Bundesinstitut
für Arzneimittel
und Medizinprodukte

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Irland

Antrag vom 01.03.2022 auf Erteilung einer Gestattung gemäß §§ 10 Absatz 1a und 11 Absatz 1c Arzneimittelgesetz -
Einfuhr und Inverkehrbringen von SPRYCEL 100 mg Filmtabletten

Arzneimittelbezeichnung	Zulassungsinhaber	Zulassungsnummer
SPRYCEL 100 mg Filmtabletten	Bristol-Myers Squibb Pharma EEIG	EU/1/06/363/011

Sehr geehrte Damen und Herren,

auf Ihren mit E-Mail vom 1. März 2022 gestellten Antrag ergeht folgender

BESCHEID:

1. Es wird im Einzelfall gestattet, dass das o. g. Arzneimittel mit der für den englischen Markt bestimmten und damit mit einer Kennzeichnung bzw. Packungsbeilage in einer anderen als der deutschen Sprache in den Verkehr gebracht wird.
2. Diese Gestattung ist befristet bis zum 15. Juli 2022.

Begründung:

Zu 1.
Nach §§ 10 Absatz 1a, 11 Absatz 1c AMG kann die zuständige Bundesoberbehörde im Fall eines drohenden oder bestehenden Versorgungsengpasses auf Antrag des Zulassungsinhabers im Einzelfall gestatten, dass das Arzneimittel befristet mit einer Kennzeichnung und Packungsbeilage in einer anderen als der deutschen Sprache in den Verkehr gebracht wird.
Diese Voraussetzungen sind vorliegend erfüllt.
Bei der von Ihnen mit dem Antrag vorgelegten und für den Markt in Großbritannien Kennzeichnung/Packungsbeilage handelt es sich um eine Kennzeichnung/Packungsbeilage in einer anderen als der deutschen Sprache.

SPRYCEL ist angezeigt für die Behandlung erwachsener Patienten mit:

- neu diagnostizierter Philadelphia-Chromosom-positiver (Ph+) chronischer myeloischer Leukämie (CML) in der chronischen Phase.
- CML in der chronischen oder akzelerierten Phase oder in der Blastenkrise mit Resistenz oder Intoleranz gegenüber einer vorherigen Behandlung einschließlich Imatinib.
- Ph+ akuter lymphatischer Leukämie (ALL) oder lymphatischer Blastenkrise der CML mit Resistenz oder Intoleranz gegenüber einer vorherigen Therapie.

SPRYCEL ist angezeigt für die Behandlung von Kindern und Jugendlichen mit:

- neu diagnostizierter Philadelphia-Chromosom-positiver (Ph+) chronischer myeloischer Leukämie (CML) in der chronischen Phase (Ph+ CML-CP) oder Ph+ CML-CP mit Resistenz oder Intoleranz gegenüber einer vorherigen Therapie einschließlich Imatinib.
- neu diagnostizierter Ph+ ALL in Kombination mit Chemotherapie.

Besonders die Versorgung von CML-Patienten ist aufgrund des bestehenden CML-Indikations-Patents durch Dasatinib-Generika nicht möglich. Somit stehen für CML-Patienten, die auf eine Versorgung mit Dasatinib angewiesen sind, keine Alternativen im deutschen Markt zur Verfügung. Bei der Erkrankung der CML handelt es sich um eine lebensbedrohliche bösartige onkologische Erkrankung des Knochenmarks.
Das Inverkehrbringen des Arzneimittels Sprycel 100 mg Filmtabletten wird als Maßnahme zur Gewährleistung der Versorgung daher befürwortet.

Zu 2.

Die Befristung stützt sich auf §§ 10 Absatz 1a, 11 Absatz 1c AMG und ist im genannten Zeitraum erforderlich, um den drohenden Versorgungsengpass mit dem o. g. Arzneimittel auf dem deutschen Markt abzuwenden. Nach derzeitigem Sachstand ist ab 16. Juli 2022 wieder von einem regulären Vertrieb von Ware in deutscher Aufmachung auszugehen.

Hinweis:

Es wird empfohlen, aus Gründen der Nachvollziehbarkeit und Transparenz ein offizielles Informationsschreiben jeder Lieferung beizufügen.

Rechtsbehelfsbelehrung:

Gegen diesen Bescheid kann innerhalb eines Monats nach Bekanntgabe Widerspruch erhoben werden. Der Widerspruch ist bei dem Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) in Bonn einzulegen.

Bonn, den 07.03.2022

Mit freundlichen Grüßen
Im Auftrag

Dr. Michael Horn

Anlagen

- Gebrauchsinformation – in englischer Aufmachung

2/5 CODE № 7173

dasatinib

SPRYCEL®

20 mg 50 mg 70 mg 80 mg 100 mg 140 mg

film-coated tablets

1295444B4

2/5 CODE № 7173

1295444B4

SPRYCEL®

20 mg 50 mg 70 mg 80 mg 100 mg 140 mg

film-coated tablets

dasatinib

Package leaflet: Information for the user

SPRYCEL 20 mg film-coated tablets
SPRYCEL 50 mg film-coated tablets
SPRYCEL 70 mg film-coated tablets
SPRYCEL 80 mg film-coated tablets
SPRYCEL 100 mg film-coated tablets
SPRYCEL 140 mg film-coated tablets

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 only. 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) in adults, adolescents and children at least 1 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.

SPRYCEL is also used to treat Philadelphia chromosome positive (Ph+) acute lymphoblastic leukaemia (ALL) in adults, adolescents and children at least 1 year of age, and lymphoid blast CML in adults who are not benefiting from prior therapies. In people with ALL, white cells called lymphocytes multiply too quickly and live too long. 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, 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 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 will also have blood tests regularly while you are taking SPRYCEL.

Children and adolescents
Do not give this medicine to children younger than one year of age. There is limited experience with the use of SPRYCEL in this age group. 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 think you 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 lactose
If you have been told by your doctor that you have an intolerance to some sugars, talk to your doctor before taking this medicine.

3. How to take SPRYCEL

SPRYCEL will only be prescribed to you 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 is prescribed for adults and children at least 1 year of age.

The starting dose recommended for adult patients with chronic phase CML is 100 mg once a day.

The starting dose recommended for adult patients with accelerated or blast crisis CML or Ph+ ALL is 140 mg once a day.

Dosing for children with chronic phase CML or Ph+ ALL is on the basis of body weight. SPRYCEL is administered orally once daily in the form of either SPRYCEL tablets or SPRYCEL powder for oral suspension. SPRYCEL tablets are not recommended for patients weighing less 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. The starting dose of SPRYCEL for children is calculated by body weight as shown below:

Body Weight (kg)[a]	Daily Dose (mg)
10 to less than 20 kg	40 mg
20 to less than 30 kg	60 mg
30 to less than 45 kg	70 mg
at least 45 kg	100 mg

[a] The tablet is not recommended for patients weighing less than 10 kg; the powder for oral suspension should be used for these patients.

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. For higher or lower doses, you may need to take combinations of the different tablet strengths.

The tablets may come in packs with calendar blisters. These are blisters showing the days of the week. There are arrows to show the next tablet to be taken according to your treatment schedule.

How to take SPRYCEL
Take your tablets at the same time every day. Swallow the tablets whole. **Do not crush, cut or chew them.** Do not take dispersed tablets. You cannot be sure you will receive the correct dose if you crush, cut, chew or disperse the tablets. SPRYCEL tablets can be taken with or without a meal.

Special handling instructions for SPRYCEL
It is unlikely that the SPRYCEL tablets will get broken. But if they do, persons other than the patient should use gloves when handling SPRYCEL.

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 many tablets, 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 tablet. 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)

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, blister or carton after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

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. Each film-coated tablet contains 20 mg, 50 mg, 70 mg, 80 mg, 100 mg or 140 mg dasatinib (as monohydrate).
- The other ingredients are:
  - *Tablet core:* lactose monohydrate (see section 2 "SPRYCEL contains lactose"); microcrystalline cellulose; croscarmellose sodium; hydroxypropylcellulose; magnesium stearate
  - *Film-coating*: hypromellose; titanium dioxide (E171); macrogol 400

BIANCA / FRONT

Bristol Myers Squibb®

Perigord Job No.:	625979	
Market:	UK(GB)	
Version No.:	03	
Date & Time:	09 November 2021	15:52
Superseded Artwork Number:	1295444B3	
Artwork Number:	1295444B4	
Drawing:	I016	
OLV Barcode type:	2/5	
OLV Barcode No.:	7173	
Artwork Description:	SPRYCEL PIL	
Description of change:	Brexit , Log update	
CMO Artwork Description:	INS SPRYCEL 440X330(90X45) GB	

Printable Colours: Black

Non Print: Profile, Technical Info

Perigord — life science artwork solutions

Bar prints 100mm @ 100%

Font information

Font family: **Arial**
Body text size: **8 pt**
Smallest text size: **8 pt**
(excluding component code)

What SPRYCEL looks like and contents of the pack

SPRYCEL 20 mg: the film-coated tablet is white to off-white, biconvex, round with “BMS” debossed on one side and “527” on the other side.

SPRYCEL 50 mg: the film-coated tablet is white to off-white, biconvex, oval with “BMS” debossed on one side and “528” on the other side.

SPRYCEL 70 mg: the film-coated tablet is white to off-white, biconvex, round with “BMS” debossed on one side and “524” on the other side.

SPRYCEL 80 mg: the film-coated tablet is white to off-white, biconvex, triangular with “BMS 80” debossed on one side and “855” on the other side.

SPRYCEL 100 mg: the film-coated tablet is white to off-white, biconvex, oval with “BMS 100” debossed on one side and “852” on the other side.

SPRYCEL 140 mg: the film-coated tablet is white to off-white, biconvex, round with “BMS 140” debossed on one side and “857” on the other side.

SPRYCEL 20 mg, 50 mg or 70 mg film-coated tablets are available in cartons containing 56 film-coated tablets in 4 calendar blisters of 14 film-coated tablets each, and in cartons containing 60 x 1 film-coated tablets in perforated unit dose blisters. They are also available in bottles with child-resistant closure containing 60 film-coated tablets. Each carton contains one bottle.

SPRYCEL 80 mg, 100 mg or 140 mg film-coated tablets are available in cartons containing 30 x 1 film-coated tablets in perforated unit dose blisters. They are also available in bottles with child-resistant closure containing 30 film-coated tablets. Each carton contains one bottle.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

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Manufacturer

Swords Laboratories T/A Bristol-Myers Squibb
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Ireland

This leaflet was last revised in November 2021

VOLTA / BACK

Bristol Myers Squibb

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