AYVAKIT®
avapritinib | 25mg tablets

The FIRST and ONLY Therapy for Adults With Indolent Systemic Mastocytosis (ISM)[1]

Please see Important Safety Information on pages 15-16 and the full Prescribing Information for AYVAKIT.

Patients with ISM can experience a high symptom burden that may impact work and daily life[2,3]

Symptoms (including skin, neurocognitive, and GI) can be heterogeneous, chronic, and potentially debilitating[2,4,5]

76%
reported experiencing skin and subcutaneous tissue disorders[3]*

65%
reported experiencing nervous system disorders[3]*

80%
reported experiencing GI disorders[3]*

Patients report impact to their work and personal life due to living with ISM[3†]

Of 32 patients with moderate to severe ISM in the Blueprint Medicines–sponsored patient survey[3†]:

56%
reported reducing work hours due to their ISM

28%
reported going on medical disability due to their ISM

72%
reported avoiding leaving home due to their ISM symptoms

*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.[3]

GI=gastrointestinal.

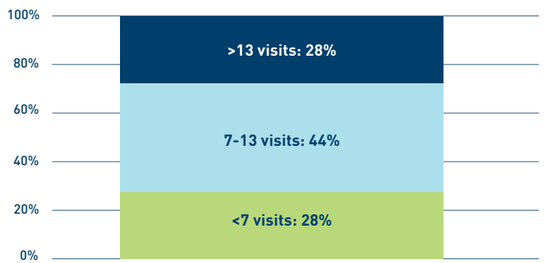
Patients may take multiple symptom-directed therapies and visit HCPs frequently due to their ISM[3†]

ISM patients in the Blueprint Medicines–sponsored patient survey

Medications Taken for ISM (n=37)[3†]

86%
reported moderate to severe symptom burden despite taking a median of 3 OTC and 2 prescription medications for their ISM symptoms[3†]

HCP Visits in 1 Year, as Reported by Patients With Moderate to Severe ISM (n=32)[3†]



Historically, there have been no approved therapies for ISM[2]

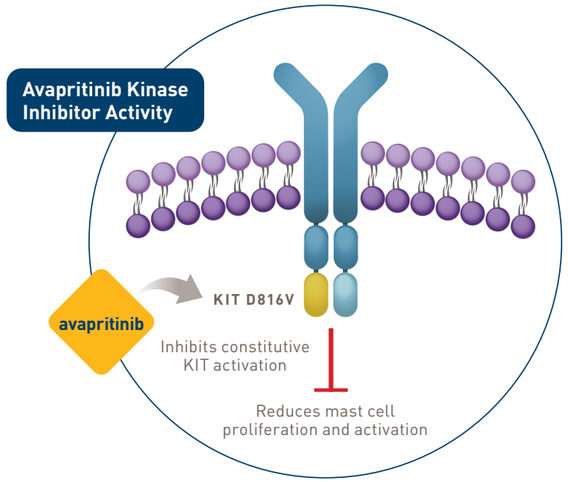
†In the Blueprint Medicines–sponsored TouchStone SM Patient Survey, US adults with a self-reported SM diagnosis (N=56) completed an online survey of 100 items. An analysis was conducted in patients with ISM (n=37), including 32 patients with moderate to severe ISM (defined as an ISM-SAF TSS ≥28) and results were analyzed using descriptive statistics. These analyses were made from the TouchStone Patient SM Survey but have not been published.[3]

HCP=healthcare provider; OTC=over the counter; SM=systemic mastocytosis.

The FIRST FDA-approved treatment for adults with ISM to target the underlying driver of disease in ~95% of patients[1,6-8]

Avapritinib is a TKI designed for potent and selective inhibition of KIT D816V[1]

Demonstrated greater inhibitory potency for KIT D816V vs wild type KIT in cellular assays.[1]



FDA=Food and Drug Administration; KIT=KIT proto-oncogene, receptor tyrosine kinase; TKI=tyrosine kinase inhibitor.

INDICATION

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

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

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.

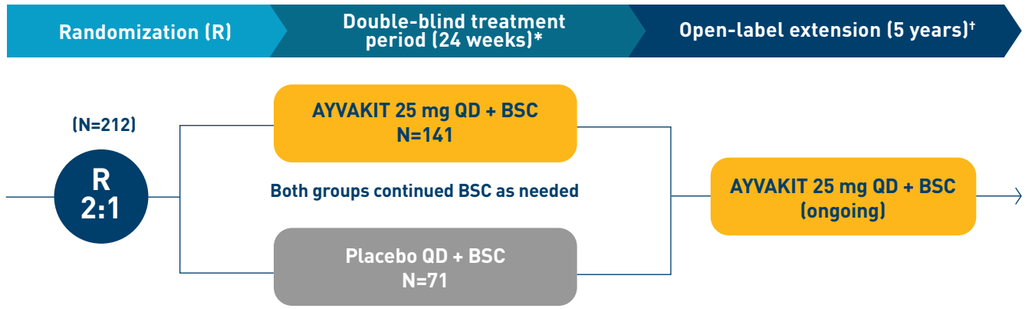
Monitor patients closely for risk factors of ICH which may include history of vascular aneurysm, ICH or cerebrovascular accident within the prior year, concomitant use of anticoagulant drugs, or thrombocytopenia.

Please see Important Safety Information on pages 15-16 and the full Prescribing Information for AYVAKIT.

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

PIONEER was a phase 2, multipart, randomized, placebo-controlled, double-blind trial evaluating the safety and efficacy of AYVAKIT 25 mg vs placebo—both with concomitant best supportive care (BSC) over 24 weeks—**in patients with moderate to severe ISM not adequately controlled on BSC alone**.[1,9]

STUDY DESIGN[1,9]



- **Primary endpoint:** Absolute mean change in ISM-SAF TSS compared with placebo + BSC from baseline to Week 24[1]
  - **Select key secondary endpoints:** Proportion of patients achieving ≥50% reduction in serum tryptase levels; ≥50% reduction in KIT D816V VAF or undetectable‡; ≥50% reduction in bone marrow mast cells or no aggregates, all compared with placebo + BSC at Week 24[1,9]
  - **Exploratory endpoints:** Mean change in ISM-SAF individual symptom scores; mean change in most severe symptom score at Week 24[3,9]
- Key eligibility criteria: ≥18 years of age; centrally confirmed ISM diagnosis per WHO criteria; uncontrolled moderate to severe ISM symptoms (defined as ISM-SAF TSS ≥28) despite ≥2 symptom-directed therapies[9]
- The recommended dose of AYVAKIT for the double-blind treatment period was identified in Part 1 of PIONEER[9]

*Data cutoff was June 23, 2022.

†OLE: The open-label study is evaluating the long-term efficacy and safety of AYVAKIT 25 mg + BSC for up to 5 years. All eligible patients either continued AYVAKIT 25 mg + BSC daily or switched from placebo + BSC to AYVAKIT 25 mg + BSC daily.

‡In peripheral blood.

ISM-SAF=Indolent Systemic Mastocytosis-Symptom Assessment Form; OLE=open-label extension; QD=every day; TSS=total symptom score; VAF=variant allele fraction; WHO=World Health Organization.

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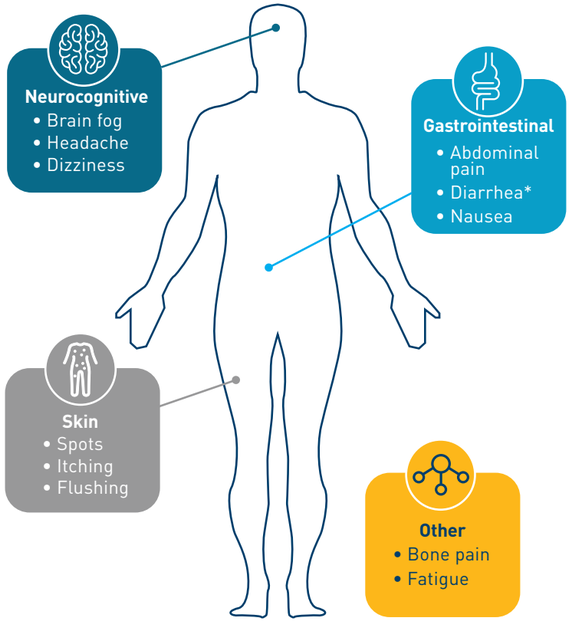
The Indolent Systemic Mastocytosis-Symptom Assessment Form (ISM-SAF) is a validated symptom assessment tool[1,10]

The ISM-SAF is a patient-reported outcome measure assessing ISM signs and symptoms[1,10]

The ISM-SAF is a 12-item questionnaire. Individual symptom scores are evaluated, and the 11 symptom severity scores are combined to calculate the TSS (0-110), with higher scores representing greater symptom severity.[1,10]*



Scoring

Individual symptoms scored 0-10 daily

0=no symptom,10=worst imaginable symptom

A biweekly average ISM-SAF TSS was used to evaluate efficacy endpoints in PIONEER

*There are 12 items in the evaluation of the 11 symptoms in the ISM-SAF. Diarrhea frequency was the 12th item evaluated but was not included in the TSS calculation.

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.

Permanently discontinue AYVAKIT if ICH of any grade occurs.

Please see Important Safety Information on pages 15-16 and the full Prescribing Information for AYVAKIT.

Patient demographics in PIONEER were similar between both arms[9]

SELECT BASELINE DEMOGRAPHIC AND DISEASE CHARACTERISTICS (N=212)[1,9]

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[9]

BSC=best supportive care.

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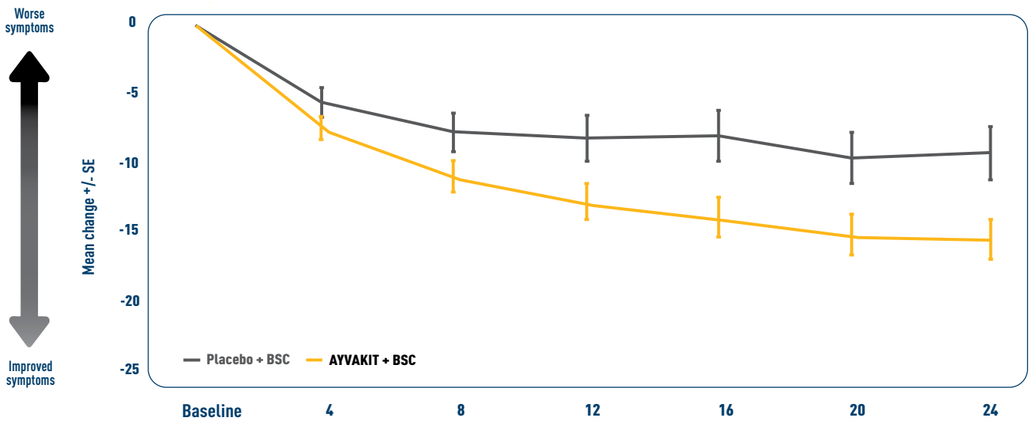
AYVAKIT demonstrated a statistically significant improvement in ISM-SAF TSS at 24 weeks[1]

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[9]



Number of patients							
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.

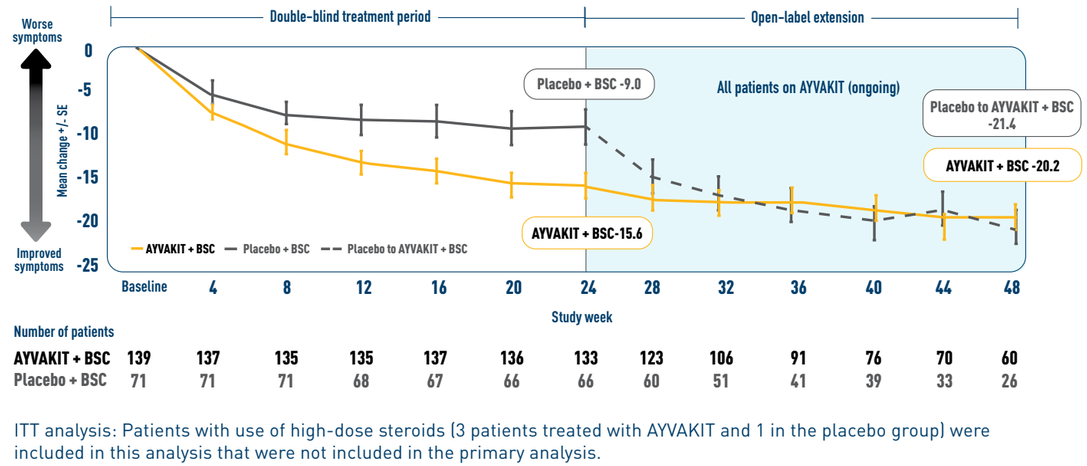
LIMITATIONS: Mean change in TSS at all time points except Week 24 were prespecified, nonranked endpoints and were not adjusted for multiplicity. Therefore, treatment differences at these time points cannot be regarded as statistically significant and results should be interpreted with caution.

ITT=intention to treat.

Exploratory endpoint: Mean change in ISM-SAF TSS through 48 weeks[9]

EXPLORATORY ENDPOINT

ISM-SAF TSS THROUGH 48 WEEKS[9]



Number of patients													
AYVAKIT + BSC	**139**	**137**	**135**	**135**	**137**	**136**	**133**	**123**	**106**	**91**	**76**	**70**	**60**
Placebo + BSC	71	71	71	68	67	66	66	60	51	41	39	33	26

ITT analysis: 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.

Missing visit data were excluded from calculations for that visit.

- In an interim analysis, a decrease in TSS was observed for patients who continued on AYVAKIT in an OLE through 48 weeks[9]

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 and conclusions cannot be drawn. In an open-label extension, there is a potential for enrichment of the long-term data in the remaining patient populations since patients who are unable to tolerate or do not respond to the drug often drop out.

ISM-SAF=Indolent Systemic Mastocytosis-Symptom Assessment Form; TSS=total symptom score.

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.

Please see Important Safety Information on pages 15-16 and the full Prescribing Information for AYVAKIT.

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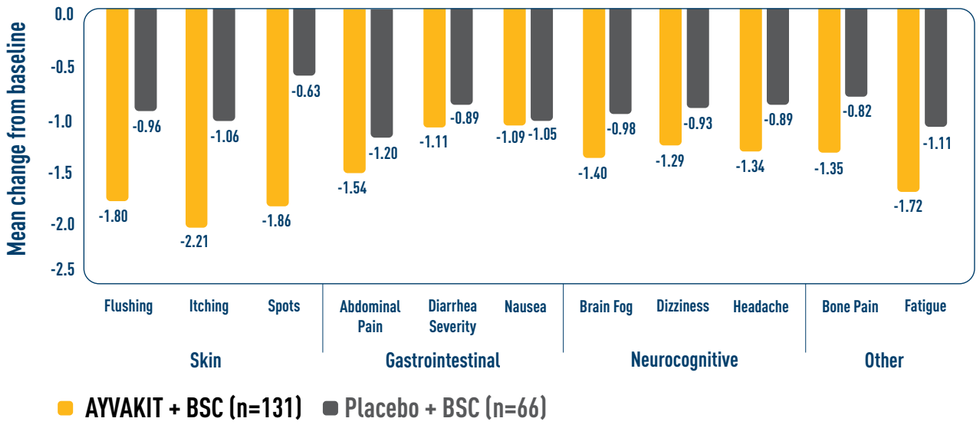
Exploratory endpoint: Individual symptom scores at 24 weeks[3]

EXPLORATORY ENDPOINT

Reductions across all individual symptom scores were observed at 24 weeks[3]

MEAN CHANGE FROM BASELINE AT 24 WEEKS BY ISM-SAF INDIVIDUAL SYMPTOM SCORE[3]



Reductions were observed in patients' most severe symptom, defined as the symptom with the highest score at baseline[9]

ITT analysis: In this analysis, if a patient was missing more than 7 days of score between baseline score and Week 2 score, it was considered as missing for the patient. If a patient missed more than 7 days of the score from the 14 days period for calculating the Week 24 score, then the Week 24 score was considered as missing.

LIMITATIONS: Individual components in a descriptive exploratory analysis were prespecified, nonranked endpoints, not adjusted for multiplicity, and not powered. Therefore, data should be interpreted with caution, conclusions cannot be drawn, and treatment differences cannot be regarded as statistically significant.

SELECT SAFETY INFORMATION

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 method of contraception during treatment with AYVAKIT and for 6 weeks after the final dose of AYVAKIT. Advise women not to breastfeed during treatment with AYVAKIT and for 2 weeks after the final dose.

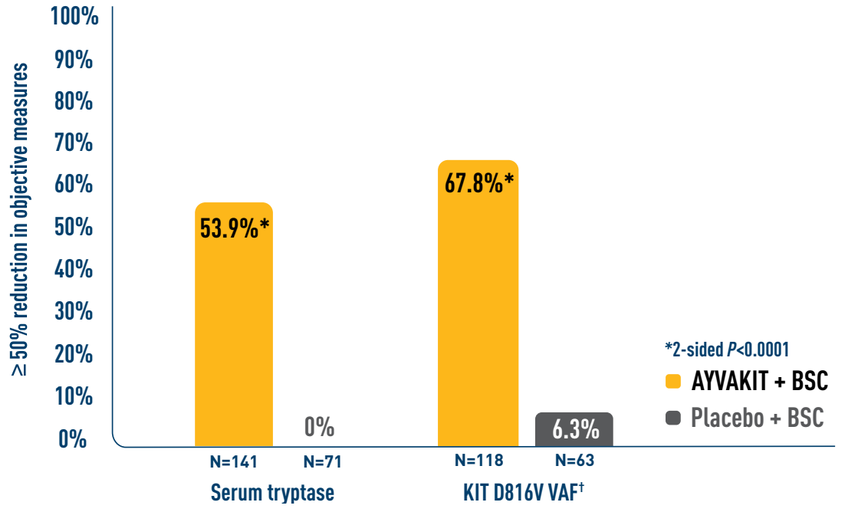
Please see Important Safety Information on pages 15-16 and the full Prescribing Information for AYVAKIT.

Significantly more patients treated with AYVAKIT had reductions in objective measures of mast cell burden at 24 weeks[1]

KEY SECONDARY ENDPOINTS

More than half of the evaluated AYVAKIT + BSC patients experienced ≥50% reductions in serum tryptase, KIT D816V VAF, and BM MC levels[1]

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



- 52.8% of 106 patients receiving AYVAKIT + BSC achieved ≥50% reduction in BM MCs vs 22.8% of 57 patients receiving placebo + BSC (2-sided $P<0.0001$)[1‡]

†Percent of patients with ≥50% reduction in peripheral blood KIT D816V VAF or undetectable.
‡Percent of patients with ≥50% reduction in BM MCs or no aggregates.

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.

BM=bone marrow; MC=mast cell.

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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]

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]

SELECT SAFETY INFORMATION

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.

Please see Important Safety Information on pages 15-16 and the full Prescribing Information for AYVAKIT.

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Important Safety Information

INDICATION

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

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

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.

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Please see Important Safety Information continued on back cover and Prescribing Information for AYVAKIT.

References: 1. AYVAKIT [prescribing information]. Cambridge, MA: Blueprint Medicines Corporation; May 2023. **2.** Pardanani A. *Am J Hematol.* 2021;96(4):508-525. **3.** Data on file. Blueprint Medicines Corporation, Cambridge, MA. 2023. **4.** Gülen T et al. *J Intern Med*. 2016;279(3):211-228. **5.** Theoharides TC et al. *N Engl J Med*. 2015;373(2):163-172. **6.** Kristensen T et al. *Am J Hematol.* 2014;89(5):493-498. **7.** Garcia-Montero AC et al. *Blood*. 2006;108(7):2366-2372. **8.** Ungerstedt J et al. *Cancers*. 2022;14(16):3942. **9.** Gotlib J et al. *NEJM Evid* 2023. Available online. doi:10.1056/EVIDoa2200339 **10.** Padilla B et al. *Orphanet J Rare Dis*. 2021;16(1):434.

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Consider AYVAKIT for your ISM patient

Patients can experience a high symptom burden that may impact work and daily life[2,3]

A once-daily oral therapy designed to target the driver of disease in ~95% of ISM cases[1,6-8]

AYVAKIT 25 mg + BSC showed improvements vs placebo + BSC in key endpoints: ISM-SAF total symptom score, KIT D816V VAF, serum tryptase, and bone marrow mast cells[1]*

The most common adverse reactions (≥10%) were eye edema, dizziness, peripheral edema, and flushing[1]*

*In a phase 2, randomized, placebo-controlled, double-blind clinical trial.

BSC=best supportive care; ISM=indolent systemic mastocytosis; VAF=variant allele fraction.

For more information, visit AYVAKITHCP.com.

Important Safety Information (Cont'd from Page 15)

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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.

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11/2023 USBP-PRAVAISM-23.049.2

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