**Semblix**® (asciminib)

Semblix® (asciminib) is the first FDA-approved allosteric inhibitor of BCR-ABL, exhibiting safety and promising single-agent activity in a Phase I study of patients with CML with failure of prior TKI therapy. This innovative treatment is approved for use in adults with Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CML-CP) and is part of the ongoing efforts to find out how Semblix works over a longer period of time. It is not known if Semblix is safe and effective in children.

**Mechanism of action:**

Semblix inhibits the ABL myristoyl pocket, which is an allosteric binding site for the BCR-ABL tyrosine kinase. By binding to this pocket, Semblix blocks the activity of the kinase, thereby inhibiting the growth and proliferation of leukemic cells. This mechanism of action was a determining factor in the accelerated approval of the drug, which is contingent upon further verification and description of clinical benefit in a confirmatory trial(s).

**Indications:**

- **Ph+ CML-CP:** Semblix is approved for use in adults with Ph+ CML in CP with the T315I mutation – representing a significant clinical challenge for patients with CML who develop mutations that cause resistance to TKI therapy. Despite significant advances in CML care over the last few decades, many patients remain at risk of disease progression, and the sequential use of currently available TKIs may not yield the desired results.

**Development:**

- **Semblix for Ph+ CML-CP:**
  - A study of oral asciminib versus other TKIs in adult patients with newly diagnosed Ph+ CML-CP.
  - A Study of Efficacy and Safety of CML-CP versus other TKIs in adult patients with previously treated Ph+ CML-CP (ASC4FIRST).
  - A Phase IIIb optimization study of asciminib in Ph+ CML-CP with and without a T315I mutation.
  - A Study of Efficacy and Safety of CML-CP in Previously Treated Patients with Chronic Myeloid Leukemia in Chronic Phase (NCT04971226).

- **Ph+ CML-CP with Failure of Prior TKI:**
  - A Study of Oral Asciminib Versus Other TKIs in Adult Patients With Newly Diagnosed Ph+ CML-CP.
  - A Study of Efficacy and Safety of CML-CP Versus Other TKIs in Adult Patients With Previously Treated Ph+ CML-CP (ASC4FIRST).

- **Ph+ CML-CP with the T315I Mutation:**
  - A Study of Efficacy and Safety of CML-CP in Previously Treated Patients With Chronic Myeloid Leukemia in Chronic Phase (NCT04971226).

**Important Safety Information:**

- **Common side effects:** Semblix can cause nausea, rash, diarrhea, fatigue, headache, and muscle spasms. Less common side effects include infections, muscle, bone, or joint pain, rash, fatigue, nausea, and diarrhea. The most common serious side effects are abnormal blood counts, infections that do not respond to antibiotics, fever, bruising, blood in the urine or stools, fever, or any signs of an infection. SCEMBLIX is in drug category classified as pregnancy category X, meaning that it is unsafe to use during pregnancy. Women should tell their doctor right away if they become pregnant or plan to become pregnant.

- **Drug interactions:** Semblix should be used with caution in patients who are also taking other medications. It may affect the way other medications work or may cause their effects to be more severe.

- **Contraindications:** Women who are pregnant or breastfeeding should not use Semblix. It is not known if Semblix is safe and effective in children.

**Further studies:**

Ongoing studies exist to find out how Semblix works over a longer period of time. No clinical information is available to show if these patients treated with Semblix live longer or if their symptoms improve. No clinical information is available to show major molecular response (MMR) rates. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).