SPRYCEL®
dasatinib

Start with SPRYCEL® in 1st line for CML[1]

Convenient once daily dosing, with or without a meal[1]

Ph+ CML-CP (adult patients)

- 76% MMR rate at 5 years[2§]
- Well-established safety profile with > 5 years follow-up[2§]

Ph+ CML -CP (pediatric patients)

- **75%** MMR rate at 2 years[1†]
- **96%** CCyR rate at 2 years[1†]

Extending our reach

Newly diagnosed ***pediatric***[#] Ph+ ALL[1]

- **64%** EFS rate at 3 years[1*]
- **96%** had BM <5% lymphoblasts[1*] by the end of induction

[#]Aged 1 year or older

***Study Design:** CA180372 is a multicenter, multiple-cohort study of pediatric patients with newly diagnosed B-cell precursor Ph+ ALL. The purpose of this study was to determine the safety and efficacy of SPRYCEL® when added to standard chemotherapy. In cohort 1, 78 patients received SPRYCEL® (60mg/m^2) in combination with chemotherapy for up to 24 months. Patients continued to receive study treatment until disease progression or the development of unacceptable toxic effects.[3]

†**Study Designs:** CA180018 was an open-label, non-randomized, phase 1 trial which evaluated the safety, efficacy and pharmacokinetics of SPRYCEL® in children or adolescents with relapsed or refractory Ph- ALL or AML. Escalating doses of SPRYCEL® (60 to 120mg/m2) were administered to patients age 1 to 21 years (n=58) with (i) imatinib-pretreated CML or Ph+ ALL and (ii) treatment-refractory Ph- ALL or AML. CA180226 was an open-label, non-randomized, single-arm phase 2 trial to further evaluate safety and efficacy of SPRYCEL® in pediatric patients with CML-CP. Three cohorts, (1) imatinib-resistant/intolerant CML-CP (n=29), (2) imatinib-resistant/intolerant CML in accelerated/blast phase or Ph+ ALL (n = 17), and (3) newly diagnosed CML-CP (n=51) were treated with SPRYCEL® tablet. Major cytogenetic response and CCyR for newly diagnosed patients were evaluated.[5]

§**Study Design:** DASISION was a multicenter, open-label, phase 3 randomized trial of adult patients with newly diagnosed CML-CP (cytogenetically confirmed as Ph+). Patients (n=519) were randomized (1:1) to receive either SPRYCEL® (100mg once daily) or imatinib (400mg once daily). All patients had no prior CML therapy, with the exception of anagrelide or hydroxyurea. Patients continued to receive study treatment until disease progression or the development of unacceptable toxic effects.[2]

Abbreviations: ALL, acute lymphoblastic leukemia; **BM,** bone marrow; **CCyR,** complete cytogenetic response; **CML,** chronic myeloid leukemia; **CP,** chronic phase; **EFS**, event-free survival; **MMR,** major molecular response; **Ph+,** Philadelphia chromosome-positive; **Ph-,** Philadelphia chromosome-negative

References: 1. SPRYCEL® (dasatinib) tablets package insert. Hong Kong: Prescribing information last revised: April 2019 (1237730A9). **2.**Cortes, J. E. *et al.* Final 5-Year Study Results of DASISION: The Dasatinib Versus Imatinib Study in Treatment-Naïve Chronic Myeloid Leukemia Patients Trial. JCO 34, 2333–2340 (2016). **3**. Pediatric Philadelphia Positive Acute Lymphoblastic Leukemia. *ClinicalTrials.gov* Available at: https://clinicaltrials.gov/ct2/show/NCT01460160. (Accessed: 22nd November 2019). **4.** Zwaan, C. M. *et al.* Dasatinib in children and adolescents with relapsed or refractory leukemia: results of the CA180-018 phase I dose-escalation study of the Innovative Therapies for Children with Cancer Consortium. *J. Clin. Oncol.* 31, 2460–2468 (2013). **5**. Gore, L. *et al.* Dasatinib in Pediatric Patients With Chronic Myeloid Leukemia in Chronic Phase: Results From a Phase II Trial. *J. Clin. Oncol.* 36, 1330–1338 (2018).

SPRYCEL® tablets
ABBREVIATED PRESCRIBING INFORMATION

ACTIVE INGREDIENT(S): Each film-coated tablet contains 20, 50, or 70 mg of dasatinib. **INDICATION(S):** SPRYCEL is indicated for the treatment of adults with: • newly diagnosed Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase. • chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib. • Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) with resistance or intolerance to prior therapy. SPRYCEL is indicated for the treatment of pediatric patients 1 year of age and older with • Ph+ CML in chronic phase. • newly diagnosed Ph+ ALL in combination with chemotherapy. **DOSAGE & ADMINISTRATION:** Chronic phase CML in adults: 100 mg once daily. Accelerated phase CML, myeloid or lymphoid blast phase CML, or Ph+ ALL in adults: 140mg once daily. Chronic phase CML and ALL in pediatrics: starting dose based on body weight. Administer orally, with or without a meal. Do not crush, cut, or chew tablets. **CONTRAINDICATIONS:** None. **SPECIAL WARNINGS AND PRECAUTIONS:** • Myelosuppression and Bleeding Events: Severe thrombocytopenia, neutropenia, and anemia may occur. Use caution if used concomitantly with medications that inhibit platelet function or anticoagulants. Monitor complete blood counts regularly. Transfuse and interrupt SPRYCEL when indicated. • Fluid Retention: Fluid retention, sometimes severe, including pleural effusions. Manage with supportive care measures and/or dose reduction. • Cardiac Dysfunction: Monitor patients for signs or symptoms and treat appropriately. • Pulmonary Arterial Hypertension (PAH): SPRYCEL may increase the risk of developing PAH which may be reversible on discontinuation. Consider baseline risk and evaluate patients for signs and symptoms of PAH during treatment. Permanently discontinue dasatinib if PAH is confirmed. • QT Prolongation: Use SPRYCEL with caution in patients who have or may develop prolongation of the QT interval. • Severe Dermatologic Reactions: Individual cases of severe mucocutaneous dermatologic reactions have been reported. • Tumor Lysis Syndrome: Tumor lysis syndrome has been reported. Maintain adequate hydration and correct uric acid levels prior to initiating therapy with SPRYCEL. • Embryo-Fetal Toxicity: Can cause fetal harm. Advise of potential risk to fetus and avoid pregnancy. • Effects on Growth and Development in Pediatric Patients: epiphyses delayed fusion, osteopenia, growth retardation, and gynecomastia have been reported. Monitor bone growth and development in pediatric patients. • Hepatitis B Virus (HBV) Reactivation: BCR-ABL TKIs have been associated with HBV reactivation including individual case reports for SPRYCEL. Consider screening for HBV before starting therapy with SPRYCEL. **ADVERSE REACTIONS:** Most common adverse reactions (>15%) in patients receiving SPRYCEL as single-agent therapy included myelosuppression, fluid retention events, diarrhea, headache, skin rash, hemorrhage, dyspnea, fatigue, nausea, and musculoskeletal pain. Most common adverse reactions (>30%) in pediatric patients receiving SPRYCEL in combination with chemotherapy included mucositis, febrile neutropenia, pyrexia, diarrhea, nausea, vomiting, musculoskeletal pain, abdominal pain, cough, headache, rash, fatigue, constipation, arrhythmia, hypertension, edema, infections (bacterial, viral and fungal), hypotension, decreased appetite, hypersensitivity, dyspnea, epistaxis, peripheral neuropathy, and altered state of consciousness. Refer to full prescribing information for other side effects.**PREGNANCY & LACTATION:** Based on limited human data, SPRYCEL can cause fetal harm when administered to a pregnant woman. Breastfeeding is not recommended during treatment with SPRYCEL and for 2 weeks after the final dose. **INTERACTIONS:** Strong CYP3A4 Inhibitors. Strong CYP3A4 Inducers. Antacids. H2 Antagonists/Proton Pump Inhibitors: concomitant use of H2 antagonists or proton pump inhibitors with SPRYCEL is not recommended.

PLEASE REFER TO FULL PRESCRIBING INFORMATION BEFORE PRESCRIBING.
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SPRYCEL®
dasatinib