ISENTRESS® 600 mg Film-Coated Tablets (raltegravir)

PRESCRIBING INFORMATION
Refer to Summary of Product Characteristics 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: 0208 1548000).
By clicking the above link you will leave the MSD website and be taken to the MHRA website.

PRESENTATION
Film-coated tablet containing 600 mg of raltegravir (as potassium).

USES
For use in combination with other anti-retroviral medicinal products for the treatment of human immunodeficiency virus (HIV-1) infection in patients weighing at least 40 kg.

DOSAGE AND ADMINISTRATION: Therapy to be initiated by a physician experienced in the management of HIV infection. *Recommended dose:* 2 x 600 mg tablets once daily for patients weighing at least 40 kg who are treatment naïve or virologically suppressed on initial raltegravir regimen of 400 mg twice daily. Refer to SmPC for full dosing information. *Elderly:* Use with caution. *Renal impairment*: No dosage adjustment required. *Hepatic impairment:* No dosage adjustment required for mild to moderate hepatic impairment. Use with caution in severe hepatic impairment.

CONTRA-INDICATIONS: Hypersensitivity to the active ingredients or excipients.

PRECAUTIONS: Advise patients that current ART does not cure HIV and has not been proven to prevent the transmission of HIV to others through blood or sexual contact. Effective viral suppression with ART has been proven to substantially reduce the risk of sexual transmissions but a residual risk cannot be excluded. Advise patients to continue with appropriate precautions.
Raltegravir has a relatively low genetic barrier to resistance. When possible, administer raltegravir with two other active ARTs to minimise the potential for virological failure and the development of resistance.
Use with caution in patients with a pre-existing history of depression or psychiatric illness.
Monitor patients with pre-existing liver dysfunction including chronic hepatitis. Consider interruption or discontinuation if evidence of worsening liver disease exists.
Patients with chronic hepatitis B or C treated with combination ART are at an increased risk for severe and potentially fatal hepatic adverse events.
Osteonecrosis has been reported. Advise patients to seek medical advice if they experience joint effects or difficulty in movement.
An inflammatory reaction to asymptomatic or residual opportunistic pathogens may arise in HIV-infected patients with severe immune deficiency. Evaluate symptoms and institute treatment when necessary. Autoimmune disorders (such as Graves' disease and autoimmune hepatitis) have been reported. These can occur many months after initiation of treatment.
Use with caution in patients with a history of myopathy and rhabdomyolysis or any risk factors associated with these conditions.
Severe, potentially life threatening and fatal skin reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported; in most cases other medications associated with these reactions were used concomitantly. Hypersensitivity reactions have been reported. Discontinue Isentress and other suspect agents immediately if signs or symptoms of severe skin reactions or hypersensitivity reactions develop. Monitor clinical status including liver aminotransferase and initiate appropriate therapy.
Rash occurred more commonly in patients receiving Isentress with darunavir compared to patients receiving either medicine alone.
Contains lactose: Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.
Contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'
Drug interactions: Refer to SmPC for full information on drug interactions. *In vitro* studies indicated that raltegravir is not a substrate of cytochrome P450 (CYP) enzymes, does not inhibit CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP3A, P-glycoprotein-mediated transport,

UDP glucuronosyltransferases (UGTs) 1A1 and 2B7, and does not induce CYP3A4.
Effect of other agents on the pharmacokinetics of raltegravir: Raltegravir is metabolised primarily via UGT1A1. As the impact of strong inducers of UGT1A1 on raltegravir 1200 mg once daily is unknown, rifampicin is not recommended. Less potent inducers (e.g., efavirenz, nevirapine, etravirine, rifabutin, glucocorticoids, St. John's wort, pioglitazone) may be used.
Co-administration of raltegravir 1200 mg once daily with either atazanavir or the combination of tipranavir/ritonavir is not recommended. Co-administration of raltegravir 1,200 mg once daily with aluminium/magnesium and calcium carbonate containing antacids is not recommended. Co-administration with iron salts leads to reduced raltegravir plasma levels. Administering iron salts at least 2 hours from raltegravir may allow to limit this effect. All interactions studies were performed in adults.

Pregnancy and Lactation: Not recommended during pregnancy or breastfeeding. An Anti-retroviral Pregnancy Registry has been established which physicians are encouraged to use.

SIDE EFFECTS
Refer to Summary of Product Characteristics for complete information on side-effects

Frequencies of adverse reactions are defined as common (≥1/100 to <1/10) and uncommon (≥1/1,000 to <1/100).
Common: decreased appetite, abnormal dreams, insomnia, nightmare, abnormal behaviour, depression, dizziness, headache, psychomotor hyperactivity vertigo, abdominal distention, abdominal pain, flatulence, diarrhoea, nausea, vomiting, dyspepsia, rash, fatigue, asthenia, pyrexia, increased ALT, AST, blood triglycerides, lipase and blood pancreatic amylase, and atypical lymphocytes.

Uncommon (serious): lymph node abscess, neutropenia, thrombocytopenia, immune reconstitution syndrome, drug hypersensitivity, diabetes mellitus, mental disorder, anxiety, confusional state, major depression, suicidal ideation, suicidal behaviour, amnesia, cognitive disorder, memory impairment, visual impairment, sinus bradycardia, ventricular extrasystoles, erosive duodenitis, pancreatitis acute, rectal haemorrhage, hepatitis, hepatic steatosis, hepatic failure, Stevens Johnson syndrome, renal failure, nephritis, renal impairment, increased blood ALP, bilirubin, increased INR, decreased platelet count, accidental overdose, drug rash with eosinophilia and systemic symptoms (DRESS).

In raltegravir 400 mg twice daily, cancers were reported. The types and rates of specific cancers were those expected in a highly immune-deficient population. The risk of developing cancer in these studies was similar in the groups receiving Isentress and in the groups receiving comparators.

Rhabdomyolysis was an uncommonly reported serious adverse reaction in post-marketing use of raltegravir 400 mg twice daily.

Paediatric population: Isentress 600 mg tablet formulation has not been studied in paediatric patients.

PACKAGE QUANTITIES AND BASIC NHS COST: Bottles of 60 tablets: £471.41

Marketing Authorisation number:
Great Britain: PLGB 53095/0033

UK (Northern Ireland): EU/1/07/436/006

Marketing Authorisation holder:
Great Britain:
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UK

UK (Northern Ireland):
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Legal Category: POM

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