

Transcript Details

This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: <https://reachmd.com/programs/medical-industry-feature/mechanism-treatment-approach-indolent-systemic-mastocytosis-ism/32766/>

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Understanding the Mechanism Behind a Treatment Approach in Indolent Systemic Mastocytosis (ISM)

Onscreen text:

[AYVAKIT 25mg logo]

AYVAKIT and its role in treating **INDOLENT SYSTEMIC MASTOCYTOSIS (ISM)**¹

INDICATION

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

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

Please see Important Safety Information near the end of this video.

See full Prescribing Information for AYVAKIT at AYVAKITPI.com.

Voice-over:

AYVAKIT and its role in treating indolent systemic mastocytosis, or ISM.

INDICATION

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

Limitations of Use: AYVAKIT is not recommended for the treatment of patients with ISM with platelet counts of less than 50,000 per microliter.

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Voice-over:

Mast cells play a key role in the immune system, particularly in allergic responses.

Voice-over:

During a typical immune response, normal mast cells degranulate, releasing inflammatory mediators such as leukotrienes, histamine, and tryptase.

Onscreen text:

leukotrienes

histamine

tryptase

Voice-over:

Stem cell factor, or SCF, regulates mast cells by binding to KIT receptors on the cell surface to drive their maturation, proliferation, and survival.

Onscreen text:

Stem cell factor

Voice-over:

In approximately 95% of ISM cases, gain-of-function mutations in the KIT gene—particularly the D816V mutation—can lead to the unregulated proliferation and activation of abnormal mast cells.

Onscreen text:

KIT mutations, like D816V, can lead to unregulated proliferation and activation of abnormal mast cells.^{2,4-8}

Voice-over:

Improper signaling caused by the KIT mutation, independent of stem cell factor, bypasses the normal checks and balances that regulate mast cells. This results in continuous reproduction, survival, and activation of abnormal mast cells.

Onscreen text:

Improper signaling results in continuous reproduction, survival, and activation of abnormal mast cells.⁴

Voice-over:

These abnormal mast cells accumulate in the body and can degranulate unpredictably, and can lead to...

Onscreen text:

Abnormal mast cells accumulate throughout the body...

Voice-over:

...organ infiltration and potentially debilitating symptoms like skin lesions, flushing, rash, brain fog, abdominal cramping, diarrhea, life-threatening anaphylaxis, and more.

Onscreen text:

...and can lead to symptoms like skin lesions, flushing, rash, brain fog, abdominal cramping, diarrhea, life threatening anaphylaxis, and more.^{2,4,5}

skin

neuropsychiatric

gastrointestinal

systemic

Voice-over:

Though symptoms sometimes can be addressed with over-the-counter or other symptom-directed therapies, they do not target the source of disease, and uncontrolled symptoms can still persist in some patients.

Onscreen text:

Over-the-counter or other symptom-directed therapies may relieve individual symptoms but don't target the source of disease.⁵

Voice-over:

AYVAKIT, a tyrosine kinase inhibitor, or TKI, was designed to target the KIT D816V mutation.

By targeting KIT D816V—the underlying cause of ISM, and not just the symptoms—AYVAKIT, as demonstrated in cellular assays, reduces the self-activation process, inhibiting the production of these abnormal mast cells responsible for the symptoms of ISM.

Onscreen text:

AYVAKIT, a tyrosine kinase inhibitor (TKI), targets the KIT D816V mutation^{1,4}

Demonstrated in cellular assays

Inhibits production of abnormal mast cells^{1,4}

Voice-over:

If abnormal mast cells remain uncontrolled, they continue to accumulate, and patients using over-the-counter or other symptom-directed therapies may still experience symptoms.

Adding AYVAKIT can help reduce the production of abnormal mast cells that are responsible for ISM symptoms.

Historically, ISM care focused on treating symptoms—AYVAKIT targets the KIT D816V mutation, the underlying cause of ISM.

Considering adding AYVAKIT for your patients with ISM.

Onscreen text:

Patients using over-the-counter or other symptom-directed therapies may still experience symptoms.

Consider adding AYVAKIT for your patients with ISM.^{1,5}

Voice-over:

INDICATION

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Limitations of Use: AYVAKIT is not recommended for the treatment of patients with ISM with platelet counts of less than 50,000 per microliter.

IMPORTANT SAFETY INFORMATION

Cognitive adverse reactions can occur in patients receiving AYVAKIT and occurred in 7.8% of patients with ISM who received AYVAKIT plus best supportive care (BSC) versus 7% of patients who received placebo plus BSC; less than 1% were Grade 3. Depending on the severity, withhold AYVAKIT and then resume at the same dose, or permanently discontinue AYVAKIT.

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.

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.

The most common adverse reactions (greater than or equal to 10%) in patients with ISM were eye edema, dizziness, peripheral edema, and flushing.

Avoid coadministration of AYVAKIT with strong or moderate CYP3A inhibitors or inducers. If contraception requires estrogen, limit ethinyl estradiol to less than or equal to 20 micrograms unless a higher dose is necessary.

AYVAKIT is available in 25-mg tablets.

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 see the accompanying full [Prescribing Information](#) for AYVAKIT.

Onscreen text:

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IMPORTANT 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 plus best supportive care (BSC) versus 7% of patients who received placebo plus BSC; less than 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 ($\geq 10\%$) 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.

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To learn more, visit AYVAKITHCP.com/ism.

[Blueprint and AYVAKIT 25mg logos]

References:

1. AYVAKIT [prescribing Information]. Cambridge, MA: Blueprint Medicines Corporation; November 2024.
2. Akin C, ed. *Mastocytosis: A Comprehensive Guide*. Springer; 2020.
3. Theoharides TC et al. *N Engl J Med*. 2015;373(2):163-172.
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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. Data on file. Blueprint Medicines Corporation, Cambridge, MA.

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