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Summarized information_English

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| Product Name | OCALIVA |
| Active substance | Obeticholic acid |
| Indication and conditions of use | <p>The program is only for the treatment of patients with primary biliary cholangitis (PBC) who completed the Long-Term Safety Extension of the POISE phase 3 trial.</p> <p>Condition of use:</p> <ul style="list-style-type: none"> • OCALIVA is indicated for the treatment of PBC in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA. • Prior to the initiation of OCALIVA, healthcare providers should determine whether the patient has decompensated cirrhosis (including Child-Pugh Class B or C) or has had a prior decompensation event because OCALIVA is contraindicated in these patients . <p>The starting dose of obeticholic acid is 5 mg once daily for the first 6 months. After the first 6 months, for patients who have not achieved an adequate reduction in alkaline phosphatase (ALP) and/or total bilirubin and who are tolerating obeticholic acid, increase to a maximum dose of 10 mg once daily. No dose adjustment of concomitant UDCA is required in patients receiving obeticholic acid.</p> <p><u>Management and dose adjustment for severe pruritus</u> Management strategies include the addition of bile acid binding resins or antihistamines.</p> <p>For patients experiencing severe intolerability due to pruritus, one or more of the following should be considered:</p> <ul style="list-style-type: none"> • The dose of obeticholic acid may be reduced to: <ul style="list-style-type: none"> ○ 5 mg every other day, for patients intolerant to 5 mg once daily ○ 5 mg once daily, for patients intolerant to 10 mg once daily • The dose of obeticholic acid may be temporarily interrupted for up to 2 weeks followed by restarting at a reduced dose. • The dose may be increased to 10 mg once daily, as tolerated, to achieve optimal response. <p>Discontinuing treatment with obeticholic acid may be considered for patients who continue to experience persistent, intolerable pruritus.</p> <p><u>Bile acid binding resins</u> For patients taking bile acid binding resins, obeticholic acid should be administered at least 4 to 6 hours before or 4 to 6 hours after taking a bile acid binding resin, or at as great an interval as possible.</p> <p><u>Missed dose</u> If a dose is missed, the missed dose should be skipped and the normal schedule should be resumed for the following dose. A double dose should not be taken to make up for the missed dose.</p> <p><u>Special populations</u></p> <p><u>Hepatic impairment</u> Obeticholic acid is contraindicated in patients with decompensated cirrhosis (e.g., Child-Pugh Class B or C) or a prior decompensation event.</p> <p>Elderly (≥ 65 years) Limited data exists in elderly patients. No dose adjustment is required for elderly patients.</p> |

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| | <p><i>Renal impairment</i> No dose adjustment is required for patients with renal impairment.</p> <p><i>Paediatric population</i> There is no relevant use of obeticholic acid in the paediatric population in the treatment of PBC.</p> <p>The tablet should be taken orally with or without food.</p> |
| <p>Conditions, delays and further rules for participation of patients</p> | <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • The treatment of patients with PBC who completed the Long-Term Safety Extension of the POISE phase 3 trial (747-301 / EudraCT 2011-004728-36). • OCALIVA is indicated for the treatment of PBC in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA. • The patient is not eligible for a clinical trial running with OCALIVA and/or a clinical trial running in the envisaged indication of this program. • The patient cannot be satisfactorily treated with the approved and commercially available alternative treatments, in accordance with clinical guidelines, because of efficacy and/or safety issues. <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of the SmPC. • Complete biliary obstruction. • Moderate or severe hepatic impairment (Child Pugh B or C or Decompensated Cirrhosis). • Age < 18 years. Expected timelines: • After the patient has signed the informed consent and the treating physician has put in a request for the patient's inclusion in the MNP with the responsible of the program, the responsible physician will make a decision within 2 to 4 weeks, after approval, the patient will be supplied with OCALIVA within 2 to 4 week . |
| <p>Duration of the program</p> | <p>Program start: as soon as this program is approved by the FAMHP</p> <p>Inclusion is dependent of patients having their final visit for the POISE trial (747-301 / EudraCT 2011-004728-36).</p> <p>The program will end as soon as reimbursement for OCALIVA is obtained, or until, in the clinical judgement of the treating physician, the patient is no longer benefiting from continuation of the treatment, or 10 years after approval of the program, whichever is sooner.</p> <p>At the moment the program ends, patients who are included in the program should switch to the commercially available medicinal product. If and as long as the medicinal product is not commercially available in Belgium in the indication of the program the applicant will continue to provide the medicinal product following the modalities of the closed program unless the program has been closed for safety issues.</p> |
| <p>Conditions of distribution</p> | <p>The drug is distributed through the UZ Leuven pharmacy</p> |

| Responsible of the program | <p>Dr Femi Adekunle Advanz Pharma Limited Suite 17, Northwood House, Northwood Avenue, Santry, Dublin 9</p> <p>T: +44 (203) – 872-5031 E: Femi.Adekunle@advanzpharma.com</p> | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| Modalities for the disposal | <p>Any unused or expired medication needs to be returned to Almac Pharma Services or destroyed in an appropriate facility as soon as possible after the patient’s discontinuation from the Medical Need Program.</p> | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| The information for registration of suspected unexpected serious adverse reactions | <p>Serious Adverse Reactions (PBRER #14; Data Lock Point 26 May 2025)</p> | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | <table border="1"> <thead> <tr> <th rowspan="3">System Organ Class (MedDRA)</th> <th rowspan="3">SARs</th> <th colspan="3">Number of subjects exposed (N) = 6,521</th> </tr> <tr> <th>All SARs</th> <th>Occurrence of fatal SARs</th> <th>Occurrence of life-threatening SARs</th> </tr> <tr> <th>n (%)</th> <th>n (%)</th> <th>n (%)</th> </tr> </thead> <tbody> <tr> <td rowspan="2">Cardiac disorders</td> <td>Palpitations</td> <td>15 (0.2%)</td> <td>0 (0.0%)</td> <td>0 (0.0%)</td> </tr> <tr> <td>Endocrine disorders</td> <td>Hypothyroidism</td> <td>21 (0.3%)</td> <td>1 (0.0%)</td> <td>0 (0.0%)</td> </tr> <tr> <td rowspan="8">Gastrointestinal disorders</td> <td>Abdominal discomfort</td> <td>4 (0.1%)</td> <td>0 (0.0%)</td> <td>0 (0.0%)</td> </tr> <tr> <td>Abdominal pain</td> <td>58 (0.9%)</td> <td>0 (0.0%)</td> <td>0 (0.0%)</td> </tr> <tr> <td>Abdominal pain lower</td> <td>4 (0.1%)</td> <td>0 (0.0%)</td> <td>0 (0.0%)</td> </tr> <tr> <td>Abdominal pain upper</td> <td>36 (0.6%)</td> <td>0 (0.0%)</td> <td>0 (0.0%)</td> </tr> <tr> <td>Abdominal tenderness</td> <td>2 (0.0%)</td> <td>0 (0.0%)</td> <td>0 (0.0%)</td> </tr> <tr> <td>Ascites</td> <td>122 (1.9%)</td> <td>0 (0.0%)</td> <td>1 (0.0%)</td> </tr> <tr> <td>Constipation</td> <td>13 (0.2%)</td> <td>0 (0.0%)</td> <td>0 (0.0%)</td> </tr> <tr> <td>Gastrointestinal pain</td> <td>1 (0.0%)</td> <td>0 (0.0%)</td> <td>0 (0.0%)</td> </tr> <tr> <td rowspan="5">General disorders and administration site conditions</td> <td>Asthenia</td> <td>19 (0.3%)</td> <td>0 (0.0%)</td> <td>0 (0.0%)</td> </tr> <tr> <td>Fatigue</td> <td>14 (0.2%)</td> <td>0 (0.0%)</td> <td>0 (0.0%)</td> </tr> <tr> <td>Oedema peripheral</td> <td>15 (0.2%)</td> <td>0 (0.0%)</td> <td>0 (0.0%)</td> </tr> <tr> <td>Peripheral swelling</td> <td>15 (0.2%)</td> <td>0 (0.0%)</td> <td>0 (0.0%)</td> </tr> <tr> <td>Pyrexia</td> <td>23 (0.4%)</td> <td>0 (0.0%)</td> <td>0 (0.0%)</td> </tr> <tr> <td rowspan="5">Hepatobiliary disorders</td> <td>Acute hepatic failure</td> <td>3 (0.0%)</td> <td>1 (0.0%)</td> <td>0 (0.0%)</td> </tr> <tr> <td>Acute on chronic liver failure</td> <td>1 (0.0%)</td> <td>1 (0.0%)</td> <td>1 (0.0%)</td> </tr> <tr> <td>Biliary cirrhosis</td> <td>6 (0.1%)</td> <td>1 (0.0%)</td> <td>0 (0.0%)</td> </tr> <tr> <td>Chronic hepatic failure</td> <td>21 (0.3%)</td> <td>6 (0.1%)</td> <td>2 (0.0%)</td> </tr> <tr> <td>Hepatic cirrhosis</td> <td>234 (3.6%)</td> <td>16 (0.2%)</td> <td>0 (0.0%)</td> </tr> </tbody> </table> | System Organ Class (MedDRA) | SARs | Number of subjects exposed (N) = 6,521 | | | All SARs | Occurrence of fatal SARs | Occurrence of life-threatening SARs | n (%) | n (%) | n (%) | Cardiac disorders | Palpitations | 15 (0.2%) | 0 (0.0%) | 0 (0.0%) | Endocrine disorders | Hypothyroidism | 21 (0.3%) | 1 (0.0%) | 0 (0.0%) | Gastrointestinal disorders | Abdominal discomfort | 4 (0.1%) | 0 (0.0%) | 0 (0.0%) | Abdominal pain | 58 (0.9%) | 0 (0.0%) | 0 (0.0%) | Abdominal pain lower | 4 (0.1%) | 0 (0.0%) | 0 (0.0%) | Abdominal pain upper | 36 (0.6%) | 0 (0.0%) | 0 (0.0%) | Abdominal tenderness | 2 (0.0%) | 0 (0.0%) | 0 (0.0%) | Ascites | 122 (1.9%) | 0 (0.0%) | 1 (0.0%) | Constipation | 13 (0.2%) | 0 (0.0%) | 0 (0.0%) | Gastrointestinal pain | 1 (0.0%) | 0 (0.0%) | 0 (0.0%) | General disorders and administration site conditions | Asthenia | 19 (0.3%) | 0 (0.0%) | 0 (0.0%) | Fatigue | 14 (0.2%) | 0 (0.0%) | 0 (0.0%) | Oedema peripheral | 15 (0.2%) | 0 (0.0%) | 0 (0.0%) | Peripheral swelling | 15 (0.2%) | 0 (0.0%) | 0 (0.0%) | Pyrexia | 23 (0.4%) | 0 (0.0%) | 0 (0.0%) | Hepatobiliary disorders | Acute hepatic failure | 3 (0.0%) | 1 (0.0%) | 0 (0.0%) | Acute on chronic liver failure | 1 (0.0%) | 1 (0.0%) | 1 (0.0%) | Biliary cirrhosis | 6 (0.1%) | 1 (0.0%) | 0 (0.0%) | Chronic hepatic failure | 21 (0.3%) | 6 (0.1%) | 2 (0.0%) | Hepatic cirrhosis | 234 (3.6%) | 16 (0.2%) | 0 (0.0%) |
| | System Organ Class (MedDRA) | | | SARs | Number of subjects exposed (N) = 6,521 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | All SARs | Occurrence of fatal SARs | Occurrence of life-threatening SARs | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | n (%) | n (%) | | n (%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Cardiac disorders | Palpitations | 15 (0.2%) | 0 (0.0%) | 0 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | Endocrine disorders | Hypothyroidism | 21 (0.3%) | 1 (0.0%) | 0 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Gastrointestinal disorders | Abdominal discomfort | 4 (0.1%) | 0 (0.0%) | 0 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | Abdominal pain | 58 (0.9%) | 0 (0.0%) | 0 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | Abdominal pain lower | 4 (0.1%) | 0 (0.0%) | 0 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | Abdominal pain upper | 36 (0.6%) | 0 (0.0%) | 0 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | Abdominal tenderness | 2 (0.0%) | 0 (0.0%) | 0 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | Ascites | 122 (1.9%) | 0 (0.0%) | 1 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | Constipation | 13 (0.2%) | 0 (0.0%) | 0 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | Gastrointestinal pain | 1 (0.0%) | 0 (0.0%) | 0 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | General disorders and administration site conditions | Asthenia | 19 (0.3%) | 0 (0.0%) | 0 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | Fatigue | 14 (0.2%) | 0 (0.0%) | 0 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | Oedema peripheral | 15 (0.2%) | 0 (0.0%) | 0 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | Peripheral swelling | 15 (0.2%) | 0 (0.0%) | 0 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | Pyrexia | 23 (0.4%) | 0 (0.0%) | 0 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Hepatobiliary disorders | Acute hepatic failure | 3 (0.0%) | 1 (0.0%) | 0 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | Acute on chronic liver failure | 1 (0.0%) | 1 (0.0%) | 1 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | Biliary cirrhosis | 6 (0.1%) | 1 (0.0%) | 0 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Chronic hepatic failure | | 21 (0.3%) | 6 (0.1%) | 2 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatic cirrhosis | | 234 (3.6%) | 16 (0.2%) | 0 (0.0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

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| | | Hepatic failure | 148 (2.3%) | 22 (0.3%) | 6 (0.1%) |
| | | Hyperbilirubinaemia | 24 (0.4%) | 0 (0.0%) | 0 (0.0%) |
| | | Jaundice | 52 (0.8%) | 2 (0.0%) | 0 (0.0%) |
| | | Jaundice cholestatic | 1 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| | | Jaundice hepatocellular | 1 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| | | Ocular icterus | 6 (0.1%) | 0 (0.0%) | 0 (0.0%) |
| | | Primary biliary cholangitis | 47 (0.7%) | 4 (0.1%) | 0 (0.0%) |
| | | Subacute hepatic failure | 1 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| | Investigations | Alanine aminotransferase increased | 10 (0.2%) | 0 (0.0%) | 0 (0.0%) |
| | | Aspartate aminotransferase increased | 8 (0.1%) | 0 (0.0%) | 0 (0.0%) |
| | | Blood alkaline phosphatase abnormal | 1 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| | | Blood alkaline phosphatase increased | 32 (0.5%) | 0 (0.0%) | 0 (0.0%) |
| | | Blood bilirubin increased | 60 (0.9%) | 1 (0.0%) | 1 (0.0%) |
| | | Blood thyroid stimulating hormone increased | 1 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| | | Heart rate irregular | 4 (0.1%) | 1 (0.0%) | 1 (0.0%) |
| | | Hepatic enzyme abnormal | 2 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| | | Hepatic enzyme increased | 19 (0.3%) | 1 (0.0%) | 0 (0.0%) |
| | | Liver function test abnormal | 8 (0.1%) | 1 (0.0%) | 0 (0.0%) |
| | | Liver function test increased | 5 (0.1%) | 0 (0.0%) | 0 (0.0%) |
| | | Musculoskeletal and connective tissue disorders | Arthralgia | 14 (0.2%) | 0 (0.0%) |
| | Dizziness | | 20 (0.3%) | 0 (0.0%) | 0 (0.0%) |
| | Nervous system disorders | Hepatic encephalopathy | 91 (1.4%) | 5 (0.1%) | 1 (0.0%) |
| | | Presyncope | 7 (0.1%) | 0 (0.0%) | 1 (0.0%) |
| | | Syncope | 43 (0.7%) | 0 (0.0%) | 1 (0.0%) |
| | | Prurigo | 1 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| | Skin and subcutaneous tissue disorders | Pruritus | 42 (0.6%) | 0 (0.0%) | 0 (0.0%) |
| | | Rash | 8 (0.1%) | 0 (0.0%) | 0 (0.0%) |
| | | Rash pruritic | 2 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| | | Rash vesicular | 2 (0.0%) | 0 (0.0%) | 0 (0.0%) |

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|--|--------------|-----------|--------------------------------|-----------------------------|-----------------------------|
| | | Urticaria | 1 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| | Total | | 1,288 (19.7%) | 63 (0.96%) | 15 (0.23%) |

Informations résumées_Français

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| Nom du médicament | OCALIVA |
| Nom de la substance active | Acide obéticholique |
| Indication et conditions d'utilisation | <p>Le programme est uniquement destiné au traitement des patients atteints de cholangite biliaire primitive (CBP) qui ont terminé l'extension de la sécurité à long terme de l'essai de phase 3 de POISE.</p> <p>Conditions d'utilisation:</p> <ul style="list-style-type: none"> • OCALIVA est indiqué dans le traitement de la CBP en association avec l'acide ursodésoxycholique (AUDC) chez les adultes insuffisamment répondeurs à l'AUDC, ou en monothérapie chez les adultes qui ne tolèrent pas l'AUDC • Avant l'instauration du traitement par acide obéticholique, il est nécessaire de connaître l'état de la fonction hépatique du patient. Il convient de déterminer au préalable si le patient est atteint d'une cirrhose décompensée (notamment classe B ou C de Child-Pugh) ou s'il a déjà présenté un épisode de décompensation car l'acide obéticholique est contre-indiqué chez ces patients. <p>La dose initiale d'acide obéticholique est de 5 mg une fois par jour pendant les 6 premiers mois. Après les 6 premiers mois, il convient d'augmenter la dose jusqu'à un maximum de 10 mg une fois par jour chez les patients qui n'ont pas obtenu une réduction adéquate du taux de phosphatases alcalines (PAL) et/ou de la bilirubine totale, et qui tolèrent l'acide obéticholique.</p> <p>Aucun ajustement de la dose de l'AUDC administrée de façon concomitante n'est nécessaire chez les patients qui reçoivent de l'acide obéticholique.</p> <p><u>Prise en charge du prurit sévère et ajustement de dose</u> Les stratégies de prise en charge incluent l'ajout de résines chélatrices des acides biliaires ou d'antihistaminiques.</p> <p>Si les patients présentent une intolérance sévère en raison du prurit, l'une, voire plusieurs, des options suivantes doivent être envisagées :</p> <ul style="list-style-type: none"> • La dose d'acide obéticholique peut être réduite à : <ul style="list-style-type: none"> ○ 5 mg un jour sur deux, chez les patients intolérants à 5 mg une fois par jour ○ 5 mg une fois par jour, chez les patients intolérants à 10 mg une fois par jour • L'administration d'acide obéticholique peut être interrompue de manière temporaire, pendant un maximum de 2 semaines, puis reprise à une dose réduite. • En fonction de la tolérance, la dose peut être augmentée à 10 mg une fois par jour, pour obtenir la réponse optimale. <p>Une interruption du traitement par acide obéticholique peut être envisagée chez les patients qui continuent de présenter un prurit persistant intolérable.</p> <p><u>Résines chélatrices des acides biliaires</u> Les patients prenant des résines chélatrices des acides biliaires doivent prendre l'acide obéticholique au moins 4 à 6 heures avant ou 4 à 6 heures après des résines chélatrices des acides biliaires, ou en respectant un intervalle aussi long que possible.</p> <p><u>Oubli d'une dose</u></p> |

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| | <p>En cas d'oubli d'une dose, la dose oubliée ne doit pas être rattrapée et la dose suivante doit être prise selon le schéma posologique habituel. Les patients ne doivent pas prendre de dose double pour compenser la dose qu'ils ont oubliée.</p> <p><u>Populations particulières</u></p> <p><i>Insuffisance hépatique</i></p> <p>L'acide obéticholique est contre-indiqué chez les patients atteints de cirrhose décompensée (par exemple, classe B ou C de Child-Pugh) ou ayant déjà subi une décompensation.</p> <p><i>Patients âgés (≥ 65 ans)</i></p> <p>Les données chez les patients âgés sont limitées. Aucun ajustement de la dose n'est nécessaire chez les patients âgés.</p> <p><i>Insuffisance rénale</i></p> <p>Aucun ajustement de la dose n'est requis chez les patients présentant une insuffisance rénale.</p> <p><i>Population pédiatrique</i></p> <p>Il n'existe pas d'utilisation</p> <p>Le comprimé doit être pris par voie orale, au moment ou en dehors des repas.</p> |
| <p>Conditions, délais et modalités selon lesquels les patients sont admis dans le programme</p> | <p>Critères d'inclusion:</p> <ul style="list-style-type: none"> • Le traitement des patients atteints de CBP qui ont terminé la prolongation de la sécurité à long terme de l'essai POISE phase 3 (747-301 / EudraCT 2011-004728-36). • OCALIVA est indiqué dans le traitement de la CBP en association avec l'acide ursodésoxycholique (AUDC) chez les adultes insuffisamment répondeurs à l'AUDC, ou en monothérapie chez les adultes qui ne tolèrent pas l'AUDC. • Le patient n'est pas éligible pour un essai clinique avec OCALIVA et / ou un essai clinique en cours dans l'indication envisagée de ce programme. • Le patient ne peut pas être traité de manière satisfaisante avec les traitements alternatifs approuvés et disponibles dans le commerce, conformément aux directives cliniques, en raison de problèmes d'efficacité et / ou d'innocuité. <p>Critères d'exclusion:</p> <ul style="list-style-type: none"> • Hypersensibilité a une des substances actives ou excipients cités dans la section 6.1 of the SmPC. • Obstruction biliaire complète. • Insuffisance Hépatique Modéré à Sévère (Child Pugh B ou C ou Cirrhose Décompensé) • Age < 18 ans. Calendrier prévu • Après que le patient a signé le consentement et que le médecin traitant a demandé l'inclusion du patient dans le MNP avec le responsable du programme, le médecin responsable prendra une décision dans les 2 à 4 semaines, après approbation , le patient sera fourni avec OCALIVA dans les 2à4 semaines. |
| <p>Durée</p> | <p>Début du Programme : dès que ce programme est approuvé par l'AFMPS Début d'inclusions en fonction de la visite finale pour l'étude POISE (747-301 / EudraCT 2011-004728-36).</p> |

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| | <p>Le programme prendra fin à l'obtention du remboursement pour OCALIVA, ou jusqu'à ce que, selon le jugement clinique du médecin traitant, le patient ne bénéficie plus de la poursuite du traitement, ou à 10 ans de l'acceptation du programme, selon la première éventualité.</p> <p>Au moment où le programme prend fin, les patients qui sont inclus dans le programme devront passer au médicament disponible sur le marché. Si et aussi longtemps que le médicament n'est pas commercialement disponible en Belgique dans l'indication du programme, le demandeur continuera à fournir le médicament selon les modalités du programme clôturé, à moins que programme n'ait été clôturé pour des raisons de sécurité.</p> | | | | |
| Conditions de distribution | Le produit est distribué par UZ Leuven Pharmacie. | | | | |
| Responsable du program | <p>Dr Femi Adekunle Advanz Pharma Limited Suite 17, Northwood House, Northwood Avenue, Santry, Dublin 9</p> <p>T: +44 (203) – 872-5031 E: Femi.Adekunle@advanzpharma.com</p> | | | | |
| Modalités selon lesquelles les médicaments non-utilisés sont traités | Tout médicament inutilisé ou périmé doit être retourné à Almac Pharma Services ou détruit dans un établissement approprié dès que possible après l'arrêt du programme médical. | | | | |
| Données pour l'enregistrement des suspicions d'effets indésirables inattendus graves | Réaction indésirables graves (PBRER n° 14 ; date limite de saisie des données: 26 mai 2025) | | | | |
| | Classe de systèmes d'organes (MedDRA) | Réaction Indésirables Graves (RIG) | Toutes les RIG n (%) | RIG fatales n (%) | RIG mettant en jeu le pronostic vital n (%) |
| | Affections cardiaques | Palpitations | 15 (0,2 %) | 0 (0,0 %) | 0 (0,0 %) |
| | Affections endocriniennes | Hypothyroïdie | 21 (0,3 %) | 1 (0,0 %) | 0 (0,0 %) |
| | Affections gastro-intestinales | Gêne abdominale | 4 (0,1 %) | 1 (0,0 %) | 0 (0,0 %) |
| | | Douleur abdominale | 58 (0,9 %) | 0 (0,0 %) | 0 (0,0 %) |
| | | Douleur abdominale basse | 4 (0.1%) | 0 (0,0 %) | 0 (0,0 %) |
| Douleur abdominal haute | | 36 (0.6%) | 0 (0,0 %) | 0 (0,0 %) | |
| Sensibilité abdominale | 2 (0.0%) | 0 (0.0%) | 0 (0.0%) | | |

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| | | Ascite | 122 (1,9 %) | 0 | 1 (0,0 %) |
| | | Constipation | 13 (0.2%) | 0 (0.0%) | 0 (0.0%) |
| | | Douleur gastrointestinale | 1 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| | Troubles généraux et anomalies au site d'administration | Asthénie | 19 (0.3%) | 0 (0.0%) | 0 (0.0%) |
| | | Fatigue | 14 (0.2%) | 0 (0.0%) | 0 (0.0%) |
| | | Oedème peripherique | 15 (0.2%) | 0 (0.0%) | 0 (0.0%) |
| | | Gonflement périfirique | 15 (0.2%) | 0 (0.0%) | 0 (0.0%) |
| | | Pyrexie | 23 (0.4%) | 0 (0.0%) | 0 (0.0%) |
| | Affections hépatobiliaires | Insuffisance hépatique aiguë | 3 (0,0 %) | 1 (0,0 %) | 1 (0,0 %) |
| | | Insuffisance hépatique aiguë sur chronique | 1 (0,0 %) | 1 (0,0 %) | 1 (0,0 %) |
| | | Cirrhose biliaire | 6 (0.1%) | 1 (0.0%) | 0 (0.0%) |
| | | Insuffisance hépatique chronique | 21 (0.3%) | 6 (0.1%) | 2 (0.0%) |
| | | Cirrhose hépatique | 234 (3.6%) | 16 (0.2%) | 0 (0.0%) |
| | | Insuffisance hépatique | 148 (2.3%) | 22 (0.3%) | 6 (0.1%) |
| | | Hyperbilirubinémie | 24 (0.4%) | 0 (0.0%) | 0 (0.0%) |
| | | Jaunisse | 52 (0.8%) | 2 (0.0%) | 0 (0.0%) |
| | | Jaunisse cholestatique | 1 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| | | Jaunisse hepatocellulaire | 1 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| | | Ictère oculaire | 6 (0.1%) | 0 (0.0%) | 0 (0.0%) |
| | | Cholangite biliaire primitive | 47 (0.7%) | 4 (0.1%) | 0 (0.0%) |
| | | Insuffisance hépatiqu sub- aigue | 1 (0.0%) | 0 (0.0%) | 0 (0.0%) |

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| Investigations | Alanine aminotransférase augmentée | 10 (0.2%) | 0 (0.0%) | 0 (0.0%) | |
| | Aspartate aminotransférase augmentée | 8 (0.1%) | 0 (0.0%) | 0 (0.0%) | |
| | Phosphatase alcaline sanguine anormale | 1 (0.0%) | 0 (0.0%) | 0 (0.0%) | |
| | Phosphatase alcaline sanguine augmentée | 32 (0.5%) | 0 (0.0%) | 0 (0.0%) | |
| | Bilirubine sanguine augmentée | 60 (0.9%) | 1 (0.0%) | 1 (0.0%) | |
| | Thyréostimuline sanguine augmentée | 1 (0.0%) | 0 (0.0%) | 0 (0.0%) | |
| | Rythme cardiaque irrégulier | 4 (0.1%) | 1 (0.0%) | 1 (0.0%) | |
| | Ezymes Hépatiques anormales | 2 (0.0%) | 0 (0.0%) | 0 (0.0%) | |
| | Enzymes hépatiques augmentées | 19 (0.3%) | 1 (0.0%) | 0 (0.0%) | |
| | Test de la fonction hépatique anormal | 8 (0.1%) | 1 (0.0%) | 0 (0.0%) | |
| | Test de la fonction hépatique augmenté | 5 (0.1%) | 0 (0.0%) | 0 (0.0%) | |
| | AFFECTIONS MUSCULOSQUELETTIQUES ET DU TISSU CONJONCTIF | Arthralgie | 14 (0.2%) | 0 (0.0%) | 0 (0.0%) |
| | Affections du système nerveux | Vertige | 20 (0.3%) | 0 (0.0%) | 0 (0.0%) |
| Encéphalopathie hépatique | | 91 (1,4 %) | 5 (0,1 %) | 1 (0,0 %) | |
| Présyncope | | 7 (0.1%) | 0 (0.0%) | 1 (0.0%) | |
| Syncope | | 43 (0.7%) | 0 (0.0%) | 1 (0.0%) | |
| Affections de la peau et du tissu sous-cutané | Prurigo | 1 (0.0%) | 0 (0.0%) | 0 (0.0%) | |
| | Prurit | 42 (0,6 %) | 0 | 0 | |
| | Rash | 8 (0.1%) | 0 (0.0%) | 0 (0.0%) | |

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| | | Rash pruritique | 2 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| | | Rash vasculaire | 2 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| | | Urticaire | 1 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| | | Total | 1 288 (19,7 %) | 63 (0,96 %) | 15 (0,23 %) |

Samengevatte informatie_Nederlands

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| Naam geneesmiddel | OCALIVA |
| Naam actieve substantie | Obeticholzuur |
| Indicatie en gebruiksvoorwaarden | <p>Het programma is alleen bedoeld voor de behandeling van patiënten met primaire gal cholangitis (PBC) die de lange-termijn veiligheidsuitbreiding van de POISE fase 3-studie hebben voltooid.</p> <p>Gebruiksvoorwaarden:</p> <ul style="list-style-type: none"> • OCALIVA is geïndiceerd voor de behandeling van primaire billiaire cholangitis (ook bekend als primaire billiaire cirrose) in combinatie met ursodeoxycholzuur (UDCA) in volwassenen met een inadequate respons op UDCA of als monotherapie in volwassenen die UDCA niet verdragen. • Alvorens de behandeling met obeticholzuur in te stellen, moet het stadium van de leverziekte van de patiënt bekend zijn. Voorafgaand aan instelling van de behandeling moet worden vastgesteld of er bij de patiënt sprake is van gedecompenseerde cirrose (inclusief Child-Pugh-klasse B of C) of dat de patiënt ooit een decompenserende gebeurtenis heeft doorgemaakt, omdat obeticholzuur bij deze patiënten gecontra-indiceerd is. <p>De startdosis van obeticholzuur is 5 mg eenmaal daags gedurende de eerste 6 maanden.</p> <p>Verhoog deze na de eerste 6 maanden tot een maximumdosis van 10 mg eenmaal daags voor patiënten</p> <ul style="list-style-type: none"> • die geen toereikende verlaging in alkalische fosfatase (AF) en/of totaal bilirubine hebben bereikt en die obeticholzuur verdragen. <p>De dosis van gelijktijdig toegediend UDCA hoeft niet te worden aangepast bij patiënten die obeticholzuur krijgen.</p> <p><u>Behandeling en dosisaanpassing voor ernstige pruritus</u> Behandelstrategieën bestaan uit het toevoegen van galzuurbindende harsen of antihistaminica.</p> <p>Voor patiënten die ernstige intolerantie ervaren vanwege pruritus, dient een of meer van de volgende situaties te worden overwogen:</p> <ul style="list-style-type: none"> • De dosis obeticholzuur kan worden verlaagd tot: <ul style="list-style-type: none"> ○ 5 mg om de andere dag, voor patiënten die 5 mg eenmaal daags niet kunnen verdragen ○ 5 mg eenmaal daags, voor patiënten die 10 mg eenmaal daags niet kunnen verdragen • De dosis obeticholzuur kan tijdelijk gedurende maximaal 2 weken worden onderbroken, waarna de behandeling opnieuw wordt gestart met een verlaagde dosis. • De dosis kan worden verhoogd tot 10 mg eenmaal daags, naargelang dit wordt verdragen, om een optimale respons te bereiken. <p>Stopzetting van de behandeling met obeticholzuur kan worden overwogen voor patiënten die onverdraagbare pruritus blijven hebben.</p> <p><u>Galzuurbindende harsen</u></p> <p>Voor patiënten die galzuurbindende harsen innemen, moet obeticholzuur minstens 4 tot 6 uur vóór of 4 tot 6 uur na inname van een galzuurbindende hars of met een zo groot mogelijke tussenperiode, worden toegediend.</p> |

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| | <p><u>Gemiste dosis</u> Als een dosis niet is ingenomen, dient de gemiste dosis te worden overgeslagen en het normale schema voor de volgende dosis te worden hervat. Er mag geen dubbele dosis worden ingenomen om de gemiste dosis in te halen.</p> <p><u>Speciale populaties</u></p> <p><u>Leverfunctiestoornis</u> Obeticholzuur is gecontra-indiceerd bij patiënten met gedecompenseerde cirrose (bijv. Child-Pughklasse B of C) of met een eerder doorgemaakte decompenserende gebeurtenis.</p> <p><u>Ouderen (≥ 65 jaar)</u> Er zijn beperkte gegevens over oudere patiënten. De dosis hoeft niet te worden aangepast voor oudere patiënten.</p> <p><u>Nierfunctiestoornis</u> De dosis hoeft niet te worden aangepast voor patiënten met een nierfunctiestoornis.</p> <p><u>Pediatrische patiënten</u> Er is geen relevante toepassing van obeticholzuur bij pediatrische patiënten voor de behandeling van PBC.</p> <p>De tablet moet oraal met of zonder voedsel worden ingenomen.</p> |
| <p>Voorwaarden, termijnen en nadere regelen waaronder patiënten worden toegelaten</p> | <p>Inclusie criteria:</p> <ul style="list-style-type: none"> • Participatie in de fase 3 POISE trial (747-301 / EudraCT 2011-004728-36). • OCALIVA is geïndiceerd voor de behandeling van primaire billiaire cholangitis (ook bekend als primaire billiaire cirrose) in combinatie met ursodeoxycholzuur (UDCA) in volwassenen met een inadequate respons op UDCA of als monotherapie in volwassen die UDCA niet verdragen. • De patiënt komt niet in aanmerking voor een klinische proef met OCALIVA en / of een klinische proef die wordt uitgevoerd in de beoogde indicatie van dit programma. • De patiënt kan niet op bevredigende wijze worden behandeld met de goedgekeurde en in de handel verkrijgbare alternatieve behandelingen, in overeenstemming met klinische richtlijnen, vanwege werkzaamheid en / of veiligheidskwesties. <p>Exclusie criteria:</p> <ul style="list-style-type: none"> • Overgevoeligheid voor de actieve stof of een van de hulpstoffen vermeld in sectie 6.1. van de SmPC. • Complete biliaire obstructie. • Matige of ernstige leverfunctiestoornis (Child Pugh B of C of gedecompenseerde cirrose). • Leeftijd < 18 jaar. Verwachte tijdlijnen: • Nadat de patiënt het informed consent heeft ondertekend en de behandelende arts een verzoek heeft ingediend om de patiënt op te nemen in het MNP bij de verantwoordelijke van het programma, zal de verantwoordelijke arts binnen 2-4 weeks een beslissing nemen, na goedkeuring zal de patiënt binnen 2-4 weeks worden voorzien van OCALIVA. |

| Looptijd | <p>Programma start: zodra dit programma is goedgekeurd door het FAGG</p> <p>Inclusie is afhankelijk van de het laatste studiebezoek van patiënt voor de POISE trial (747-301 / EudraCT 2011-004728-36).</p> <p>Het programma zal eindigen zodra terugbetaling voor OCALIVA behaald is of totdat, in het klinische oordeel van de behandelend arts, de patiënt niet langer baat heeft bij voortzetting van de behandeling, of 10 jaar na goedkeuring van het programma, naargelang wat zich eerder voordoet.</p> <p>Op het moment dat het programma eindigt, dienen patiënten die in het programma zijn opgenomen over te stappen op het commercieel beschikbare geneesmiddel. Indien en zolang het geneesmiddel in België niet commercieel beschikbaar is in de indicatie van het programma, blijft de aanvrager het geneesmiddel verstrekken volgens de modaliteiten van het afgesloten programma, tenzij het programma is afgesloten wegens veiligheidsproblemen.</p> | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| Distributievoorwaarden | Het geneesmiddel wordt geleverd via de apotheek van het UZ Leuven. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Verantwoordelijke van het programma | <p>Dr Femi Adekunle Advanz Pharma Limited Suite 17, Northwood House, Northwood Avenue, Santry, Dublin 9</p> <p>T: +44 (203) – 872-5031 E: Femi.Adekunle@advanzpharma.com</p> | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Modaliteiten voor de behandeling van niet-gebruikt geneesmiddel | Al het ongebruikte of verlopen geneesmiddel moet worden teruggebracht naar Almac Pharma Services of worden vernietigd in een geschikte faciliteit, zo snel mogelijk nadat de patiënt het medische noodprogramma is gestopt. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Gegevens voor de registratie van vermoedens van onverwachte ernstige bijwerkingen | <p>Ernstige bijwerkingen (PBRER #14; Data Lock Point 26 mei 2025)</p> <table border="1" data-bbox="523 1312 1538 2009"> <thead> <tr> <th rowspan="3">Systeem Orgaan Klasse (MedDRA)</th> <th rowspan="3">SAR's</th> <th colspan="3">Aantal blootgestelde proefpersonen (N) = 6.521</th> </tr> <tr> <th>Alle SAR's</th> <th>Voorkomen van fatale SAR's</th> <th>Voorkomen van levensbedreigende SAR's</th> </tr> <tr> <th>n* (%)</th> <th>n (%)</th> <th>n (%)</th> </tr> </thead> <tbody> <tr> <td>Hartaandoeningen</td> <td>Palpitaties</td> <td>15 (0,2%)</td> <td>0 (0,0%)</td> <td>0 (0,0%)</td> </tr> <tr> <td>Endocriene aandoeningen</td> <td>Hypothyreoïdie</td> <td>21 (0,3%)</td> <td>1 (0,0%)</td> <td>0 (0,0%)</td> </tr> <tr> <td rowspan="7">Maagdarmstelselaandoeningen</td> <td>Buikongemak</td> <td>4 (0,1%)</td> <td>0 (0,0%)</td> <td>0 (0,0%)</td> </tr> <tr> <td>Buikpijn</td> <td>58 (0,9%)</td> <td>0 (0,0%)</td> <td>0 (0,0%)</td> </tr> <tr> <td>Pijn in onderbuik</td> <td>4 (0,1%)</td> <td>0 (0,0%)</td> <td>0 (0,0%)</td> </tr> <tr> <td>Pijn in bovenbuik</td> <td>36 (0,6%)</td> <td>0 (0,0%)</td> <td>0 (0,0%)</td> </tr> <tr> <td>Buikgevoeligheid</td> <td>2 (0,0%)</td> <td>0 (0,0%)</td> <td>0 (0,0%)</td> </tr> <tr> <td>Ascites</td> <td>122 (1,9%)</td> <td>0 (0,0%)</td> <td>1 (0,0%)</td> </tr> <tr> <td>Obstipatie</td> <td>13 (0,2%)</td> <td>0 (0,0%)</td> <td>0 (0,0%)</td> </tr> <tr> <td rowspan="2">Algemene aandoeningen en toedieningsplaa</td> <td>Asthenie</td> <td>19 (0,3%)</td> <td>0 (0,0%)</td> <td>0 (0,0%)</td> </tr> <tr> <td>Vermoeidheid</td> <td>14 (0,2%)</td> <td>0 (0,0%)</td> <td>0 (0,0%)</td> </tr> </tbody> </table> | Systeem Orgaan Klasse (MedDRA) | SAR's | Aantal blootgestelde proefpersonen (N) = 6.521 | | | Alle SAR's | Voorkomen van fatale SAR's | Voorkomen van levensbedreigende SAR's | n* (%) | n (%) | n (%) | Hartaandoeningen | Palpitaties | 15 (0,2%) | 0 (0,0%) | 0 (0,0%) | Endocriene aandoeningen | Hypothyreoïdie | 21 (0,3%) | 1 (0,0%) | 0 (0,0%) | Maagdarmstelselaandoeningen | Buikongemak | 4 (0,1%) | 0 (0,0%) | 0 (0,0%) | Buikpijn | 58 (0,9%) | 0 (0,0%) | 0 (0,0%) | Pijn in onderbuik | 4 (0,1%) | 0 (0,0%) | 0 (0,0%) | Pijn in bovenbuik | 36 (0,6%) | 0 (0,0%) | 0 (0,0%) | Buikgevoeligheid | 2 (0,0%) | 0 (0,0%) | 0 (0,0%) | Ascites | 122 (1,9%) | 0 (0,0%) | 1 (0,0%) | Obstipatie | 13 (0,2%) | 0 (0,0%) | 0 (0,0%) | Algemene aandoeningen en toedieningsplaa | Asthenie | 19 (0,3%) | 0 (0,0%) | 0 (0,0%) | Vermoeidheid | 14 (0,2%) | 0 (0,0%) | 0 (0,0%) |
| Systeem Orgaan Klasse (MedDRA) | SAR's | | | Aantal blootgestelde proefpersonen (N) = 6.521 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | | | Alle SAR's | Voorkomen van fatale SAR's | Voorkomen van levensbedreigende SAR's | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | n* (%) | n (%) | n (%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hartaandoeningen | Palpitaties | 15 (0,2%) | 0 (0,0%) | 0 (0,0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Endocriene aandoeningen | Hypothyreoïdie | 21 (0,3%) | 1 (0,0%) | 0 (0,0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Maagdarmstelselaandoeningen | Buikongemak | 4 (0,1%) | 0 (0,0%) | 0 (0,0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Buikpijn | 58 (0,9%) | 0 (0,0%) | 0 (0,0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Pijn in onderbuik | 4 (0,1%) | 0 (0,0%) | 0 (0,0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Pijn in bovenbuik | 36 (0,6%) | 0 (0,0%) | 0 (0,0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Buikgevoeligheid | 2 (0,0%) | 0 (0,0%) | 0 (0,0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Ascites | 122 (1,9%) | 0 (0,0%) | 1 (0,0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Obstipatie | 13 (0,2%) | 0 (0,0%) | 0 (0,0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Algemene aandoeningen en toedieningsplaa | Asthenie | 19 (0,3%) | 0 (0,0%) | 0 (0,0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Vermoeidheid | 14 (0,2%) | 0 (0,0%) | 0 (0,0%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

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|------------|---|-------------------------------|-----------------------------------|-----------|----------|
| | tscondities | Perifeer oedeem | 15 (0,2%) | 0 (0,0%) | 0 (0,0%) |
| | | Zwelling van ledematen | 15 (0,2%) | 0 (0,0%) | 0 (0,0%) |
| | | Koorts | 23 (0,4%) | 0 (0,0%) | 0 (0,0%) |
| | Lever- en galwegaan doeningen | Acuut leverfalen | 3 (0,0%) | 1 (0,0%) | 0 (0,0%) |
| | | Acuut op chronisch leverfalen | 1 (0,0%) | 1 (0,0%) | 1 (0,0%) |
| | | Galkanaalcirrose | 6 (0,1%) | 1 (0,0%) | 0 (0,0%) |
| | | Chronisch leverfalen | 21 (0,3%) | 6 (0,1%) | 2 (0,0%) |
| | | Levercirrose | 234 (3,6%) | 16 (0,2%) | 0 (0,0%) |
| | | Leverfalen | 148 (2,3%) | 22 (0,3%) | 6 (0,1%) |
| | | Hyperbilirubinemie | 24 (0,4%) | 0 (0,0%) | 0 (0,0%) |
| | | Geelzucht | 52 (0,8%) | 2 (0,0%) | 0 (0,0%) |
| | | Cholestatische geelzucht | 1 (0,0%) | 0 (0,0%) | 0 (0,0%) |
| | | Hepatocellulaire geelzucht | 1 (0,0%) | 0 (0,0%) | 0 (0,0%) |
| | | Oculaire icterus | 6 (0,1%) | 0 (0,0%) | 0 (0,0%) |
| | | Primaire biliare cholangitis | 47 (0,7%) | 4 (0,1%) | 0 (0,0%) |
| | | Subacuut leverfalen | 1 (0,0%) | 0 (0,0%) | 0 (0,0%) |
| | | Onderzoeken | Alanine-aminotransferase verhoogd | 10 (0,2%) | 0 (0,0%) |
| | Aspartaat-aminotransferase verhoogd | | 8 (0,1%) | 0 (0,0%) | 0 (0,0%) |
| | Alkalische fosfatase abnormaal | | 1 (0,0%) | 0 (0,0%) | 0 (0,0%) |
| | Alkalische fosfatase verhoogd | | 32 (0,5%) | 0 (0,0%) | 0 (0,0%) |
| | Bilirubine in bloed verhoogd | | 60 (0,9%) | 1 (0,0%) | 1 (0,0%) |
| | TSH in bloed verhoogd | | 1 (0,0%) | 0 (0,0%) | 0 (0,0%) |
| | Onregelmatige hartslag | | 4 (0,1%) | 1 (0,0%) | 1 (0,0%) |
| | Abnormale leverenzymen | | 2 (0,0%) | 0 (0,0%) | 0 (0,0%) |
| | Leverenzymen verhoogd | | 19 (0,3%) | 1 (0,0%) | 0 (0,0%) |
| | Abnormale leverfunctietest | | 8 (0,1%) | 1 (0,0%) | 0 (0,0%) |
| | Verhoogde leverfunctietest | | 5 (0,1%) | 0 (0,0%) | 0 (0,0%) |
| | Musculoskeletale en bindweefselaan doeningen | Artralgie | 14 (0,2%) | 0 (0,0%) | 0 (0,0%) |
| | Zenuwstelse laandoeningen | Duizeligheid | 20 (0,3%) | 0 (0,0%) | 0 (0,0%) |
| | | Hepatische encefalopathie | 91 (1,4%) | 5 (0,1%) | 1 (0,0%) |
| Presyncope | | 7 (0,1%) | 0 (0,0%) | 1 (0,0%) | |

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| | | Syncope | 43 (0,7%) | 0 (0,0%) | 1 (0,0%) |
| | Huid- en onderhuidaan doeningen | Prurigo | 1 (0,0%) | 0 (0,0%) | 0 (0,0%) |
| | | Jeuk | 42 (0,6%) | 0 (0,0%) | 0 (0,0%) |
| | | Uitslag | 8 (0,1%) | 0 (0,0%) | 0 (0,0%) |
| | | Jeukende uitslag | 2 (0,0%) | 0 (0,0%) | 0 (0,0%) |
| | | Blaasvormige uitslag | 2 (0,0%) | 0 (0,0%) | 0 (0,0%) |
| | | Netelroos | 1 (0,0%) | 0 (0,0%) | 0 (0,0%) |
| | | Totaal | | 1,288 (19.7%) | 63 (0.96%) |