For adults with indolent systemic mastocytosis

Patient portrayal

AYVAKIT®
avapritinib | 25mg tablets

The **First** and **Only** FDA-approved therapy to treat ISM[1]

FDA=Food and Drug Administration; ISM=indolent systemic mastocytosis.

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.

Target the source, not just the symptoms[1,2]

Symptom-directed therapies (SDT) alone may not be enough[1,2]

SDT may help address ISM symptoms but do not treat the underlying cause of the symptoms: the KIT D816V mutation[1,2]

AYVAKIT inhibits the autophosphorylation of KIT in cellular assays, which ultimately blocks overproduction of abnormal and hyperactive mast cells thought to cause the symptoms of ISM[1,2]

AYVAKIT targets the KIT D816V mutation—the primary driver of ISM[1-5]

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

- **PIONEER:** A phase 2, multipart, randomized, placebo-controlled, double-blind trial (N=212) 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 best supportive care (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 at Week 24 in: serum tryptase levels, KIT D816V VAF or undetectable in peripheral blood, BM MCs or no aggregates[1,6]
- **ISM-SAF TSS:** Validated patient-reported outcome assessing 11 ISM signs and symptoms (abdominal pain, nausea, diarrhea, spots, itching, flushing, bone pain, fatigue, dizziness, headache, and brain fog)[1,7†]

PIONEER reflects a heterogeneous population of patients living with ISM[1,6]

SELECT BASELINE DEMOGRAPHICS AND PATIENT CHARACTERISTICS (AYVAKIT + BSC, n=141; PLACEBO + BSC, n=71)[1,6]

AGE RANGE	**Median age, years (range)** AYVAKIT + BSC: 50 (18-77) Placebo + BSC: 54 (26-79)	**SEX**	AYVAKIT + BSC: 71% female, 29% male Placebo + BSC: 76% female, 24% male
VARIED TRYPTASE LEVELS	**Median serum tryptase, ng/mL (range)** AYVAKIT + BSC: 38.4 (3.6-256) Placebo + BSC: 43.7 (5.7-501.6)	**MAST CELL BURDEN**	**Mast cell aggregates present** AYVAKIT + BSC: 75% Placebo + BSC: 80%
VARIED SYMPTOM SEVERITY	**Mean ISM-SAF TSS (SD)** AYVAKIT + BSC: 50.2 (19.1) Placebo + BSC: 52.4 (19.8)	**POLY-PHARMACY BURDEN**	**Median No. of BSC (range)** AYVAKIT + BSC: 3 (0-11) Placebo + BSC: 4 (1-8)

- 93% of patients in the AYVAKIT + BSC arm were KIT positive, with 7% KIT undetectable[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]

*Data cutoff was June 23, 2022.[6]
†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.[1,7]
BM=bone marrow; GI=gastrointestinal; ISM-SAF=Indolent Systemic Mastocytosis-Symptom Assessment Form; KIT=KIT proto-oncogene, receptor tyrosine kinase; MC=mast cell; TSS=total symptom score; VAF=variant allele fraction.

AYVAKIT reduced symptom and mast cell burden[1]

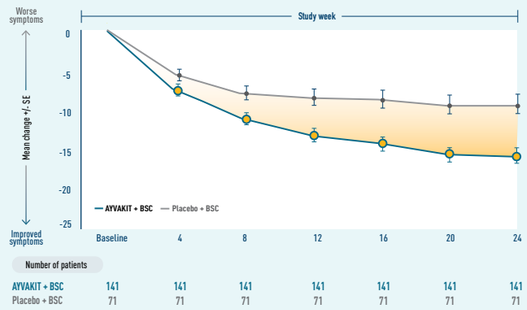
PRIMARY ENDPOINT AT 24 WEEKS[1]

Adding AYVAKIT to BSC demonstrated significantly greater symptom reduction vs Placebo + BSC[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.

MEAN CHANGE IN ISM-SAF TSS AT 24 WEEKS[6]

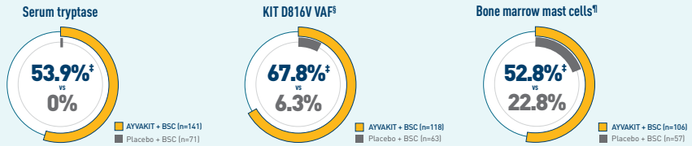


ITT analysis: Markov chain Monte Carlo simulation was used to impute the missing values. Patients with use of high-dose steroids (3 patients treated with AYVAKIT and 1 in the placebo group) were included in this analysis that were not included in the primary analysis.

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.

KEY SECONDARY ENDPOINTS AT 24 WEEKS[1]

PROPORTION OF PATIENTS ACHIEVING ≥50% REDUCTION IN OBJECTIVE MEASURES OF MAST CELL BURDEN AT 24 WEEKS[1]



ITT analysis: For patients with high-dose steroid use within 7 days before Week 24, or greater than 14 consecutive days at any point from baseline to Week 24, the Week 24 score was set to missing.
‡2-sided *P*<0.0001.
§Percent of patients with ≥50% reduction in peripheral blood KIT D816V VAF or undetectable.
¶Percent of patients with ≥50% reduction in bone marrow mast cells or no aggregates.

ITT=intention to treat.

SELECT SAFETY INFORMATION

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.

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AYVAKIT was generally well tolerated in PIONEER[1]

SAFETY AT 24 WEEKS[1]

- Serious adverse reactions occurred in 1 patient (0.7%) who received AYVAKIT due to pelvic hematoma[1]
- Permanent discontinuation of AYVAKIT due to adverse reactions 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]

Adverse reactions occurring in patients with ISM during the 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, and retinal hemorrhage.

SELECT SAFETY INFORMATION

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.

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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. If contraception requires estrogen, limit ethinyl estradiol to ≤20 mcg unless a higher dose is necessary.

To report suspected adverse reactions, contact Blueprint Medicines Corporation at 1-888-258-7768 or the FDA at 1-800-FDA-1088 or visit 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; November 2024. **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.** Akin C, ed. *Mastocytosis: A Comprehensive Guide.* Springer; 2020. **6.** Gotlib J et al. *NEJM Evidence.* 2023;2(6). Published online May 23, 2023. doi:10.1056/EVIDoa2200339 **7.** Padilla B et al. *Orphanet J Rare Dis.* 2021;16(1):434. **8.** Data on file. Blueprint Medicines Corporation, Cambridge, MA. 2024.

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 coadministration of AYVAKIT with strong or moderate CYP3A inhibitors or inducers. If contraception requires estrogen, limit ethinyl estradiol to ≤20 mcg unless a higher dose is necessary.[1]

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

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