PIFELTRO®▼
Doravirine

DELSTRIGO®▼
Doravirine/Lamivudine/Tenofovir disoproxil fumarate

PRESCRIBING INFORMATION
Refer to Summary of Product Characteristics (SmPC) before prescribing

Adverse events should be reported. Reporting forms and information 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 MSD, UK (Tel: 01992 467272). By clicking the above link you will leave the MSD website and be taken to the MHRA website.

PRESENTATION
Pifeltro: film-coated tablet containing 100 mg doravirine.
Delstrigo: film-coated tablet containing 100 mg doravirine, 300 mg lamivudine and 300 mg tenofovir disoproxil fumarate, equivalent to 245 mg of tenofovir disoproxil.

USES
Pifeltro: For use in combination with other antiretrovirals, for the treatment of HIV-1 without past or present evidence of resistance to non-nucleoside reverse transcriptase inhibitors (NNRTI).
Delstrigo: For the treatment of HIV-1 without past or present evidence of resistance to NNRTIs, lamivudine or tenofovir.

DOSAGE AND ADMINISTRATION
Therapy should be initiated by a physician experienced in HIV infection management. **Pifeltro:** One 100 mg tablet once daily. **Delstrigo:** One 100/300/245 mg tablet once daily. **Pifeltro and Delstrigo**: If co-administered with rifabutin or other moderate CYP3A inducers, increase doravirine dose to 100 mg twice daily (12 hours apart). **Pifeltro:** *Elderly*: No dose adjustment necessary. *Renal impairment*: No dose adjustment necessary. *Hepatic impairment*: mild to moderate: no dosage adjustment required; severe: use with caution. **Delstrigo:** *Elderly*: Special care advised. *Renal impairment*: estimated creatinine clearance (CrCl) ≥ 50 mL/min: no dose adjustment necessary; estimated CrCl <50 mL/min: not recommended. *Hepatic impairment*: mild to moderate: no adjustment required; severe hepatic: use with caution.

CONTRA-INDICATIONS
Hypersensitivity to the active substance or excipients
Co-administration with strong CYP3A inducers.

PRECAUTIONS
A residual risk of sexual transmission of HIV-1 cannot be excluded and precautions should be taken in accordance with national guidelines. Use with CYP3A inducers may reduce the exposure of doravirine. Autoimmune disorders and immune reactivation syndrome have been reported in patients treated with combination antiretroviral therapy which may require investigation and treatment. Contains lactose monohydrate.
Delstrigo: Post-treatment exacerbation of HBV (including hepatic decompensation and liver failure) have been reported in patients co-infected with HIV-1 and HBV following discontinuation of lamivudine or tenofovir disproxil. Monitor patients co-infected with HIV-1 and HBV after discontinuation of Delstrigo and if appropriate initiate anti-HBV therapy. Renal impairment, including acute renal failure and Fanconi syndrome have been reported with tenofovir disoproxil. Assess estimated CrCl prior to initiation and during therapy. In patients at risk of renal dysfunction, serum phosphorus, urine glucose, and urine protein should also be assessed. Discontinue therapy if estimated CrCl declines below 50 mL/min. Avoid with concurrent or recent use of nephrotoxic medicinal products (e.g. high-dose or multiple NSAIDs). Evaluation of renal function is recommended for persistent or worsening bone pain, pain in extremities, fractures, and/or muscular pain or weakness. Assessment of bone mineral density should be considered for patients who have a history of pathologic bone fracture or other risk factors for osteoporosis or bone loss. Hypophosphatemia and osteomalacia secondary to proximal renal tubulopathy should be considered in patients at risk of renal dysfunction who present with persistent or worsening bone or muscle symptoms. Doravirine/lamivudine/tenofovir disoproxil must not be co-administered with other medicinal products containing lamivudine, tenofovir disoproxil, or tenofovir alafenamide or with adefovir dipivoxil. Doravirine/lamivudine/tenofovir disoproxil should not be administered with doravirine unless needed for dose adjustment (e.g. co-administered with rifabutin).
Drug interactions: Refer to SmPC for full information on drug interactions. **Pifeltro and Delstrigo:** Doravirine is metabolized primarily by CYP3A. Do not co-administer with strong CYP3A enzyme inducers. If co-administeration with rifabutin or other moderate CYP3A inducers cannot be avoided, increase doravirine dose to 100 mg twice daily (taken 12 hours apart). Use with caution when co-administering doravirine with medicinal products that are sensitive CYP3A substrates that have a narrow therapeutic window (e.g., midazolam,

tacrolimus and sirolimus). **Delstrigo:** Do not administer with other antiretroviral medicinal products. Co-administration of doravirine/lamivudine/tenofovir disoproxil with medicinal products that reduce renal function or compete for active tubular secretion may increase serum concentrations of lamivudine. Co-administration of doravirine/lamivudine/tenofovir disoproxil with medicinal products that reduce renal function or compete for active tubular secretion via OAT1, OAT3 or MRP4 may increase serum concentrations of tenofovir. Avoid with concurrent or recent use of nephrotoxic medicinal products.
Pregnancy and Lactation: Pifeltro and Delstrigo: Avoid use during pregnancy. An Antiretroviral Pregnancy Registry has been established. Breastfeeding is not recommended.

SIDE EFFECTS
Refer to SmPC for complete information on side-effects.
Pifeltro and Delstrigo: ***Common:*** abnormal dreams, insomnia, headache, dizziness, somnolence, nausea, diarrhoea, abdominal pain, vomiting, rash, fatigue, flatulence, increased alanine aminotransferase. ***Uncommon:*** depression, hypophosphataemia, suicidal ideation, paraesthesia, asthenia. ***Rare***: rash pustular, hypomagnesaemia, aggression, hallucination, dyspnoea, acute kidney injury, renal disorder, calculus urinary, nephrolithiasis, chest pain. **Delstrigo:** ***Common:*** cough, nasal symptoms, alopecia, muscle disorders, fever. ***Uncommon:*** neutropenia, anaemia, thrombocytopenia, pancreatitis, rhabdomyolysis, proximal renal tubulopathy (including Fanconi syndrome). ***Rare:*** lactic acidosis, hepatitis, angioedema, myopathy, acute renal failure, renal failure, acute tubular necrosis, nephritis (including acute interstitial) and nephrogenic diabetes insipidus. ***Very Rare:*** pure red cell aplasia, peripheral neuropathy (or paraesthesia).

Delstrigo: Lactic acidosis has been reported with tenofovir disoproxil alone or in combination with other antiretrovirals. Predisposing factors such as decompensated liver disease, or patients receiving concomitant medications known to induce lactic acidosis are at increased risk of experiencing severe lactic acidosis during tenofovir disoproxil treatment, including fatal outcomes.

PACKAGE QUANTITIES AND BASIC NHS COST
Pifeltro: Bottle of 30 tablets £471.41
Delstrigo: Bottle of 30 tablets £578.55

Marketing Authorisation number
Pifeltro: EU/1/18/1332/001
Delstrigo: EU/1/18/1333/001

Marketing Authorisation holder
Merck Sharp & Dohme B.V.
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The Netherlands

Legal Category: POM

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