Package leaflet: Information for the user

SPRYCEL 10 mg/mL powder for oral suspension
dasatinib

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What SPRYCEL is and what it is used for

SPRYCEL contains the active substance dasatinib. This medicine is used to treat chronic myeloid leukaemia (CML) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukaemia (ALL) in adolescents and children from at least one year of age. Leukaemia is a cancer of white blood cells. These white cells usually help the body to fight infection. In people with CML, white cells called granulocytes start growing out of control. SPRYCEL inhibits the growth of these leukaemic cells.

If you have any questions about how SPRYCEL works or why this medicine has been prescribed for you or your child, ask your doctor.

2. What you need to know before you take SPRYCEL

Do not take SPRYCEL
- if **you are allergic** to dasatinib or any of the other ingredients of this medicine (listed in section 6).

If you or your child could be allergic, ask your doctor for advice.

Warnings and precautions
Talk to your doctor or pharmacist before using SPRYCEL
- if you are taking **medicines to thin the blood** or prevent clots (see "Other medicines and SPRYCEL")
- if you have a liver or heart problem, or used to have one
- if you start **having difficulty breathing, chest pain, or a cough** when taking SPRYCEL: this may be a sign of fluid retention in the lungs or chest (which can be more common in patients aged 65 years and older), or due to changes in the blood vessels supplying the lungs
- if you have ever had or might now have a hepatitis B infection. This is because SPRYCEL could cause hepatitis B to become active again, which can be fatal in some cases. Patients will be carefully checked by their doctor for signs of this infection before treatment is started.
- if you experience bruising, bleeding, fever, fatigue and confusion when taking SPRYCEL, contact your doctor. This may be a sign of damage to blood vessels known as thrombotic microangiopathy (TMA).

Your doctor will regularly monitor your condition to check whether SPRYCEL is having the desired effect. You or your child will also have blood tests regularly while taking SPRYCEL.

Children and adolescents
Do not give this medicine to children younger than one year of age.
Bone growth and development will be closely monitored in children taking SPRYCEL.

Other medicines and SPRYCEL
Tell your doctor if you are taking, have recently taken or might take any other medicines.

SPRYCEL is mainly handled by the liver. Certain medicines may interfere with the effect of SPRYCEL when taken together.

These medicines are not to be used with SPRYCEL:
- ketoconazole, itraconazole - these are **antifungal medicines**
- erythromycin, clarithromycin, telithromycin - these are **antibiotics**
- ritonavir - this is an **antiviral medicine**
- phenytoin, carbamazepine, phenobarbital - these are treaments for **epilepsy**
- rifampicin - this is a treatment for **tuberculosis**
- famotidine, omeprazole - these are medicines that **block stomach acids**
- St. John's wort - a herbal preparation obtained without a prescription, used to treat **depression** and other conditions (also known as *Hypericum perforatum*)

Do not take medicines that neutralise stomach acids (**antacids** such as aluminium hydroxide or magnesium hydroxide) in the **2 hours before or 2 hours after taking SPRYCEL.**

Tell your doctor if you are taking **medicines to thin the blood** or prevent clots.

SPRYCEL with food and drink
Do not take SPRYCEL with grapefruit or grapefruit juice.

Pregnancy and breast-feeding
If you are pregnant or may be pregnant, **tell your doctor immediately. SPRYCEL is not to be used during pregnancy** unless clearly necessary. Your doctor will discuss with you the potential risk of taking SPRYCEL during pregnancy.
Both men and women taking SPRYCEL will be advised to use effective contraception during treatment.

If you are breast-feeding, tell your doctor. You should stop breast-feeding while you are taking SPRYCEL.

Driving and using machines
Take special care when driving or using machines in case you experience side effects such as dizziness and blurred vision.

SPRYCEL contains sucrose
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.
Contains 0.29 g of sucrose per mL of oral suspension. This should be taken into account in patients with diabetes mellitus. May be harmful to the teeth.

SPRYCEL contains sodium
This medicinal product contains 2.1 mg sodium (main component of cooking/table salt) per mL of SPRYCEL oral suspension. At the maximum daily dose of 16 mL oral suspension, this is equivalent to 1.7% of the WHO recommended maximum daily dietary intake of 2 g sodium for an adult.

SPRYCEL contains benzoic acid and sodium benzoate
SPRYCEL contains 0.25 mg benzoic acid in each mL of oral suspension and 0.25 mg sodium benzoate in each mL of oral suspension.
Benzoic acid/Benzoate salt may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old).

SPRYCEL contains benzyl alcohol
SPRYCEL contains 0.017 mg benzyl alcohol in each mL of oral suspension.
Benzyl alcohol may cause allergic reactions.

Use of SPRYCEL is not recommended during pregnancy. Ask your doctor or pharmacist for advice if you are pregnant or breast feeding. This is because large amounts of benzyl alcohol can build-up in your body and may cause side effects (called "metabolic acidosis").

Ask your doctor or pharmacist for advice if you have a liver or kidney disease. This is because large amounts of benzyl alcohol can build-up in your body and may cause side effects (called "metabolic acidosis").

SPRYCEL contains sulphur dioxide (E220)
May rarely cause severe hypersensitivity reactions and bronchospasm.

3. How to take SPRYCEL

SPRYCEL will only be prescribed by a doctor with experience in treating leukaemia. Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

SPRYCEL oral suspension is taken once daily. Your doctor will decide the right dose based on your weight. The starting dose of SPRYCEL is calculated by body weight as shown below:

Body Weight (kg)	Daily Dose, mL (mg)
5 to less than 10 kg	4 mL (40 mg)
10 to less than 20 kg	6 mL (60 mg)
20 to less than 30 kg	9 mL (90 mg)
30 to less than 45 kg	10.5 mL (105 mg)
at least 45 kg	12 mL (120 mg)

SPRYCEL is also available as tablets for use in adults and children from one year of age and weighing more than 10 kg. The powder for oral suspension should be used for patients weighing less than 10 kg and patients who cannot swallow tablets. A change in dose may occur when switching between formulations (i.e., tablets and powder for oral suspension), so you should not switch from one to the other. Your doctor will decide the right formulation and dose based on your weight, any side effects and response to treatment.

There is no dose recommendation for SPRYCEL with children under 1 year of age.

Depending on how you respond to the treatment, your doctor may suggest a higher or lower dose, or even stopping treatment briefly.

How to take SPRYCEL
Your pharmacist or qualified healthcare professional will constitute (mix to form a liquid) SPRYCEL powder for oral suspension to form SPRYCEL oral suspension before dispensing to you.

SPRYCEL should be taken at the same time every day. SPRYCEL can be taken with or without a meal. SPRYCEL oral suspension may be mixed with milk, yogurt, apple juice, or applesauce.

See the "Instructions for administration to the patient" at the end of the package leaflet for how to give a dose of SPRYCEL oral suspension.

Special handling instructions for SPRYCEL
Persons other than the patient should use gloves when handling SPRYCEL.
Pregnant or breast-feeding women should avoid exposure to SPRYCEL powder for oral suspension.

How long to take SPRYCEL
Take SPRYCEL daily until your doctor tells you to stop. Make sure you take SPRYCEL for as long as it is prescribed.

If you take more SPRYCEL than you should
If you have accidentally taken too much SPRYCEL, talk to your doctor **immediately.** You may require medical attention.

If you forget to take SPRYCEL
Do not take a double dose to make up for a forgotten dose. Take the next scheduled dose at the regular time.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following can all be signs of serious side effects:
- if you have chest pain, difficulty breathing, coughing and fainting
- if you experience **unexpected bleeding or bruising** without having an injury
- if you find blood in your vomit, stools or urine, or have black stools
- if you get **signs of infections** such as fever, severe chills
- if you get fever, sore mouth or throat, blistering or peeling of your skin and/or mucous membranes

Contact your doctor immediately if you notice any of the above.

Very common side effects (may affect more than 1 in 10 people)
- **Infections** (including bacterial, viral and fungal)
- **Heart and lungs:** shortness of breath
- **Digestive problems:** diarrhoea, feeling or being sick (nausea, vomiting)
- **Skin, hair, eye, general:** skin rash, fever, swelling around the face, hands and feet, headache, feeling tired or weak, bleeding
- **Pain:** pain in the muscles (during or after discontinuing treatment), tummy (abdominal) pain
- **Tests may show:** low blood platelet count, low white blood cells count (neutropaenia), anaemia, fluid around the lungs

Common side effects (may affect up to 1 in 10 people)
- **Infections:** pneumonia, herpes virus infection (including cytomegalovirus - CMV), upper respiratory tract infection, serious infection of the blood or tissues (including uncommon cases with fatal outcomes)
- **Heart and lungs:** palpitations, irregular heartbeat, congestive heart failure, weak heart muscle, high blood pressure, increased blood pressure in the lungs, cough
- **Digestive problems:** appetite disturbances, taste disturbance, bloated or distended tummy (abdomen), inflammation of the colon, constipation, heartburn, mouth ulceration, weight increase, weight decrease, gastritis
- **Skin, hair, eye, general:** skin tingling, itching, dry skin, acne, inflammation of the skin, persistent noise in ears, hair loss, excessive perspiration, visual disorder (including blurred

vision and disturbed vision), dry eye, bruise, depression, insomnia, flushing, dizziness, contusion (bruising), anorexia, somnolence, generalised oedema
- **Pain:** pain in joints, muscular weakness, chest pain, pain around hands and feet, chills, stiffness in muscles and joints, muscle spasm
- **Tests may show:** fluid around the heart, fluid in the lungs, arrhythmia, febrile neutropaenia, gastrointestinal bleeding, high uric acid levels in the blood

Uncommon side effects (may affect up to 1 in 100 people)
- **Heart and lungs:** heart attack (including fatal outcome), inflammation of the lining (fibrous sack) surrounding the heart, irregular heartbeat, chest pain due to lack of blood supply to the heart (angina), low blood pressure, narrowing of airway that may cause breathing difficulties, asthma, increased blood pressure in the arteries (blood vessels) of the lungs
- **Digestive problems:** inflammation of the pancreas, peptic ulcer, inflammation of the food pipe, swollen tummy (abdomen), tear in the skin of the anal canal, difficulty in swallowing, inflammation of the gallbladder, blockage of bile ducts, gastro-oesophageal reflux (a condition where acid and other stomach contents come back up into the throat)
- **Skin, hair, eye, general:** allergic reaction including tender, red lumps on the skin (erythema nodosum), anxiety, confusion, mood swings, lower sexual drive, fainting, tremor, inflammation of the eye which causes redness or pain, a skin disease characterized by tender, red, well-defined blotches with the sudden onset of fever and raised white blood cell count (neutrophilic dermatosis), loss of hearing, sensitivity to light, visual impairment, increased eye tearing, disturbance in skin colour, inflammation of fatty tissue under the skin, skin ulcer, blistering of the skin, nail disorder, hair disorder, hand-foot disorder, renal failure, urinary frequency, breast enlargement in men, menstrual disorder, general weakness and discomfort, low thyroid function, losing balance while walking, osteonecrosis (a disease of reduced blood flow to the bones, which can cause bone loss and bone death), arthritis, skin swelling anywhere in the body
- **Pain:** inflammation of vein which can cause redness, tenderness and swelling, inflammation of the tendon
- **Brain:** loss of memory
- **Tests may show:** abnormal blood test results and possibly impaired kidney function caused by the waste products of the dying tumour (tumour lysis syndrome), low levels of albumin in the blood, low levels of lymphocytes (a type of white blood cell) in the blood, high level of cholesterol in the blood, swollen lymph nodes, bleeding in the brain, irregularity of the electrical activity of the heart, enlarged heart, inflammation of the liver, protein in the urine, raised creatine phosphokinase (an enzyme mainly found in the heart, brain and skeletal muscles), raised troponin (an enzyme mainly found in the heart and skeletal muscles), raised gamma-glutamyltransferase (an enzyme mainly found in the liver), milky-appearing fluid around the lungs (chylothorax)

Rare side effects (may affect up to 1 in 1,000 people)
- **Heart and lungs:** enlargement of the right ventricle in the heart, inflammation of the heart muscle, collection of conditions resulting from blockage of blood supply to the heart muscle (acute coronary syndrome), cardiac arrest (stopping of blood flow from the heart), coronary (heart) artery disease, inflammation of the tissue covering the heart and lungs, blood clots, blood clots in the lungs
- **Digestive problems:** loss of vital nutrients such as protein from your digestive tract, bowel obstruction, anal fistula (an abnormal opening from the anus to the skin around the anus), impairment of kidney function, diabetes
- **Skin, hair, eye, general:** convulsion, inflammation of the optic nerve that may cause a complete or partial loss of vision, blue-purple mottling of the skin, abnormally high thyroid function, inflammation of the thyroid gland, ataxia (a condition associated with lack of muscular coordination), difficulty walking, miscarriage, inflammation of the skin blood vessels, skin fibrosis
- **Brain:** stroke, temporary episode of neurologic dysfunction caused by loss of blood flow, facial nerve paralysis, dementia
- **Immune system:** severe allergic reaction
- **Musculoskeletal and connective tissue:** delayed fusion of the rounded ends that form joints

(epiphyses); slower or delayed growth

Other side effects that have been reported with frequency not known (cannot be estimated from the available data)
- Inflammation of the lungs
- Bleeding in the stomach or bowels that can cause death
- Recurrence (reactivation) of hepatitis B infection when you have had hepatitis B in the past (a liver infection)
- A reaction with fever, blisters on the skin, and ulceration of the mucous membranes
- Disease of the kidneys with symptoms including oedema and abnormal laboratory test results such as protein in the urine and low protein level in the blood
- Damage to blood vessels known as thrombotic microangiopathy (TMA), including decreased red blood cell count, decreased platelets, and formation of blood clots

Your doctor will check for some of these effects during your treatment.

Reporting of side effects
If you get any side effects, **talk to your doctor or pharmacist.** This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store SPRYCEL

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle label and carton after EXP. The expiry date refers to the last day of that month.

Powder
Store below 25°C.

After constitution
Store in a refrigerator (2°C - 8°C). Do not freeze. Discard any unused suspension 60 days after constitution.

Constituted oral suspension mixed with milk, yogurt, apple juice, or applesauce may be stored at or below 25°C for up to 1 hour.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What SPRYCEL contains
- The active substance is dasatinib. One bottle of powder for oral suspension contains 990 mg of dasatinib (as monohydrate). After constitution, one bottle contains 99 mL of oral suspension. Each mL of oral suspension contains 10 mg of dasatinib (as monohydrate).
- The other ingredients are: sucrose, carmellose sodium, simethicone emulsion (consisting of simeticone, polyethylene glycol sorbitan tristearate, polyethoxylate stearate, glycerides, methylcellulose, xanthan gum, benzoic acid, sorbic acid, sulfuric acid), tartaric acid, trisodium citrate anhydrous, sodium benzoate (E211), silica hydrophobic colloidal, mixed berry flavour (containing: benzyl alcohol, sulphur dioxide) (see section 2 "What you need to know before you take SPRYCEL").

What SPRYCEL looks like and contents of the pack
SPRYCEL is supplied as a white to off-white powder for oral suspension which forms a white to yellow opaque suspension after constitution with water.

One 120-mL plastic bottle (with child-resistant closure) contains 33 g of powder for oral suspension.

Once constituted, the bottle contains 99 mL of oral suspension, of which 90 mL is intended for dosing and administration.

Each pack also contains a press-in-bottle adapter (PIBA) and a 12-mL oral dosing syringe in a sealed plastic bag.

Each carton contains one bottle.

Marketing Authorisation Holder
Bristol-Myers Squibb Pharma EEIG
Plaza 254
Blanchardstown Corporate Park 2
Dublin 15, D15 T867
Ireland

Manufacturer
Swords Laboratories Unlimited Company T/A
Lawrence Laboratories Unit 12 & 15, Distribution Centre
Shannon Industrial Estate
Shannon, Co. Clare, V14 DD39
Ireland

This leaflet was last revised in March 2022

Instructions for administration to the patient

These instructions show you how to give a dose of SPRYCEL oral suspension to the patient. Once constituted by your pharmacist or healthcare professional, the oral suspension should only be administered using the oral dosing syringe supplied with each pack. Your doctor will decide the right dose based on age and weight. Make sure that you read and understand these instructions before using the oral suspension.

What you need to know before using this medicine

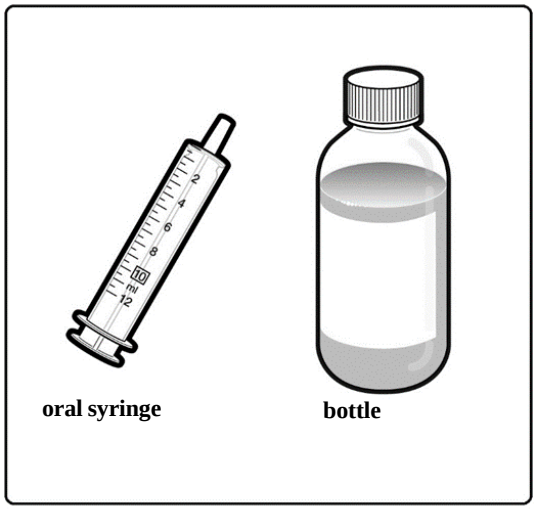
- Take SPRYCEL oral suspension on an empty or full stomach.
- Wash your hands before and after each use.
- Store the constituted oral suspension in a refrigerator (2°C - 8°C). Do not freeze.
- Review total prescribed dose and determine number of milliliters (mL) you will need.
- If the amount needed is greater than 11 mL, it must be split into 2 doses as shown below:

How to split a dose that is greater than 11 mL

Total prescribed dose (mL)	First dose (mL)	Second dose (mL)
12	6	6
13	7	6
14	7	7
15	8	7
16	8	8

Before you prepare a dose of SPRYCEL oral suspension for administration to the patient, get the following supplies ready:

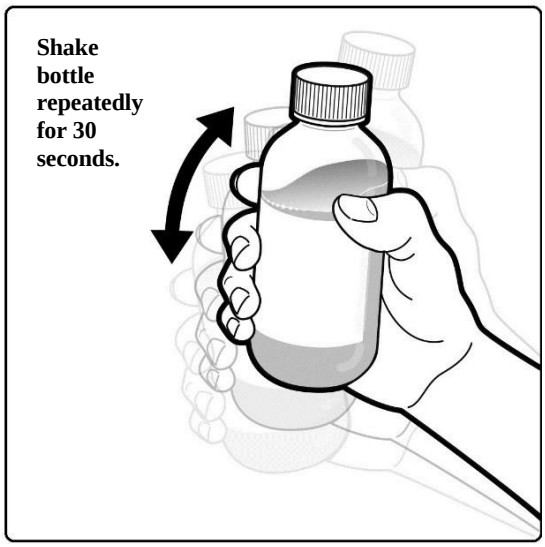
- Paper towel
- 1 SPRYCEL oral suspension bottle containing a white to yellow opaque suspension.
- 12-mL oral syringe provided with the bottle.
- A small container filled with water to use to rinse the syringe.



Carefully prepare the SPRYCEL oral suspension for administration, measure the dose, and fill the syringe, like this:

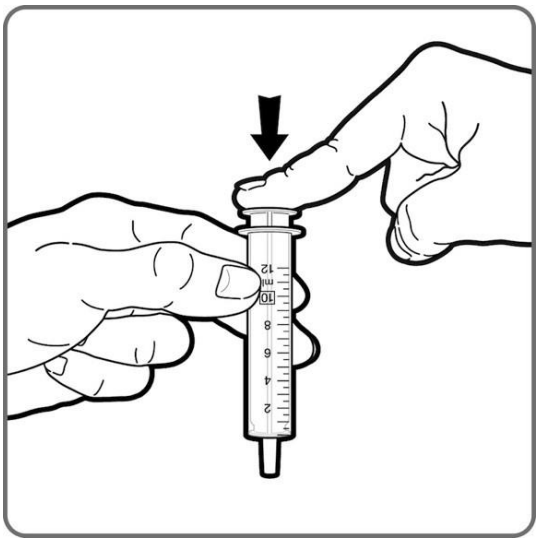
1. Mix the SPRYCEL oral suspension in the closed bottle by shaking for 30 seconds.

- Shake well before each use.

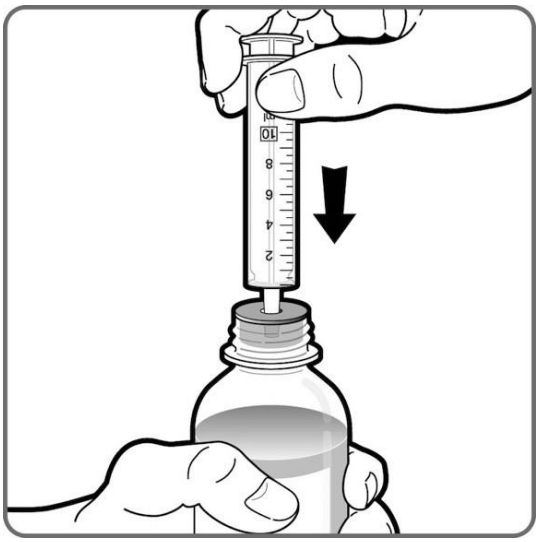


2. Remove the closure from the bottle. Make sure the adapter provided on the bottle for syringe placement is firmly pressed into the bottle.

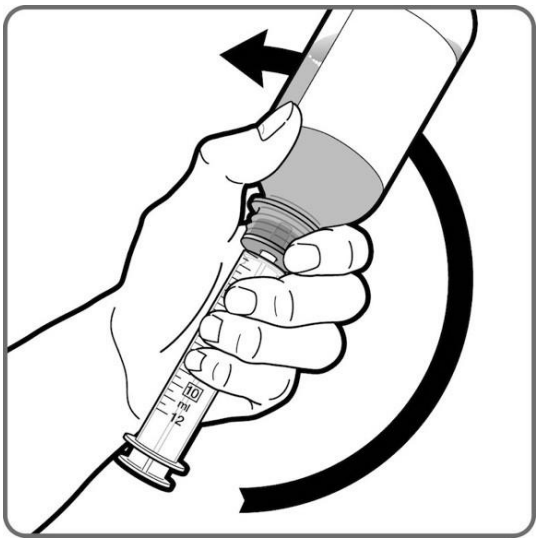
3. Look at the measurements on the side of the syringe so you can see how much to fill it before you begin. Note that the markings on the syringe are in mL. Find the marking that matches the dose that was prescribed by your doctor. Before each use, make sure the syringe plunger is pushed to the bottom of the syringe barrel.



4. With the bottle in an upright position, insert the tip of the syringe firmly into the bottle adapter.



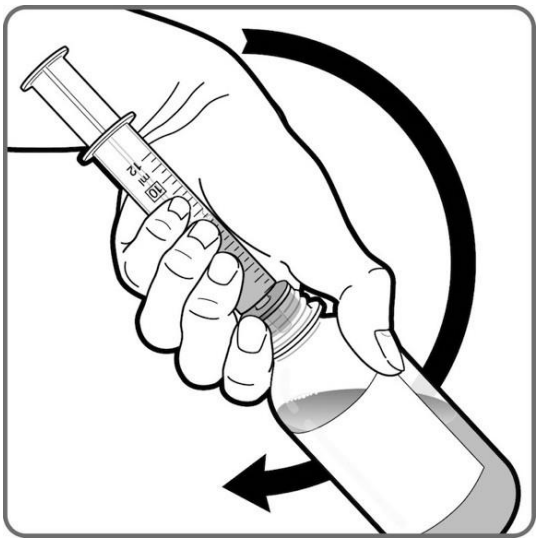
5. Holding the syringe tip firmly into the bottle, turn the bottle with the syringe upside down.



6. Slowly withdraw the amount of SPRYCEL oral suspension prescribed by pulling the syringe plunger until it reaches the marking of the dose prescribed.

- Hold plunger to prevent it from moving. There may be a vacuum pulling the plunger back into barrel.
- If unable to fill with one bottle, use the second bottle to complete the full prescribed dose. Make sure the second bottle is shaken before use.

7. Holding the syringe tip firmly in the bottle, turn the bottle with the syringe upright again.



8. Remove the syringe from the bottle being careful not to depress the plunger.

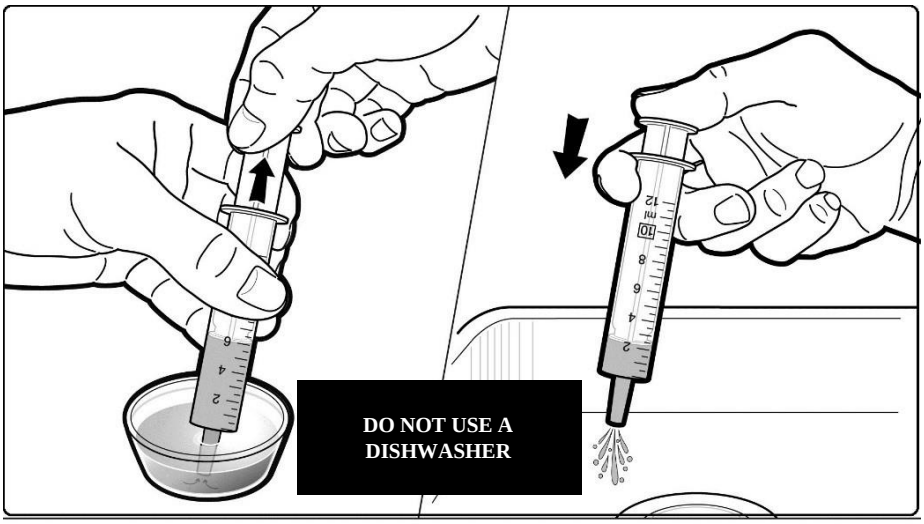
9. With the patient in an upright position, place the tip of the syringe into the mouth between the side of the mouth and the tongue. Slowly push the plunger down until all of the dose has been given.

- Check to make sure the patient has swallowed all of the dose.
- If a second dose is needed to complete the total prescribed dose, repeat steps 3 through 10.
- Put closure back on the bottle and close tightly. Store upright.

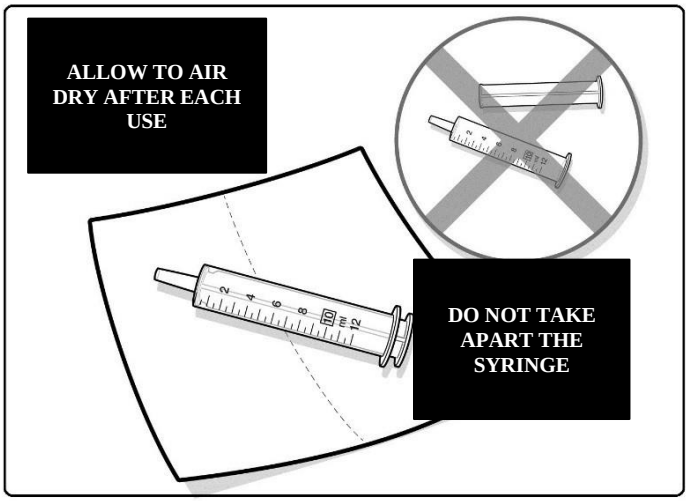
10. Wash the outside and the inside of the syringe with water and allow to air dry after each use to re-use for the next day.

- **Do not wash in a dishwasher.**

- **Do not take the syringe apart in order to avoid damaging it.**



11. Refer to the package leaflet (see section 5 ‘How to store SPRYCEL’) for instructions on discarding any unused medicine, syringe and bottle.



If you have any questions on how to prepare or give a dose of SPRYCEL oral suspension, talk to your doctor, pharmacist or nurse.

The following information is intended for healthcare professionals only:

Instructions for constitution of powder for oral suspension

SPRYCEL powder for oral suspension is to be constituted as follows:
Note: If you have to constitute more than one bottle, complete one bottle at a time.
Wash your hands before initiating the constitution. This procedure should be performed on a clean surface.

Step 1: Tap bottom of each bottle (containing 33 g SPRYCEL powder for oral suspension) gently to loosen the powder. Remove child-resistant closure and foil seal. Add 77.0 mL of purified water all at once to the bottle and close tightly with closure.
Step 2: Immediately invert the bottle and shake vigorously for no less than 60 seconds to obtain a uniform suspension. If there are still visible clumps, continue shaking until no clumps are visible.

Constitution in this way produces 90 mL (deliverable volume) of 10 mg/mL SPRYCEL oral suspension.
Step 3: Remove the closure, insert the press-in bottle adapter (PIBA) into the bottle neck, and close the bottle tightly with the child-resistant closure.
Step 4: Write the date of expiry of the constituted oral suspension on the bottle label (the date of expiry of the constituted oral suspension is 60 days from the date of constitution).
Step 5: Dispense the bottle with inserted PIBA, package leaflet, and oral dosing syringe in the original carton to the patient or caregiver. Remind the patient or caregiver to shake the bottle vigorously prior to each use.