

The ONLY Targeted Therapy for Advanced Systemic Mastocytosis

Designed for **potent and selective inhibition of KIT D816V¹**

INDICATION

AYVAKIT[®] (avapritinib) is indicated for the treatment of adult patients with Advanced SM (AdvSM) including patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated hematological neoplasm (SM-AHN), and mast cell leukemia (MCL).

Limitations of Use: AYVAKIT is not recommended for the treatment of patients with AdvSM with platelet counts of $<50 \times 10^9/L$.

SELECT IMPORTANT SAFETY INFORMATION

There are no contraindications for AYVAKIT.

Serious intracranial hemorrhage (ICH) may occur with AYVAKIT treatment; fatal events occurred in $<1\%$ of patients. Overall, ICH (eg, subdural hematoma, ICH, and cerebral hemorrhage) occurred in 2.9% of 749 patients who received AYVAKIT. In AdvSM patients who received AYVAKIT at 200 mg daily, ICH occurred in 2 of 75 patients (2.7%) who had platelet counts $\geq 50 \times 10^9/L$ prior to initiation of therapy and in 3 of 80 patients (3.8%) regardless of platelet counts. Monitor patients closely for risk of ICH including those with thrombocytopenia, vascular aneurysm or a history of ICH or cerebrovascular accident within the prior year. Permanently discontinue AYVAKIT if ICH of any grade occurs.

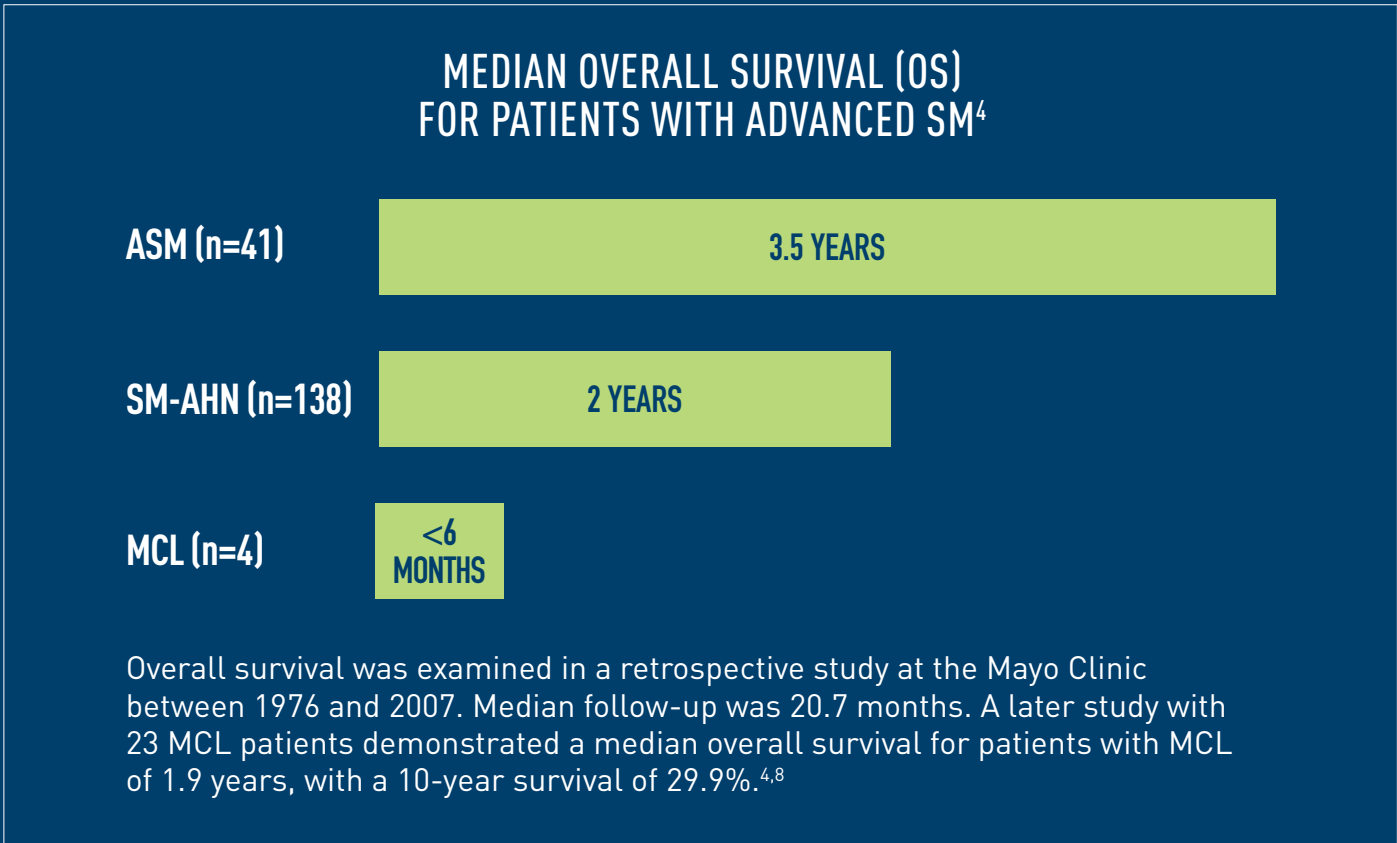
Please see Important Safety Information on pages 12-13 and the full [Prescribing Information](#) for AYVAKIT.

Advanced SM can lead to significant disease burden and shortened overall survival²⁻⁴

Advanced SM is a clonal mast cell neoplasm **causing significant symptom burden and impact to quality of life.**^{2,3}

Patients may exhibit debilitating mast cell mediator symptoms, such as rash and life-threatening anaphylaxis.³

Additionally, patients with Advanced SM can experience organ damage, including ascites, osteolytic lesions, pleural effusion, liver dysfunction, weight loss, cytopenias, and hypersplenism.^{3,5-7}



Advanced SM may be missed in patients with other myeloid neoplasms.⁹

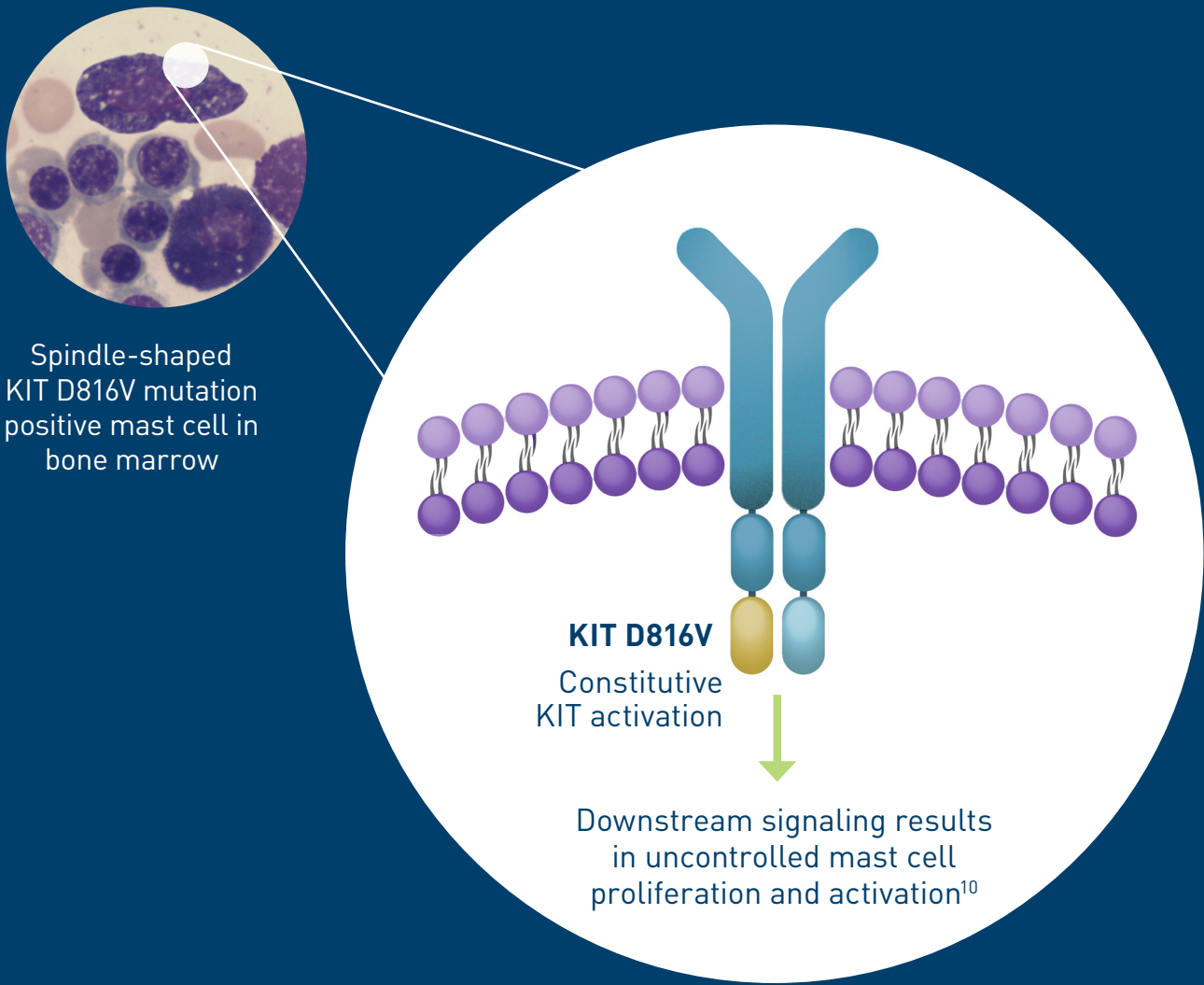
The median time from symptom onset to diagnosis for patients with Advanced SM is 3 years.^{3*}

*Based on a survey in patients with Advanced SM (n=13).

ASM=aggressive systemic mastocytosis; MCL=mast cell leukemia; SM=systemic mastocytosis; SM-AHN=systemic mastocytosis with an associated hematological neoplasm.

Advanced SM is driven by KIT D816V in ~95% of cases^{6,10,11}

The KIT D816V mutation constitutively activates downstream pathways regulating cellular functions including proliferation and survival of abnormal mast cells.^{12,13}



Historically, patients with Advanced SM had **no treatment options that selectively targeted the underlying mutation.**^{5,14}

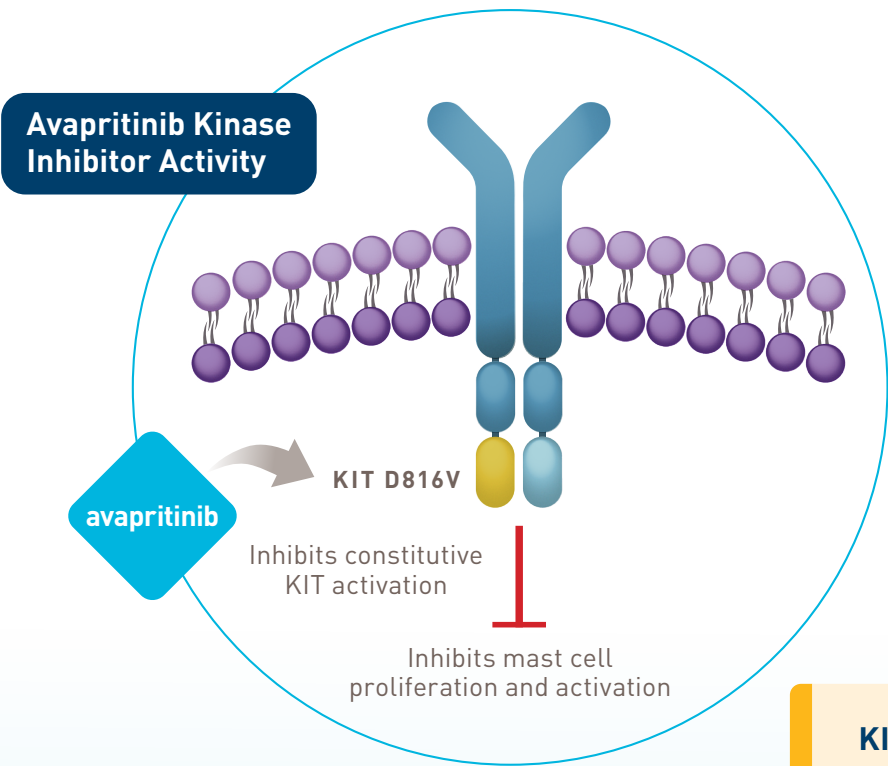
KIT=KIT proto-oncogene, receptor tyrosine kinase.

The ONLY treatment to selectively target the underlying mutation¹

AVAPRITINIB IS A TYROSINE KINASE INHIBITOR DESIGNED FOR POTENT AND SELECTIVE INHIBITION OF KIT D816V



AYVAKIT potently and selectively inhibits autophosphorylation of the KIT receptor produced by the KIT D816V mutation, with an IC₅₀ of 4 nanomoles in selective cellular assays.



KIT D816V testing is not required for AYVAKIT treatment.

SELECT IMPORTANT SAFETY INFORMATION

A platelet count must be performed prior to initiating therapy. AYVAKIT is not recommended in AdvSM patients with platelet counts <50 x 10⁹/L. Following treatment initiation, platelet counts must be performed every 2 weeks for the first 8 weeks. After 8 weeks of treatment, monitor platelet counts every 2 weeks or as clinically indicated based on platelet counts. Manage platelet counts of <50 x 10⁹/L by treatment interruption or dose reduction.

Please see Important Safety Information on pages 12-13 and the full [Prescribing Information](#) for AYVAKIT.

The efficacy and safety of AYVAKIT were evaluated in EXPLORER and PATHFINDER¹

MULTICENTER, SINGLE-ARM, OPEN-LABEL CLINICAL TRIALS FOR PATIENTS WITH ADVANCED SM



53 patients were evaluable for a response across the 2 trials, with median follow-up of 11.6 months [95% CI: 9.9 to 16.3 months].*

EXPLORER¹⁵

- Phase 1 dose-finding study to determine maximum tolerated dose
- Patients received a starting, once-daily dose of 30-400 mg

PATHFINDER¹⁶

- Phase 2 study evaluating efficacy and safety
- Patients received a starting, once-daily dose of 200 mg

Efficacy was based on overall response rate (ORR) in 53 patients with Advanced SM dosed at up to 200 mg daily, per modified IWG-MRT-ECNM criteria as adjudicated by the central committee. In the subgroup of patients with MCL, the efficacy was based on CR.

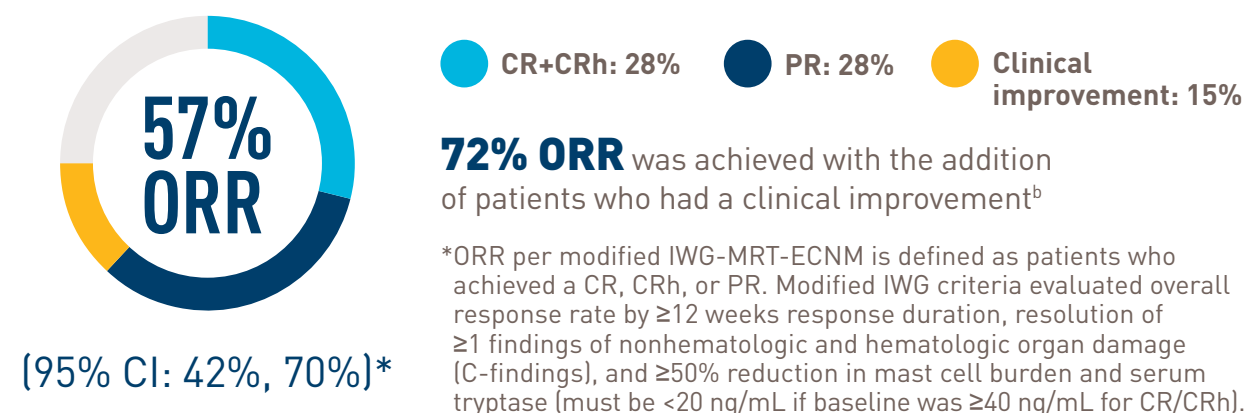
Demographic Characteristics at Baseline (N=53)	
Median age	67 years (37-85)
Gender	58% male, 42% female
ECOG PS	0-1: 68%
	2-3: 32%
Ongoing corticosteroid use	40%
Presence of KIT D816V mutation	94% (as measured by ddPCR)
Prior antineoplastic therapy	66%
Prior midostaurin	47%
Advanced SM subtypes	ASM: 3.8% (n=2)
	SM-AHN: 75.5% (n=40)
	MCL: 20.7% (n=11)
Baseline platelet count ≥50 x 10 ⁹ /L	91%

*Response-evaluable patients: Confirmed diagnosis of Advanced SM per WHO criteria and deemed evaluable by modified IWG-MRT-ECNM criteria at baseline. Received at least 1 dose of AYVAKIT, had at least 2 post-baseline bone marrow assessments, and were on study for at least 24 weeks, or had an end-of-study visit.

CR=complete remission; ddPCR=droplet digital polymerase chain reaction; ECOG PS=Eastern Cooperative Oncology Group Performance Status; IWG-MRT-ECNM=International Working Group-Myeloproliferative Neoplasia Research and Treatment-European Competence Network on Mastocytosis; WHO=World Health Organization.

Proven efficacy and demonstrated duration of response¹

ORR across all evaluable Advanced SM patients (N=53)^a who were dosed up to 200 mg daily



^aMedian duration of follow-up was 11.6 months [95% CI: 9.9, 16.3].

^bClinical improvement is defined as having a response duration of ≥12 weeks and fulfillment of 1 or more of the nonhematologic and/or hematologic response criteria.⁷

CR=complete remission; CRh=complete remission with partial hematologic recovery; PR=partial remission.

Median DOR across all Advanced SM patients

38.3 MONTHS

[95% CI: 19, NE]
driven primarily by SM-AHN patients

PATIENT TIME TO TREATMENT RESPONSE:

2.1 MONTHS

Median time to response (n=30)

9.2 MONTHS

Median time to CR and CRh (n=15)¹⁷

DOR=duration of response; NE=not estimable.

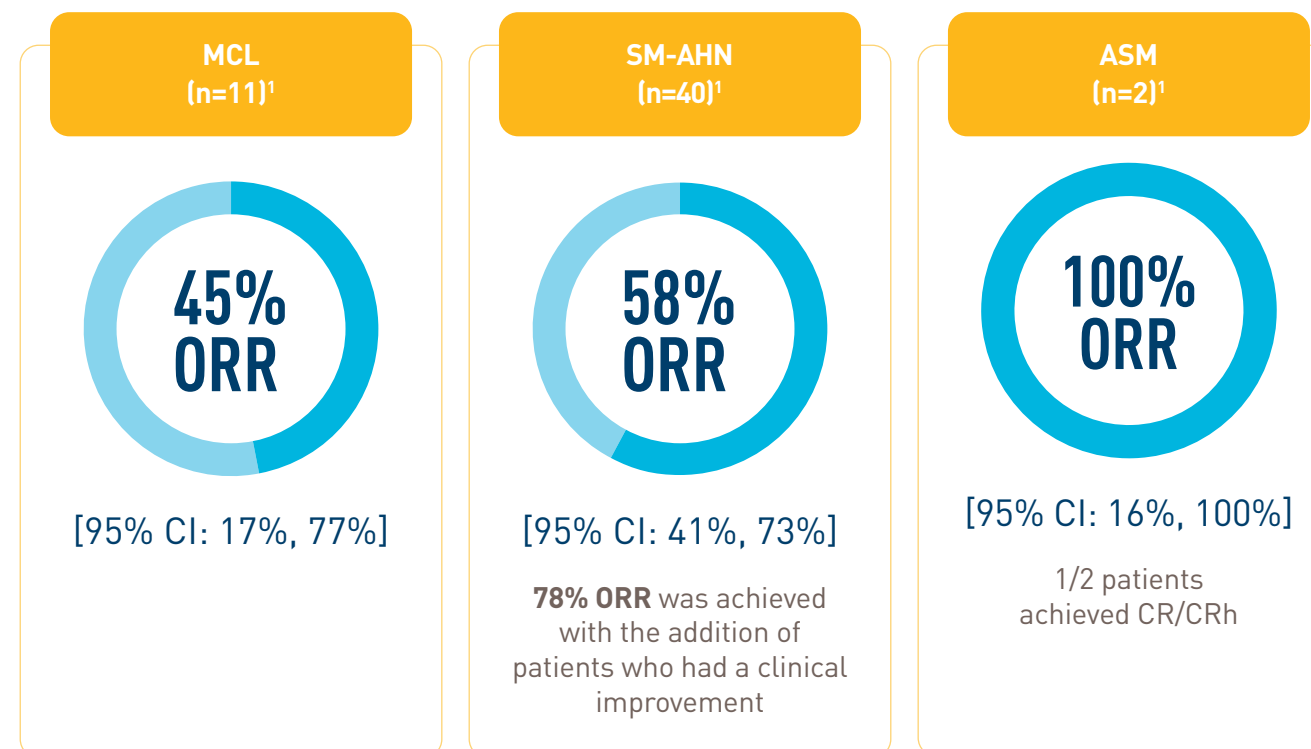
SELECT IMPORTANT SAFETY INFORMATION

Cognitive adverse reactions can occur in patients receiving AYVAKIT. Cognitive adverse reactions occurred in 39% of 749 patients and in 28% of 148 SM patients (3% were Grade >3). Memory impairment occurred in 16% of patients; all events were Grade 1 or 2.

Please see Important Safety Information on pages 12-13 and the full [Prescribing Information](#) for AYVAKIT.

Proven efficacy across subtypes and regardless of prior antineoplastic therapy^{1,17}

EFFICACY ACROSS ADVANCED SM SUBTYPES¹



ASM=aggressive systemic mastocytosis; MCL=mast cell leukemia; SM-AHN=systemic mastocytosis with an associated hematological neoplasm.

IN A PRE-PLANNED SUBGROUP ANALYSIS, AYVAKIT DEMONSTRATED EFFICACY REGARDLESS OF PRIOR ANTINEOPLASTIC THERAPY¹⁷

In treatment-naïve patients (n=18), **ORR was 72.2%** (95% CI: 46.5%, 90.3%)

In patients with prior antineoplastic therapy (including midostaurin) (n=35), **ORR was 48.6%** (95% CI: 31.4%, 66%)

SELECT IMPORTANT SAFETY INFORMATION

Cognitive disorder occurred in 10% of patients; <1% of these events were Grade 3. Confusional state occurred in 6% of patients; <1% of these events were Grade 3. Other events occurred in <2% of patients. Depending on the severity, withhold AYVAKIT and then resume at same dose or at a reduced dose upon improvement, or permanently discontinue.

Please see Important Safety Information on pages 12-13 and the full [Prescribing Information](#) for AYVAKIT.

See adverse reactions from clinical trials >

AYVAKIT was generally well tolerated¹

THE MAJORITY OF ADVERSE REACTIONS WERE GRADE 1 OR 2

Adverse reactions (≥10%) for patients receiving 200 mg once-daily starting dose in EXPLORER and PATHFINDER (N=80)*

Adverse Reactions	All Grades %	Grade ≥3 %
General		
Edema ^a	79	5
Fatigue/asthenia	23	4
Gastrointestinal		
Diarrhea	28	1
Nausea	24	1
Vomiting	18	3
Abdominal pain ^b	14	1
Constipation	11	0
Nervous system		
Headache	15	0
Cognitive effects ^c	14	1
Taste effects ^d	13	0
Dizziness	13	0
Musculoskeletal and connective tissue		
Arthralgia	10	1
Respiratory, thoracic, and mediastinal		
Epistaxis	11	0

Among patients receiving AYVAKIT, 70% were treated for 6 months or longer and 37% were exposed for greater than 1 year.

For patients receiving the recommended starting dose of 200 mg in clinical trials (N=80):

- **Serious adverse reactions were seen in 34% of patients**
- **Fatal adverse reactions occurred in 2.5% [2/80] of patients**
- **No specific adverse reaction leading to death was reported in more than 1 patient**
- **10% of patients permanently discontinued due to any adverse reaction**

Lab abnormalities (≥10%) for patients receiving 200 mg once-daily starting dose in EXPLORER and PATHFINDER (N=80)

Laboratory Abnormality	All Grades %	Grade ≥3 %
Hematology		
Decreased platelets	64	21
Decreased hemoglobin	55	23
Decreased neutrophils	54	25
Decreased lymphocytes	34	11
Increased activated partial thromboplastin time	14	1
Increased lymphocytes	10	0
Chemistry		
Decreased calcium	50	3
Increased bilirubin	41	3
Increased aspartate aminotransferase	38	1
Decreased potassium	26	4
Increased alkaline phosphatase	24	5
Increased creatinine	20	0
Increased alanine aminotransferase	18	1
Decreased sodium	18	1
Decreased albumin	15	1
Decreased magnesium	14	1
Increased potassium	11	0

*Per National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03 and 5.0.

^aEdema includes face swelling, eyelid edema, orbital edema, periorbital edema, face edema, peripheral edema, edema, generalized edema, and peripheral swelling.

^bAbdominal pain includes abdominal pain, upper abdominal pain, and abdominal discomfort.

^cCognitive effects include memory impairment, cognitive disorder, confusional state, delirium, and disorientation.

^dTaste effects include dysgeusia.

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.

Clinically relevant adverse reactions occurring in <10% of patients were:

Cardiac: cardiac failure (2.5%) and cardiac failure congestive (1.3%). Gastrointestinal: ascites (5%), gastrointestinal hemorrhage (1.3%), and large intestine perforation (1.3%). Hepatobiliary: cholelithiasis (1.3%). Infections and infestations: upper respiratory tract infection (6%), urinary tract infection (6%), and herpes zoster (2.5%). Vascular: flushing (3.8%), hypertension (3.8%), hypotension (3.8%), and hot flush (2.5%). Nervous: insomnia (6%). Musculoskeletal and connective tissue: pain in extremity (6%). Respiratory, thoracic, and mediastinal: dyspnea (9%) and cough (2.5%). Skin and subcutaneous tissue: rash (rash and rash maculo-papular) (8%), alopecia (9%), pruritus (8%), and hair color changes (6%). Metabolism and nutrition: decreased appetite (8%). Eye: lacrimation increased (9%). Laboratory abnormality: decreased phosphate (9%).

Please see Important Safety Information on pages 12-13 and the full [Prescribing Information](#) for AYVAKIT.

Starting AYVAKIT—dosing, cognitive effects, and platelet monitoring¹

THE RECOMMENDED DOSAGE OF AYVAKIT FOR ADVANCED SM IS 200 MG ORALLY ONCE DAILY

AYVAKIT should be taken:



One tablet orally



One time each day



On an empty stomach, at least 1 hour before or 2 hours after a meal

Treatment should continue until disease progression or unacceptable toxicity. Dose reductions as described in the AYVAKIT Prescribing Information may also be considered for adverse reactions as clinically appropriate. Do not initiate AYVAKIT in patients with platelet counts $<50 \times 10^9/L$.

IT WAS COMMON TO MODIFY AYVAKIT DOSAGE

Many patients in the EXPLORER and PATHFINDER trials had their dose reduced or interrupted due to adverse reactions.

Dose modifications for patients in clinical trials who started at 200 mg (N=80):

- Dose interruption: **60%**
- Dose reduction: **68%** (median time to reduction: 6.9 weeks)¹⁷
- Permanent discontinuation due to adverse reaction: **10%**

Adverse reactions requiring dosage interruption or dose reduction in $>2\%$ of patients who received AYVAKIT at 200 mg once daily:

- Thrombocytopenia
- Neutropenia
- Anemia
- Elevated blood alkaline phosphatase
- Cognitive disorder
- Peripheral edema
- Periorbital edema
- Fatigue
- Arthralgia

Review the AYVAKIT Prescribing Information and download the AYVAKIT Dosing and Patient Management Guide at [AYVAKIT.com/HCP](https://www.ayvakit.com/HCP) for more detailed information on dose modifications.

SELECT IMPORTANT SAFETY INFORMATION

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 12-13 and the full Prescribing Information for AYVAKIT.

PLATELET MONITORING FOR ICH IS ESSENTIAL FOR TREATMENT WITH AYVAKIT

Platelet monitoring schedule

Time on therapy	Monitoring and treatment plan
Prior to initiation	Perform a platelet count. AYVAKIT is not recommended in Advanced SM patients with platelet counts $<50 \times 10^9/L$.
First 8 weeks	Perform platelet count every 2 weeks regardless of baseline platelet count.
After 8 weeks	Monitor platelet counts: <ul style="list-style-type: none"> • Every 2 weeks if values are $<75 \times 10^9/L$ (or more frequently as clinically indicated) • Every 4 weeks if values are $75-100 \times 10^9/L$ • As clinically indicated if values are $>100 \times 10^9/L$

Due to risk of ICH, dose interruption or reduction should be considered if platelet counts decrease below $50 \times 10^9/L$ during treatment. If platelet count $<50 \times 10^9/L$ occurs, interrupt AYVAKIT until platelet count is $\geq 50 \times 10^9/L$, then resume at reduced dose. If platelet counts do not recover above $50 \times 10^9/L$, consider platelet support.

Platelet monitoring must be performed prior to initiating therapy and throughout treatment with AYVAKIT.

Serious ICH may occur with AYVAKIT treatment. ICH occurred in 2.7% (2/75) of the patients with Advanced SM who had platelet counts of $\geq 50 \times 10^9/L$ at initiation of the recommended 200-mg dose and in 3.8% (3/80) of patients regardless of platelet counts. Fatal events of ICH have occurred in $<1\%$ of Advanced SM patients treated with any dose of AYVAKIT.

Thrombocytopenia was generally reversible by reducing or interrupting AYVAKIT. Dose interruptions and dose reductions for thrombocytopenia occurred in 20% and 22% of AYVAKIT-treated patients, respectively. Manage platelet counts of $<50 \times 10^9/L$ by treatment interruption or dose reduction of AYVAKIT.

Use with caution in patients with potential increased risk of ICH, including those with thrombocytopenia, vascular aneurysm, or a history of ICH or cerebrovascular accident within the prior year.

MONITOR PATIENTS FOR COGNITIVE EFFECTS DURING TREATMENT WITH AYVAKIT

Cognitive adverse reactions can occur in patients receiving AYVAKIT. For patients with Advanced SM started at the 200-mg recommended dose, cognitive effects occurred in 14% of 80 patients. Of the 148 patients with SM who received AYVAKIT at all doses, cognitive effects occurred in 28% of patients, with a median time to onset for the first cognitive adverse reaction of 13.3 weeks (range: 1 day to 1.8 years). Among patients who experienced a cognitive effect of Grade 2 or worse, the median time to improvement to Grade 1 or complete resolution was 8.1 weeks.

Cognitive effects include memory impairment, cognitive disorder, confusional state, delirium, and disorientation.



Advise patients and their caregivers of the potential cognitive effects, and the importance of notifying their healthcare provider of any new or worsening symptoms. Advise patients not to drive or operate hazardous machinery if they are experiencing cognitive adverse reactions.

Embryo-Fetal Toxicity: Based on findings from animal studies and its mechanism of action, AYVAKIT can cause fetal harm when administered to pregnant women. Advise females and males of reproductive potential of the potential risk to a fetus and to use effective contraception.

Review the full Prescribing Information and visit [AYVAKIT.com/HCP](https://www.ayvakit.com/HCP)

For additional information on:

- Dose modifications
- Patient monitoring
- Clinical data
- Support resources

Important Safety Information

Important Safety Information

INDICATION

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Limitations of Use: AYVAKIT is not recommended for the treatment of patients with AdvSM with platelet counts of $<50 \times 10^9/L$.

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Serious intracranial hemorrhage (ICH) may occur with AYVAKIT treatment; fatal events occurred in $<1\%$ of patients. Overall, ICH (eg, subdural hematoma, ICH, and cerebral hemorrhage) occurred in 2.9% of 749 patients who received AYVAKIT. In AdvSM patients who received AYVAKIT at 200 mg daily, ICH occurred in 2 of 75 patients (2.7%) who had platelet counts $\geq 50 \times 10^9/L$ prior to initiation of therapy and in 3 of 80 patients (3.8%) regardless of platelet counts. Monitor patients closely for risk of ICH including those with thrombocytopenia, vascular aneurysm or a history of ICH or cerebrovascular accident within the prior year. Permanently discontinue AYVAKIT if ICH of any grade occurs. A platelet count must be performed prior to initiating therapy. AYVAKIT is not recommended in AdvSM patients with platelet counts $<50 \times 10^9/L$. Following treatment initiation, platelet counts must be performed every 2 weeks for the first 8 weeks. After 8 weeks of treatment, monitor platelet counts every 2 weeks or as clinically indicated based on platelet counts. Manage platelet counts of $<50 \times 10^9/L$ by treatment interruption or dose reduction.

Cognitive adverse reactions can occur in patients receiving AYVAKIT. Cognitive adverse reactions occurred in 39% of 749 patients and in 28% of 148 SM patients (3% were Grade >3). Memory impairment occurred in 16% of patients; all events were Grade 1 or 2. Cognitive disorder occurred in 10% of patients; $<1\%$ of these events were Grade 3. Confusional state occurred in 6% of patients; $<1\%$ of these events were Grade 3. Other events occurred in $<2\%$ of patients. Depending on the severity, withhold AYVAKIT and then resume at same dose or at a reduced dose upon improvement, or permanently discontinue.

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.

The most common adverse reactions ($\geq 20\%$) were edema, diarrhea, nausea, and fatigue/asthenia.

Avoid coadministration of AYVAKIT with strong and moderate CYP3A inhibitors. If coadministration with a moderate CYP3A inhibitor cannot be avoided, reduce dose of AYVAKIT. Avoid coadministration of AYVAKIT with strong and moderate CYP3A 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 see the full [Prescribing Information](#) for AYVAKIT.

The ONLY targeted therapy for Advanced SM designed for potent and selective inhibition of KIT D816V¹



Advanced SM is driven by the KIT D816V mutation in ~95% of cases.^{6,10,11}



Proven efficacy across all Advanced SM subtypes and regardless of prior antineoplastic therapy.^{1,17}



One tablet, once-daily dosing starting at 200 mg.¹



Generally well tolerated with specific guidelines for patient monitoring and management; most common adverse reactions were Grade 1 or 2.¹

SELECT IMPORTANT SAFETY INFORMATION

The most common adverse reactions (≥20%) at all doses were edema, diarrhea, nausea, and fatigue/asthenia.

Please see Important Safety Information on pages 12-13 and the full [Prescribing Information](#) for AYVAKIT.

Support for you and your patients

YourBlueprint™ provides dedicated, personalized assistance to help your patients. Through this program, your patients will have a specialized support team that provides:

- Benefits investigation
- Prior authorization support
- Financial assistance options
- Helpful resources



To see how we can help:

- ☎ Call **1-888-BLUPRNT (1-888-258-7768)**
Monday-Friday, 8 AM-8 PM Eastern Time (ET)
- Visit **www.YourBlueprint.com/HCP**

References: 1. AYVAKIT [prescribing information]. Cambridge, MA: Blueprint Medicines Corporation; June 2021. 2. Theoharides TC et al. *N Engl J Med*. 2015;373(2):163-172. 3. Jennings SV et al. *Immunol Allergy Clin North Am*. 2018;38(3):505-525. 4. Lim K-H et al. *Blood*. 2009;113(23):5727-5736. 5. Gülen T et al. *J Intern Med*. 2016;279(3):211-228. 6. Verstovsek S. *Eur J Haematol*. 2013;90(2):89-98. 7. Gotlib J et al. *Blood*. 2013;121(13):2393-2401. 8. Sperr WR et al. *Lancet Haematol*. 2019;6(12):e638-e649. 9. Schwaab J et al. *J Allergy Clin Immunol Pract*. 2020;8(9):3121-3127. 10. Gilreath JA et al. *Clin Pharmacol*. 2019;11:77-92. 11. Garcia-Montero AC et al. *Blood*. 2006;108(7):2366-2372. 12. da Silva EZM et al. *J Histochem Cytochem*. 2014;62(10): 698-738. 13. Valent P et al. *Blood*. 2017;129(11): 1420-1427. 14. Evans EK et al. *Sci Transl Med*. 2017;9(414):eaao1690. 15. EXPLORER Study. ClinicalTrials.gov. NCT02561988. Accessed May 9, 2022. 16. PATHFINDER Study. ClinicalTrials.gov. NCT03580655. Accessed May 9, 2022. 17. Data on file. Blueprint Medicines Corporation, Cambridge, MA. 2021.



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