AYVAKIT®
avapritinib | 25mg tablets

The FIRST and ONLY targeted therapy for adults with indolent systemic mastocytosis (ISM)[1]

INDICATION

AYVAKIT® (avapritinib) is indicated for the treatment of adult patients with indolent systemic mastocytosis (ISM).

Limitations of Use: AYVAKIT is not recommended for the treatment of patients with ISM with platelet counts of <50 x 10^9/L.

Please see Important Safety Information on page 5 and click here to see the full Prescribing Information for AYVAKIT.

ISM is a clonal mast cell disorder that can be associated with heterogeneous, chronic, and potentially debilitating symptoms[2-4]

76% reported experiencing skin and subcutaneous tissue disorders[5]*

65% reported experiencing nervous system disorders[5]*

80% reported experiencing GI disorders[5]*

The efficacy and safety of AYVAKIT in patients with ISM were evaluated in PIONEER[1]

- **PIONEER:** Phase 2, multipart, randomized, placebo-controlled, double-blind trial evaluating the safety and efficacy of AYVAKIT 25 mg (N=141) vs placebo (N=71)—both + BSC over 24 weeks—in adult patients (≥18 years of age) with moderate to severe ISM symptoms not adequately controlled on BSC alone[1,6†]
- **Primary endpoint:** Absolute mean change from baseline to Week 24 in ISM-SAF TSS[1]
- **Select key secondary endpoints:** Patients (%) achieving ≥50% reduction in: serum tryptase levels, KIT D816V VAF or undetectable in peripheral blood, BM MCs or no aggregates at Week 24[1,6]
- **ISM-SAF:** Patient-reported outcome assessing 11 ISM signs and symptoms (abdominal pain, nausea, diarrhea, spots, itching, flushing, bone pain, fatigue, dizziness, headache, and brain fog)[1‡]

Select baseline demographics and disease characteristics[1,6]

Patient Demographic	AYVAKIT + BSC (n=141)	Placebo + BSC (n=71)
Median age (range)	50 years (18-77)	54 years (26-79)
Female	71%	76%
Mean ISM-SAF TSS (SD)	50.2 (19.1)	52.4 (19.8)
Median no. of BSC treatments (range)	3 (0-11)	4 (1-8)
Median serum tryptase, ng/mL (range)	38.4 (3.6-256.0)	43.7 (5.7-501.6)
Mast cell aggregates present	75%	80%

- 93% of patients in the AYVAKIT + BSC arm had a KIT D816V mutation[1]
- BSC medications allowed in the PIONEER study included anti-immunoglobulin E antibody (omalizumab), glucocorticoids, cromolyn sodium, H1 antihistamines, H2 antihistamines, leukotriene inhibitors, and proton pump inhibitors[6]

~99% of patients (n=207/210) reported ≥7 symptoms measured by the ISM-SAF at baseline[§]

~61% of patients (n=129/210) reported experiencing all 11 symptoms measured by the ISM-SAF at baseline[§]

*Data based on ongoing medical history events in the PIONEER study (N=212). Events ≥10% in 1 or both trial arms from 3 of the organ classes include pruritus, urticaria pigmentosa, urticaria, rash maculo-papular for skin and subcutaneous tissue disorders; headache, dizziness, migraine, memory impairment, disturbance in attention for nervous system disorders; and diarrhea, abdominal pain, nausea, gastroesophageal reflux disease, abdominal distension, constipation for gastrointestinal disorders.[5]

†Data cutoff was June 23, 2022.

‡11 symptom severity scores (scored 0 [no symptoms] to 10 [worst imaginable symptoms] daily) are combined to calculate the TSS from 0-110, with higher scores representing greater symptom severity. A biweekly average in ISM-SAF TSS was used to evaluate efficacy endpoints.[1]

§210 of 212 patients with ISM-SAF TSS values at baseline; baseline TSS values missing for 2 patients in avapritinib + BSC arm.

BM=bone marrow; BSC=best supportive care; GI=gastrointestinal; ISM-SAF=Indolent Systemic Mastocytosis-Symptom Assessment Form; MC=mast cell; SD=standard deviation; TSS=total symptom score; VAF=variant allele fraction.

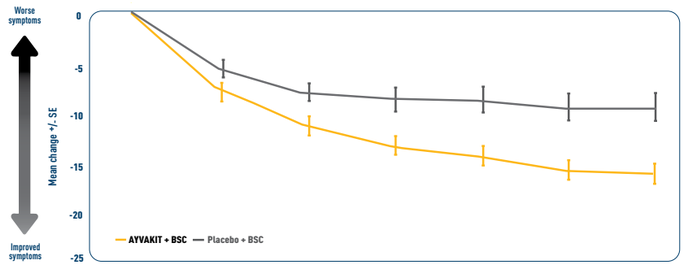
AYVAKIT demonstrated a statistically significant improvement in ISM-SAF TSS at 24 weeks[1]

PRIMARY ENDPOINT[1]

Week 24	AYVAKIT + BSC (N=141)	Placebo + BSC (N=71)	2-sided *P* value
Absolute mean change in the ISM-SAF TSS (95% CI)	**-15.33** (-18.36, -12.31)	**-9.64** (-13.61, -5.68)	**0.012**

ITT analysis: Markov chain Monte Carlo simulation was used to impute the missing values at Baseline or Week 24.

ISM-SAF TSS over time[6]



Number of patients	Baseline	4	8	12	16	20	24
AYVAKIT + BSC	141	141	141	141	141	141	141
Placebo + BSC	71	71	71	71	71	71	71

ITT analysis: Markov chain Monte Carlo simulation was used to impute the missing values.

LIMITATIONS: Mean change in TSS at all time points except Week 24 were prespecified, nonranked endpoints and were not adjusted for multiplicity. Therefore, treatment differences at these time points cannot be regarded as statistically significant and results should be interpreted with caution.

ITT=intention to treat.

KEY SECONDARY ENDPOINTS[1]

- **Serum tryptase:** 53.9% of 141 patients receiving AYVAKIT + BSC achieved ≥50% reduction in serum tryptase vs 0% of 71 patients receiving placebo + BSC at Week 24 (2-sided *P*<0.0001)
- **KIT D816V:** 67.8% of 118 patients in the AYVAKIT + BSC arm vs 6.3% of 63 patients in the placebo + BSC arm had a ≥50% reduction in KIT D816V VAF or undetectable in peripheral blood at Week 24 (2-sided *P*<0.0001)
- **BM MC levels:** 52.8% of 106 patients in the AYVAKIT + BSC arm achieved ≥50% reduction in BM MCs or no aggregates vs 22.8% of 57 patients in the placebo + BSC arm at Week 24 (2-sided *P*<0.0001)

SELECT SAFETY INFORMATION

Intracranial Hemorrhage (ICH)—Serious ICH may occur with AYVAKIT treatment; fatal events occurred in <1% of patients. No events of ICH occurred in the 246 patients with ISM who received any dose of AYVAKIT in the PIONEER study.

Please see Important Safety Information on page 5 and click here to see the full Prescribing Information for AYVAKIT.

AYVAKIT was generally well tolerated in PIONEER[1]

Adverse reactions occurring in patients with ISM during PIONEER trial[1]

Adverse Reaction[a,b]	AYVAKIT (25 mg once daily) + BSC N=141, %	Placebo + BSC N=71, %
Eye edema[c]	13	7
Dizziness[d]	13	10
Peripheral edema[d]	12	6
Flushing[d]	11	4
Respiratory tract infection[e]	8	1
Face edema	7	1
Rash[d]	6	4
Liver transaminase increased[d]	6	3
Insomnia	6	3
Hematoma[f]	6	1
Blood alkaline phosphatase increased	6	1
Hemorrhage[g]	5	3

[a]Adverse reactions that occurred in ≥5% of AYVAKIT-treated patients and ≥2% more than placebo-treated patients.

[b]Per National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.

[c]Eye edema includes periorbital edema, eye edema, swelling of eyelid, orbital edema, eye swelling, eyelid edema and eyelid ptosis.

[d]Term includes several similar terms.

[e]Respiratory tract infection includes pneumonia, upper respiratory tract infection, bronchitis and respiratory tract infection.

[f]Hematoma includes contusion, hematoma and pelvic hematoma.

[g]Hemorrhage includes epistaxis, gingival bleeding, hematochezia, rectal hemorrhage, retinal hemorrhage.

- Serious adverse reactions occurred in 1 patient (0.7%) who received AYVAKIT due to pelvic hematoma[1]
- Permanent discontinuation of AYVAKIT due to an adverse reaction occurred in 1 patient (0.7%) due to dyspnea and dizziness[1]
- Dosage interruptions of AYVAKIT due to an adverse reaction occurred in 5% of patients[1]
- Of all adverse reactions, 55% were Grade 1, 38% were Grade 2, and 7% were Grade 3[1]
- Among patients with edema adverse reactions, 95% were Grade 1 and 5% were Grade 2. Among patients with hemorrhage adverse reactions, 86% were Grade 1 and 14% were Grade 2[1]

SELECT SAFETY INFORMATION

Intracranial Hemorrhage (ICH) (cont'd)—Monitor patients closely for risk factors of ICH which may include history of vascular aneurysm, ICH or cerebrovascular accident within the prior year, concomitant use of anticoagulant drugs, or thrombocytopenia.

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Important Safety Information

There are no contraindications for AYVAKIT.

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Monitor patients closely for risk factors of ICH which may include history of vascular aneurysm, ICH or cerebrovascular accident within the prior year, concomitant use of anticoagulant drugs, or thrombocytopenia.

Symptoms of ICH may include headache, nausea, vomiting, vision changes, or altered mental status. Advise patients to seek immediate medical attention for signs or symptoms of ICH.

Permanently discontinue AYVAKIT if ICH of any grade occurs.

Cognitive Effects—Cognitive adverse reactions can occur in patients receiving AYVAKIT and occurred in 7.8% of patients with ISM who received AYVAKIT + best supportive care (BSC) versus 7.0% of patients who received placebo + BSC; <1% were Grade 3. Depending on the severity, withhold AYVAKIT and then resume at the same dose, or permanently discontinue AYVAKIT.

Photosensitivity—AYVAKIT may cause photosensitivity reactions. In all patients treated with AYVAKIT in clinical trials (n=1049), photosensitivity reactions occurred in 2.5% of patients. Advise patients to limit direct ultraviolet exposure during treatment with AYVAKIT and for one week after discontinuation of treatment.

Embryo Fetal Toxicity—AYVAKIT can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females and males of reproductive potential to use an effective contraception during treatment with AYVAKIT and for 6 weeks after the final dose. Advise women not to breastfeed during treatment with AYVAKIT and for 2 weeks following the final dose.

Adverse Reactions—The most common adverse reactions (≥10%) in patients with ISM were eye edema, dizziness, peripheral edema, and flushing.

Drug Interactions—Avoid coadministration of AYVAKIT with strong or moderate CYP3A inhibitors or inducers.

To report suspected adverse reactions, contact Blueprint Medicines Corporation at 1-888-258-7768 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please click here to see the full Prescribing Information for AYVAKIT.

References: 1. AYVAKIT [prescribing information]. Cambridge, MA: Blueprint Medicines Corporation; May 2023. **2.** Pardanani A. *Am J Hematol*. 2023;98(7):1097-1116. **3.** Gülen T et al. *J Intern Med*. 2016;279(3):211-228. **4.** Theoharides TC et al. *N Engl J Med*. 2015;373(2):163-172. **5.** Data on file. Blueprint Medicines Corporation, Cambridge, MA. 2023. **6.** Gotlib J et al. *NEJM Evidence*. 2023;2(6). Published online May 23, 2023. doi:10.1056/EVIDoa2200339

AYVAKIT® avapritinib 25mg tablets

The recommended dosage for patients with ISM is 25 mg, orally, once daily[1]

AYVAKIT should be taken[1]:

- One 25-mg tablet orally
- On an empty stomach, at least 1 hour before or at least 2 hours after a meal
- Once a day

A modified starting dosage of AYVAKIT is recommended for patients with severe hepatic impairment (Child-Pugh Class C): 25 mg orally every other day.[1]

Avoid concomitant use of AYVAKIT with strong or moderate CYP3A inhibitors or inducers.[1]

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Monday-Friday, 8 AM-8 PM Eastern Time (ET)

Read the terms and conditions and learn more: **www.YourBlueprint.com/HCP**

To learn more about AYVAKIT for ISM, visit AYVAKITHCP.com.

SELECT SAFETY INFORMATION

Intracranial Hemorrhage (ICH) (cont'd)—Symptoms of ICH may include headache, nausea, vomiting, vision changes, or altered mental status. Advise patients to seek immediate medical attention for signs or symptoms of ICH.

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