1. Emerging treatment paradigms with FLT3 inhibitors in acute myeloid leukemia; Short NJ et al. Ther Adv Hematol 2019;Vol.10:1–18.
2. XOSPATA™ Product information: www.swissmedicinfo.ch

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XOSPATA™ IS NEWLY APPROVED BY SWISSMEDIC

www.swissmedicinfo.ch

GILTERITINIB IS NOW XOSPATA™

XOSPATA™ is the first 2nd generation[1] tyrosine kinase inhibitor for FLT3m+ R/R AML patients approved in Switzerland.[2]

PRODUCT	PIVOTAL STUDY	PRESCRIBING INFORMATION

I would like to be informed as soon there is Swiss product in stock.

XOSPATA™
gilteritinib 40 mg tablets

PRODUCT

Indication

Xospata™ is indicated for the treatment of adult patients who have relapsed or refractory acute myeloid leukaemia (AML) with FMS-like tyrosine kinase 3 (FLT3) mutations.
(full product information on www.swissmedicinfo.ch)

- XOSPATA™ is orally administered[2] and therefore can be given in an in-patient or out-patient setting.

- XOSPATA™ film-coated tablets (three 40 mg tablets) should be taken orally once-daily with or without food.[2]

XOSPATA™
gilteritinib 40 mg tablets

PIVOTAL STUDY

For a summary of the ADMIRAL study click **here**

Please send me an electronic copy of the ADMIRAL study

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XOSPATA™

gilteritinib 40 mg tablets

Abridged prescribing information for XOSPATA™

Comp: Film-coated tablets with 40 mg of gilteritinib. Ind: Xospata is indicated for the treatment of adult patients who have relapsed or refractory acute myeloid leukaemia (AML) with FMS-like tyrosine kinase 3 (FLT3) mutations. Pos/Adm: The recommended starting dose is 120 mg gilteritinib (three 40 mg tablets) once-daily. The treatment can be continued up to disease progression or intolerable toxicity. Before taking gilteritinib, relapsed or refractory AML patients must have confirmation of FMS-like tyrosine kinase 3 (FLT3) mutation (internal tandem duplication [ITD] or tyrosine kinase domain [TKD]) using a validated test. Blood chemistries, including creatine phosphokinase, have to be assessed prior to the initiation of treatment with Xospata, on day 15 of cycle 1 and monthly for the duration of therapy. An electrocardiogram (ECG) has to be performed prior to initiation of treatment with Xospata, on day 8 and 15 of cycle 1, and prior to the start of the next two subsequent cycles. Response may be delayed; therefore, continuation of treatment at the prescribed dose for a period of 6 months should be considered to allow time for a clinical response. No dose adjustment is required for patients with mild or moderate (Child-Pugh Class A, B) hepatic impairment. Gilteritinib has not been studied in patients with severe hepatic impairment (Child-Pugh Class C). No dose adjustment is required in patients with mild (CrCL 60 - <90 ml/min) or moderate (CrCL 30 - <60 ml/min) renal impairment. There is no clinical experience in patients with severe renal impairment (CrCL <30 ml/min). No dose adjustment is required in patients ≥65 years of age. Gilteritinib is not recommended for use in children and adolescents. Xospata tablets should be taken orally once-daily with or without food. CI: Hypersensitivity to the active substance or any excipients of the product. Anaphylactic reactions have been reported. Warn/Precaut: Please refer to the full prescribing information, which is published at www.swissmedicinfo.ch. IA: Pharmacokinetic interactions: Gilteritinib exposure (AUCinf) decreased approximately 70% when Xospata was coadministered with a strong CYP3A/P-gp inducer. Gilteritinib Cmax decreased by 30%. Gilteritinib exposure increased approximately to 2.2-fold when Xospata was coadminstered with a strong CYP3A inhibitor in healthy adult subjects and approximately to 1.5-fold in patients with relapsed or refractory AML. Pharmacodynamic interactions: Based on in vitro data, gilteritinib may reduce the effects of drugs that target 5HT2B receptor or sigma nonspecific receptor. Avoid concomitant use of these drugs with gilteritinib unless use is considered essential for the care of the patient. Concomitant use of gilteritinib with drugs that are strong inducers of CYP3A/P-gp should be avoided as they can decrease the plasma exposure of gilteritinib. Concomitant use of gilteritinib with drugs that are strong inhibitors of CYP3A should be avoided as they can increase the plasma exposure of gilteritinib. Alternatives should be considered. However, the patient should be monitored more closely for adverse reactions if a combination with strong CYP3A4 inhibitors cannot be avoided. Drugs that are strong inhibitors of P-gp may increase the plasma exposure of gilteritinib. Avoid concomitant use of these drugs with gilteritinib unless use is considered essential for the care of the patient. Gilteritinib is not an inhibitor or inducer of CYP3A4 or an inhibitor of MATE1 in vivo. AE: The safety evaluation of gilteritinib is based on 319 patients with relapse or refractory AML who have received at least one dose of 120 mg gilteritinib daily. The most common undesirable effects (≥10%) were alanine aminotransferase (ALT) increased, aspartate aminotransferase (AST) increased, diarrhoea, fatigue, nausea, constipation, cough, peripheral oedema, dyspnoea, blood alkaline phosphatase increased, dizziness, hypotension, pain in extremity, asthenia, blood creatine phosphokinase increased, arthralgia and myalgia. The most frequent serious undesirable effects (≥2%) reported in patients were acute kidney injury, diarrhoea, ALT increased, AST increased, hypotension, dyspnoea and differentiation syndrome. Undesirable effects observed during clinical studies are listed below by frequency category. Frequency categories are defined as follows: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); isolated cases (frequency cannot be estimated from the available data). Within each grouping, undesirable effects are presented in order of decreasing frequency. Cardiac disorders Common: electrocardiogram QT prolonged, pericardial effusion, pericarditis, cardiac failure. Gastrointestinal disorders Very common: diarrhoea (35.1%), nausea (29.8%), constipation (28.2%), stomatitis (13.5%), abdominal pain (13.2%). Hepatobiliary disorders Very common: alanine aminotransferase increased (82.1%)*, aspartate aminotransferase increased (80.6%)*. General disorders and administration site conditions Very common: pyrexia (41.1%), fatigue (30.4%), peripheral oedema (24.1%), asthenia (13.8%). Common: malaise. Immune system disorders Common: anaphylactic reaction. Metabolism and nutrition disorders Very common: hyperglycaemia (88.1%)*, hypocalcaemia (64.9%)*, hypoalbuminaemia (59.9%)*, hypophosphataemia (51.1%)*, hypokalaemia (33.9%)*, hyponatraemia (32.0%)*, hypomagnesaemia (18.8%)*, reduced appetite (17.2%). Psychiatric disorders Very common: insomnia/sleeplessness (15%). Musculoskeletal and connective tissue disorders Very common: blood alkaline phosphatase increased (68.7%)*, blood creatine phosphokinase increased (53.9%)*, pain in extremity (14.7%), arthralgia (12.5%), myalgia (12.5%). Common: musculoskeletal pain. Nervous system disorders Very common: dizziness (20.4%), headache (23.5%), dysgeusia (11%). Uncommon: posterior reversible encephalopathy syndrome. Respiratory, thoracic and mediastinal disorders Very common: cough (28.2%), dyspnoea (24.1%). Common: differentiation syndrome. Vascular disorders Very common: hypotension (17.2%). Renal and urinary disorders Common: acute kidney injury. * Investigations (frequency is based on central laboratory values) Description of selected adverse reactions Differentiation syndrome Of 319 patients treated with Xospata in the clinical studies, 11 (3%) experienced differentiation syndrome. Differentiation syndrome is associated with rapid proliferation and differentiation of myeloid cells and may be life-threatening or fatal if not treated. Symptoms and clinical findings of differentiation syndrome in patients treated with Xospata included fever, dyspnoea, pleural effusion, pericardial effusion, pulmonary oedema, hypotension, rapid weight gain, peripheral oedema, rash, and renal dysfunction. Some cases had concomitant acute febrile neutrophilic dermatosis. Differentiation syndrome occurred as early as one day and up to 82 days after Xospata initiation and has been observed with or without concomitant leukocytosis. Of the 11 patients who experienced differentiation syndrome, 9 (82%) recovered after treatment or after dose interruption of Xospata. PRES Of the 319 patients treated with Xospata in the clinical studies, 0.6% experienced posterior reversible encephalopathy syndrome (PRES). PRES is a rare, reversible, neurological disorder, which can present with rapidly evolving symptoms including seizure, headache, confusion, visual and neurological disturbances, with or without associated hypertension. Symptoms have resolved after discontinuation of treatment. QT prolongation Of the 317 patients treated with gilteritinib at 120 mg with a post-baseline QTC value in clinical studies, 4 patients (1%) experienced a QTcF >500 msec. Additionally, across all doses, 12 patients (2.3%) with relapsed/refractory AML had a maximum post-baseline QTcF interval >500 msec. A concentration related increase in change from baseline of QTcF (ΔQTcF) was observed across gilteritinib doses ranging from 20 to 450 mg. The predicted mean change from baseline of QTcF at the mean steadystate Cmax (282.0 ng/ml) at the 120 mg daily dose was 4.96 msec with an upper 1-sided 95% CI = 6.20 msec. Reporting suspected adverse reactions after authorisation of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions online via the ElViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch. P: 84 film-coated tablets, 40 mg each, dispensing category: A For further information, please refer to the full prescribing information, which is published at www.swissmedicinfo.ch. Astellas Pharma AG, Richtiring 28, 8304 Wallisellen. www.astellas.ch

For full prescribing information, please refer to swissmedicinfo.ch

References

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