

**PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE
PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986**

The medicine is dispensed with a physician's prescription only

Tivicay 5 mg dispersible tablets

Each tablet contains:

Tivicay 5 mg: **dolutegravir (as sodium) 5 mg**

For the list of inactive and allergenic ingredients in the preparation, see section 2 – “Important information regarding some of the ingredients of the medicine” and section 6 - “Further information”.

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the physician or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Tivicay is used as combination therapy (in combination with other anti-retroviral medicines) to treat **HIV (human immunodeficiency virus) infection** in adults, adolescents and children of at least 4 weeks of age or older, and who weigh at least 3 kg.

Tivicay does not cure HIV infection; it reduces the amount of virus in your body, and keeps it at a low level. As a result of this, it also increases the CD4 cell count in your blood. CD4 cells are a type of white blood cells that are important in helping your body fight infection.

Not everyone responds to treatment with Tivicay in the same way. Your physician will monitor the effectiveness of your treatment.

Tivicay is always used in combination with other anti-retroviral medicines (*combination therapy*). To control your HIV infection and to stop your illness from getting worse, you must keep taking all your medicines, unless your physician tells you to stop taking any.

Therapeutic group

Tivicay contains the active ingredient dolutegravir. This medicine belongs to a group of anti-retroviral medicines called *integrase inhibitors (INIs)*.

2. BEFORE USING THE MEDICINE

Do not use the medicine:

- if you (or your child, if he/she is the patient) are sensitive (allergic) to the active ingredient or any of the additional ingredients contained in the medicine (listed in section 6).
 - if you (or your child) are taking another medicine called fampridine (also known as dalfampridine - used to treat multiple sclerosis).
- If you think any of these apply to you (or your child), **tell your physician.**

Special warnings regarding use of the medicineLook out for important symptoms

Some people taking medicines for HIV infection develop other conditions, which can be serious. These include:

- symptoms of infections and inflammation
- joint pain, stiffness and bone problems

You need to know about important signs and symptoms to look out for while you (or your child, if he/she is the patient) are taking Tivicay.

→ **Read the information in Section 4 of this leaflet.**

Children

Do not give this medicine to children under 4 weeks of age, who weigh less than 3 kg, or with HIV infection that is resistant to other medicines similar to Tivicay. The use of Tivicay dispersible tablets in children under 4 weeks of age or weighing less than 3 kg has not yet been studied.

It is important to schedule **planned physician's appointments** for children (for more information, see "children and adolescents" in Section 3).

Drug interactions

If you (or your child) are taking, if you have recently taken, or if you (or your child) plan to take other medicines, including non-prescription medicines and nutritional supplements, inform the physician or pharmacist.

Do not take Tivicay with the following medicine:

- fampridine (also known as dalfampridine), used to treat **multiple sclerosis**.

Some medicines can affect how Tivicay works, or make it more likely that you will have side effects. Tivicay can also affect how some other medicines work.

Tell your physician if you (or your child) are taking any of the medicines *on the following list*.

- metformin, to treat **diabetes**.
- medicines called **antacids**, to treat **indigestion and heartburn**. **Do not take an antacid** during the 6 hours before you take Tivicay, or for at least 2 hours after you take it (*See also Section 3*).
- calcium supplements, iron supplements and multivitamins. **Do not take a calcium supplement, iron supplement or multivitamin** during the 6 hours before you take Tivicay, or for at least 2 hours after you take it (*see also*

Section 3).

- etravirine, efavirenz, fosamprenavir/ritonavir, nevirapine or tipranavir/ritonavir, to treat **HIV infection**.
 - rifampicin, to treat tuberculosis (TB) and other **bacterial infections**.
 - phenytoin and phenobarbital, to treat **epilepsy**.
 - oxcarbazepine and carbamazepine, to treat **epilepsy** or **bipolar disorder**.
 - **St. John's wort** (*Hypericum perforatum*), an herbal remedy to treat **depression**.
- **Tell your physician** if you (or your child) are taking any of these medicines. Your physician may decide to adjust the dosage of the medicinal treatment or to perform extra tests.

Pregnancy, breastfeeding and fertility

If you are pregnant, think you may be pregnant, or if you are planning a pregnancy:

→ **Talk to your physician** about the risks and benefits of taking Tivicay.

Taking Tivicay at the time of becoming pregnant or during the first 6 weeks of pregnancy, may increase the risk of a type of birth defect, called neural tube defect, such as spina bifida (malformed spinal cord).

If you could get pregnant while taking Tivicay:

→ **Talk to your physician** and discuss whether there is a need for contraception, such as a condom or pills.

Tell the physician immediately if you become pregnant or are planning to become pregnant. Your physician will review your treatment. Do not stop taking Tivicay without consulting your physician, as this may harm you and your unborn baby.

Breastfeeding

Breastfeeding is **not recommended** in women living with HIV because HIV infection can be passed on to the baby in breast milk.

A small amount of the ingredients in Tivicay can pass into your breast milk.

If you are breastfeeding, or thinking about breastfeeding, **you should discuss it with your physician as soon as possible**.

Driving and using machinery

→ **Tivicay can make you dizzy and have other side effects that make you less alert.**

→ **Do not drive or operate machinery** unless you are sure you are not affected.

Important information regarding some of the ingredients of the medicine Tivicay contains less than 1 mmol (23 mg) sodium per tablet; that is to say is essentially 'sodium-free'.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the physician's instructions. Check

with the physician or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

The dosage and treatment regimen will be determined by the physician only.

The recommended dosage is generally:

Adults

- The usual adult dose is 30 mg (six 5 mg dispersible tablets), **once a day**.
- If you are taking **certain other medicines**, the dose is 30 mg (six 5 mg dispersible tablets), **twice a day**.
- **For treatment of HIV that is resistant** to other medicines similar to Tivicay, the usual dose is 30 mg (six 5 mg dispersible tablets), **twice a day**.

Your physician will decide on the correct dose for you.

Children and adolescents

- **Children's dose** should to be adjusted as they get older or gain weight.
→ It is important therefore to schedule for children **planned physician's appointments**.
- Children and adolescents weighing at least 20 kg can take the adult dose of 30 mg once a day or 15 mg twice daily. The physician will decide how Tivicay should be taken.
- For children aged at least 4 weeks and weighing between 3 and 20 kg: the physician will decide on the correct dose of Tivicay, depending on the weight and age of your child.
- If children are swallowing a whole tablet with water, to reduce the risk of choking, **it is important to swallow each tablet separately**.
- Tivicay should **not** be used in children and adolescents with **HIV infection that is resistant** to other medicines similar to Tivicay.

Do not exceed the recommended dose.

How to take the dispersible tablets

- The dispersible tablets can be dispersed in drinking water or swallowed whole with drinking water.

When dispersed, the amount of water needed will depend on the number of tablets prescribed. The tablet(s) should be fully dispersed before swallowing.

See **separate instructions for use** regarding how to disperse and administer the tablets using a dosing cup and oral syringe provided in this pack.

- **Do not** chew, halve or crush the tablet.
- Tivicay can be taken **with or without food**. When Tivicay is taken twice a day, the physician may advise you to take it with food.

Tivicay is also available as **film-coated tablets**. Film-coated tablets and dispersible tablets are not the same; therefore, **you must not switch** between the film-coated and dispersible tablets without first consulting the physician.

Antacid medicines

Antacids, to treat **indigestion and heartburn**, can stop Tivicay being absorbed

into your body and make it less effective. **Do not take an antacid** during the 6 hours before you take Tivicay, or for at least 2 hours after you take it. Other acid-lowering medicines like ranitidine and omeprazole can be taken at the same time as Tivicay.

→ Talk to your physician for further advice on taking acid-lowering medicines with Tivicay.

Calcium supplements, iron supplements or multivitamins

Calcium supplements, iron supplements, or multivitamins can stop Tivicay being absorbed into your body and make it less effective.

Do not take a calcium supplement, iron supplement or multivitamins during the 6 hours before you take Tivicay, or for at least 2 hours after you take it.

→ Talk to your physician for further advice on taking calcium supplements, iron supplements or multivitamins with Tivicay.

If you accidentally took a higher dosage

If you (or your child) accidentally took too many tablets of Tivicay, **contact a physician or pharmacist for advice**. If possible, show them the Tivicay pack.

If a child has accidentally swallowed the medicine, refer immediately to a physician or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forget to take the medicine

If you (or if your child) miss a dose, take it as soon as you remember. But if your next dose is due within 4 hours, skip the dose you missed and take the next one at the usual time. Then continue the treatment as usual.

Do not take a double dose to make up for a missed dose.

Do not stop taking Tivicay without consulting the physician

Adhere to the treatment regimen as recommended by the physician. Even if there is an improvement in your health, do not stop treatment with the medicine without consulting a physician.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the physician or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Tivicay may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Allergic reactions

These are uncommon in people taking Tivicay. Signs include:

- skin rash
- fever

- lack of energy (*fatigue*)
- swelling, sometimes of the mouth or face (*angioedema*), causing difficulty in breathing
- muscle or joint aches

→ **See a physician immediately.** Your physician may decide to carry out tests on your liver, kidneys or blood, and may tell you to stop taking Tivicay.

Very common side effects

These may affect **more than 1 in 10 people**:

- headache
- diarrhea
- nausea.

Common side effects

These may affect **up to 1 in 10 people**:

- rash
- itching
- vomiting
- abdominal pain
- abdominal discomfort
- weight gain
- insomnia
- dizziness
- abnormal dreams
- depression (feelings of deep sadness and unworthiness)
- anxiety
- lack of energy (*fatigue*)
- wind (*flatulence*)
- increased level of liver enzymes
- increased level of enzymes produced in the muscles (*creatine phosphokinase*).

Uncommon side effects

These may affect **up to 1 in 100 people**:

- inflammation of the liver (*hepatitis*)
- suicide attempt*
- suicidal thoughts*
- panic attack
- joint pain
- muscle pain

*Particularly in patients who have had depression or mental health problems before

Rare side effects

These may affect **up to 1 in 1,000 people**:

- liver failure (signs may include yellowing of the skin and the whites of the

- eyes or unusually dark urine)
 - increase in bilirubin level in the blood (a liver function test)
 - suicide (particularly in patients who have had depression or mental health problems before)
- **Tell your physician immediately** if you experience any mental health problems (see also other mental health problems above).

Symptoms of infection and inflammation

People with advanced HIV infection (AIDS) have a weak immune system, and are more likely to develop serious infections (*opportunistic infections*). Such infections may have been “silent” and not detected by the weak immune system before treatment was started. After starting treatment, the immune system becomes stronger, and may attack the infections, which can cause symptoms of infection or inflammation. Symptoms usually include **fever**, plus some of the following:

- headache
- stomach ache
- breathing difficulties

In rare cases, as the immune system becomes stronger, it can also attack healthy body tissue (*autoimmune disorders*). The symptoms of autoimmune disorders may develop many months after you start taking medicine to treat your HIV infection. Symptoms may include:

- palpitations (rapid or irregular heartbeat) or tremor
- hyperactivity (restlessness and excessive movement)
- weakness beginning in the hands and feet and moving up towards the trunk of the body.

If you (or your child) get any symptoms of infection and inflammation or if you notice any of the symptoms above:

→ **Tell your physician immediately.** Do not take other medicines for the infection without consulting your physician.

Joint pain, stiffness and bone problems

Some people taking combination therapy for HIV develop a condition called *osteonecrosis*. With this condition, parts of the bone tissue die because of reduced blood supply to the bone. People may be more likely to get this condition:

- if they have been taking combination therapy for a long time
- if they are also taking anti-inflammatory medicines called corticosteroids
- if they drink alcohol
- if their immune system is very weak
- if they are overweight.

Signs of osteonecrosis include:

- stiffness in the joints
- aches and pains in the joints (especially in the hip, knee or shoulder)

- difficulty moving.

If you notice any of these symptoms:

→ **Tell your physician.**

Weight, blood lipid and blood glucose effect

During HIV therapy, there may be an increase in weight and in levels of blood lipids and glucose. These effects are partly linked to restored health and lifestyle, and sometimes to the HIV medicines themselves. Your physician will test for these changes.

If a side effect occurs, if one of the side effects worsens, or if you are suffering from a side effect not mentioned in the leaflet, consult the physician.

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:

<https://sideeffects.health.gov.il>

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the physician.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- Store below 30°C. Store in the original package to protect from moisture. Keep the bottle tightly closed. Do not remove the desiccant. Do not swallow the desiccant.

Do not dispose of medicines via the waste water or household waste. Consult a pharmacist as to how to dispose of medicines that are not being used. These measures will help protect the environment.

6. FURTHER INFORMATION

- In addition to the active ingredient, the medicine also contains - Silicified Microcrystalline Cellulose, Mannitol, Crospovidone (Type B), Microcrystalline Cellulose, Calcium sulfate dihydrate, Povidone K29/32, Sodium Starch Glycolate (Type A), Sodium Stearyl Fumarate, Sucralose, Strawberry Cream Flavour Permaseal PHS-132963, Hypromellose, Titanium dioxide (E171), Macrogol.
- What the medicine looks like and the contents of the pack:
Tivicay 5 mg dispersible tablets are white, round, biconvex and marked with “SV H7S” on one side and “5” on the other side. The bottle contains a desiccant. Keep the desiccant in the bottle after opening; do not remove it.

The dispersible tablets are provided in bottles containing 60 tablets. In addition, the package of the preparation contains a dosing cup and oral syringe.

- The bottle is closed with a child-resistant cap.
 - Opening instructions: To remove the cap, press down while turning left (counterclockwise).
 - Closing instructions: Place the cap on the open side of the bottle and turn right (clockwise) until it is fully closed.
- Registration holder: GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach Tikva.
- Manufacturer: ViiV Healthcare UK Ltd., Brentford, UK.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 174-13-37177

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Tiv DT PT v2A

Step by step instructions for use

Read these instructions for use before giving a dose of the medicine.

Follow the steps, using clean drinking water to prepare and give a dose to an infant or a child who cannot swallow the tablets.

Important information

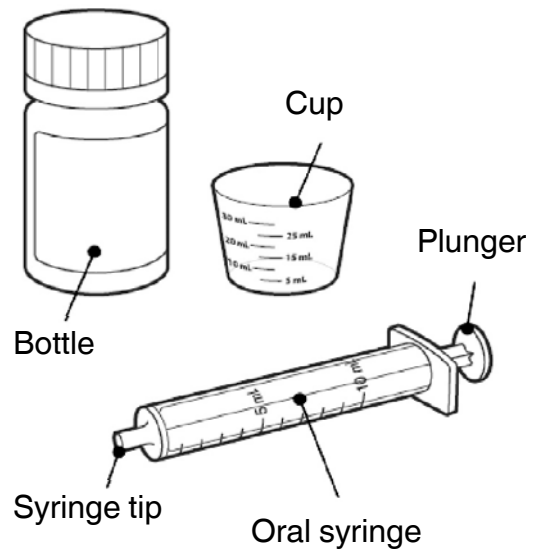
Always give this preparation exactly as instructed by the physician. Check with the physician or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

Do not chew, halve, or crush the tablet.

If you forget to give a dose, give it as soon as you remember. But if your next dose is due within 4 hours, skip the dose you missed and take the next one at the usual time. Then, continue your treatment as before. Do not give 2 doses at the same time or give more than prescribed by the physician.

If you gave an overdose, get emergency medical help right away.

If your child is able and prefers to swallow the tablets, then you may skip the following steps.



The pack contains:

- A bottle containing 60 tablets
- Dosing kit:
 - **Cup:** use this to prepare and give the medicine **to the child.**
 - **Oral Syringe:** use this to give the medicine **to an infant.**

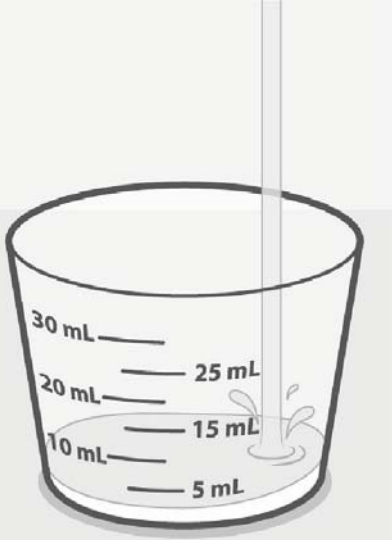
You will also need:

- Clean drinking water.

Getting ready

1. Pour water

Water Volume Guide						
Number of tablets	1	2	3	4	5	6
Volume of water	5 mL			10 mL		

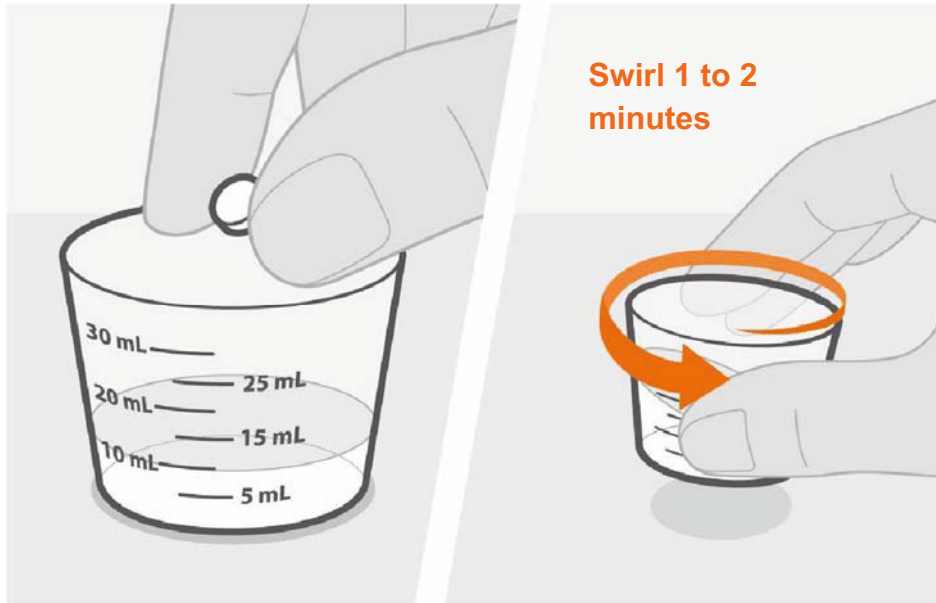


The illustration shows a cup with volume markings at 5 mL, 10 mL, 15 mL, 20 mL, 25 mL, and 30 mL. A stream of water is being poured into the cup from above, creating a splash.

- Pour clean drinking water into the cup.
The Water Volume Guide above shows the amount of water needed for the prescribed dose.
Use drinking water only.

Do not use food or any other beverage to prepare the dose.

2. Prepare the medicine



- Add the prescribed number of tablets to the water.
- Swirl the cup gently for one or two minutes to disperse the tablet(s). The medicine will become cloudy. Be careful not to spill any of the medicine.
- Check that the medicine is ready. If there are any lumps of tablet, swirl the cup until they are gone.

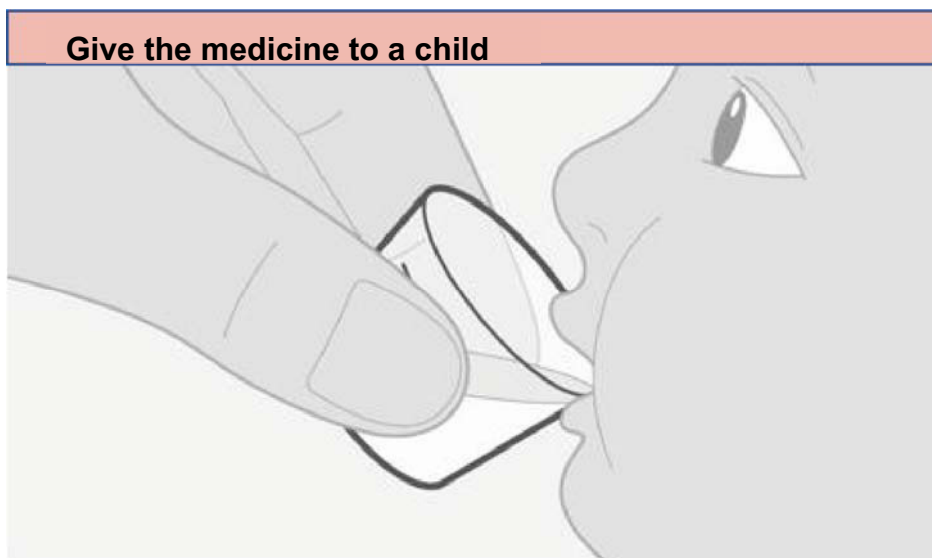
If you spill any medicine, clean up the spill.

Throw away the rest of the prepared medicine and make a new dose.

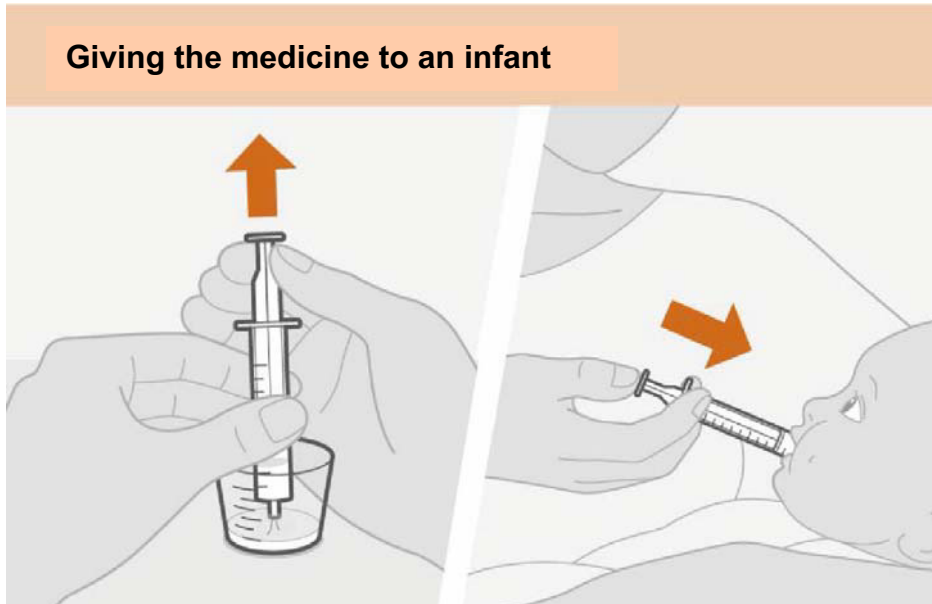
You must give the dose of medicine within 30 minutes of preparing the dose. If it has been more than 30 minutes, wash the dose away and prepare a new dose of medicine.

Giving the medicine

3. Give the medicine



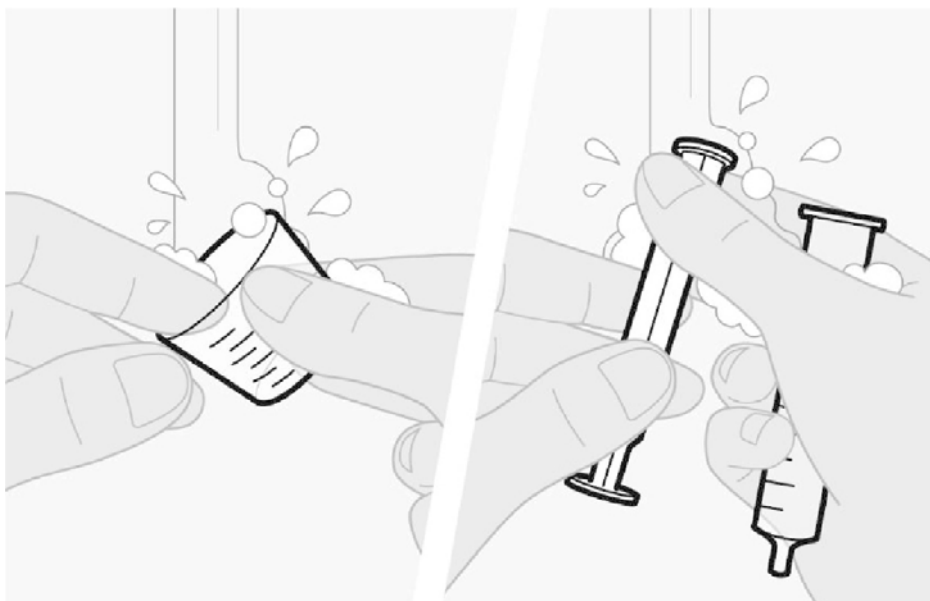
- Make sure that the child is upright. Give all the prepared medicine to the child.
- Add another 5 mL of drinking water to the cup, swirl and give it all to the child.
- Repeat if any medicine remains to make sure the child gets the full dose.



- Place the tip of the oral syringe into the prepared medicine and draw up all the medicine into the oral syringe by pulling up on the plunger.
- Place the tip of the oral syringe against the inside of the infant's cheek. Gently push down the plunger to give the dose slowly.
- Add another 5 mL of drinking water to the cup and swirl. Draw up the remaining medicine into the oral syringe and give it all to the infant.
- Repeat if any medicine remains to make sure the infant gets the full dose.
- Allow the infant time to swallow the medicine.

Cleaning

4. Cleaning the dosing items



- Wash the cup with water.
- Pull the plunger out of the oral syringe and wash the syringe parts separately in water. Allow parts to dry completely before reassembling and storing.
- All parts will need to be clean before preparing the next dose.

Storage instructions

Keep the tablets in the bottle. Keep the bottle tightly closed.

The bottle contains a desiccant canister which helps keep the tablets dry. **Do not** eat the desiccant. **Do not** remove the desiccant from the bottle.

Keep this medicine and all medicines in a safe place, out of reach and sight of children and/or infants.

Disposal instructions

When all the tablets in the bottle have been taken, throw away the bottle, cup and oral syringe.

You will get a new cup and oral syringe in your next pack.