XOSPATA™

gilteritinib 40 mg film-coated tablets

Case Simulation-
Unfit Patient

MAT-IN-XOS-2025-00053 For the use of registered medical practitioners only.

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only, Additional Information Available on request.

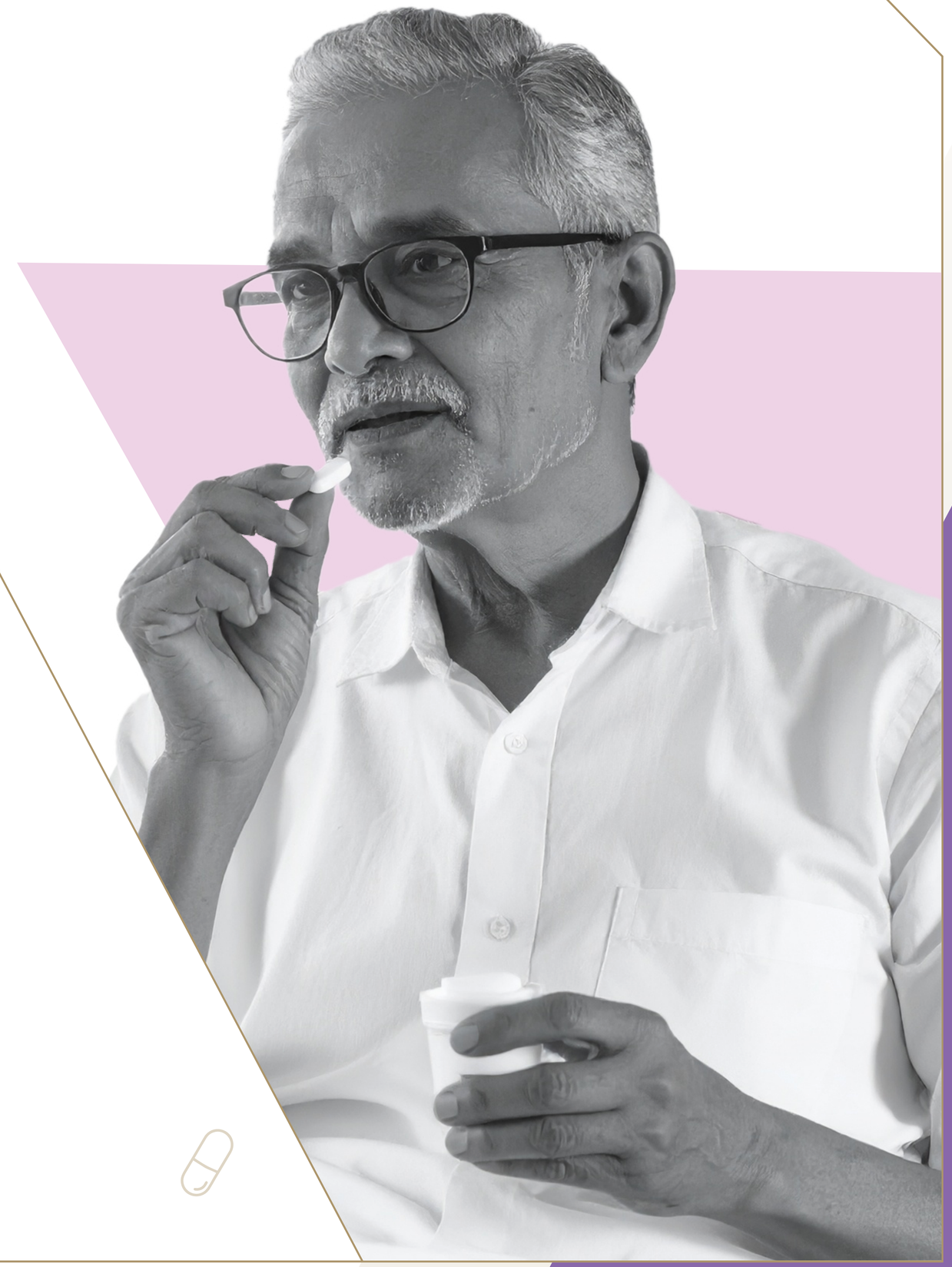
Date of preparation: August 2025

Scan for Prescibing Information

- A patient diagnosed with FLT3+ AML.
- Patient is old and frail. Not eligible for high intensity chemo.
- Started on Midostaurin + Azacitidine + Venetoclax.

- Blast counts keep increasing.
- Patient refractory to initial therapy. Unfit for intensive therapy.
- Ineligible for transplant.

Patient started on Xospata



BASELINE CHARACTERISTICS IN ADMIRAL TRIAL[1]

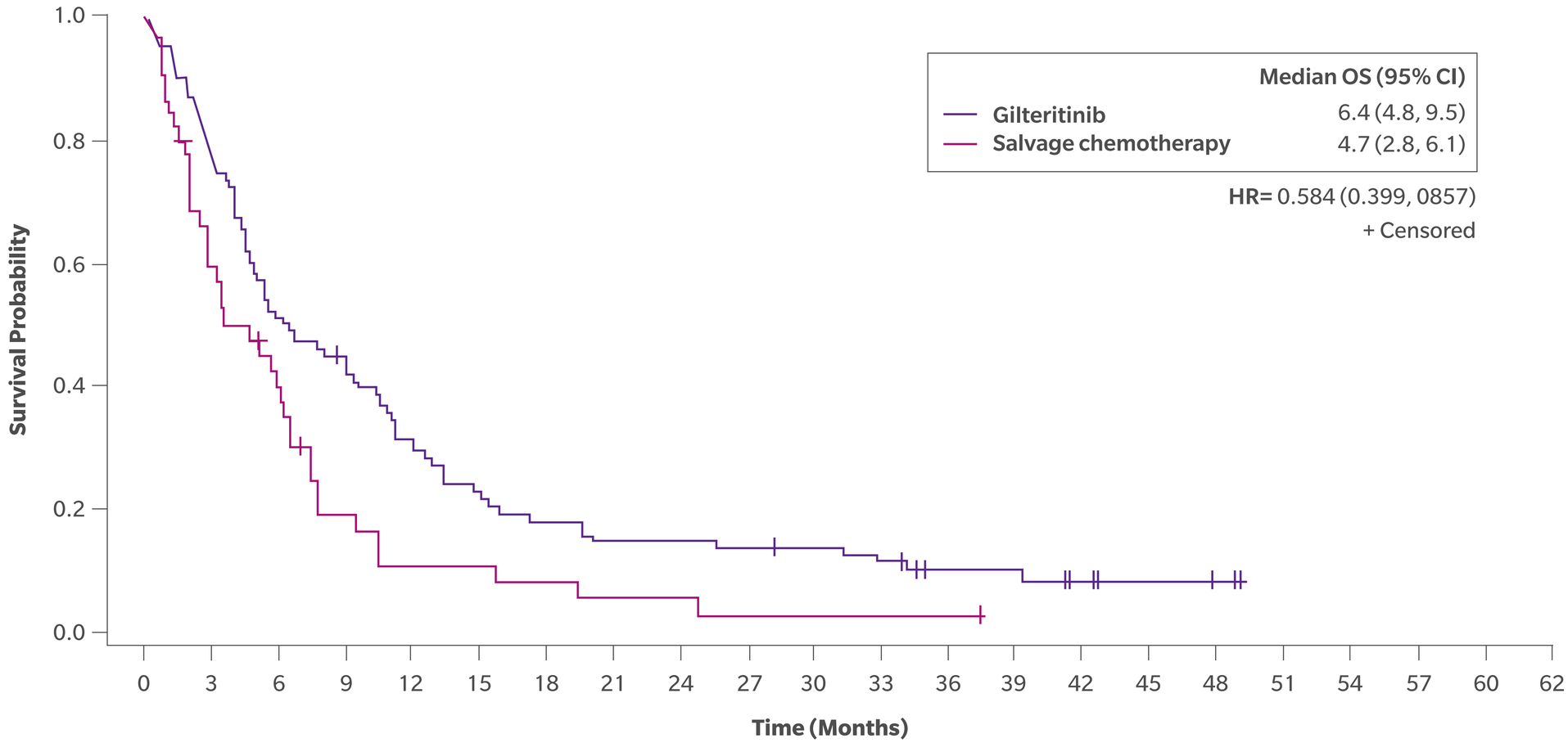
Characteristic	All patients (N=371)	Gilteritinib (n=247)	Salvage chemotherapy (n=124)
Age, year			
Median	62.0	62.0	61.5
Range	19.0–85.0	20.0–84.0	19.0–85.0
Sex, n (%)			
Female	201 (54.2)	131 (53.0)	70 (56.5)
Cytogenetic risk status, n (%)			
Favourable	5 (1.3)	4 (1.6)	1 (0.8)
Intermediate	271 (73.0)	182 (73.7)	89 (71.8)
Unfavourable	37 (10.0)	26 (10.5)	11 (8.9)
Unknown	58 (15.6)	35 (14.2)	23 (18.5)
Previous therapy for AML, n (%)			
Anthracycline	311 (83.8)	205 (83.0)	106 (85.5)
FLT3 inhibitor	46 (12.4)	32 (13.0)	14 (11.3)
HSCT	74 (19.9)	48 (19.4)	26 (21.0)
Response to first-line therapy before enrolment, n (%)†			
Relapse	225 (60.6)	149 (60.3)	76 (61.3)
Primary refractory AML without HSCT	146 (39.4)	98 (39.7)	48 (38.7)
Preselected salvage chemotherapy per IRT, n (%)			
High-intensity chemotherapy	224 (60.4)	149 (60.3)	75 (60.5)
Low-intensity chemotherapy	147 (39.6)	98 (39.7)	49 (39.5)
***FLT3* mutation subtype, n (%)‡**			
ITD only	328 (88.4)	215 (87.0)	113 (91.1)
TKD only	31 (8.4)	21 (8.5)	10 (8.1)
ITD and TKD	7 (1.9)	7 (2.8)	0

*ITT population included all patients who underwent randomisation; Percentages may not total 100 because of rounding. †Response based on IRT findings.
‡Central laboratory confirmed *FLT3* mutation status; unconfirmed *FLT3* mutation (n=5, 1.3%); n=4 (1.6%) assigned to gilteritinib, n=1 (0.8%) to chemotherapy.

Ref1. Perl AE, Martinelli G, Cortes JE, et al. *N Engl J Med.* 2019;381:1728–1740.

RESULTS: OVERALL SURVIVAL[1]

Patients Pre-selected for Low-Intensity Chemotherapy



	Median OS (95% CI)
Gilteritinib	6.4 (4.8, 9.5)
Salvage chemotherapy	4.7 (2.8, 6.1)

HR= 0.584 (0.399, 0857)

\+ Censored

Patients at risk (n)																					
Gilteritinib	74	74	70	41	25	21	17	14	14	13	12	10	3	3	3	2	1	0	0	0	0	0
Salvage chemotherapy	40	24	10	7	4	4	3	2	2	1	1	1	1	0	0	0	0	0	0	0	0	0

Survival benefit of gilteritinib was maintained in patients preselected for low-intensity chemotherapy

Abbreviations: CI, confidence interval; HR, hazard ratio; IRT, interactive response technology; ITD, internal tandem duplication; OS, overall survival; TKD, tyrosine kinase domain.

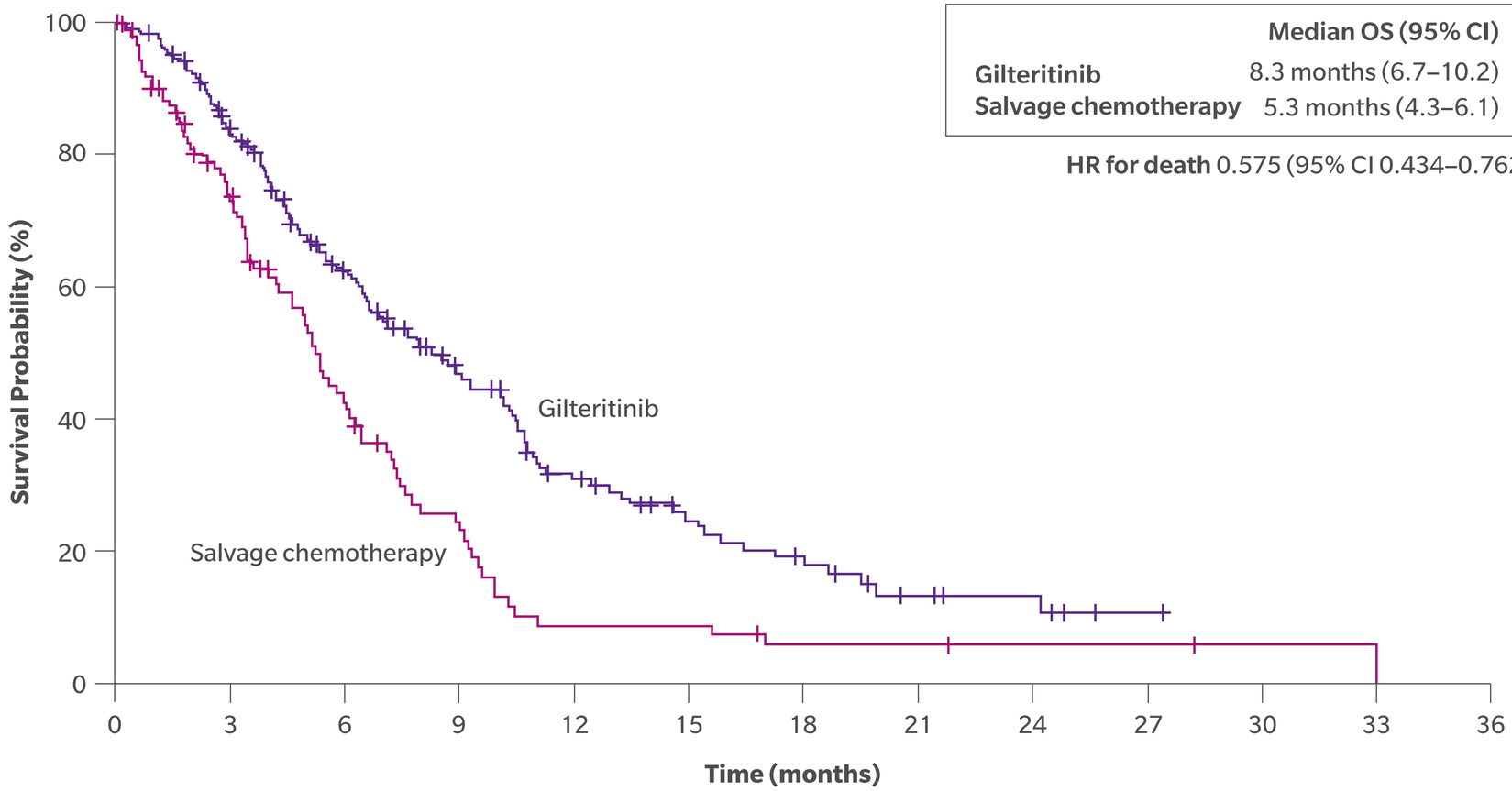
1.Perl A et al. Follow-up of patients with R/R FLT3-mutation-positive AML treated with gilteritinib in the phase 3 ADMIRAL trial. Blood 2022 Jun 9;139(23):3366-3375.

CR Rate			Risk Difference
	Xospata	Salvage Chemotherapy	
Patients eligible for Low-intensity chemotherapy	15.30%	2%	13.30%

Perl AE, Martinelli G, Cortes JE, et al. *N Engl J Med*. 2019;381:1728–1740

For all randomised patients, OS advantage with XOSPATA group was maintained after censoring at the time of transplantation[1]

Xospata has better survival as compared to chemotherapy even without transplant



	Median OS (95% CI)
Gilteritinib	8.3 months (6.7–10.2)
Salvage chemotherapy	5.3 months (4.3–6.1)

HR for death 0.575 (95% CI 0.434–0.762)

Patients at risk (n)													
Gilteritinib 120 mg/day	247	182	110	62	35	21	15	7	5	1	0	0	0
Salvage chemotherapy	124	70	36	18	6	6	3	3	2	2	1	0	0

Two-sided p-values were determined according to the log-rank test; the Kaplan–Meier method, combined with the Greenwood formula, were used to determine OS and corresponding 95% CIs.

OS advantage with XOSPATA was maintained after HSCT censoring

1.Perl AE, Martinelli G, Cortes JE, et al. *N Engl J Med.* 2019;381:1728–1740.

Perl AE, Martinelli G, Cortes JE, et al. *N Engl J Med.* 2019;381:1728–1740 (Supplementary appendix).

XOSPATA AS PALLIATIVE THERAPY: CONCLUSIONS[1]

1. Gilteritinib is equally effective in patients with *FLT3*-mutated R/R AML preselected for low intensity chemo[1].

2. OS advantage was maintained after censoring at the time of transplantation[1].

3. These data points suggest that Xospata can be an effective strategy as a palliative therapy amongst patients with R/R FLT3+ AML.

AML, acute myeloid leukemia; CI, confidence interval; *FLT3*, FMS-like tyrosine kinase; ITD, internal tandem duplication; R/R, relapsed or refractory; SC, salvage chemotherapy; TKD, tyrosine kinase domain; TKI, tyrosine kinase inhibitor.

1. Perl AE, Martinelli G, Cortes JE, et al. *N Engl J Med*. 2019;381:1728–1740.

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ABBREVIATED PRESCRIBING INFORMATION OF XOSPATA™ 40 mg film-coated tablets

(Please refer the full prescribing information for further details)

1. Name of the medicinal product: XOSPATA™ 40 mg film-coated tablets **2. QUALITATIVE AND QUANTITATIVE COMPOSITION:** Each film-coated tablet contains 40 mg gilteritinib (as fumarate). **3. PHARMACEUTICAL FORM:** Film-coated tablet (tablet). **4. CLINICAL PARTICULARS 4.1 Therapeutic indication:** Xospata is indicated as monotherapy for the treatment of adult patients who have relapsed or refractory acute myeloid leukaemia (AML) with a FLT3 mutation. **4.2 Posology and method of administration** Posology: The recommended starting dose is 120 mg gilteritinib (three 40 mg tablets) once daily. Blood chemistries and ECG monitoring should be performed before initiation and during the treatment as recommended. Treatment should continue until the patient is no longer clinically benefiting from Xospata or until unacceptable toxicity occurs. Response may be delayed; therefore, continuation of treatment at the prescribed dose for up to 6 months should be considered to allow time for a clinical response. In the absence of a response after 4 weeks of treatment, the dose can be increased to 200 mg once daily, if tolerated or clinically warranted. *Dose modifications:* Xospata should be administered at about the same time each day. If a dose is missed or not taken at the usual time, the dose should be administered as soon as possible on the same day, and patients should return to the normal schedule the following day. If vomiting occurs after dosing, patients should not take another dose but should return to the normal schedule the following day. *Elderly:* No dose adjustment is required in patients ≥65 years of age. *Hepatic impairment:* No dose adjustment is required for patients with mild or moderate hepatic impairment. Xospata is not recommended for use in patients with severe hepatic impairment, as safety and efficacy have not been evaluated in this population. *Renal impairment:* No dose adjustment is necessary in patients with mild or moderate renal impairment. There is no clinical experience in patients with severe renal impairment . *Paediatric population:* The safety and efficacy of Xospata in children aged below 18 years has not yet been established. No data is available. Due to in vitro binding to 5HT2B, there is a potential impact on cardiac development in patients less than 6 months of age. **4.3 Contraindications:** Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 (Kindly refer full prescribing information). **4.4 Special warnings and precautions for use:** Differentiation syndrome: If differentiation syndrome is suspected, corticosteroid therapy should be initiated along with hemodynamic monitoring until symptom resolution. If severe signs and/or symptoms persist for more than 48 hours after initiation of corticosteroids, Xospata should be interrupted until signs and symptoms are no longer severe. Corticosteroids can be tapered after resolution of symptoms and should be administered for a minimum of 3 days. Symptoms of differentiation syndrome may recur with premature discontinuation of corticosteroid treatment. Posterior reversible encephalopathy syndrome: There have been reports of posterior reversible encephalopathy syndrome (PRES) in patients receiving Xospata (see section 4.6). If PRES is suspected, it should be confirmed by brain imaging, preferably magnetic resonance imaging (MRI). Discontinuation of Xospata in patients who develop PRES is recommended. Prolonged QT interval: QT prolongation can be observed in the first three months of treatment with gilteritinib. Therefore, electrocardiogram (ECG) should be performed prior to initiation of treatment, on day 8 and 15 of cycle 1, and prior to the start of the next three subsequent months of treatment. Caution is warranted in patients with relevant cardiac history. Hypokalaemia or hypomagnesaemia may increase the QT prolongation risk. Hypokalaemia or hypomagnesaemia should therefore be corrected prior to and during Xospata treatment. Xospata should be interrupted in patients who have a QTcF >500 msec. The decision to re-introduce gilteritinib treatment after an event of QT prolongation should be based on a careful consideration of benefits and risks. If Xospata is re-introduced at a reduced dose, ECG should be performed after 15 days of dosing, and prior to the start of the next three subsequent months of treatment. In clinical studies, 12 patients had QTcF >500 msec. Three patients interrupted and re-initiated treatment without recurrence of QT prolongation. Pancreatitis: Xospata should be interrupted and can be resumed at a reduced dose when the signs and symptoms of pancreatitis have resolved. Interactions: Co-administration of CYP3A/P-gp inducers may lead to decreased gilteritinib exposure and consequently a risk for lack of efficacy. Therefore, concomitant use of gilteritinib with strong CYP3A4/P-gp inducers should be avoided. Caution is required when concomitantly prescribing gilteritinib with medicinal products that are strong inhibitors of CYP3A, P-gp and/or breast cancer resistant protein (BCRP) because they can increase gilteritinib exposure. In situations where satisfactory therapeutic alternatives do not exist, patients should be closely monitored for toxicities during administration of gilteritinib. Concomitant use of gilteritinib with medicinal products that target 5HT2B receptor or sigma nonspecific receptors should be avoided unless use is considered essential for the care of the patient since gilteritinib may reduce the effect of these drugs. Embryofoetal toxicity and contraception: Pregnant women should be informed of the potential risk to a foetus. Females of reproductive potential should be advised to have a pregnancy test within seven days prior to starting treatment with Xospata and to use effective contraception during treatment with Xospata and for at least 6 months after stopping treatment. Women using hormonal contraceptives should add a barrier method of contraception. Males with female partners of reproductive potential should be advised to use effective contraception during treatment and for at least 4 months after the last dose of Xospata. **4.5 Effects on ability to drive and use machines:** Dizziness has been reported in patients taking Xospata and should be considered when assessing a patient's ability to drive or use machines. **4.6 Undesirable effects:** Summary of the safety profile: The safety of Xospata was evaluated in 319 patients with relapsed or refractory AML who have received at least one dose of 120 mg gilteritinib. The most frequent adverse reactions with gilteritinib were alanine aminotransferase (ALT) increased (82.1%), aspartate aminotransferase (AST) increased (80.6%), blood alkaline phosphatase increased (68.7%), blood creatine phosphokinase increased (53.9%), diarrhoea (35.1%), fatigue (30.4%), nausea (29.8%), constipation (28.2%), cough (28.2%), peripheral oedema (24.1%), dyspnoea (24.1%), dizziness (20.4%), hypotension (17.2%), pain in extremity (14.7%), asthenia (13.8%), arthralgia (12.5%) and myalgia (12.5%). The most frequent serious adverse reactions were acute kidney injury (6.6%), diarrhoea (4.7%), ALT increased (4.1%), dyspnoea (3.4%), AST increased (3.1%) and hypotension (2.8%). Other clinically significant serious adverse reactions included differentiation syndrome (2.2%), electrocardiogram QT prolonged (0.9%) and posterior reversible encephalopathy syndrome (0.6%). **OVERDOSE:** There is no known specific antidote for Xospata. In the event of an overdose, treatment with Xospata should be stopped. Patients must be closely monitored for signs or symptoms of adverse reactions, and appropriate symptomatic and supportive treatment initiated, taking into consideration the long half-life estimated at 113 hours. For **full prescribing information please write to: MARKETING AUTHORISATION HOLDER: Astellas Pharma India Private Limited**, 301, 3rd Floor, C and B Square, 127 Andheri Kurla Road, Chakala, Andheri (East), Mumbai - 400 069. (Version: XOSPATA/aPI/India/Ver.2.0/Apr2024).