AYVAKYT® ▼
(avapritinib)

The Only Targeted Therapy Designed for Potent and Highly Selective Inhibition of *KIT* D816V for the Treatment of Advanced Systemic Mastocytosis[1–3]

INDICATION

AYVAKYT is indicated as a 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.**[1]

▼ 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.

Abbreviated Prescribing Information can be found on page 14.

Advanced SM is associated with shortened overall survival[4,5]

Advanced SM is a clonal mast-cell neoplasm, causing **shortened survival as well as symptom burden and impact to quality of life.[4–8]**

Patients may exhibit debilitating mast cell mediator symptoms, such as rash and life-threatening anaphylaxis.[5–7]

Additionally, patients with Advanced SM can experience organ damage, including ascites, osteolytic lesions, pleural effusion, liver dysfunction, weight loss, cytopenias, and hypersplenism.[5–7, 9–11]

HISTORICAL MEDIAN OVERALL SURVIVAL (OS) FOR PATIENTS WITH ADVANCED SM[5]

Adapted from Lim K-H, *et al*. 2009.

Overall survival was examined in a retrospective study at the Mayo Clinic between 1976 and 2007. Median follow-up was 20.7 months.[5]

*A later study with 23 MCL patients demonstrated a median overall survival for patients with MCL of 1.9 years, with a 10-year survival of 29.9%.[4]

Advanced SM may be missed in patients with other myeloid neoplasms.[12]

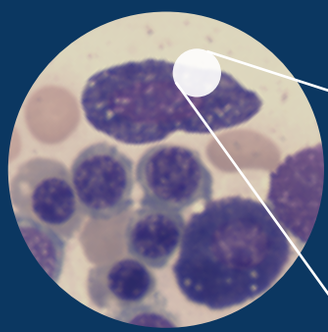
The median time from symptom onset to diagnosis for patients with Advanced SM is 3 years.[6†]

[†]Based on data from patients with self-reported Advanced SM (n=13) in the US Mast Cell Connect registry in the Jennings 2018 study.[6]

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

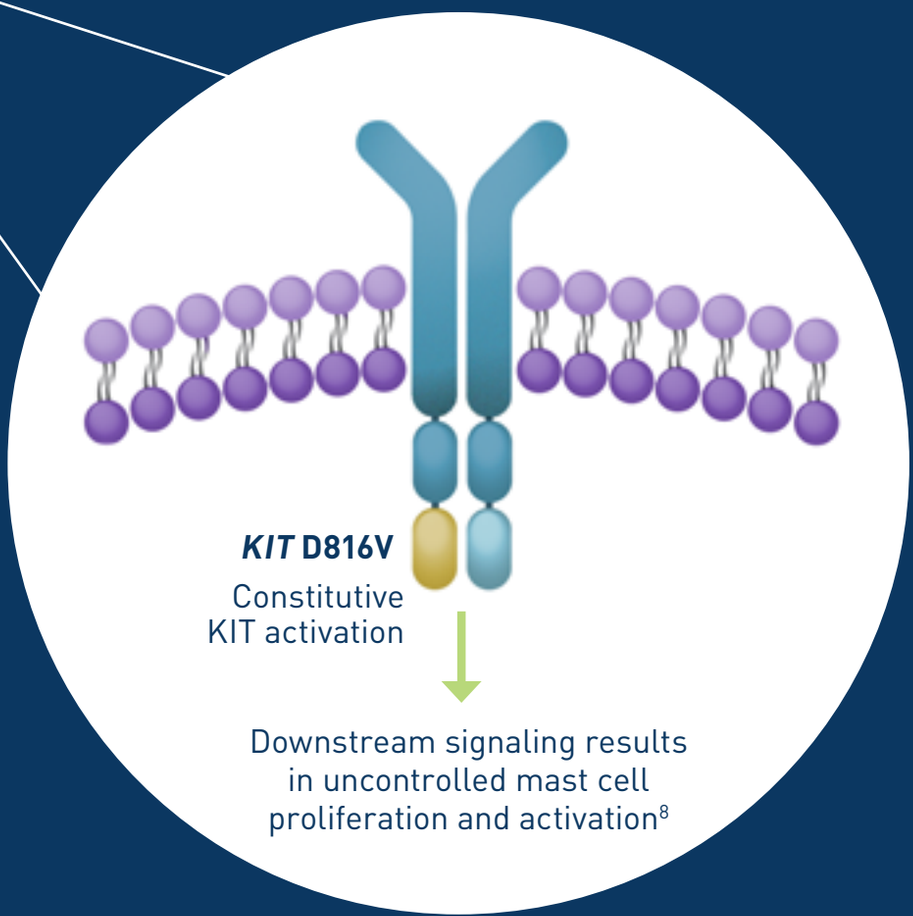
Advanced SM is driven by *KIT* D816V in ~95% of cases[8,10,13,14]

The *KIT* D816V mutation constitutively activates downstream pathways regulating cellular functions including proliferation and survival of abnormal mast cells.[15,16]



Spindle-shaped *KIT* D816V mutation positive mast cell in bone marrow

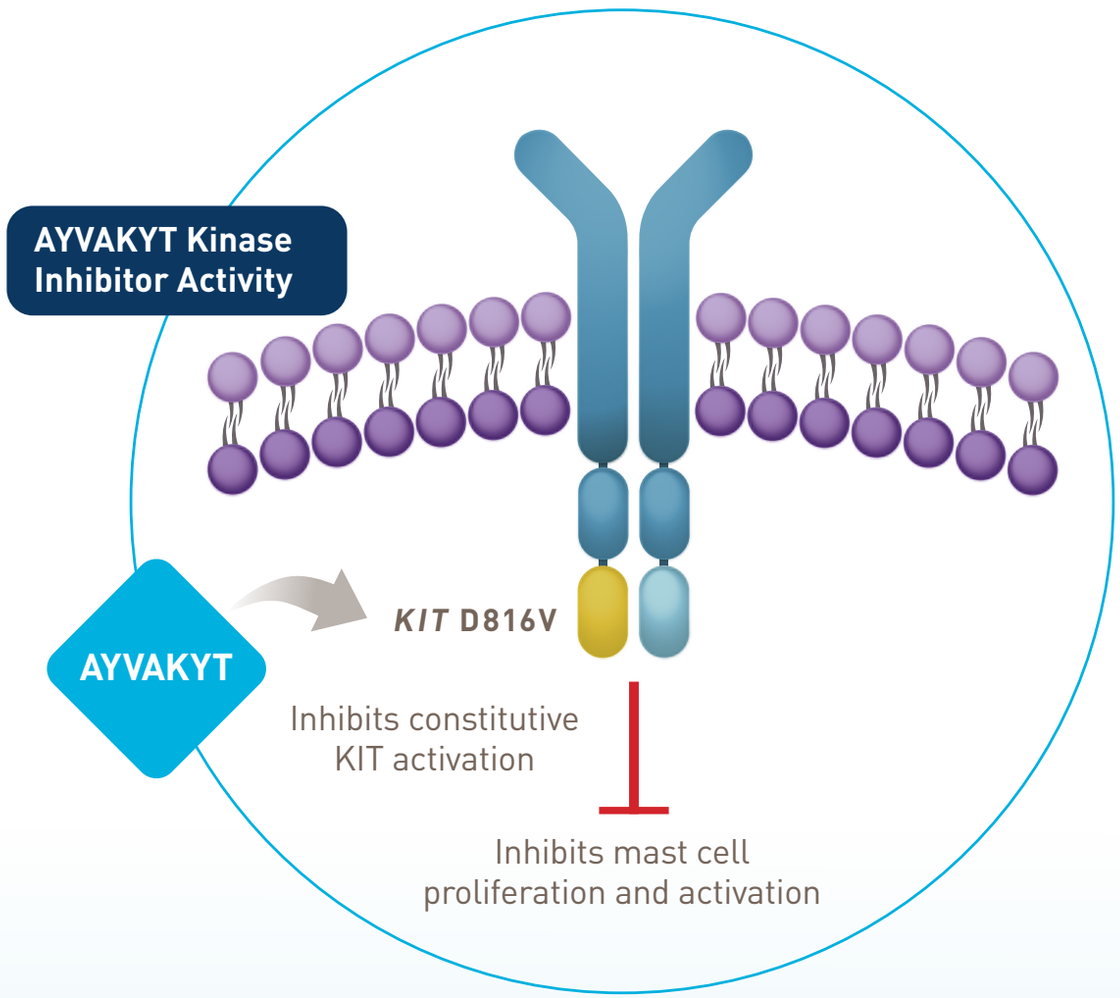
Image: Prof. H.-P. Horny, LMU Munich, all rights reserved, with kind approval.



Adapted from Gilreath JA, *et al*. Clinical Pharmacology 2019.

The only targeted therapy designed for potent and highly selective inhibition of *KIT* D816V[1–3]

AYVAKYT is a tyrosine kinase inhibitor that potently and selectively inhibits the autophosphorylation of *KIT* D816V, with an IC_{50} of 0.27 nanomolar in in-vitro biochemical assays.[1–3]



Adapted from Gilreath JA, *et al*. Clinical Pharmacology 2019.

Please note: To initiate treatment with AYVAKYT, patients will need a platelet count of >50 x 10^9/L.[1]

IC_{50}, half maximal inhibitory concentration.

The efficacy and safety of AYVAKYT were studied in patients with Advanced SM[1]

PATHFINDER WAS A MULTI-CENTRE, SINGLE-ARM, OPEN-LABEL PHASE 2 CLINICAL STUDY[1,2]

Patients enrolled in PATHFINDER study were treated at starting dose of 200 mg orally once daily.[2] Efficacy was based on overall response rate (ORR) in 47 patients with Advanced SM evaluable according to the mIWG-MRT-ECNM response criteria,* who:[1]

- Received at least one prior systemic therapy
- Had at least 2 post-baseline bone marrow assessments
- Had been on study for at least 24 weeks or had an end of study visit
- Median duration of follow-up at last data cut: 12 months

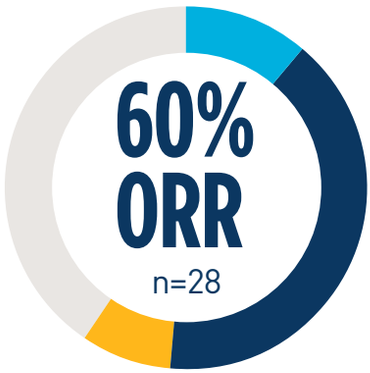
Demographic Characteristics at Baseline (n=47)[1]	
Median Age	69 years (31–86)
Gender	70% male, 30% female
ECOG PS	0–1: 66%
	2–3: 34%
Presence of *KIT* D816V mutation	89%
Median *KIT* D816V mutant allele fraction	26.2%
Prior antineoplastic therapy	100%
• midostaurin	78.7%
• cladribine	17.0%
• interferon alpha	14.9%
• hydroxycarbamide	10.6%
• azacytidine	6.4%
Advanced SM subtypes	ASM: 17% (n=8)
	SM-AHN: 62% (n=29)
	MCL: 21% (n=10)
Median bone marrow mast cell infiltrate	70%
Median serum tryptase level	325 ng/mL

*mIWG-MRT-ECNM response criteria evaluate overall response rate by ≥12 weeks duration, resolution of ≥1 C-findings and ≥50% reduction in biomarker response.[11,17]

ASM, aggressive systemic mastocytosis; ECOG PS, Eastern Cooperative Oncology Group Performance Status; mIWG-MRT-ECNM, modified International Working Group-Myeloproliferative Neoplasms Research and Treatment, European Competence Network on Mastocytosis; MCL, mast cell leukaemia; ORR, overall response rate; SM, systemic mastocytosis; SM-AHN, systemic mastocytosis with an associated haematological neoplasm.

Proven efficacy and demonstrated duration of response[1]

In evaluable Advanced SM (ASM, SM-AHN, MCL) patients (n=47) receiving 200 mg daily after at least one prior systemic therapy:[1]



(95% CI: 44.3%, 73.6%)

- **CR+CRh: 11% (n=5)**
- **PR: 40% (n=19)**
- **Clinical improvement:* 9% (n=4)**

The mIWG-MRT-ECNM criteria valuates ORR by:[11,17]

- ≥12 weeks response duration
- Resolution of ≥1 findings of non-haematological and haematological organ damage (C-findings)†
- ≥50% reduction in biomarker response (bone marrow mast cell aggregates and serum tryptase)‡

TIME TO TREATMENT RESPONSE[1]

1.9 MONTHS
Median time to response (n=28)

3.7 MONTHS
Median time to CR and CRh (n=5)

DURATION OF RESPONSE[1§]

100%
At 12 months (n=28)

85.6%
At 24 months (n=28)

*Clinical improvement is defined as having a response duration of ≥12 weeks and fulfilment of 1 or more of the non-haematologic and/or haematologic response criteria.[11,17]

†C-findings: Bone marrow dysfunction manifested by 1 or more cytopenia (ANC <1 x 10^9/L, Hb <10 g/dL, or platelets <100 x 10^9/L); palpable hepatomegaly with impairment of liver function, ascites, and/or portal hypertension; skeletal involvement with large osteolytic lesions and/or pathological fractures; palpable splenomegaly with hypertension; malabsorption with weight loss from gastrointestinal tract mast cell infiltrates.[11,17]

‡Serum tryptase must be <20 ng/mL if baseline was ≥40 ng/mL for CR or CRh.[11]

§Estimated from Kaplan-Meier analysis. DOR (months), median (95% confidence interval).[1]

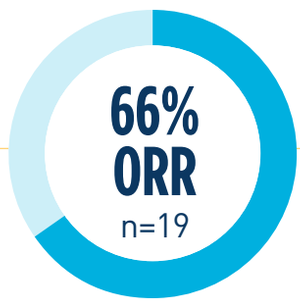
CI, confidence interval; CR, complete remission; CRh, complete remission with partial haematologic recovery; m, months; mIWG-MRT-ECNM, modified International Working Group-Myeloproliferative Neoplasms Research and Treatment and European Competence Network on Mastocytosis; ORR, overall response rate; PR, partial remission.

Proven efficacy across all subtypes of Advanced SM[1]

AGGRESSIVE SYSTEMIC MASTOCYTOSIS (ASM) (N=8)[1]

[95% CI: 24.5%, 91.5%]

SYSTEMIC MASTOCYTOSIS WITH AN ASSOCIATED HAEMATOLOGICAL NEOPLASM (SM-AHN) (N=29)[1]



[95% CI: 45.7%, 82.1%]

MAST CELL LEUKAEMIA (MCL) (N=10)[1]

[95% CI: 12.2%, 73.8%]

AYVAKYT was generally well tolerated[2,18]

THE MAJORITY OF ADVERSE REACTIONS WERE GRADE 1 OR 2[1*]

The safety of AYVAKYT was evaluated in 193 patients with Advanced SM in EXPLORER and PATHFINDER. Patients received a starting dose ranging from 30 mg to 400 mg orally once daily, including 126 patients who received the recommended starting dose of 200 mg once daily.[1†]

Serious adverse reactions occurred in 12% of patients receiving avapritinib. The most common serious adverse reactions during treatment with avapritinib were subdural haematoma (2%), anaemia (2%), and haemorrhage (2%).[1]

7.1% of patients permanently discontinued treatment due to any adverse reactions at the recommended starting dose of 200 mg.[1]

The most common adverse reactions of any grade during treatment with AYVAKYT at a starting dose of 200 mg were periorbital oedema, thrombocytopenia, oedema peripheral and anaemia.[1]

Adverse reactions (≥10%) reported in clinical studies in patients with Advanced SM treated with AYVAKYT starting at 200 mg[1]

Adverse reactions*	All grades %	Grade ≥3 %
Blood and lymphatic system disorders		
Thrombocytopenia‡	46.8	23.0
Anaemia‡	23.0	11.9
Neutropenia‡	21.4	19.0
General disorders and administration site conditions		
Oedema§	69.8	4.8
Fatigue‡	18.3	2.4
Gastrointestinal disorders		
Diarrhoea	14.3	1.6
Nausea	12.7	-
Nervous system disorders		
Taste effect‡	15.9	0.8
Cognitive disorder	11.9	1.6
Skin and subcutaneous tissue disorders		
Hair colour changes	15.1	-

Adverse reactions occurring in <10% of patients (all grades)[1]

- Leukopenia (8.7%)‡
- Vomiting (8.7%)‡
- Headache (7.9%)
- Hyperbilirubinaemia (7.9%)‡
- Rash (7.9%)‡
- Alopecia (7.1%)
- Lacrimation increased (6.3%)
- Weight increased (6.3%)
- Memory impairment (5.6%)‡
- Dizziness (5.6%)
- Epistaxis (5.6%)
- Neuropathy peripheral (4.8%)**
- Blood alkaline phosphatase increased (4.8%)
- Transaminases increased (4.8%)‡
- Gastroesophageal reflux disease (4.8%)‡
- Arthralgia (4.8%)
- Ascites (4.0%)‡
- Dryness (4.0%)‡
- Constipation (3.2%)
- Abdominal pain (3.2%)‡
- Pain (3.2%)
- Contusion (3.2%)
- Intracranial haemorrhage (2.4%)††
- Gastrointestinal haemorrhage (2.4%)‡‡
- Pleural effusion (2.4%)
- Electrocardiogram QT prolonged (1.6%)
- Confusional state (1.6%)
- Pericardial effusion (0.8%)
- Photosensitivity reaction (0.8%)
- Acute kidney injury (0.8%)‡

*The severity of adverse reactions graded by the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 and 5.0.

†See description of the safety profile according to the results from the EXPLORER[18] and PATHFINDER[2] studies in the AYVAKYT SmPC, date of information March 2023.[1]

‡Comprises pooled terms representing similar medical concepts.

§Oedema (including periorbital oedema, oedema peripheral, face oedema, eyelid oedema, fluid retention, generalised oedema, oedema, periphereal swelling, swelling face, eye swelling, conjunctival oedema, laryngeal oedema, localised oedema.

**Neuropathy peripheral (including paraesthesia, neuropathy peripheral, hypoaesthesia).

††Intracranial haemorrhage (including haemorrhage intracranial, subdural haematoma).

‡‡Gastrointestinal haemorrhage (including gastric haemorrhage, gastrointestinal haemorrhage, melaena).

Starting AYVAKYT – one tablet, once-daily dosing[1]

THE RECOMMENDED DOSAGE FOR ADVANCED SM IS 200 MG ONCE DAILY[1]

AYVAKYT should be taken:

One tablet orally

One time each day

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

The dose for patients with Advanced SM must not exceed 200 mg once daily.

To initiate treatment with AYVAKYT, patients will need a platelet count of >50 x 10^9/L. Treatment should continue until disease progression or unacceptable toxicity occurs.

Concomitant use of AYVAKYT with strong or moderate CYP3A inhibitors should be avoided. If concomitant use with a moderate CYP3A inhibitor cannot be avoided, the starting dose of AYVAKYT must be reduced from 200 mg to 50 mg orally once daily.

DOSE MODIFCATIONS IN CLINICAL TRIALS[1*]

EXPLORER & PATHFINDER

Among Advanced SM patients in clinical trials who started at 200 mg (n=126):

7.1%

Permanent discontinuation due to adverse reaction[1]

PATHFINDER

Patients with Advanced SM who received at least one prior systemic therapy and a starting dose of 200 mg AYVAKYT (n=47):

79% (n=37)

Dose reduction (median time to reduction, 6 weeks)[1]

Adverse reactions leading to a dose reduction included thrombocytopenia, neutropenia, periorbital oedema, cognitive disorder, oedema peripheral, platelet count decreased, neutrophil count decreased, anaemia, asthenia, fatigue, arthralgia, blood alkaline phosphatase increased, blood bilirubin increased, and white blood cell count decreased.[1]

*See description of the safety profile according to the results from the EXPLORER[18] and PATHFINDER[2] studies in the AYVAKYT SmPC, date of information March 2023.[1]

Platelet monitoring[1]

MONITOR YOUR PATIENTS AT INITIATION AND AS INDICATED DURING TREATMENT TO HELP REDUCE AND MANAGE POTENTIAL ADVERSE REACTIONS

Time on therapy	Monitoring plan	Treatment plan
Prior to initiation	Perform platelet count.	**AYVAKYT is not recommended in Advanced SM patients with platelet counts <50 x 10^9/L**
First 8 weeks	Perform platelet count every 2 weeks regardless of baseline platelet count.	If platelet count <50 x 10^9/L occurs, interrupt AYVAKYT until platelet count is ≥50 x 10^9/L, then resume at reduced dose. If platelet count does not recover above 50 x 10^9/L, consider platelet support.
After 8 weeks	Monitor platelet counts: • Every 2 weeks if values are <75 x 10^9/L (or more frequently as clinically indicated) • Every 4 weeks if values are 75–100 x 10^9/L • As clinically indicated if values are >100 x 10^9/L	

Manage platelet counts of <50 x 10^9/L by treatment interruption until platelet count is ≥50 x 10^9/L, then resume at a reduced dose. If platelet count does not recover above 50 x 10^9/L, consider platelet support.

Thrombocytopenia was generally reversible by reducing or interrupting treatment with AYVAKYT.

23% of patients treated with AYVAKYT experienced a Grade ≥3 thrombocytopenia in clinical studies.

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

Please refer to the SmPC for additional information on dose modifications, patient monitoring and administration of AYVAKYT.

Special warnings and precautions for use[1]

HAEMORRHAGES

AYVAKYT has been associated with an increased incidence of haemorrhagic adverse reactions, including serious and severe adverse reactions, like gastrointestinal haemorrhage and intracranial haemorrhage in patients with Advanced SM (see section 4.8 of the SmPC).

Routine surveillance of haemorrhagic adverse reactions must include physical examination. Complete blood counts, including platelets, and coagulation parameters must be monitored, particularly in patients with conditions predisposing to bleeding, and in those treated with anticoagulants (e.g. warfarin and phenprocoumon) or other concomitant medicinal products that increase the risk of bleeding.

INTRACRANIAL HAEMORRHAGES

Adverse reactions of intracranial haemorrhage occurred in patients who received AYVAKYT. Before initiating AYVAKYT the risk for intracranial haemorrhage should be carefully considered in patients with potential increased risk including those with thrombocytopenia, vascular aneurysm or a history of intracranial haemorrhage or cerebrovascular accident within the prior year.

Patients who experience clinically relevant neurological signs and symptoms (e.g. severe headache, vision problems, somnolence, and/or focal weakness) during treatment with AYVAKYT must interrupt dosing of AYVAKYT and inform their healthcare professional immediately. Brain imaging by magnetic resonance imaging (MRI) or computed tomography (CT) may be performed at the discretion of the physician based on severity and the clinical presentation.

For patients with observed intracranial haemorrhage during treatment with AYVAKYT, regardless of severity grade, AYVAKYT must be permanently discontinued (see section 4.2 of the SmPC).

Serious adverse reactions of intracranial haemorrhage were reported in patients with Advanced SM receiving AYVAKYT (see section 4.8 of the SmPC). The exact mechanism is unknown. The incidence of intracranial haemorrhage was higher in patients with platelet counts <50 x 10^9/L and in patients with a starting dose of ≥300 mg.

Considering the above, a platelet count must be performed prior to initiating therapy. AYVAKYT is not recommended in patients with platelet counts <50 x 10^9/L. Following treatment initiation, platelet counts must be performed every 2 weeks for the first 8 weeks regardless of baseline platelet count. After 8 weeks of treatment, monitor platelet counts every 2 weeks (or more frequently as clinically indicated) if values are less than 75 x 10^9/L, every 4 weeks if values are between 75 and 100 x 10^9/L, and as clinically indicated if values are greater than 100 x 10^9/L.

Manage platelet counts of <50 x 10^9/L by temporarily interrupting AYVAKYT. Platelet support may be necessary, and the recommended dose modification in Table 2 must be followed (see section 4.2 of the SmPC). Thrombocytopenia was generally reversible by reducing or interrupting AYVAKYT in clinical studies. The maximum dose for patients with AYVAKYT must not exceed 200 mg once daily.

COGNITIVE EFFECTS

Cognitive effects, such as memory impairment, cognitive disorder, confusional state and encephalopathy, can occur in patients receiving AYVAKYT (see section 4.8 of the SmPC). The mechanism of the cognitive effects is not known.

It is recommended that patients are clinically monitored for signs and symptoms of cognitive events such as new or increased forgetfulness, confusion and/or difficulty with cognitive functioning. Patients must notify their healthcare professional immediately if they experience new or worsening cognitive symptoms.

For patients with observed cognitive effects related to treatment with AYVAKYT, the recommended dose modification in Table 2 must be followed (see section 4.2 of the SmPC). In clinical studies, dose reductions or interruptions improved Grade ≥2 cognitive effects compared to no action.

FLUID RETENTION

In patients with Advanced SM, localised (facial, periorbital, peripheral, pulmonary oedema, pericardial and/or pleural effusion) or generalised oedema, and ascites have been observed with a frequency category of at least common (see section 4.8 of the SmPC). Other localised oedemas (laryngeal oedema) have been reported uncommonly.

Therefore, it is recommended that patients be evaluated for these adverse reactions including regular assessment of weight and respiratory symptoms. An unexpected rapid weight gain or respiratory symptoms indicating fluid retention must be carefully investigated and appropriate supportive care and therapeutic measures, such as diuretics, should be undertaken. For patients presenting with ascites, it is recommended to evaluate the aetiology of ascites.

QT INTERVAL PROLONGATION

Prolongation of QT interval has been observed in patients with Advanced SM treated with AYVAKYT in clinical studies. QT interval prolongation may induce an increased risk of ventricular arrhythmias, including Torsade de pointes.

AYVAKYT should be used with caution in patients with known QT interval prolongation or at risk of QT interval prolongation (e.g. due to concomitant medicinal products, pre-existing cardiac disease and/or electrolyte disturbances). Concomitant administration with strong or moderate CYP3A4 inhibitors should be avoided due to the increased risk of adverse reactions, including QT prolongation and related arrhythmias (see section 4.5 of the SmPC). If concomitant use of moderate CYP3A4 inhibitors cannot be avoided, see section 4.2 of the SmPC for dose modification instructions.

Interval assessments of QT by electrocardiogram (ECG) should be considered if AYVAKYT is taken concurrently with medicinal products that can prolong QT interval.

GASTROINTESTINAL DISORDERS

Diarrhoea, nausea and vomiting were the most commonly reported gastrointestinal adverse reactions in patients with Advanced SM (see section 4.8 of the SmPC). Patients who present with diarrhoea, nausea and vomiting should be evaluated to exclude disease-related aetiologies. Supportive care for gastrointestinal adverse reactions requiring treatment may include medicinal products with antiemetic, antidiarrheal or antacid properties.

The hydration status of patients experiencing gastrointestinal adverse reactions must be closely monitored and treated as per standard clinical practice.

LABORATORY TESTS

Treatment with AYVAKYT in patients with Advanced SM is associated with anaemia, neutropenia and/or thrombocytopenia. Complete blood counts must be performed on a regular basis during the treatment with AYVAKYT. See also intracranial haemorrhages above in this section and in section 4.8 of the SmPC.

Treatment with AYVAKYT is associated in patients with Advanced SM with elevations in bilirubin and liver transaminases (see section 4.8 of the SmPC). Liver function (transaminases and bilirubin) should be monitored regularly in patients receiving AYVAKYT.

CYP3A4 INHIBITORS AND INDUCERS

Co-administration with strong or moderate CYP3A inhibitors should be avoided because it may increase the plasma concentration of AYVAKYT (see sections 4.2 and 4.5 of the SmPC).

Co-administration with strong or moderate CYP3A inducers should be avoided because it may decrease the plasma concentrations of AYVAKYT (see section 4.5 of the SmPC).

PHOTOSENSITIVITY REACTION

Exposure to direct sunlight must be avoided or minimised due to the risk of phototoxicity associated with AYVAKYT. Patients must be instructed to use measures such as protective clothing and sunscreen with high sun protection factor (SPF).

SODIUM

This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially "sodium-free".

Please refer to the SmPC for additional information on dosing and administration of AYVAKYT.

Abbreviated Prescribing Information (EN)

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.

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.

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 2022

AYVAKYT is the only targeted therapy designed for potent and highly selective inhibition of *KIT* D816V[1–3]

AYVAKYT is indicated as a 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.[1]

~95%

Advanced SM is driven by the *KIT* D816V mutation in ~95% of cases[8,10,13,14]

Proven efficacy across all Advanced SM subtypes (ASM, SM-AHN, MCL)[1]

AYVAKYT treatment resulted in reductions of all objective measures of mast cell burden[1]

Generally well tolerated[2,18] with specific guidelines for patient monitoring and management; most common adverse reactions of any grade were periorbital oedema, thrombocytopenia, oedema peripheral, and anaemia[1]

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

ASM, aggressive systemic mastocytosis; MCL, mast cell leukaemia; SM, systemic mastocytosis; SM-AHN, systemic mastocytosis with an associated haematological neoplasm.

References: 1. AYVAKYT® (avapritinib). Summary of Product Characteristics; March 2023. Available at: https://www.ema.europa.eu/en/documents/product-information/ayvakyt-epar-product-information_en.pdf. **2.** Gotlib *J, et al. Nat Med*. 2021;27(12):2192–2199. doi:10.1038/s41591-021-01539-8 **3.** Evans EK, *et al. Sci Transl Med*. 2017;9(414):eaao1690. **4.** Sperr WR, *et al. Lancet Haematol*. 2019;6(12):e638–e649. **5.** Lim K-H, *et al. Blood*. 2009;113(23):5727–5736. **6.** Jennings SV, *et al. Immunol Allergy Clin North Am*. 2018;38(3):505–525. **7.** Theoharides TC, *et al. N Engl J Med*. 2015;373(2):163–172. **8.** Gilreath JA, *et al. Clin Pharmacol*. 2019;11:77–92. **9.** Gulen T, *et al. J Intern Med*. 2016;279(3):211–228. **10.** Verstovsek S. Eur J Haematol. 2013;90(2):89–98. **11.** Gotlib J, *et al. Blood*. 2013;121(13):2393–2401. **12.** Schwaab J, *et al. J Allergy Clin Immunol Pract*. 2020;8(9):3121–3127. **13.** Garcia-Montero AC, *et al. Blood*. 2006;108(7):2366–2372. **14.** Kristensen T, *et al. J Mol Diagn*. 2011;13:180–188. **15.** da Silva EZM, *et al. J Histochem Cytochem*. 2014;62(10):698–738. **16.** Valent P, *et al. Blood*. 2017;129(11):1420–1427. **17.** Shomali W & Gotlib J. *Int J Mol Sci*. 2021;22(6)2983. **18.** DeAngelo DJ, *et al. Nat Med*. 2021;27(12):2183–2191.

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