



Dosing and Patient Management Guide

An educational resource about
AYVAKIT® (avapritinib) for healthcare
professionals, including patient and
caregiver counseling information.

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

DOSING AND
MODIFICATIONS

ADVERSE
REACTIONS

PATIENT
COUNSELING

IMPORTANT SAFETY
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CASE
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HELPFUL
RESOURCES

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INDICATION

AYVAKIT® (avapritinib) is indicated for the treatment of adult patients with unresectable or metastatic gastrointestinal stromal tumor (GIST) harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutations.

SELECT SAFETY INFORMATION

Intracranial Hemorrhage—Serious intracranial hemorrhage (ICH) may occur with AYVAKIT treatment; fatal events occurred in <1% of patients. Overall, ICH (e.g., subdural hematoma, ICH, and cerebral hemorrhage) occurred in 2.9% of 749 patients who received AYVAKIT in clinical trials. In GIST patients, ICH occurred in 3 of 267 patients (1.1%) and two (0.7%) of the events were Grade ≥3 and resulted in discontinuation.


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.

DOSING


► Dosing¹

The recommended dosage of AYVAKIT is 300 mg orally once daily in patients with GIST.


PATIENTS SHOULD TAKE:



1 AYVAKIT tablet



1 time each day



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

Select patients for treatment with AYVAKIT based on the presence of a PDGFRA exon 18 mutation.

Additional instructions:

- Treatment should be continued until disease progression or unacceptable toxicity
- Do not make up for a missed dose within 8 hours of the next scheduled dose
- Do not repeat dose if vomiting occurs after AYVAKIT but continue with the next scheduled dose
- Avoid coadministration of AYVAKIT with strong or moderate CYP3A inhibitors. If coadministration with a moderate CYP3A inhibitor cannot be avoided, reduce dose of AYVAKIT
- Avoid coadministration of AYVAKIT with strong or moderate CYP3A inducers
- If contraception requires estrogen, limit ethinyl estradiol to ≤ 20 mcg unless a higher dose is necessary

SELECT SAFETY INFORMATION

Cognitive Effects—Cognitive adverse reactions can occur in patients receiving AYVAKIT and occurred in 33% of 995 patients overall in patients who received AYVAKIT in clinical trials including: 41% of 601 GIST patients (5% were Grade ≥ 3). 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 and 13 and click here to see the full [Prescribing Information](#) for AYVAKIT.

► Dose strengths¹

AYVAKIT is available in 100-mg, 200-mg, and 300-mg dose strengths. If your patient experiences any adverse reactions while taking AYVAKIT, consider interrupting dose, reducing dose, or permanently discontinuing AYVAKIT.



Available in bottles of 30 tablets.

Dose Strength	Description
100-mg tablet	Round, white film-coated, printed with blue ink "BLU" on one side and "100" on the other side
200-mg tablet	Capsule shaped, white film-coated, printed with blue ink "BLU" on one side and "200" on the other side
300-mg tablet	Capsule shaped, white film-coated, printed with blue ink "BLU" on one side and "300" on the other side

► In the NAVIGATOR Study, it was common to modify AYVAKIT doses¹

Approximately 50% patients in the clinical trial experienced dose reduction and/or interruption due to an adverse reaction.¹ Sixteen percent of patients who received AYVAKIT permanently discontinued due to adverse reactions.

Recommended Dosage Modifications for AYVAKIT for Adverse Reactions¹

Recommend 200 mg once daily for first dose reduction and 100 mg once daily for second dose reduction.^{1a}

Adverse Reaction	Severity ^b	Dosage Modification
Intracranial Hemorrhage	Any grade	Permanently discontinue AYVAKIT.
Cognitive Effects	Grade 1	Continue AYVAKIT at same dose or reduced dose or withhold until improvement to baseline or resolution. Resume at same dose or reduced dose.
	Grade 2 or Grade 3	Withhold AYVAKIT until improvement to baseline, Grade 1, or resolution. Resume at same dose or reduced dose.
	Grade 4	Permanently discontinue AYVAKIT.
Other	Grade 3 or Grade 4	Withhold AYVAKIT until improvement to less than or equal to Grade 2. Resume at same dose or reduced dose, as clinically appropriate.

^a Permanently discontinue AYVAKIT in patients who are unable to tolerate a dose of 100 mg once daily.

^b Severity as defined by the National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0.

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 12 and 13 and click here to see the full [Prescribing Information](#) for AYVAKIT.

► Dosing considerations for PDGFRA exon 18 GIST

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) recommend avapritinib (AYVAKIT) as a preferred treatment option for unresectable, progressive or metastatic GIST with PDGFRA exon 18 mutations that are insensitive to imatinib (including PDGFRA D842V) and also recommend continued use of avapritinib (AYVAKIT) at the same dose in cases of limited progression.²

Post hoc analyses of the NAVIGATOR trial showed that each studied dose of AYVAKIT is associated with variable exposure levels across individual patients, supporting need for clinically guided dose adjustments based on adverse reactions.³

► Dose strengths of NAVIGATOR PDGFRA exon 18 trial patients (n=36) still receiving AYVAKIT at 6 months⁴



The recommended dosage of AYVAKIT is 300 mg orally once daily.¹

*400 mg is not an approved dose of AYVAKIT.

Data cutoff date: November 2018.



The **YourBlueprint[®] Dose Exchange Program** is available to help ensure continuity of care for patients by allowing patients taking AYVAKIT to trade in their remaining medication for a new dosage in the event of a prescribed dose adjustment at no cost.

See page 17 for more information about YourBlueprint.



NCCN=National Comprehensive Cancer Network.

Adverse reactions observed in patients with GIST in the NAVIGATOR trial^{1,4}

The recommended dosage of AYVAKIT is 300 mg orally once daily.¹

ADVERSE REACTIONS (≥10%) IN PATIENTS RECEIVING AYVAKIT*				
Adverse Reactions	AYVAKIT 300 mg n=154		AYVAKIT 300/400 mg N=204	
	All Grades %	Grade ≥3 %	All Grades %	Grade ≥3 %
General				
Edema ^a	71	1.3	72	2
Fatigue/asthenia	58	6	61	9
Pyrexia	12	0	14	0.5
Gastrointestinal				
Nausea	60	1.3	64	2.5
Vomiting	33	1.9	38	2
Diarrhea	37	4.5	37	4.9
Abdominal pain ^b	32	7	31	6
Constipation	22	1.9	23	1.5
Dyspepsia	16	-	16	0
Nervous system				
Cognitive impairment ^c	44	3.9	48	4.9
Dizziness	16	0.6	22	0.5
Headache	16	0.6	17	0.5
Sleep disorders ^d	15	0	16	0
Taste effects ^e	18	0	15	0
Mood disorders ^f	11	0	13	1
Metabolism and nutrition				
Decreased appetite	36	1.9	38	2.9
Eye				
Increased lacrimation	30	-	33	0
Skin and subcutaneous tissue				
Rash ^g	18	1.3	23	2.1
Hair color changes	19	0	21	0.5
Alopecia	11	-	13	-
Respiratory, thoracic and mediastinal				
Dyspnea	14	1.9	17	2.5
Pleural effusion	12	1.3	12	2
Investigations				
Weight decreased	14	1.3	13	1

The safety profile to the left reflects exposure to AYVAKIT in patients with unresectable or metastatic GIST enrolled in NAVIGATOR. Patients received a starting dose of AYVAKIT 300 mg or 400 mg orally once daily (N=204). Among patients receiving AYVAKIT, 56% were exposed for 6 months or longer and 44% were exposed for greater than 1 year.¹

The median age of patients who received AYVAKIT was 62 years (range: 29 to 90 years), 60% were <65 years, 62% were male, and 69% were White. Patients had received a median of 3 prior kinase inhibitors (range: 0 to 7).

Clinically relevant adverse reactions occurring in <10% of patients were¹:

Vascular: hypertension (8%)

Endocrine: thyroid disorders (hyperthyroid, hypothyroid) (3%)

Skin and subcutaneous: palmar-plantar erythrodysesthesia (1%).

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.

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

^aEdema includes face swelling, conjunctival edema, eye edema, eyelid edema, orbital edema, periorbital edema, face edema, mouth edema, pharyngeal edema, peripheral edema, edema, generalized edema, localized edema, peripheral swelling, testicular edema.

^bAbdominal pain includes abdominal pain, upper abdominal pain, abdominal discomfort, lower abdominal pain, abdominal tenderness, and epigastric discomfort.

^cCognitive impairment includes memory impairment, cognitive disorder, confusional state, disturbance in attention, amnesia, mental impairment, mental status changes, encephalopathy, dementia, abnormal thinking, mental disorder, and retrograde amnesia.

^dSleep disorders includes insomnia, somnolence, and sleep disorder.

^eTaste effects includes dysgeusia and ageusia.

^fMood disorders includes agitation, anxiety, depression, depressed mood, dysphoria, irritability, mood altered, nervousness, personality change, and suicidal ideation.

^gRash includes rash, rash maculo-papular, rash erythematous, rash macular, rash generalized, and rash papular.

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

 **AYVAKIT**[®]
avapritinib | tablets

Select warnings and precautions

INTRACRANIAL HEMORRHAGE IS A POSSIBLE EFFECT OF AYVAKIT¹

Serious intracranial hemorrhage (ICH) may occur with AYVAKIT treatment; fatal events occurred in less than 1% of patients. Overall, ICH (eg, subdural hematoma, ICH, and cerebral hemorrhage) occurred in 2.9% of 749 patients who received AYVAKIT in clinical trials. In GIST patients, ICH occurred in 3 of 267 patients (1.1%). Two (0.7%) of the events were Grade ≥ 3 and resulted in discontinuation of study drug. Monitor patients closely for risk factors of ICH which may include history of vascular aneurysm, intracranial hemorrhage or cerebrovascular accident within the prior year, concomitant use of anticoagulant drugs, or thrombocytopenia. Permanently discontinue AYVAKIT if ICH of any grade occurs.

Advise patients to contact their healthcare provider immediately if experiencing neurologic signs and symptoms that may be associated with intracranial hemorrhage (ie, headache, nausea, vomiting, vision changes, or altered mental status).

COGNITIVE EFFECTS CAN OCCUR WHEN TAKING AYVAKIT¹

Cognitive adverse reactions can occur in patients receiving AYVAKIT. These cognitive adverse reactions occurred in 33% of 995 patients and in 41% of 601 patients with GIST who received AYVAKIT (5% were Grade ≥ 3). Memory impairment occurred in 21% of patients; <1% of these events were Grade 3. Cognitive disorder occurred in 12% of patients; 1.2% of these events were Grade 3. Confusional state occurred in 6% of patients; <1% of these events were Grade 3. Amnesia occurred in 3% of patients; <1% of these events were Grade 3. Somnolence and speech disorder occurred in 2% of patients; none of these events were Grade 3. Other events occurred in less than 2% of patients.

The median time to onset of the first cognitive adverse reaction was 8.4 weeks (range: 1 day to 4 years).

Depending on severity, withhold AYVAKIT and then resume at the same dose or at a reduced dose upon improvement, or permanently discontinue AYVAKIT.

INFORMATION REGARDING COGNITIVE EFFECTS:

Among patients who experienced a cognitive effect of Grade 2 or worse (impacting activities of daily living), the median time to improvement to Grade 1 or complete resolution was 7.9 weeks.¹

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.¹

Make a monitoring plan with your patients and their caregivers

Help your patients and their caregivers understand that they should be looking out for cognitive effects such as forgetfulness, confusion, getting lost, trouble thinking, drowsiness, trouble staying awake (somnolence), word finding problems, seeing objects or hearing things that are not there (hallucinations), or changes in mood or behavior. Advise patients not to drive or operate hazardous machinery if they are experiencing cognitive adverse reactions.¹

For example, create a list of questions to help your patients identify any changes in cognitive effects if they arise. Use the questions to educate patients and their caregivers about how to identify changes quickly and notify you as soon as possible to enable timely dose modifications.⁵

Work with your patients and their caregivers to establish a baseline, then set a schedule for periodic monitoring.⁵

Caregivers can ask patients taking AYVAKIT how often within the prior week they experienced difficulty with the following⁵:

1. Finding their way to familiar places, like places of work
2. Remembering where they put commonly used personal items (eg, phone, keys)
3. Recalling the name of an object during conversation
4. Keeping track of why they walked into a room
5. Speaking or thinking clearly
6. Completing a task without losing track of what they were doing

Although not comprehensive, this list can help guide the plan you make with your patient and their caregiver to monitor for cognitive effects.*

*These discussion points were adapted from FACT-Cog V3, Copyright 2006, 2016 by David Cella, PhD.⁵

Be sure to tell your patient and their caregiver how important it is that they monitor for and inform you about any adverse reactions, including possible CNS effects. Help them understand that sharing this information enables timely dose modifications.

IMPORTANT SAFETY INFORMATION

Intracranial Hemorrhage—Serious intracranial hemorrhage (ICH) may occur with AYVAKIT treatment; fatal events occurred in <1% of patients. Overall, ICH (e.g., subdural hematoma, ICH, and cerebral hemorrhage) occurred in 2.9% of 749 patients who received AYVAKIT in clinical trials. In GIST patients, ICH occurred in 3 of 267 patients (1.1%) and two (0.7%) of the events were Grade ≥ 3 and resulted in discontinuation.

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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 of AYVAKIT. Advise women not to breastfeed during treatment with AYVAKIT and for 2 weeks following the final dose.

Adverse Reactions—The most common adverse reactions ($\geq 20\%$) were edema, nausea, fatigue/asthenia, cognitive impairment, vomiting, decreased appetite, diarrhea, increased lacrimation, abdominal pain, constipation, rash, dizziness, and hair color changes.

Drug Interactions—Avoid coadministration of AYVAKIT with strong or moderate CYP3A inhibitors. If coadministration with a moderate CYP3A inhibitor cannot be avoided, reduce dose of AYVAKIT. Avoid coadministration of AYVAKIT with strong or moderate CYP3A 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 www.fda.gov/medwatch.

AYVAKIT is available in 100-mg, 200-mg, and 300-mg tablets.

Please click here to see the full [Prescribing Information](#) for AYVAKIT.

The following case studies are fictional but based on clinical trial experience with avapritinib. Healthcare providers should make all treatment decisions based on the prescribing information, individual patient profile, and their clinical judgment. Individual results may vary.



64-year-old female diagnosed with GIST

INITIAL TREATMENT

- Patient undergoes resection of a primary GIST of the stomach (9 cm)
- Mutational testing confirms patient's tumor harbors the PDGFRA D842V mutation; imatinib considered not an appropriate adjuvant treatment
- Patient is considered intermediate risk for relapse
- One year after initial resection, patient relapses and metastatic disease is confirmed

INTRODUCTION OF AYVAKIT

- Patient is prescribed AYVAKIT 300 mg once daily
- Approximately 1 month into treatment, patient's husband notices she keeps misplacing her keys
- Patient is determined as having Grade 1 memory impairment
- Per dosing guidelines, dosage is interrupted until improvement. After a 5-day break, patient resumes at 200 mg once daily while monitoring continues

CONTINUED TREATMENT

- After 3 months of therapy at 200 mg daily, patient's spouse notifies nurse practitioner that the patient has been experiencing forgetfulness and word-finding difficulty
- Patient's memory impairment is determined to have progressed to Grade 2
- Per dosing guidelines, dosage is once again interrupted until resolution and eventually lowered to 100 mg; monitoring continues
- After 1 year of treatment, patient continues to be maintained on therapy at 100 mg daily and is tolerating it well without any new signs of cognitive impairment



71-year-old male with metastatic GIST

PATIENT HISTORY AND INTRODUCTION OF AYVAKIT

- Patient harbors the PDGFRA exon 18 mutation
- Previously treated with imatinib and sunitinib
- Patient is prescribed AYVAKIT 300 mg once daily

ADVERSE EVENTS

- After 3 months of treatment, patient is tolerating the drug despite a mild periorbital edema
- Patient experienced a similar adverse event during previous treatment with imatinib
- Patient noted to have Grade 1 periorbital edema. No dose adjustment required; care team proceeds with continued monitoring

CONTINUED TREATMENT

- After 6 months of therapy, patient presents with worsening periorbital edema (now Grade 2) and Grade 3 anemia
- Per dosing guidelines, dose is interrupted due to onset of Grade 3 anemia
- Patient takes a break from dosing for 7 days
- Hemoglobin improves to 9.8 g/dL (Grade 2)
- Patient then resumes at 200 mg once daily
- Patient continues regimen of AYVAKIT 200 mg daily; no new notable adverse events reported

► **It is important to review the benefits and risks associated with AYVAKIT before initiating patients on therapy**



IN THE NAVIGATOR STUDY IT WAS COMMON TO MODIFY AYVAKIT DOSES¹

The recommended dosage of AYVAKIT is 300 mg orally once daily. Dosage may be lowered to 200 mg once daily for first dose reduction and 100 mg once daily for second dose reduction for adverse reactions.



SIDE EFFECTS

Recognizing any changes in how your patient is tolerating AYVAKIT, early and throughout treatment, is important. AYVAKIT may cause certain side effects that the patient did not experience while on other medicines. Ensure your patients are discussing any potential side effects of AYVAKIT with their family or caregiver. Encourage patients and their caregivers to contact you if they experience side effects.



RESOURCES

There are various resources for patients starting AYVAKIT that are available in print, online, or over the phone. Review these with your patient or contact your local Blueprint Medicines representative if you need help accessing them.

► **Support and financial assistance options for your patients taking AYVAKIT**



Enroll your patients at time of prescription to support the patient experience and access to programs.

YourBlueprint® provides dedicated, personalized support to help your patients from Day 1.

Blueprint Medicines offers a series of programs to support patient access, including:

- Co-pay Support
- Patient Assistance Program
- Quick Start
- Prior Authorization Support
- Coverage Interruption

To see how we can help:



Call: **1-888-BLUPRNT (1-888-258-7768)**

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

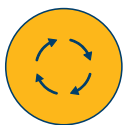
Email: info@yourblueprint.com

Fax: **1-866-370-3082**

Visit: www.YourBlueprint.com/HCP

AYVAKIT®
avapritinib | tablets

Managing your patients taking AYVAKIT



INITIATE

The recommended dosage of AYVAKIT in patients with GIST is 300 mg orally once daily. AYVAKIT is also available in 100-mg and 200-mg dose strengths.¹



MONITOR

Note your patient's baseline signs and symptoms and observe them for early signs of adverse reactions to determine if dose modifications may be appropriate.¹



OPTIMIZE

In the NAVIGATOR Study it was common to modify AYVAKIT doses. Modify dose as needed for each individual patient and see the detailed dose modification information within this guide and the AYVAKIT prescribing information.^{1,3}

For additional information about AYVAKIT, visit AYVAKITHCP.com/GIST-HCP.

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 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 following the final dose.

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

References: **1.** AYVAKIT [prescribing information]. Cambridge, MA: Blueprint Medicines Corporation; November 2024. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Gastrointestinal Stromal Tumors V.1.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed May 15, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **3.** Joseph CP, et al. *Oncologist*. 2021;26(4):e622-e631. **4.** Data on file. Blueprint Medicines Corporation, Cambridge, MA. 2021. **5.** Cella D. FACIT Measurement System. FACT-Cog: For patients with Cognitive function issues. FACIT. Accessed May 15, 2024. <https://www.facit.org/measures/FACT-Cog>