XOSPATA™ (gilteritinib)

HCP Educational Information Brochure

This HCP Educational Information Brochure is an Additional Risk Minimisation Measure of the XOSPATA Risk Management Plan provided by Astellas Pharma Co., Ltd.

HCP – healthcare professional

For prescribing information, please refer to the XOSPATA Summary of Product Characteristics available at www.medicines.ie.

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astellas

This HCP Educational Information Brochure aims to provide information about Differentiation Syndrome related to XOSPATA, to minimise the risk associated with this safety concern.

Every healthcare professional must read and understand this HCP Educational tool before prescribing XOSPATA.

Please refer to this brochure to support the health and safety of your patients, and advise your patients to understand the risk of developing Differentiation Syndrome before using XOSPATA.

Other adverse events associated with XOSPATA are listed in the Summary of Product Characteristics.

For prescribing information, please refer to the XOSPATA Summary of Product Characteristics available at www.medicines.ie.

XOSPATA

XOSPATA (gilteritinib fumarate) is a FMS-like tyrosine kinase 3 (FLT3) and AXL inhibitor. XOSPATA inhibits FLT3 receptor signalling and proliferation in cells exogenously expressing FLT3 including FLT3 internal tandem duplication (FLT3-ITD), FLT3-D835Y, and FLT3-ITD-D835Y, and induces apoptosis in leukaemic cells expressing FLT3-ITD.[1]

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.[1]

SERIOUS ADVERSE REACTIONS

319 patients have been treated with XOSPATA in the gilteritinib clinical development programme. The most frequent serious adverse reactions were:[1]

- Acute kidney injury (6.6%)
- Diarrhoea (4.7%)
- Alanine aminotransferase (ALT) increased (4.1%)
- Dyspnoea (3.4%)
- Aspartate aminotransferase (AST) increased (3.1%)
- Hypotension (2.8%)

Other clinically significant serious adverse reactions included:[1]

- Differentiation Syndrome (2.2%)
- Electrocardiogram QT prolonged (0.9%)
- Posterior Reversible Encephalopathy Syndrome (0.6%)

IMPORTANT INFORMATION ON DIFFERENTIATION SYNDROME ASSOCIATED WITH XOSPATA

Differentiation Syndrome may be life-threatening or fatal if not treated.[1] This HCP Educational Information Brochure provides information about Differentiation Syndrome related to XOSPATA to minimise the risk associated with this safety concern.

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DIFFERENTIATION SYNDROME

INCIDENCE OF DIFFERENTIATION SYNDROME IN AML PATIENTS TREATED WITH XOSPATA

Of the 319 patients treated with XOSPATA in the clinical development programme, 11 (3.4%) experienced Differentiation Syndrome (all grades). In 7 out of these 11 patients, Differentiation Syndrome was reported as Grade ≥3.[1]

AETIOLOGY AND PATHOGENESIS

Differentiation Syndrome develops in patients with acute promyelocytic leukaemia (APL) and other AML subtypes treated with agents that can affect differentiation, such as FLT3 inhibitors like gilteritinib.[1,2]

The precise mechanism implicated in the pathogenesis of Differentiation Syndrome is not known, but it has been linked to the production of inflammatory cytokines released by rapid proliferation and differentiation of myeloid cells into neutrophils, causing a systemic inflammatory response and a capillary-leak syndrome.[3] XOSPATA can induce differentiation of myeloblasts in patients with AML.[4]

Post-mortem studies in patients with APL showed leukaemic infiltration of lymph nodes, spleen, lung, liver, pleura, kidney, pericardium and skin.[3]

SIGNS AND SYMPTOMS

Differentiation Syndrome occurred as early as 1 day and up to 82 days after XOSPATA initiation and has been observed with or without concomitant leukocytosis.[1]

Symptoms and clinical findings of Differentiation Syndrome in patients treated with XOSPATA included:[1]

- Fever
- Dyspnoea
- Pleural effusion
- Pericardial effusion
- Pulmonary oedema
- Hypotension
- Rapid weight gain
- Peripheral oedema
- Rash
- Renal dysfunction
- Some cases had concomitant acute febrile neutrophilic dermatosis

Musculoskeletal pain, hyperbilirubinaemia and pulmonary haemorrhage were also reported as findings of Differentiation Syndrome in patients treated for APL.[5]

DIAGNOSIS

No single sign or symptom is considered sufficient to diagnose Differentiation Syndrome, and any possible alternative cause explaining the clinical features should be ruled out first.

The diagnosis of Differentiation Syndrome is mostly based on the presence of the above clinical and radiological criteria, and supported by the striking response to early therapy with intravenous corticosteroids.[5]

DIFFERENTIAL DIAGNOSIS

The differential diagnosis should always include lung infection, sepsis, thromboembolism and heart failure.[6]

TREATMENT

- The experience in the treatment of gilteritinib-related Differentiation Syndrome is very limited
- Corticosteroids (dexamethasone 10 mg IV every 12 hours or an equivalent dose of an alternative oral or IV corticosteroid) should be administered at the earliest clinical suspicion of Differentiation Syndrome, along with haemodynamic monitoring until improvement[1,2]
- Gilteritinib should be interrupted if severe signs and/or symptoms persist for more than 48 hours after the initiation of corticosteroids[1]
- Gilteritinib can be resumed at the same dose when signs and symptoms improve to Grade 2 or lower[1]
- Corticosteroids can be tapered after resolution of symptoms and should be administered for a minimum of 3 days[1]
- Symptoms of Differentiation Syndrome may recur with premature discontinuation of corticosteroid treatment[1]
- Delayed administration of corticosteroids is associated with poor outcomes in APL Differentiation Syndrome[5,6]

IV – intravenously

For prescribing information, please refer to the XOSPATA Summary of Product Characteristics available at www.medicines.ie.

PATIENT ALERT CARD

Your patients will receive a Patient Alert Card in their XOSPATA package. This card will help them understand Differentiation Syndrome better. Please instruct your patients to:

- Fill the Patient Alert Card and carry it with them at all times
- Show the Patient Alert Card to any healthcare professional they might interact with for any medical treatment (including pharmacy), or at any visits to the hospital or clinic

Tell your patients to talk to you immediately or go to the nearest hospital emergency room if they develop fever, trouble breathing, rash, dizziness or lightheadedness, rapid weight gain, or swelling of arms or legs.

REPORTING OF SUSPECTED ADVERSE REACTIONS

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

Healthcare professionals are asked to report any suspected adverse reactions via:

HPRA Pharmacovigilance
Website: www.hpra.ie

Astellas Pharma Co. Ltd.
Tel.: 01 467 1555
E-mail: irishdrugsafety@astellas.com

CONTACT DETAILS

For medical information enquiries, requests for additional copies of this HCP Educational Information Brochure or any questions regarding XOSPATA please contact:

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REFERENCES

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