LONG-TERM PROPHYLAXIS IN HEREDITARY ANGIOEDEMA: IS IT WORTH THE EFFORT?

This is a promotional meeting that has been organised and paid for by BioCryst UK Ltd. The meeting has been endorsed by the British Society for Immunology (BSI) Clinical Immunology Professional Network (CIPN) and is for healthcare professionals only.

BIOCRYST UK WEBINAR
Monday 17th April 2023
18:00–19:30

On behalf of BioCryst UK Ltd., we are pleased to invite you to join us for a promotional webinar, on Monday 17th April 2023, 18:00–19:30

The focus for this meeting is to discuss the value of long-term prophylaxis for patients with hereditary angioedema (HAE). In addition, the meeting will cover the importance of taking a holistic view of long-term HAE management, looking at the utility of quality of life measures in assessing the patient’s burden and response to therapy, and will touch on the latest clinical data for Orladeyo (berotralstat).

Long-term prophylaxis in hereditary angioedema: is it worth the effort?
Date: Monday 17th April 2023
Chair: Dr Sorena Kiani

AGENDA

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<td>18.00</td>
<td>Chair’s Welcome &amp; Introduction</td>
<td>Dr Sorena Kiani, Consultant Immunologist, Royal Free Hospital London NHS Foundation Trust</td>
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<td>18.10</td>
<td>The value of long-term prophylaxis for Hereditary Angioedema</td>
<td>Professor Marcus Maurer, Professor of Dermatology and Allergy, Charité - Universitätsmedizin, Berlin</td>
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<td>18.30</td>
<td>A holistic view of long-term HAE management in the UK</td>
<td>Dr Lavanya Diwakar, Consultant Clinical Immunologist, University Hospitals of North Midlands NHS Trust</td>
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<td>HAE patient case study</td>
<td>Dr Anthony Dorr, ST7 Immunology, Barts Health NHS Trust, London</td>
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<td>19.05</td>
<td>Chair’s meeting summary</td>
<td>Dr Sorena Kiani, Consultant Immunologist, Royal Free Hospital London NHS Foundation Trust</td>
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<td>19.15</td>
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To book a place for this webinar please use the following link

We look forward to you joining us virtually

UK.ORL.00239; February 2023
Great Britain and Northern Ireland combined prescribing information

Orladeyo ▼ (berotralstat) 150mg hard capsules.

Consult Summary of Product Characteristics before prescribing.

**Presentation:** Each hard capsule contains 150mg berotralstat (as dihydrochloride).

**Indication:** Routine prevention of recurrent attacks of hereditary angioedema (HAE) in adults and adolescents aged 12 years and over.

**Dosage and administration:** 150mg orally once daily, at any time of day with food in patients weighing ≥40kg. Missed doses to be taken as soon as possible without exceeding one dose per day.

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

**Warnings and Precautions:** Not intended for the treatment of acute HAE attacks. No clinical data available on use in patients with normal C1-INH activity. Not suitable for use in patients weighing <40kg.

**Risk of QT Prolongation:** Avoid use in: Patients with moderate or severe hepatic impairment due to risk of increased berotralstat concentrations, and in end stage renal disease requiring haemodialysis. Avoid use or consider ECG monitoring in patients with severe renal impairment. **Avoid use or consider appropriate monitoring e.g. ECGs in patients with:** known pre-existing QT prolongation or with risk factors for QT prolongation e.g. electrolyte disturbances or advancing age. **Avoid concomitant use of:** Drugs mainly metabolised by CYP2D6, CYP3A4 or P-gp substrates with a narrow therapeutic index or other drugs known to prolong QT (e.g. citalopram, escitalopram, amitriptyline and ondansetron). If treatment is required, consider appropriate monitoring e.g. ECG and dose adjustment of these medicines.

**Interactions:**

**Effects of other medicines on Orladeyo:** No dose adjustment is necessary for P-gp and BCRP inhibitors but close monitoring for adverse events is recommended when used with P-gp and BCRP inhibitors such as cyclosporine or grapefruit juice. Concomitant use of P-gp and BCRP inducers e.g. rifampicin, St. John’s wort is not recommended due to risk of reduced efficacy.

**Effects of Orladeyo on other medicines:** Refer to the SmPC of concomitant medications that are mainly metabolised by CYP3A4, CYP2D6 or are P-gp substrates. Orladeyo increases concentrations of the CYP3A4 substrates midazolam, amiodipine and of the CYP2D6 substrates dextromethorphan, desipramine. Dose adjustments may be required for drugs with a narrow therapeutic index or where therapeutic monitoring is recommended e.g. CYP3A4 substrates: cyclosporine, fentanyl; CYP2D6: thioridazine, pimozide, tricyclic antidepressants and P-gp substrates: digoxin, dabigatran. Orladeyo increases tolbutamide concentrations, but no dose adjustment is required for drugs mainly metabolised by CYP2C9.
**Oral contraceptives:** Berotralstat may increase the concentrations of oral contraceptives metabolised by CYP3A4. There was negligible effect on CYP2C9 conversion of desogestrel to the active metabolite etonogestrel. The AUC of etonogestrel was increased, however Cmax was not affected and no dose adjustment of concomitant desogestrel is recommended.

**Women of childbearing potential, pregnancy and lactation:**

Not recommended in women of childbearing potential unless using effective contraception, which should be continued for at least a month after the last dose of Orladeyo. Use in pregnancy not recommended due to no or limited data. Unable to exclude risk to child from excretion in breast milk therefore avoid/discontinue breast feeding or Orladeyo depending on balance of benefit to child and mother.

**Undesirable effects:** Please consult the SmPC for full list of side effects. Very common (≥1/10): headache, abdominal pain, diarrhoea. Common (≥1/100 to <1/10): vomiting, gastroesophageal reflux, flatulence, rash and elevations in ALT and AST. Abdominal pain and diarrhoea events were mostly reported within 1 to 3 months of initiation, were mild-moderate and resolved without specific treatment while Orladeyo was continued. Median duration of diarrhoea and abdominal pain was 3.2 and 3.5 days, respectively. LFT elevations were primarily seen in patients discontinuing androgens within 14 days of starting Orladeyo. Abrupt discontinuation of androgens immediately prior to initiation should be avoided.

**Package quantities and basic NHS Price:** Orladeyo 150mg hard capsules 28 day blister pack £10,205 excluding VAT.

**Marketing Authorisation Holder:** Biocryst Ireland Limited, Block 4, Harcourt Centre, Harcourt Road, Dublin 2, D02HW77, Ireland.

**Marketing Authorisation Numbers:** PLGB 50680/0001, EU/1/21/1544/001 and EU/1/21/1544/002

**Legal category:** POM

**Date of last revision of prescribing information:** October 2022

**Full Prescribing Information is available from** medinfoeurope@biocryst.com

UK.ORL.00195 | October 2022

Adverse events should be reported. Reporting forms and information for the United Kingdom can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Biocryst Ltd by email medinfoeurope@biocryst.com or by telephone +353 1 477 3087 and the UK on +44 20 3885 0789.