AYVAKYT® ▼
(avapritinib)

AYVAKYT® (avapritinib) is indicated for the treatment of adult patients with indolent systemic mastocytosis (ISM) with moderate to severe symptoms inadequately controlled on symptomatic treatment.[1]

The First Targeted Therapy for Adults With Indolent Systemic Mastocytosis (ISM)[1,2]

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 of the Summary of Product Characteristics (SmPC) for how to report adverse reactions.

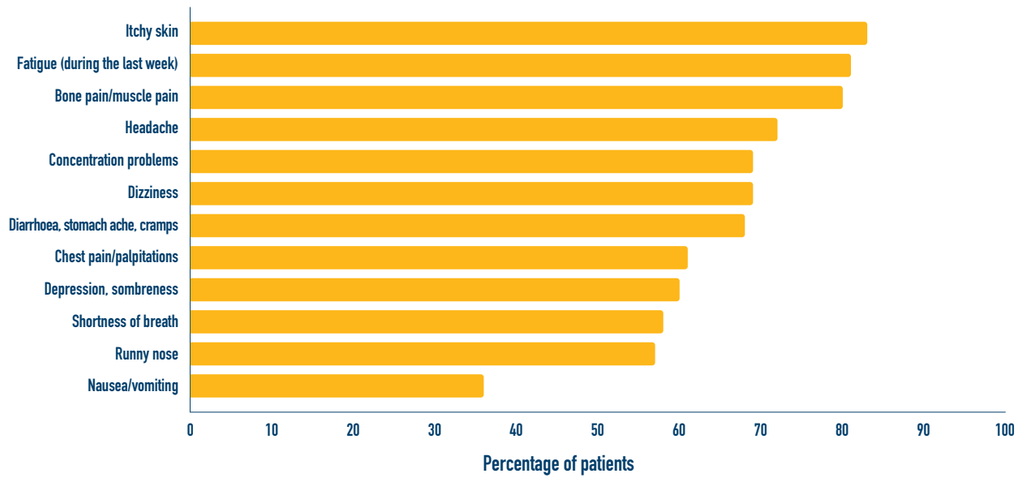
Intended for healthcare professionals only

Please see Prescribing Information on pages 14 and 15.

Patients with ISM suffer disrupted quality of life despite symptomatic treatment[2–5]

Indolent systemic mastocytosis (ISM) is a rare and potentially debilitating mast cell disease.[2,4] Patients with ISM can suffer from a wide range of symptoms[2]

SYMPTOMS OF INDOLENT SYSTEMIC MASTOCYTOSIS (N=164)[6]



Modified from van Anrooj B, *et al.* 2016. Based on a Dutch cohort of 164 patients with ISM.[6]

Results from the PRISM Europe survey showed:[3]

Between 9% and 42% of HCPs perceived that ISM impacts their patients 'quite a bit'*

Patients with ISM experience **high symptom burden** even with an average lifetime use of 8 medications†

Despite current care, **43% of patients with ISM reported an impact on work**, with 24% reducing work hours and 17% taking medical disability‡

*The reported values reflect the range observed across countries (Italy [n=201], Germany [n=122], UK [n=110], Austria [n=63], France [n=52], Switzerland [n=44] and Spain [n=19]). HCPs scored each statement on a 1–5 scale with the following items: A great deal; Quite a bit; Somewhat; A little bit; Not at all.[3]

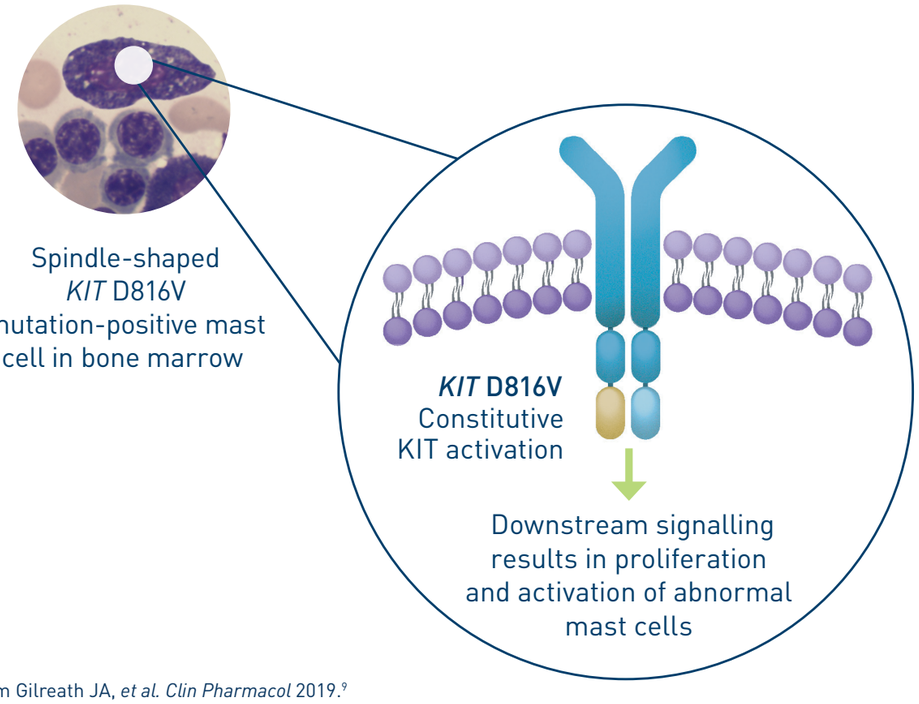
†Data based on 237 patients with an ISM diagnosis who participated in the PRISM patient survey.[3]

‡Please note that these numbers represent the summed values of specific underlying scores. Patients scored each statement on a 1–5 scale with the following items: Yes, frequently part-time; Yes, frequently unemployed; Yes, frequently dismissed; No; Unsure.[3]

ISM is driven by the *KIT* D816V mutation in ~95% of cases[7,8]

Historically, there have been no approved treatments that selectively target the underlying driver of disease in ISM[2]

The *KIT* D816V mutation constitutively activates downstream signalling pathways regulating cellular functions, including proliferation and survival of abnormal mast cells.[9]



Adapted from Gilreath JA, *et al. Clin Pharmacol* 2019.[9]

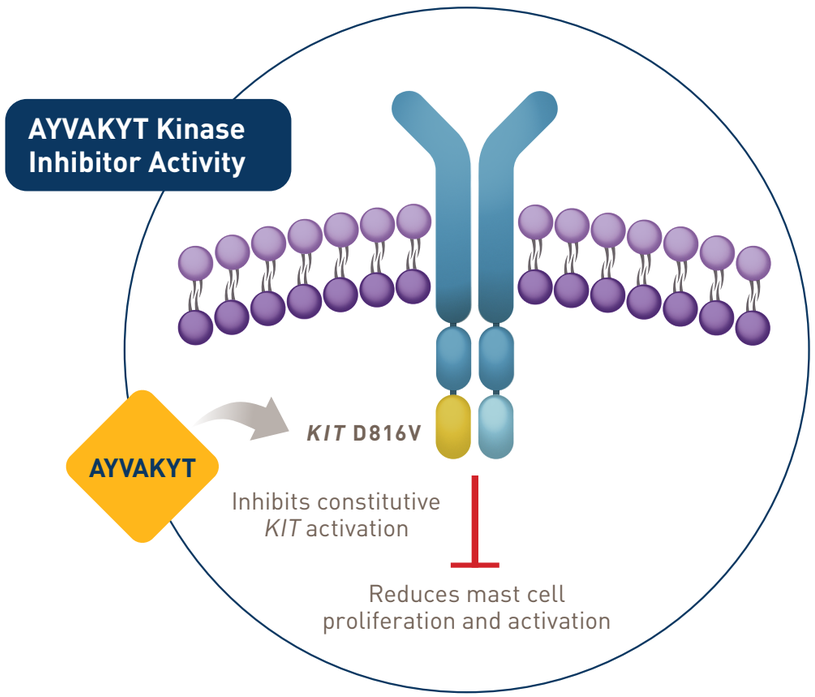
KIT=KIT proto-oncogene, receptor tyrosine kinase

AYVAKYT® (avapritinib)

AYVAKYT is a highly selective inhibitor of the underlying driver of disease, *KIT* D816V[1,2]

AYVAKYT potently and selectively inhibits *KIT* D816V[1]

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



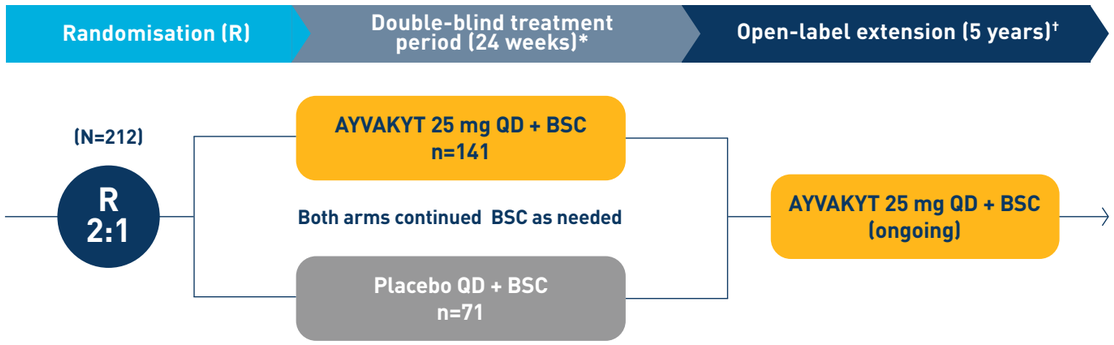
Adapted from Gilreath JA, *et al. Clin Pharmacol* 2019.[9]

KIT=KIT proto-oncogene, receptor tyrosine kinase.

AYVAKYT was evaluated in the largest ever trial of patients with ISM, PIONEER[1,2]

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

STUDY DESIGN[1,2]



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

- Key eligibility criteria: ≥18 years of age; ISM confirmed by central pathology review; uncontrolled moderate to severe ISM, defined as ISM-SAF TSS ≥28[1,2]
- **Primary endpoint:** Mean change in ISM-SAF TSS from baseline to Week 24[1,2]
  - **Select key secondary endpoints:** ≥50% reduction in serum tryptase levels; ≥50% reduction in *KIT* D816V VAF; ≥50% reduction in bone marrow mast cells[1,2]
  - **Additional select secondary endpoints:** Mean change in ISM-SAF individual symptom scores (defined as the most severe symptom with the highest score at baseline in each patient)[2]

BSC=best supportive care; ISM-SAF=Indolent Systemic Mastocytosis-Symptom Assessment Form; OLE=open-label extension; QD=once daily; TSS=total symptom score; VAF=variant allele fraction.

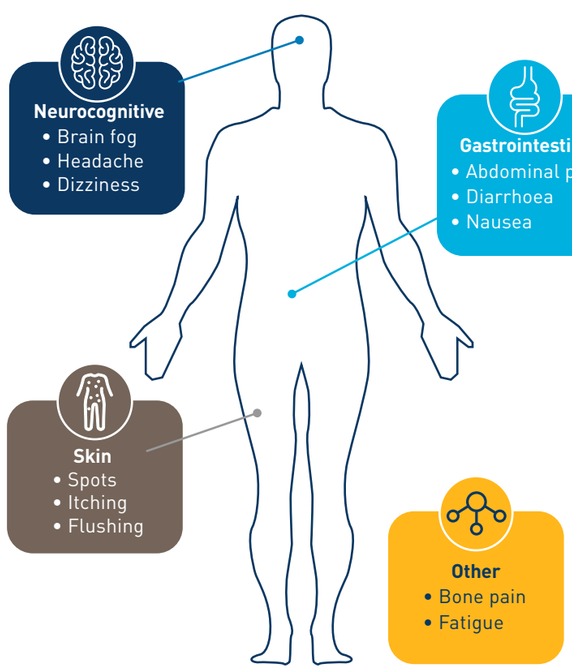
Please see Prescribing Information on pages 14 and 15.

AYVAKYT® (avapritinib)

In PIONEER, symptom severity in ISM was assessed using ISM–SAF TSS, a validated clinical endpoint[2]

The ISM-SAF was developed to measure the severity of 11 ISM-related symptoms and was designed with input from regulatory authorities, patients and therapeutic area experts[10]

Individual symptom scores are evaluated, and the 11 symptom severity scores are combined to calculate the TSS (0–110).[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[2]

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

Patient characteristics in PIONEER were balanced between both arms[2]

Patients in PIONEER were required to have failed to achieve adequate symptom control for one or more ISM symptoms with at least two symptomatic treatments.[1,2]

SELECT BASELINE PATIENT CHARACTERISTICS (N=212)[2]

Patient characteristics	AYVAKYT + BSC (n=141)	Placebo + BSC (n=71)
Median age (range)	50 years (18–77)	54 years (26–79)
Sex	~71% female, ~29% male	~76% female, ~24% male
Mean ISM-SAF TSS (SD)	50.2 (19.1)	52.4 (19.8)
Median number 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)
KIT D816V VAF in peripheral blood (≥0.02%)	~84%	~89%
Mast cell aggregates present	~75%	~80%

Modified from the Gotlib 2023 study.[2]

- BSC medications allowed in the PIONEER study included the following classes of agents that block the action of histamine at H1 and H2 receptors; proton pump inhibitors; osteoclast inhibitors (such as bisphosphonates, denosumab); leukotriene receptor antagonists and synthesis inhibitors; corticosteroids (<20 mg of prednisone or equivalent); cromolyn sodium and other mast-cell stabilisers such as ketotifen; and the anti-immunoglobulin E antibody therapy, omalizumab
- Other baseline characteristics were similar between treatment groups[2]

BSC=best supportive care; ISM-SAF=Indolent Systemic Mastocytosis-Symptom Assessment Form; *KIT*=KIT proto-oncogene, receptor tyrosine kinase; SD=standard deviation; TSS=total symptom score; VAF=variant allele fraction.

Please see Prescribing Information on pages 14 and 15.

Please see Prescribing Information on pages 14 and 15.

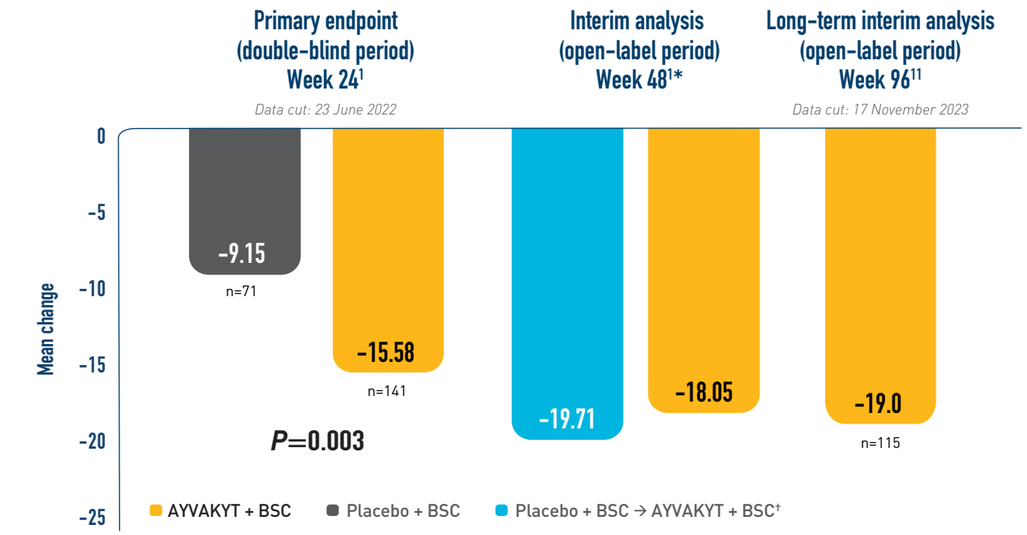
AYVAKYT® (avapritinib)

AYVAKYT + BSC demonstrated significant improvement in patients' overall symptom burden vs placebo + BSC at Week 24[1,2]

PRIMARY ENDPOINT[1]

Week 24	AYVAKYT + BSC n=141[1]	Placebo + BSC n=71[1]	*P*-value
Mean change in ISM-SAF TSS (95% CI)[1]	−15.58 (−18.61, −12.55)	−9.15 (−13.12, −5.18)	0.003

MEAN CHANGE IN ISM-SAF TSS AT WEEKS 24



*For AYVAKYT-treated patients who rolled over into the open-label long-term study, PIONEER Part 3. Overall, 201 patients rolled over from Part 2 into Part 3 of PIONEER.[1]

†Placebo patients were allowed to move into an open-label ongoing AYVAKYT crossover arm, with TSS data available from Week 24 onwards.[1]

AYVAKYT treatment delivered consistent symptom improvement through to Week 96.[1,2,11] Patients in the AYVAKYT + BSC arm continued to report improvements in TSS over time, with a mean TSS reduction of -19.0 from baseline at Week 96[11]

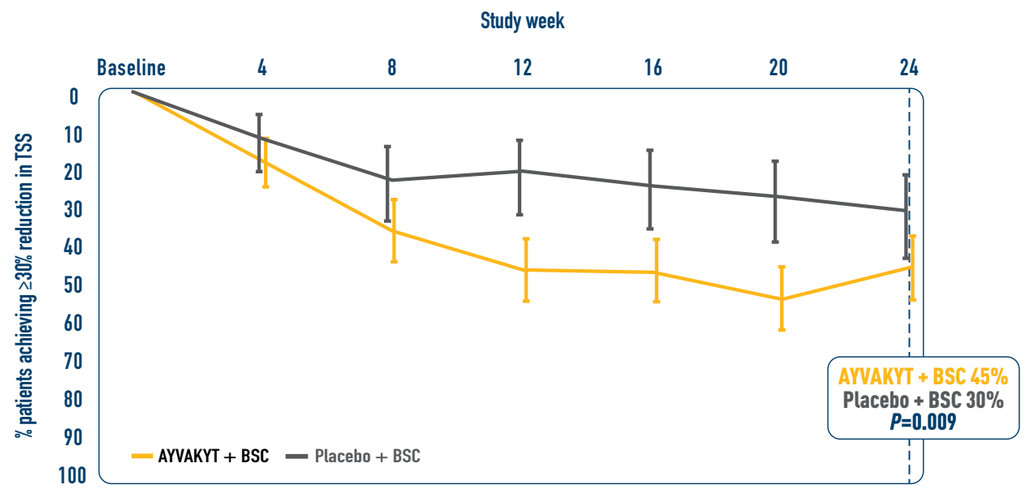
AYVAKYT + BSC showed a statistically significant improvement in ISM-SAF TSS vs placebo at Week 24[1,2]

BSC=best supportive care; CI=confidence interval; ISM-SAF=Indolent Systemic Mastocytosis-Symptom Assessment Form; TSS=total symptom score.

AYVAKYT demonstrated statistically significant improvements using ≥30% TSS threshold[1]

KEY SECONDARY ENDPOINT[1]

PROPORTION OF PATIENTS ACHIEVING ≥30% REDUCTION IN ISM-SAF TSS THROUGH 24 WEEKS[1,2]



Number of patients							
AYVAKYT + BSC	139	135	133	133	135	134	131
Placebo + BSC	71	71	71	68	67	66	66

A 30% reduction in TSS was selected as a valid and conservative threshold to represent the clinically important response or improvement at the individual level[2,10]

Patients in the AYVAKYT + BSC arm demonstrated clinically meaningful reductions in TSS vs placebo + BSC at Week 24, as judged using a well established threshold for %TSS reduction[1,2,10]

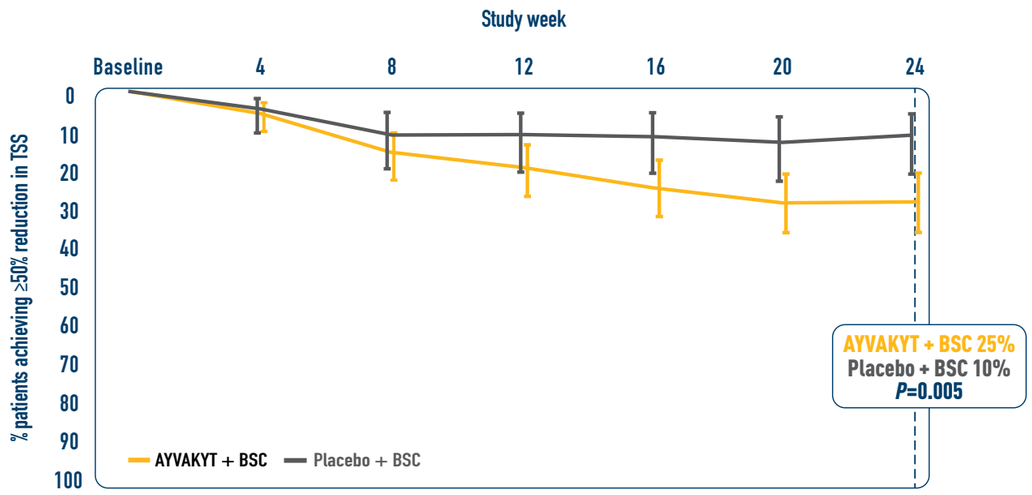
BSC=best supportive care; ISM-SAF=Indolent Systemic Mastocytosis-Symptom Assessment Form; TSS=total symptom score.

AYVAKYT® (avapritinib)

AYVAKYT demonstrated statistically significant improvements using ≥50% TSS threshold[1]

KEY SECONDARY ENDPOINT[1]

PROPORTION OF PATIENTS ACHIEVING ≥50% REDUCTION IN ISM-SAF TSS THROUGH 24 WEEKS[1,2]



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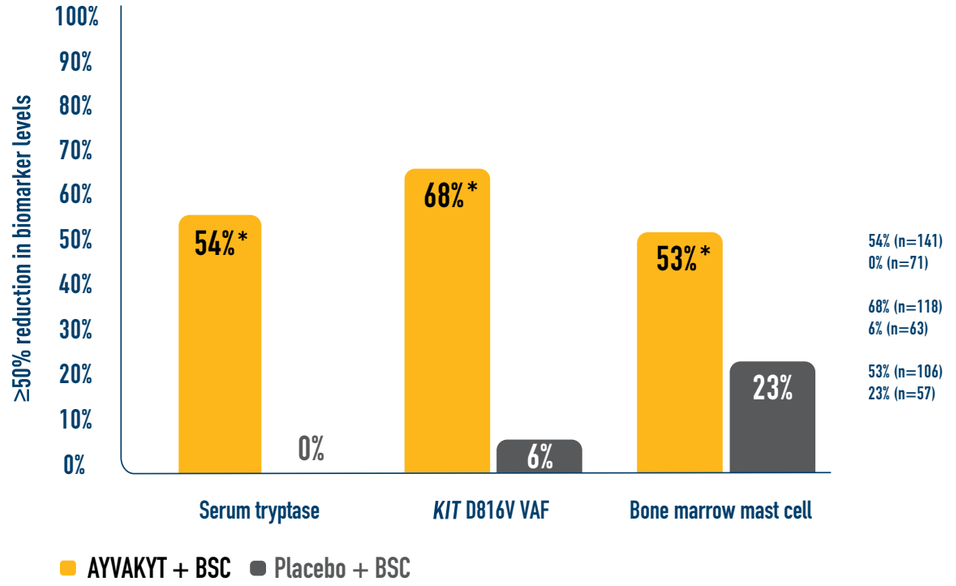
BSC=best supportive care; ISM-SAF=Indolent Systemic Mastocytosis-Symptom Assessment Form; TSS=total symptom score.

AYVAKYT + BSC showed significant improvements in objective mast cell measures vs placebo + BSC at Week 24[1]

KEY SECONDARY ENDPOINTS[1]

More than half of patients treated with AYVAKYT + BSC experienced ≥50% reductions in serum tryptase, *KIT* D816V VAF and bone marrow mast cell levels[1]

PROPORTION OF PATIENTS ACHIEVING ≥50% REDUCTION IN BIOMARKER LEVELS AT 24 WEEKS[1]



* *P*<0.0001 for the difference between AYVAKYT + BSC and placebo + BSC.

ITT analysis: For patients with high-dose glucocorticoid 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 considered missing for the primary efficacy analysis but was included in the figures of change over time.[2]

BSC=best supportive care; ITT=intention to treat; *KIT*=KIT proto-oncogene, receptor tyrosine kinase; VAF=variant allele fraction.

AYVAKYT® (avapritinib)

25 mg AYVAKYT daily is well tolerated at Week 24,[1,2] with a consistent safety profile observed through 96 weeks[11]

Week 24

The most common AEs reported in the AYVAKYT plus BSC treatment arm were flushing and oedema of which almost all were Grade 1 or 2[1]*

ADVERSE REACTIONS REPORTED IN CLINICAL STUDIES OF AYVAKYT IN PATIENTS WITH ISM[1]

Adverse reactions*	AYVAKYT + BSC All grades, n=141 (%)	AYVAKYT + BSC Grades ≥3, n=141 (%)
Insomnia	5.7	-
Flushing	9.2	1.4
Photosensitivity reaction	2.8	-
Peripheral oedema†	12.1	-
Face oedema	7.1	-
Blood alkaline phosphatase increased	6.4	0.7

*The severity of adverse reactions graded by the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) versions 4.03 and 5.0. Adverse reactions reported in Part 2 of the PIONEER study in ≥5% of patients.

†Including oedema peripheral and peripheral swelling.

-No adverse reactions reported.

Week 96 (Data cut: 17 November 2023)

AEs with 25 mg AYVAKYT daily up to 96 weeks were mainly mild to moderate, most commonly headache, peripheral oedema, periorbital oedema, and nausea[11]

AYVAKYT patients had **a discontinuation rate** of 2% (n=5), and 1% (n=2) had a **treatment-related serious AE** over 96 weeks[11]

3% (n=6) of patients **had hair depigmentation** after 96 weeks on AYVAKYT[11]

Over 96 weeks on AYVAKYT 3% (n=7) of patients had **transaminase elevations**, all mild or moderate only[11]

AE=adverse event; BSC=best supportive care.

AYVAKYT is recommended as one daily tablet in ISM[1]

AYVAKYT should be taken:[1]

- As one 25 mg tablet orally
- Once daily
- On an empty stomach, at least 1 hour before or at least 2 hours after a meal

A modified starting dose of AYVAKYT is recommended for patients with severe hepatic impairment (Child-Pugh Class C): 25 mg orally once every other day. Patients requiring dose reduction below 25 mg once every other day must discontinue treatment.[1]

Concomitant use of AYVAKYT with strong or moderate CYP3A inhibitors must be avoided.[1]

AYVAKYT® (avapritinib)

Abbreviated Prescribing Information

AYVAKYT 25 mg film-coated tablets
AYVAKYT 50 mg film-coated tablets
AYVAKYT 100 mg film-coated tablets
AYVAKYT 200 mg film-coated tablets
AYVAKYT 300 mg film-coated tablets
Active substance: avapritinib

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 of the Summary of Product Characteristics (SmPC) for how to report adverse reactions.

Qualitative and quantitative composition:
AYVAKYT 25 mg film-coated tablets Each film-coated tablet contains 25 mg of avapritinib.
AYVAKYT 50 mg film-coated tablets Each film-coated tablet contains 50 mg of avapritinib.
AYVAKYT 100 mg film-coated tablets Each film-coated tablet contains 100 mg of avapritinib.
AYVAKYT 200 mg film-coated tablets Each film-coated tablet contains 200 mg of avapritinib.
AYVAKYT 300 mg film-coated tablets Each film-coated tablet contains 300 mg of avapritinib.

List of excipients:
Tablet core: microcrystalline cellulose, copovidone, croscarmellose sodium, magnesium stearate; tablet coat: talc, macrogol 3350, poly(vinyl alcohol), titanium dioxide (E171); printing ink (only 100 mg, 200 mg and 300 mg film-coated tablets): shellac glaze 45% (20% esterified) in ethanol, brilliant blue FCF (E133), titanium dioxide (E171), black iron oxide (E172), propylene glycol.

Therapeutic indications:
Unresectable or metastatic gastrointestinal stromal tumour (GIST)

AYVAKYT is indicated as monotherapy for the treatment of adult patients with unresectable or metastatic gastrointestinal stromal tumours (GIST) harbouring the platelet-derived growth factor receptor alpha (PDGFRA) D842V mutation.

Advanced systemic mastocytosis (AdvSM)

AYVAKYT is indicated as monotherapy for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated haematological neoplasm (SM-AHN) or mast cell leukaemia (MCL), after at least one systemic therapy.

Indolent systemic mastocytosis (ISM)

AYVAKYT is indicated for the treatment of adult patients with indolent systemic mastocytosis (ISM) with moderate to severe symptoms inadequately controlled on symptomatic treatment.

Contraindications: Hypersensitivity to the active substance or to any of the excipients.

Undesirable effects:
Unresectable or metastatic GIST: *very common (≥ 1/10):* anaemia, white blood cell count decreased, neutrophil count decreased, decreased appetite, memory impairment, cognitive disorder, dizziness, taste effect, lacrimation increased, abdominal pain, vomiting, diarrhoea, nausea, dryness, gastroesophageal reflux disease, hyperbilirubinaemia, hair colour changes, rash, oedema, fatigue, transaminases increased; *common (≥ 1/100, < 1/10):* conjunctivitis, thrombocytopenia, lymphocyte count decreased, hypophosphataemia, hypokalaemia, hypomagnesaemia, hyponatraemia, dehydration, hypoalbuminaemia, hypocalcaemia, confusional state, depression, anxiety, insomnia, intracranial haemorrhage, mental impairment, neuropathy peripheral, somnolence, aphasia, hypokinesia, headache, balance disorder, speech disorder, tremor, ocular haemorrhage, vision blurred, conjunctival haemorrhage, photophobia, vertigo, hypertension, pleural effusion, dyspnoea, nasal congestion, cough, gastrointestinal haemorrhage, ascites, constipation, dysphagia, stomatitis, flatulence, salivary hypersecretion, palmar-plantar erythrodysaesthesia syndrome, photosensitivity reaction, skin hypopigmentation, pruritus, alopecia, myalgia, arthralgia, back pain, muscle spasms, acute kidney injury, blood creatinine increased, haematuria, asthenia, pyrexia, malaise, feeling cold, electrocardiogram QT prolonged, blood creatine phosphokinase increased, weight decreased, weight increased, blood lactate dehydrogenase increased; *uncommon (≥ 1/1.000, < 1/100):* tumour haemorrhage, encephalopathy, pericardial effusion, hepatic haemorrhage.

Advanced systemic mastocytosis: *very common (≥ 1/10):* thrombocytopenia, anaemia, neutropenia, taste effect, cognitive disorder, diarrhoea, nausea, hair colour changes, oedema, fatigue; *common (≥ 1/100, < 1/10):* leukopenia, confusional state, headache, memory impairment, dizziness, neuropathy peripheral, intracranial haemorrhage, lacrimation increased, epistaxis, pleural effusion, vomiting, gastroesophageal reflux disease, ascites, dryness, constipation, abdominal pain, gastrointestinal haemorrhage, hyperbilirubinaemia, rash, alopecia, arthralgia, pain, weight increased, blood alkaline phosphatase increased, transaminase increased, electrocardiogram QT prolonged, contusion; *uncommon (≥ 1/1.000, < 1/100)*: pericardial effusion, photosensitivity reaction, acute kidney injury.

Indolent systemic mastocytosis: *very common (≥ 1/10):* peripheral oedema; *common (≥1/100, < 1/10):* insomnia, flushing, photosensitivity reaction, face oedema, blood alkaline phosphatase increased.

General classification for supply: Germany: medicinal product subject to medical prescription. Austria: available only on prescription and only in pharmacies, repeated dispensation prohibited.

Pharmacotherapeutic group: antineoplastic agents, protein kinase inhibitor, ATC code: L01EX18.

Pharmaceutical entrepreneur/Marketing authorisation holder: Blueprint Medicines (Netherlands) B.V., Gustav Mahlerplein 2, 1082 MA Amsterdam, Netherlands.

Further information: For detailed information on warnings and precautions for use, interactions, pregnancy and lactation as well as undesirable effects, please refer to the published Summary of Product Characteristics.

Status: March 2024

AYVAKYT® ▼
(avapritinib)

AYVAKYT is the first targeted therapy approved for ISM[1,2]

ISM is a mast cell-driven disease that can cause multiple and individual symptoms.[2,4]

AYVAKYT is a **highly selective inhibitor of the underlying driver of disease, *KIT* D816V**[1,2]

25 mg AYVAKYT daily is well tolerated at Week 24,[1,2] **with a consistent safety profile** observed through 96 weeks[11]

AYVAKYT-targeted inhibition of *KIT* D816V demonstrated **sustained clinical benefits across primary and key secondary endpoints in ISM**[1,2,11]

AEs with 25 mg AYVAKYT daily up to 96 weeks were **mainly mild to moderate, most commonly headache, peripheral oedema, periorbital oedema, and nausea**[11]

Please see Prescribing Information on pages 14 and 15, and the accompanying full Prescribing Information for AYVAKYT.

References: 1. AYVAKYT (avapritinib). Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/ayvakyt-epar-product-information_en.pdf. Last accessed March 2026. **2.** Gotlib J, *et al. NEJM Evid.* 2023;2(6):EVIDoa2200339. **3.** Triggiani M, *et al. Clin Exp Allergy.* 2025;55(9):784–794. **4.** Mesa RA, *et al. Cancer.* 2022;128(20):3700–3708. **5.** Kurtin S, *et al. J Adv Pract Oncol.* 2025:1-11. **6.** van Anrooj B, *et al. Allergy.* 2016;71(11):1585–1593.**7.** Muñoz-González JI, *et al. Blood.* 2019;134(5):456–468. **8.** Ungerstedt J, *et al. Cancers.* 2022;14(16):3942. **9.** Gilreath JA, *et al. Clin Pharmacol.* 2019:11:77-92. **10.** Padilla B, *et al. Orphanet J Rare Dis.* 2021;16:434. **11.** Castells M, *et al. J Allergy Clin Immunol Pract.* 2025;13(8):2194-2196.e1.

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