

# To all users of **MINIRIN MELT® OD Tablets** and their families

For the patients with Arginine Vasopressin Deficiency  
(AVP-D), formerly known as  
central diabetes insipidus (CDI)

**Supervised by Akira Takeshita, MD, PhD.  
Department of Endocrinology and Metabolism  
Toranomon Hospital, Tokyo, Japan**

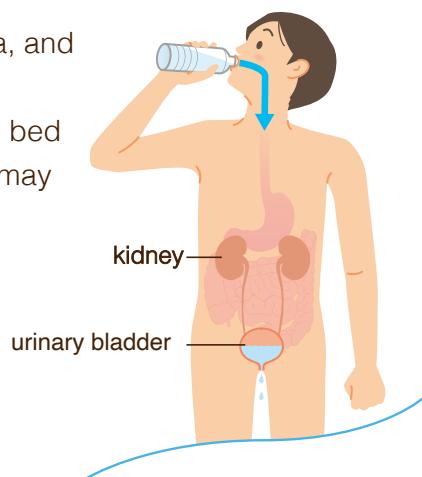
**English version translated by Akira Takeshita, MD, PhD.**

## What is diabetes insipidus?

The disease is characterized by "polyuria," which is the loss of a large amount of urine in a stream. In this situation, the patient wants to drink a lot of water because he or she produces a lot of urine; rather, the patient produce a lot of urine because he or she drinks a lot of water. Normally, an adult urinates 1-2 liters (1,000-2,000 mL) per day, but with enuresis, the "polyuria" can be at least more than 3 liters and more than 10 liters in those who urinate more. For example, if 10 liters of urine is produced in 24 hours, the amount of urine per hour is about 0.4 liters (400 mL). Since the bladder capacity of an adult is 400-500 mL, this means that the patient must go to the toilet almost every hour. This makes it difficult to go out during the day if you cannot use the restroom, and it is difficult to get a good night's sleep during the night if you have to get up several times to go to the restroom. Polyuria causes the body to lose water, making the patient very thirsty (thirst), and if the patient does not drink enough water to match the amount of urine (polydipsia), he or she will become dehydrated.

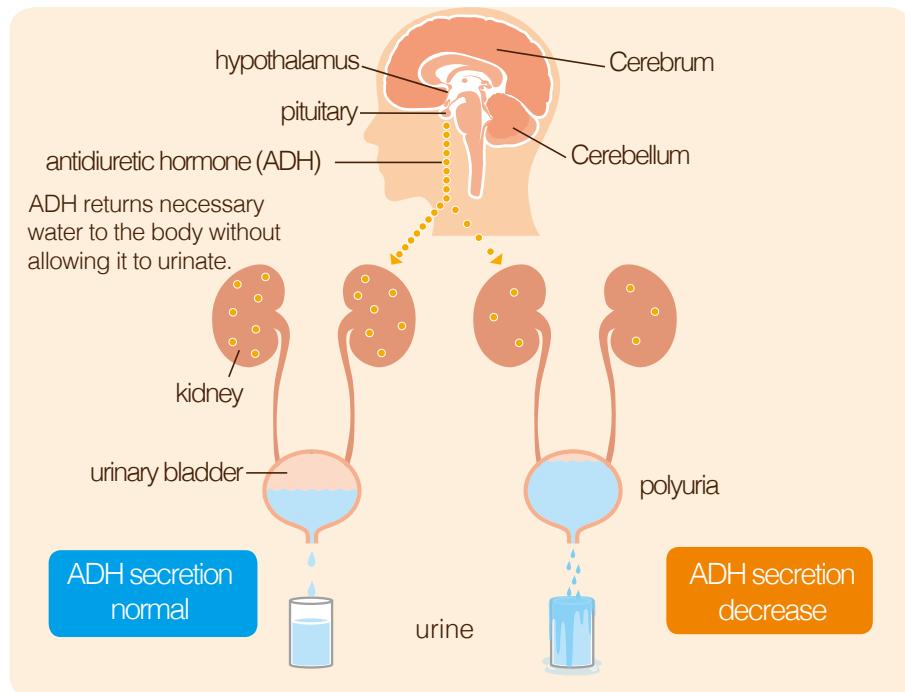
Thus, diabetes insipidus (DI) is characterized by thirst, polydipsia, and polyuria. In children, it may be mistaken for simple wetting of the bed or bed-wetting, and its detection may be delayed.

Drinking water is absorbed by the body. The water in the body is converted to urine by the kidneys, stored in the bladder, and excreted.



# ◆ Regulation of water balance by kidney◆

The function of the kidneys can be divided into two main categories: regulation of water and excretion of waste products such as ammonia that have accumulated in the body. In DI, water regulation fails, resulting in polyuria, but there is no problem with the excretion of waste products. The water in urine comes from the blood that flows through the kidneys. In a healthy person, the kidneys filter about 100 mL of blood per minute, i.e., 144 liters (equivalent to a small bath) over a 24-hour period, to make primitive urine, which is the source of urine. As the urine flows through the kidneys, 99% of the water in the primitive urine is returned to the blood vessels by "reabsorption," and only 1%, or 1-2 liters, of the water is actually made into urine. For this reabsorption, "antidiuretic hormone (ADH)" secreted by the pituitary gland is necessary.

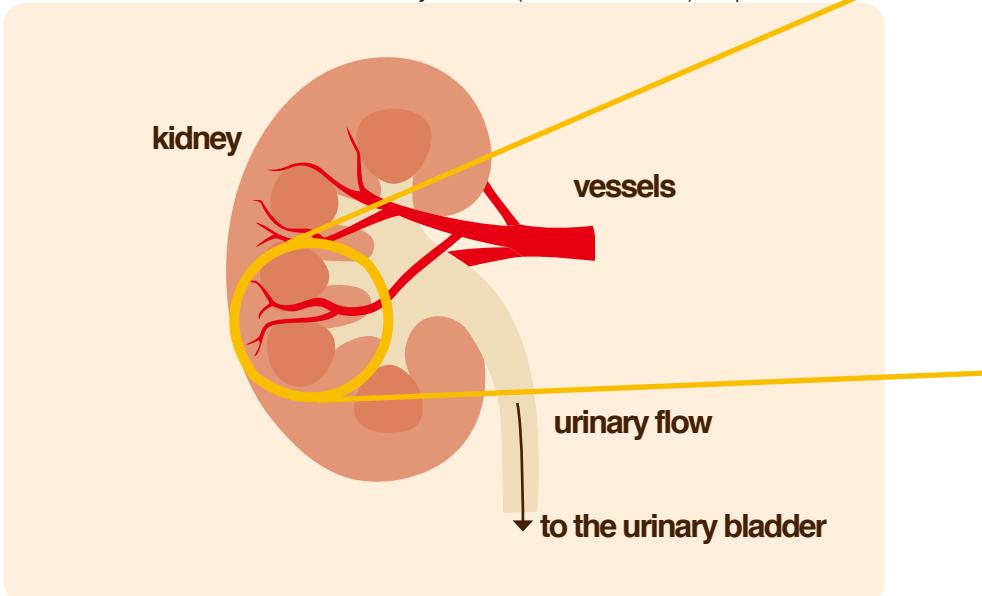


## 💧 What is antidiuretic hormone (ADH)? 💧

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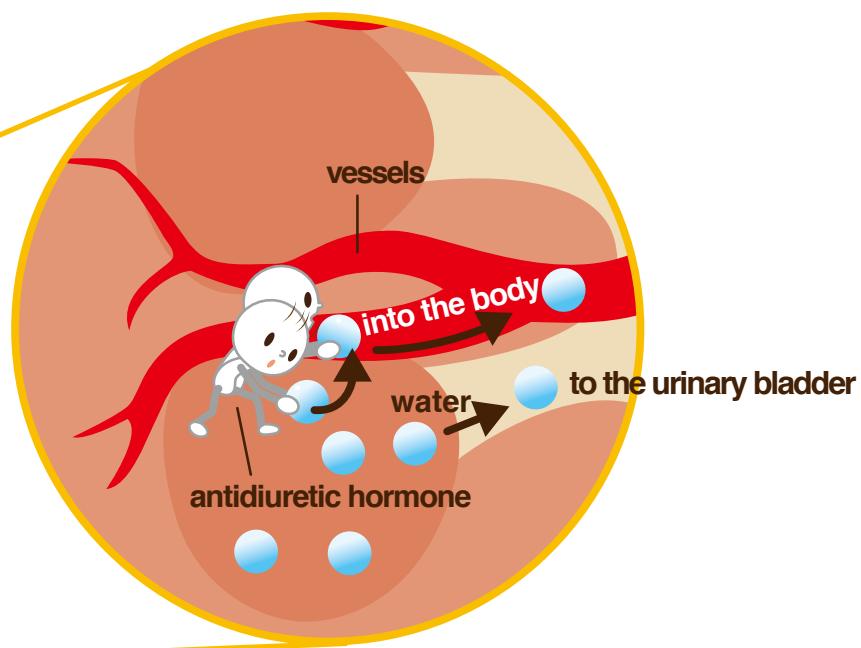
Various hormones are produced in the body to maintain the body's balance. One of these hormones is antidiuretic hormone, also called ADH, AVP, or vasopressin, which acts on the kidneys to regulate the body's water content. Antidiuretic hormone is produced in the hypothalamus of the brain, stored in the pituitary gland, and then secreted. Antidiuretic hormone is a hormone that "fights" (resists) increases of urine output (diuresis) and reduces urine output. For example, when a person sweats profusely in hot weather and does not drink enough water, the amount of urine is reduced, resulting in dark yellow urine (concentrated urine). This is because the pituitary gland secretes a lot of anti-diuretic hormone due to the lack of water in the body, resulting in less urine.

Conversely, if too much water accumulates in the body, such as by drinking a lot of water, the secretion of antidiuretic hormone is reduced and a lot of thin, watery urine (diluted urine) is produced.



## What is central diabetes insipidus (CDI)?

Diabetes insipidus (DI) can be classified into two types: Central DI (CDI) is caused by a lack of secretion of antidiuretic hormone (ADH) by the pituitary gland. The other is nephrogenic DI, which is caused by the unresponsiveness to ADH in kidneys. CDI can be caused by head trauma, hypothalamic or pituitary gland disease, or surgery, or it can be of unknown cause ("idiopathic"). CDI can be treated with "ADH" medications to control urine output.



Antidiuretic hormone (ADH) helps to return water flowing to the bladder back into the blood vessels.

For those with central DI, refraining from drinking water does not result in the production of more ADH. Do not be reluctant to drink water unless treated.

# The formulation of this drug and active ingredients

brand name	Minirin Melt® OD tablet 60 µg	Minirin Melt® OD tablet 120 µg	Minirin Melt® OD tablet 240 µg
generic name (active ingredients)	Desmopressin acetate aqueous agent		
content per tablet (as desmopressin)	60 µg	120 µg	240 µg
color of tablet	white		
size of tablet	diameter 12 mm, thickness 3 mm		
outline of tablet (top surface)			

OD tablet=Orally disintegrating tablet

1 µg = 1/1000 mg

Minirin Melt® OD tablet 60 µg



Minirin Melt® OD tablet 120 µg



Minirin Melt® OD tablet 240 µg



\* The perforation at the edge of the sheet is only on the right side of the "ear" at the top of the sheet.

The sheet containing the tablets is made of aluminum, paper, polyethylene, etc.

# How this drug works and intended use

The active ingredient in Minirin Melt® is desmopressin (DDAVP). Desmopressin is a substance that acts like antidiuretic hormone and improves polyuria by replacing antidiuretic hormone, which has the same effect and prevents the body from urinating the water it needs. As polyuria improves, thirst and polydipsia also improve.

## What you should know before using this medicine

- ▶ **Take it continuously.**

This medication is not a cure for the cause of antidiuretic hormone deficiency and should be used continuously as long as antidiuretic hormone deficiency continues.

- ▶ **This medicine should be placed under the tongue and taken without water.**

This is not a pill to be swallowed with water like ordinary tablets. When placed under the tongue, it dissolves quickly and should be taken without water. The medicine is tasteless and odorless.

- ▶ **Be careful not to drink too much water after starting Minirin Melt®.**

As a side effect of this drug, one should be aware of "water intoxication," which occurs when excess water accumulates in the body (see "Side effects and their countermeasures" section for details).

- ▶ **Consult your physician if you have any of the following.**

People who have had a rash after taking a drug before, people who are taking other drugs, pregnant/breastfeeding women, people who have a habit of drinking large amounts of water, people with impaired kidney or heart function (e.g., high blood pressure, heart failure, angina pectoris).



# How to use this medicine

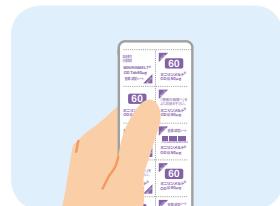
✓ Do not remove the medicine from the sheet until just before taking.

(This drug is altered by moisture and light.)

✓ This sheet is designed to make it difficult to remove the drug.

(The childproof construction prevents small children  
from opening the sheet without permission.)

1 Hold the sheet with the side that can read the letters facing you.



2 Fold back and forth along the perforations at the "ear" of the top of the sheet.

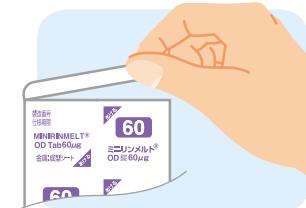
\* If the ear portion at the top of the sheet has already been detached, go to 4.



3 Cut off the "ear" from the right side.

\* The left side of the ear is not perforated to the edge of the sheet.

\* Take out the drug just before use.



4

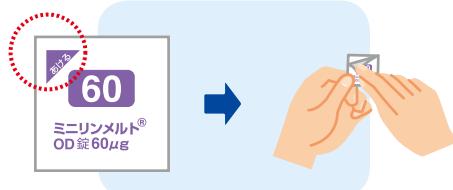
Separate one tablet from the perforation in the center of the sheet downward (arrow ①) and outward (arrow ②).

\* Sheet is not perforated at both ends.



5

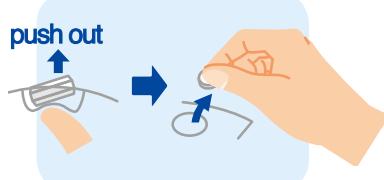
Remove the sticker from the corner of "あける (open)".



6

Without clawing, push out the center of the bulge with the tip of the finger to take out the tablet.

\* Do not try to force the tablet out.  
\* Do not touch the tablet with wet hands.  
\* Because the tablet is soft, it may chip or break when it is taken out. However, they should be taken together.



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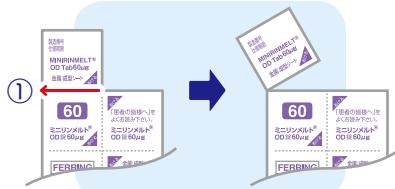
The taken-out tablet dissolves quickly when placed under the tongue.

\* Take the tablet without water.



8

If you continue taking out the tablet, detach the portion of one tablet toward the outside (arrow ①).



## 💧 Dosage and time to take this medicine 💧



### Start with a small amount and adjust the dosage

The effects of the drug vary from person to person. Therefore, it is necessary to start with a small amount of this medicine and determine the dosage that suits each individual.

First of all, the dosage is set with the goal of being able to sleep without waking up to use the restroom during sleep, so please use it as directed by your doctor.

After that, you will adjust the amount you take during the daytime and decide over time on the amount and timing of the dose that is right for you.

Do not increase or decrease the dose at your own discretion. Elderly patients and those with impaired kidney function often require smaller doses of medication and need to decide more carefully how much to take.



### Timing of medication is important

This drug is less likely to be absorbed with food. For this reason, it should not be taken within 30 minutes before or after a meal (especially just before a meal). Do not change the time of day when you take the drug, for example,

"Yesterday I took the drug before breakfast, and today I took it after breakfast. Since drinking large amounts of water may become a habit, weigh the patient once a day at the same time, especially at the beginning of the day (just wake up in the morning), to confirm that there is no change in the patient's weight.

Mc i 'WUb 'YUh'

30 min 30 min

You can eat.

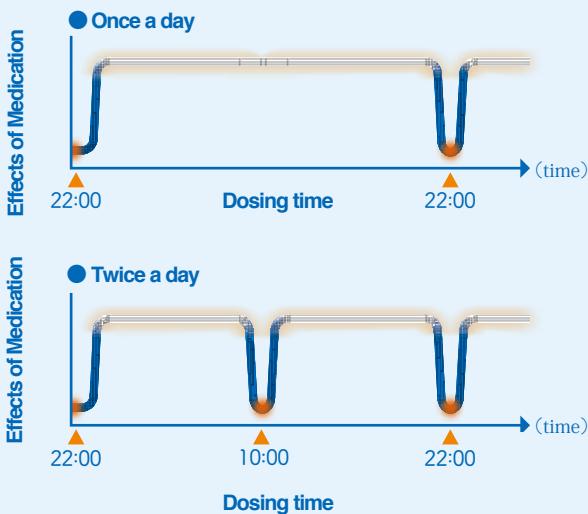
Taking Minirin Melt®

## Allow time for the effects to wear off

Once a day or so, allow time for the effects of the drug to wear off. Take it before bedtime, when it is less likely to affect your daily life. After the effect of the medication wears off and you confirm that you experience symptoms of polyuria (i.e., feeling as if there is a lot of urine in the bladder, going to the toilet earlier, and becoming thirsty), take the next dose of the medication. At first, consult with your doctor.

The purpose is to prevent water intoxication (read next page), a side effect caused by too much medication.

### Examples of Medication Specific times to be determined with your doctor.



## Side effects and their countermeasures

Drugs may cause undesirable effects other than the intended effect. The most important thing to keep in mind when using this drug is the accumulation of excess water in the body (water intoxication). Water intoxication is caused by excessive water retention in the body and blood thinning, resulting in a low sodium level in the blood (hyponatremia), when the amount of urine is reduced by the drug and too much water is consumed or when the drug is used in large quantities. Water intoxication can cause headache, loss of appetite, nausea, vomiting, dizziness, bloating, swelling, and in severe cases, coma and convulsions.



If you experience any unusual symptoms, consult your doctor or pharmacist immediately.

## Countermeasures for Water intoxication

- ▶ While the drug is working (when urine output is decreasing), take extra precautions to avoid drinking too much water.
- ▶ Do not increase the amount of medication taken at your own discretion.
- ▶ Consult your doctor if an intravenous drip is administered or if you are experiencing an illness (e.g., fever) that would cause an increase in the amount of water you drink.
- ▶ Since excessive water intake will cause weight gain, weigh yourself at the same time (e.g., upon waking) every day if possible to ensure that there are no fluctuations. Any illness accompanied by weight gain may be water intoxication.
- ▶ If symptoms such as headache, loss of appetite, nausea, vomiting, dizziness, bloating, swelling, or cramps appear, stop using the product and contact your doctor immediately.

※ Newborns and infants are unable to take in water freely on their own, so fluid intake should be managed by referring to weight measurements.

※ It is difficult to adjust appropriate fluid intake for those who do not feel thirst (dry mouth) due to brain damage. Measure the patient's weight at the same time every day (e.g., upon waking up) to confirm that there are no large fluctuations. If there are large fluctuations, consult your doctor.

## Q & A

### Q1

Can I take this medicine with water without putting it under my tongue?



### Q2

Can I drink water or eat immediately after taking the drug?



Since this drug is mainly absorbed through the mucous membranes of the mouth, drinking water immediately after taking the drug may weaken its effect.

If possible, start drinking water or eating about 30 minutes after taking the drug. If thirsty, drink water before taking the medicine.

Refrain from drinking water for 30 min after taking Minirin Melt®



Taking Minirin Melt®

### Q3

Is there any problem if I take this medicine together with other medicines?



Take this medicine without water after taking other medicines first. Also, some medications may cause problems if taken together, so be sure to inform your doctor that you are taking this medication when you visit a different medical institution for other illnesses.

## **Q4**

I accidentally took too much medicine.  
Is there any problem?



The duration of action is longer than usual and water intoxication may occur. Water intoxication can cause side effects such as headache and nausea. If this happens, do not take the next dose until the effects of the medication wear off, and consult your doctor or pharmacist immediately.

## **Q5**

The medicine broke when I took it out.  
What should I do?



Please take the chipped or broken portion together with the medicine. The effect will not change.  
Since this medicine is soft, it may chip or break when it is taken out.

## **Q6**

Does the effect of the drug change from day to day?



The length of time the drug remains effective may vary from day to day, depending on the absorption of the drug and slightly on other factors. To be sure, check that there are no problems with the way the drug is taken (e.g., if it is taken with water).

This drug is an oral formulation (taken by mouth). There is also a nasal spray (a liquid spray in the nose) that contains the same active ingredient (desmopressin) as this medicine. The type of drug is selected based on ease of use and other factors. Please consult your doctor if necessary.



[医療機関名]

[主治医名]

[薬剤師名]



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2020年5月