valproate is known to potentiate the CNS-depressant effects of diazepam; therefore, DIASTAT should be used with caution in patients expected to have high plasma concentrations of valproic acid.

Effects of Diazepam on the Metabolism of Other Drugs

There are no reports as to which isozymes could be inhibited or induced by diazepam. But, based on the fact that diazepam is a substrate for CYP2C19 and CYP3A4, it is possible that diazepam may interfere with the metabolism of drugs which are substrates for CYP2C19, (e.g., omeprazole, propranolol, and imipramine) and CYP3A4 (e.g., cyclosporine, paclitaxel, terfenadine, theophylline and warfarine) leading to a potential drug-drug interaction.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Animal and in vitro studies indicate that diazepam acts to suppress seizures through an allosteric influence on the α-aminobutyric acid (GABA) receptors of the A-type (GABAA). GABA acts at this receptor to open the membrane channel allowing chloride ions to flow into neurons. Entry of chloride ions causes an inhibitory potential that reduces the ability of neurons to depolarize to the threshold potential necessary to produce action potentials. Excessive depolarization of neurons is implicated in the generation and spread of seizures.

The benzodiazepine binding site is associated with the GABAA receptor. Diazepam binds to this site and enhances the actions of GABA by causing GABA to bind more tightly to the GABAA receptor, increasing the opening of the chloride channel and increasing the chloride ion influx into the neuron. At doses in the lower therapeutic range, diazepam decreases the spread of seizures from the active site or focus by increasing inhibition in the surrounding neurons. At high therapeutic doses, diazepam may suppress seizures originating at the active focus as well.

10.3 Pharmacokinetics

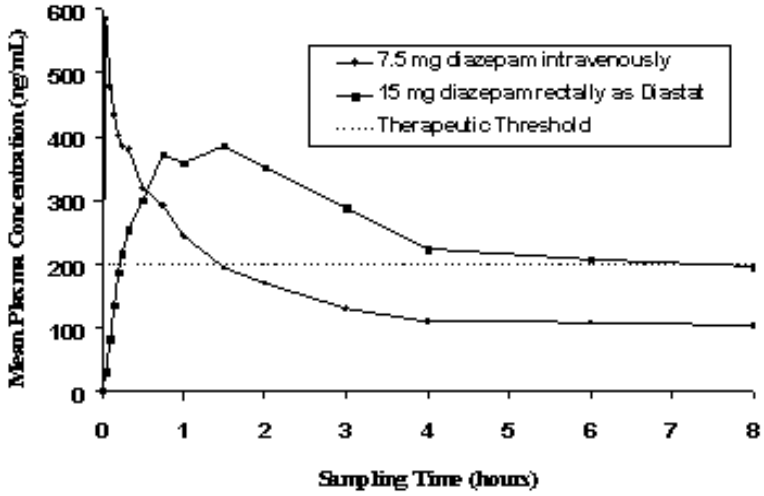
The absorption, distribution, metabolism and excretion of diazepam are well characterized.

Absorption:

Protein binding is high, ranging from 96.8%-98.6%. After diazepam gel administration, the absorption of diazepam from the rectum is rapid with an absolute bioavailability of 90.4% relative to an intravenous dose. The following figure shows diazepam plasma levels following rectal administration of 15 mg diazepam as diazepam gel and intravenous administration of 7.5 mg diazepam. Following rectal dosing, diazepam plasma levels reach 200 ng/mL within 15 minutes, reaching peak plasma concentrations within 1.5 hours. Intravenous dosing results in a quicker rise in plasma levels followed quickly by a fall as diazepam is sequestered in muscle and fat.

Distribution:

Following rectal dosing, absorptive and redistribution phases overlap, and therapeutic levels of diazepam are maintained for at least 4 hours without having the high peak concentrations of intravenous diazepam, which are often associated with adverse events. The time to maximum plasma concentration (T_{max}) following rectal administration is not different in children and adults given doses normalized to body weight.



Metabolism:

It has been reported in the literature that diazepam is extensively metabolized to one major active metabolite (desmethyldiazepam) and two minor active metabolites, 3-hydroxydiazepam (temazepam) and 3-hydroxy-N-diazepam (oxazepam) in plasma. At therapeutic doses, desmethyldiazepam is found in plasma at concentrations equivalent to those of diazepam while oxazepam and temazepam are not usually detectable. The metabolism of diazepam is primarily hepatic and involves demethylation (involving primarily CYP2C19 and CYP3A4) and

3-hydroxylation (involving primarily CYP3A4), followed by glucuronidation. The marked inter-individual variability in the clearance of diazepam reported in the literature is probably attributable to variability of CYP2C19 (which is known to exhibit genetic polymorphism; about 3-5% of Caucasians have little or no activity and are "poor metabolizers") and CYP3A4. No inhibition was demonstrated in the presence of inhibitors selective for CYP2A6, CYP2C9, CYP2D6, CYP2E1, or CYP1A2, indicating that these enzymes are not significantly involved in metabolism of diazepam.

The primary metabolite of diazepam following a single dose is desmethyldiazepam in both children and adults.

Elimination:

The elimination kinetics of diazepam are similar following rectal and intravenous administration.

Special Populations and Conditions:

- **Pediatrics:** Clinical studies have not been conducted to establish the efficacy and safety of DIASTAT in children under 2 years of age. Prolonged CNS depression has been observed in neonates treated with diazepam, apparently due to an inability to biotransform diazepam into inactive metabolites.
- **Geriatrics:** The effects of DIASTAT in patients over 60 years of age have not been well characterized. In elderly patients, DIASTAT should be used with caution due to an increase in half-life with a corresponding decrease in the clearance of free diazepam.
- **Hepatic Insufficiency:** Precautions in treating patients with impaired hepatic function should be observed because patients with severely impaired hepatic function may be unable to biotransform diazepam to inactive metabolites.
- **Renal Insufficiency:** Metabolites of diazepam are excreted by the kidney; to avoid their excess accumulation, caution should be exercised in the administration to patients with compromised kidney function.

11 STORAGE, STABILITY AND DISPOSAL

Store at controlled room temperature 15 - 30ºC (59 - 86ºF).

DIASTAT should be stored securely to avoid theft or misuse.

Keep out of sight and reach of children.

12 SPECIAL HANDLING INSTRUCTIONS

There are no special handling instructions for this product.

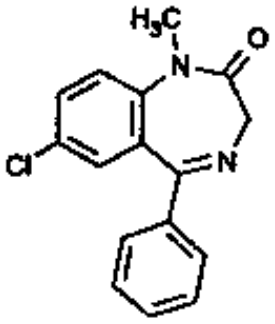
PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name:	Diazepam	
Chemical name:	7-chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one	
Molecular formula and molecular mass:	$C_{16}H_{13}ClN_2O$	284.75 g/mol

Structural formula:



Physicochemical properties:

Description:	Diazepam is a crystalline powder.
Solubility:	Freely soluble in chloroform, soluble in ethanol and propylene glycol, and practically insoluble in water.
pKa:	Diazepam has a pKa of 3.4.
Partition coefficient:	A partition coefficient of 382 (octanol : phosphate).
Melting range:	131-135ºC.

14 CLINICAL TRIALS

14.1 Clinical Trials by Indication

The Management of Selected, Refractory Patients with Epilepsy

The usefulness of DIASTAT (diazepam gel) as an adjunct in treatment of bouts of increase seizure activity has been established in 2 adequate and well-controlled clinical studies in children and adults. These studies confirmed the efficacy of rectal diazepam as treatment for acute seizures as established in numerous scientific reports.

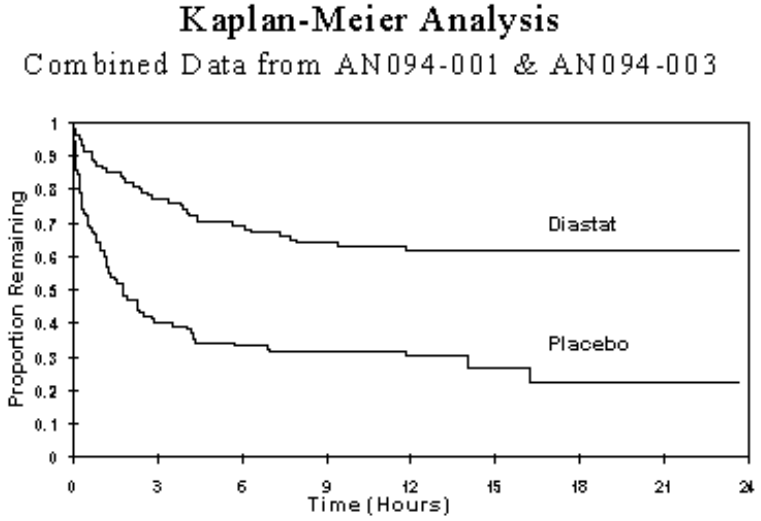
Table 6: Summary of Patient Demographics for Clinical Trials in The Management of Selected, Refractory Patients with Epilepsy

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
1	The first double-blind study compared sequential doses of DIASTAT and placebo. The first dose was given at the onset of the defined episode.	Children could be dosed again 4 hours after the first dose and were observed for 12 hours. Adults could be dosed again 4 and 12 hours after the first dose and were observed for 24 hours	91 patients	47 children 44 adults	N/A
2	A second double-blind study compared single doses of DIASTAT and placebo. The dose was given at the onset of the defined episode	Patients were observed for 12 hours.	114 patients	53 children 61 adults	N/A

Table 7: Results of Study in The Management of Selected, Refractory Patients with Epilepsy

Primary Endpoints	Associated value and statistical significance for Placebo or active control
DIASTAT significantly reduced seizure frequency ($p < 0.0001$) and increased the time to the next seizure ($p = 0.0002$).	In addition, 62% of patients treated with DIASTAT were seizure-free during the observation period compared to 20% of placebo patients. Overall, caregivers judged DIASTAT to be much more effective than placebo ($p < 0.0001$).
DIASTAT significantly reduced seizure counts ($p = 0.029$) and increased the time to the next seizure ($p=0.0072$).	In addition, 55% of patients treated with DIASTAT were seizure-free during the observation period compared to 34% of placebo patients. Overall, caregivers judged DIASTAT to be more effective than placebo ($p=0.018$). In addition, investigators also evaluated the effectiveness of DIASTAT and judged DIASTAT to be more effective than placebo ($p < 0.001$).

The following figure shows the proportion of patients remaining seizure-free following treatment of an episode with DIASTAT. This analysis of the combined data from both double-blind, placebo-controlled studies, confirms that the anti-seizure effect of DIASTAT is maintained throughout the observation period.



Long-term experience has been evaluated in 2 open-label studies following the double-blind studies. Patients in these studies were prescribed DIASTAT for treatment of bouts of increased seizure activity. Patients' episodes could be treated with DIASTAT no more frequently than

every 5 days and no more than 5 times per month. There was no evidence for development of tolerance to the effect of DIASTAT over time.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

Refer to 10.1 Mechanism of Action.

Studies in animals have provided information that is relevant to the pharmacology of diazepam in humans. Diazepam, unlike chlorpromazine and reserpine, has no demonstrable peripheral autonomic blocking action, nor does it produce extrapyramidal side effects; however, animals treated with diazepam do have a transient ataxia at higher doses. Diazepam was found to have transient cardiovascular depressor effects in dogs. Long-term experiments in rats revealed no disturbances of endocrine function. It is expected that rectal administration of diazepam will not alter the pharmacologic or toxic effects previously observed with other formulations of diazepam. No irritation was observed following repeated rectal administration of diazepam gel to rabbits.

Genotoxicity: The data currently available are inadequate to determine the mutagenic potential of diazepam.

Carcinogenicity: The carcinogenic potential of rectal diazepam has not been evaluated. In studies in which mice and rats were administered diazepam in the diet (orally) at a dose of 75 mg/kg/day (approximately 6 and 12 times, respectively, the maximum recommended human dose) for 80 and 104 weeks, respectively, an increased incidence of liver tumors was observed in males of both species.

Reproductive and Developmental Toxicology: Reproduction studies in rats showed a decrease in the number of pregnancies and surviving offspring at an oral dose of 100 mg/kg [approximately 100 times the highest diazepam gel treatment dose]. These effects may be secondary to prolonged sedation. Normal neonatal survival rates were observed at doses lower than 100 mg/kg.

PATIENT MEDICATION INFORMATION
READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

T/C DIASTAT®
Diazepam gel

Read this carefully before you start receiving **DIASTAT** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **DIASTAT**.

Serious Warnings and Precautions

Addiction, Abuse and Misuse

Even if you take DIASTAT exactly as you were told to, you are at risk for abuse, misuse, addiction, physical dependence and withdrawal. Abuse and misuse can result in an overdose or death, especially if you take DIASTAT with:

- opioids
- alcohol or
- illicit drugs

Your doctor should:

- talk to you about the risks of treatment with DIASTAT as well as other treatment (including non-drug) options
- assess your risk for these behaviours before prescribing DIASTAT
- monitor you while you are taking DIASTAT for the signs and symptoms of misuse and abuse. If you feel like you are craving DIASTAT, or not using it as directed, talk to your doctor right away.

Store DIASTAT in a secure place to avoid theft or misuse.

Withdrawal

If you suddenly stop taking DIASTAT, lower your dose too fast, or switch to another medication, you can experience severe or life-threatening withdrawal symptoms (see Other warnings you should know about)

- Always contact your doctor before stopping, or lowering your dose of DIASTAT or changing your medicine.

DIASTAT with Opioids

Taking DIASTAT with opioid medicines can cause:

- severe drowsiness
- decreased awareness

- breathing problems
- coma
- death

What is DIASTAT used for?

- DIASTAT is used in addition to other anti-epileptic medicines to help control bouts of increased seizure activity. It is given through the rectum in a pre-filed syringe.
- DIASTAT is not for use in children less then 2 years of age.
- If you are 65 years or older, talk to your doctor before starting DIASTAT. DIASTAT may not be an effective treatment for you and you may be more sensitive to experiencing side effects.

How does DIASTAT work?

DIASTAT works by increasing the actions of an amino acid in the brain called “gamma-aminobutyric acid" (GABA). By increasing the action of GABA in the brain, DIASTAT is able to help control seizures.

What are the ingredients in DIASTAT?

Medicinal ingredients: Diazepam

Non-medicinal ingredients: Benzoic Acid, Benzyl Alcohol (1.5%), Ethyl Alcohol (10%), Hydroxypropyl Methylcellulose, Propylene Glycol, Sodium Benzoate, and Water.

DIASTAT comes in the following dosage forms:

- Gel; 5 mg/mL, 10 mg/2mL, 15 mg/3mL

Do not use DIASTAT if:

- You are allergic to diazepam or any of the other ingredients in DIASTAT.
- You have a serious eye condition that may cause loss of visions (narrow angle glaucoma).

To help avoid side effects and ensure proper use, talk to your healthcare professional before you receive DIASTAT. Talk about any health conditions or problems you may have, including if you:

- have ever had a problem with:
  - substance use, including prescribed or illegal drugs, or
  - alcohol
- have ever had seizures or convulsions (violent uncontrollable shaking of the body with or without loss of consciousness)
- are pregnant or trying to become pregnant. DIASTAT should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

- are breast feeding.
- have kidney problems, liver problems, or respiratory problems (asthma, pneumonia).
- are 60 years of age or older.

Other warnings you should know about:

Withdrawal
If you suddenly stop your treatment, lower your dose too fast, or switch to another medication, you can experience withdrawal symptoms that can range from mild symptoms to severe or life threatening. Some of your withdrawal symptoms can last for months after you stop DIASTAT.

Your risk of going through withdrawal is higher if you are taking DIASTAT for a long time or at high doses. However, symptoms can still occur if you are taking DIASTAT as directed for a short period of time or slowly reducing the dose.
The symptoms of withdrawal often resemble the condition that you are being treated for. After stopping your treatment, it may be hard to tell if you are experiencing withdrawal or a return of your condition (relapse).

Tell your doctor **right away** if you experience any symptoms of withdrawal after changing or stopping your treatment.

Severe symptoms of withdrawal include:
- feeling like you cannot move or respond (catatonia)
- severe confusion, shivering, irregular heartrate and excessive sweating (delirium tremens)
- feeling depressed
- feeling disconnected from reality (dissociation)
- seeing or hearing things that are not there (hallucinations)
- overactive behavior and thoughts (mania)
- believing in things that are not true (psychosis)
- convulsions (seizures), including some that do not stop
- thoughts or actions of suicide

For other symptoms of withdrawal, see the **Serious side effects and what to do about them** table (below).

To reduce your chances of going through withdrawal:
- always contact your doctor before stopping or reducing your dose of DIASTAT or changing medications
- always follow your doctor's instructions on how to reduce your dose carefully and safely
- tell your doctor **right away** if you experience any unusual symptoms after changing or stopping your treatment

DIASTAT with Opioids
Taking DIASTAT with opioid medicines can cause severe drowsiness and breathing problems.

Tell your doctor if you:
- are taking opioid medicines
- are prescribed an opioid medicine after you start taking DIASTAT

Do NOT drive or operate heavy machinery or do tasks that require special attention until you know how taking an opioid medicine and DIASTAT affects you.

Falls and Fractures
Benzodiazepines like DIASTAT can cause you to feel sleepy, dizzy and affect your balance. This increases your risks of falling, which can cause fractures or other fall related-injuries, especially if you:

- take other sedatives
- consume alcohol
- are elderly or
- have a condition that causes weakness or frailty

Driving and Using Machines
Before you drive or do tasks that require special attention, wait until you know how DIASTAT affects you.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with DIASTAT:

Serious Drug Interactions
Taking DIASTAT and opioids may cause: • severe drowsiness • trouble breathing • coma • death

Diazepam, the active ingredient of DIASTAT, is known to interact with:

- Medicines to treat ulcers or gastroesophageal reflux disease (GERD) (such as cimetidine)
- Medicines to treat heart problems (such as quinidine, propranolol, warfarin)
- Medicines to treat depression (such as tranylcypromine, imipramine, monoamine oxidase inhibitors)
- Medicines to treat bacterial infections (such as rifampicin)
- Medicines to treat fungal infections (such as ketoconazole)
- Medicines to treat skin infections (such as clotrimazole)
- Medicines to treat seizures (such as carbamazepine, phenytoin, phenobarbital, valproate)
- Medicines to treat inflammatory conditions (such as dexamethasone)
- Immunosuppressants (used to weaken the immune system) (such as cyclosporine)
- Medicines used to treat cancer (such as paclitaxel)
- Antihistamines (drugs used to treat allergies) (such as terfenadine)
- Antipsychotics (drugs to stabilize thinking and behavior) (such as phenothiazines)
- Narcotics (used to treat pain)
- Alcohol

How DIASTAT is given:

- DIASTAT will be given to you by your caregiver or healthcare professional.
  - If you are a **caregiver**, give DIASTAT exactly as directed.

Usual dose

- Your dose will depend on your age and weight.
- Your doctor will monitor your health throughout your treatment. Your doctor may interrupt or lower your dose or stop your treatment.
  - Your doctor will slowly decrease your dose and will tell you when to stop taking the medicine.
    Always follow your doctor's instructions on how to lower your dose carefully and safely to avoid experiencing withdrawal symptoms.

Overdose:

Some of the signs of an overdose could be:

- sleepiness,
- confusion,
- unconsciousness, and
- slow reactions.

If you think you, or a person you are caring for, have ben given too much DIASTAT, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using DIASTAT?

These are not all the possible side effects you may have when taking DIASTAT. If you experience any side effects not listed here, tell your healthcare professional.

- Falls and fractures
- Sleepiness
- Dizziness
- Headache
- Pain
- Diarrhea
- Sense of well being
- Clumsiness
- Nervousness
- Movement disorder
- Weakness
- Hiccups
- Vomiting
- Nausea
- Shakiness
- Twitching
- Increased cough

- Changes in skin color
- Sweating

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
UNCOMMON			
Increased acid levels of the blood and body tissues		√	
Convulsion: seizure, spasms, shaking or fits		√	
Difficulty breathing		√	
Not enough oxygen being supplied to body tissues		√	
Kidney failure (severe kidney problems): confusion; itchiness or rashes; puffiness in your face and hands; swelling in your feet or ankles; urinating less or not at all; weight gain.		√	
Pneumonia (infection in the lungs): chest pain when you breath or cough, confusion, cough which may produce phlegm, fatigue, fever, sweating and shaking chills, nausea, vomiting or diarrhea, shortness of breath		√	
Stupor (Unconsciousness)		√	
UNKNOWN			
Overdose: extreme sleepiness, confusion, slurred speech, slow reflexes, slow shallow breathing, coma, loss of balance and coordination, uncontrolled rolling of the eyes, and low blood pressure.			√
Respiratory Depression: slow, shallow or weak breathing.			√
Withdrawal: **Severe symptoms include:** **Catatonia:** feeling like you cannot move or respond		√	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Delirium Tremens: severe confusion, shivering, irregular heartrate and excessive sweating **Feeling depressed** **Dissociation:** feeling disconnected from reality **Hallucinations:** seeing or hearing things that are not there **Mania:** overactive behaviour and thoughts **Psychosis:** believing in things that are not true **Convulsions:** (seizures – including some that do not stop): loss of consciousness with uncontrollable shaking **Thoughts or actions of suicide** **Other symptoms include:** stomach cramps; trouble remembering or concentrating; diarrhea; feeling uneasy or restless; severe anxiety or panic-attacks; headache; sensitivity to light, noise or physical contact; shaking; vomiting; trouble sleeping; feeling irritable; muscle pain or stiffness; a burning or prickling feeling in the hands, arms, legs or feet; sweating.			

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store at controlled room temperature (15 - 30ºC).

Keep out of reach and sight of children.

If you want more information about DIASTAT:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website (www.bauschhealth.ca), or by calling 1-800-361-4261.

This leaflet was prepared by Bausch Health, Canada Inc.

Bausch Health, Canada Inc.
2150 St-Elzear Blvd. West
Laval (Quebec) H7L 4A8
www.bauschhealth.ca

Last Revised: August 16, 2021