Interactions with Duvyzat® (givinostat) – Key information

Duvyzat® Summary of Product Characteristics

Effect of other medicinal products on givinostat pharmacokinetics

Avoid concomitant use of Duvyzat® with other product(s) with a known potential to prolong the QTc interval. If concomitant use cannot be avoided, obtain ECGs when initiating, during concomitant use, and as clinically indicated (see section 4.4). Withhold Duvyzat® if the QTc interval is > 500 ms or the change from baseline is > 60 ms.

Duvyzat® can cause QTc interval prolongation. Caution is advised when prescribing Duvyzat® with medicinal products known to prolong the QTc interval with known or possible risk for torsades de pointes, e.g. anaesthetics (e.g. sevoflurane, propofol), class III antiarrhythmics (e.g. amiodarone, sotalol), antiemetics (ondansetron), antibiotics (fluconazole, azithromycin, clarithromycin, ciprofloxacin), antipsychotics (aripiprazole, risperidone), and antihistamines (e.g. famotidine). This list is indicative and not exhaustive.[1]

Effect of givinostat on pharmacokinetics of other medicinal products

Givinostat is a weak intestinal CYP3A4 inhibitor.

Closely monitor when Duvyzat® is used in combination with orally administered CYP3A4 sensitive substrates (e.g., alfentanil, tacrolimus, sirolimus, lovastatin, simvastatin, indinavir, sildenafil, eletriptan, midazolam) for which a small change in substrate plasma concentration may lead to serious toxicities.

Givinostat is a weak inhibitor of the renal uptake transporter OCT2.

Closely monitor when Duvyzat® is used in combination with drugs known as a sensitive substrate of the OCT2 transporter (e.g.: metformin, dofetilide) for which a small change in substrate plasma concentration may lead to serious toxicities.[1]

Information from Phase III trial EPIDYS

EPIDYS was a phase III randomised, double-blind, parallel-group, placebo-controlled clinical study in boys with DMD who were ambulant. It included 179 patients randomised 2:1 givinostat:placebo.[2]

Givinostat or placebo were administered in addition to a stable dose of corticosteroids throughout the study. A total of 28 (23.7%) subjects in the givinostat group and 14 (23.0%) subjects in the placebo group received prior steroid treatments. Additionally, drugs known to increase the QT interval were to be used with caution. After the screening visit, medication to treat minor treatment-emergent illnesses were permitted during EPIDYS.[3]

Further Information

Contacting the manufacturer of the other medication may also provide further advice or information.

Noting the givinostat SmPC list of medicinal products known to prolong the QTc interval is not exhaustive, other sources of drug information can be consulted, such as the CredibleMeds database [4] or Medicines Complete Stockley's Drug Interactions.[5]

Duvyzat®

(givinostat) 8.86 mg/mL Oral suspension

Prescribing information

Please refer to the Summary of Product Characteristics before prescribing.

Indication: For the treatment of Duchenne muscular dystrophy (DMD) in patients 6 years of age and older.
Presentation: Oral suspension. White to off-white or faintly pink, peach-cream flavoured suspension. Each mL contains 8.86 mg of givinostat (equivalent to 10 mg of givinostat hydrochloride monohydrate).
Posology and administration: Obtain and evaluate baseline platelet counts and triglycerides prior to initiation of givinostat. Do not initiate givinostat in patients with a platelet count less than 150 x 10^9/L. Monitor platelet counts and triglycerides as recommended during treatment. In patients with underlying cardiac disease or taking concomitant medications that cause QT prolongation, obtain electrocardiograms (ECGs) when initiating treatment with givinostat, during concomitant use, and as clinically indicated.
Posology: The recommended dosage of givinostat is based on body weight and administered orally twice daily (bd) with food.

Weight	Dosage	Oral suspension volume
10 kg to <20 kg	22.2 mg bd	2.5 mL bd
20 kg to <40 kg	31 mg bd	3.5 mL bd
40 kg to <60 kg	44.3 mg bd	5 mL bd
60 kg or more	53.2 mg bd	6 mL bd

± Based on actual body weight.

Dose modification: For decrease in platelets, diarrhoea, increase in triglycerides. Givinostat may cause adverse reactions, which may necessitate a dosage modification if the following occur; moderate or severe diarrhoea; platelet count <150 x 10^9/L; fasting triglycerides >3.42 mmol/L both verified by two assessments 1 week apart. Based on the severity of these adverse reactions, treatment interruption prior to dosage modification should be considered, see table.

	First dosage modification*		Second dosage modification**	
Weight	Dosage	Oral suspension	Dosage	Oral suspension
10 to <20 kg	17.7 mg bd	2 mL bd	13.3 mg bd	1.5 mL bd
20 to <40 kg	22.2 mg bd	2.5 mL bd	17.7 mg bd	2 mL bd
40 to <60 kg	31 mg bd	3.5 mL bd	26.6 mg bd	3 mL bd
60 kg or more	39.9 mg bd	4.5 mL bd	35.4 mg bd	4 mL bd

*If any of the adverse reaction(s) persist after the first dosage modification, proceed to the second dosage modification. **If the adverse reaction(s) persist after the second dosage modification, givinostat should be discontinued. Withhold givinostat if the QTc interval is >500 ms or the change from baseline is >60 ms.

Administration: For oral use only. Before use, shake the givinostat suspension for at least 30 seconds by inverting the bottle by 180°. Visually verify the homogeneity of the suspension. Using a graduated oral syringe, measure the appropriate volume of suspension corresponding to the prescribed dose of givinostat. Administer orally.
Missed dose: If a dose is missed, patients should not take double or extra doses.
Renal impairment: The pharmacokinetics and safety of givinostat have not been studied in patients with renal impairment. However, renal impairment is not expected to impact the exposure of givinostat because renal excretion is not a significant route of givinostat elimination.
Hepatic impairment: No data is available. Givinostat is highly metabolised, and the impact of hepatic impairment cannot be excluded.
Paediatrics: Safety and effectiveness in paediatric patients below the age of 6 years have not been established.
Contraindications: ***Hypersensitivity to givinostat or any of the excipients:*** polysorbate 20, glycerol, tragacanth gum, sodium benzoate, peach flavour (natural flavouring substances, flavouring substances, propylene glycol), cream flavour (natural flavouring substances, flavouring substances, propylene glycol), saccharin sodium, liquid sorbitol, tartaric acid, sodium hydroxide, purified water.
Warnings and precautions: ***Haematological changes:*** Givinostat can cause dose-related thrombocytopenia and other signs of myelosuppression, including decreased haemoglobin and neutropenia. In the study EPIDYS, thrombocytopenia occurred in 33% of patients treated with givinostat. The maximum decrease in platelets occurred within the first 2 months and remained low throughout the course of therapy. In a few patients, thrombocytopenia was associated with bleeding events including epistaxis, haematoma or contusions. Low platelet counts resulted in givinostat dose reduction in 28% of patients. Decreased levels of haemoglobin and neutrophils were also observed in patients treated with givinostat compared to placebo. Blood counts should be monitored every 2 weeks for the first 2 months of treatment, at month 3 and then every 3 months thereafter. If a patient develops signs or symptoms of thrombocytopenia, a platelet count should be obtained as soon as possible, and dosing should be held until platelet count is confirmed.
Increased triglycerides: Givinostat can cause elevations in triglycerides. In the EPIDYS study, hypertriglyceridemia occurred in 23% of patients treated with givinostat (one of whom had familial hypertriglyceridemia). High triglycerides (i.e. levels greater than 3.42 mmol/L) resulted in discontinuation and led to dosage modification in 2% and 8%, respectively, of patients treated with givinostat. Triglyceride levels should be monitored at 1 month, 3 months, 6 months and then every 6 months thereafter. The dosage should be modified if fasting triglycerides are verified >3.42 mmol/L. Treatment with givinostat should be discontinued if triglycerides remain elevated despite adequate dietary intervention and dosage adjustment.
Gastrointestinal disturbances: Gastrointestinal disturbances, including diarrhoea, nausea/vomiting and abdominal pain were common adverse reactions in givinostat clinical trials in DMD. In the EPIDYS study, diarrhoea was reported in 37% of patients treated with givinostat (with one severe case reported). Diarrhoea usually occurred within the first few weeks of initiation of treatment with givinostat. Vomiting and nausea, sometimes severe and usually occurring within the first 2 months of treatment, occurred in 32% of patients treated with givinostat. Abdominal pain occurred in 34% of patients treated with givinostat compared with 25% of patients on placebo. One case of abdominal pain was serious. Antiemetics or antidiarrheal medications may be considered during treatment with givinostat. Fluid and electrolytes should be replaced as needed to prevent dehydration.
QTc prolongation: Givinostat can cause prolongation of QTc. Avoid use of givinostat in patients who are at an increased risk for ventricular arrhythmias (including torsades de pointes), such as those with congenital long QT syndrome, coronary artery disease, electrolyte disturbance, concomitant use of other medicinal products known to cause QT prolongation. In patients with underlying cardiac disease or in patients who are taking concomitant medications that cause QT prolongation, obtain ECGs prior to initiating treatment with givinostat, during concomitant use and as clinically indicated.
Excipients with known effects: Patients with hereditary fructose intolerance (HFI) should not take this medicinal product. This medicinal product contains 400 mg of sorbitol in each mL, which is equivalent to 40 mg/kg. The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account. The content of sorbitol in medicinal products for oral use may affect the bioavailability of other medicinal products for oral use administered concomitantly. This medicinal product contains 4.4 mg of sodium benzoate in each mL, which is equivalent to 0.44 mg/kg.
Sodium content: This medicinal product contains less than 1 mmol of sodium (23 mg) per dose and, therefore, is essentially 'sodium-free'.
Interactions: ***Effect of other medicinal products on givinostat pharmacokinetics:*** Avoid concomitant use of givinostat with other product(s) with a known potential to prolong the QTc interval. If concomitant use cannot be avoided, obtain ECGs when initiating, during concomitant use and as clinically indicated. Givinostat can cause QTc interval prolongation. Caution is advised when prescribing givinostat with medicinal products known to prolong the QTc interval with known or possible risk for torsades de pointes, e.g. anaesthetics (e.g. sevoflurane, propofol), class III antiarrhythmics (e.g. amiodarone, sotalol), antiemetics (ondansetron), antibiotics (fluconazole, azithromycin, clarithromycin, ciprofloxacin), antipsychotics (aripiprazole, risperidone) and antihistamines (e.g. famotidine). This list is indicative and not exhaustive.
Effect of givinostat on pharmacokinetics of other medicinal products: Givinostat is a weak intestinal CYP3A4 inhibitor. Closely monitor when givinostat is used in combination with orally administered CYP3A4 sensitive substrates (e.g. alfentanil, tacrolimus, sirolimus, lovastatin, simvastatin, indinavir, sildenafil, eletriptan, midazolam) for which a small change in substrate plasma concentration may lead to serious toxicities. Givinostat is a weak inhibitor of the renal uptake transporter OCT2. Closely monitor when givinostat is used in combination with drugs known as a sensitive substrate of the OCT2 transporter (e.g. metformin, dofetilide) for which a small change in substrate plasma concentration may lead to serious toxicities.
Fertility, pregnancy and lactation: There are no data from the use of givinostat in pregnant women. Reproductive toxicity studies in animal species have shown changes in reproduction at doses causing maternal toxicity. Givinostat should not be used during pregnancy. It is unknown whether givinostat or its metabolites are excreted in human milk. A risk to the suckling child cannot be excluded. Givinostat should not be used during breastfeeding. There are no human data on the effect of givinostat on fertility. Givinostat had no obvious adverse effects on fertility in male and female rats.
Effects on ability to drive and use machines: The effect of givinostat on driving or using machines has not been tested.
Undesirable effects: ***Very common (≥1/10):*** Thrombocytopenia, diarrhoea, nausea/vomiting, abdominal pain, pyrexia, hypertriglyceridemia. ***Common (≥1/100 to <1/10):*** Constipation, fatigue, decreased appetite, myalgia, arthralgia, rash. Please refer to the Summary of Product Characteristics for additional information on selected adverse reactions.
Overdose: In the event of a suspected overdose, supportive medical care, including cardiac monitoring, should be provided.
Storage: Store in original packaging, no special temperature required. Shelf life after first opening is 60 days.
Package quantities: 140 mL child resistant bottle, 1 graduated oral 5 mL syringe
Price: Single 140 mL bottle £13846.00
Legal category: POM
Marketing Authorisation number: PLGB 13297/0017
Marketing Authorisation Holder: Italfarmaco S.p.A. Viale F. Testi, 330 20126 Milano Italy
Full prescribing information (SmPC) is available from: ITF Pharma Ltd. 27 Old Gloucester Street, London, WC1N 3AX
Date of preparation: April 2025
Job code: UK-DVZ-25-00034

Adverse event reporting
Adverse events should be reported. Reporting forms and information can be found at **https://yellowcard.mhra.gov.uk/**
Adverse events with this product should also be reported to **UK.Medical.Information@Italfarmacogroup.com**
For further information about this medicine, please telephone **08000984040** or email **UK.Medical.Information@Italfarmacogroup.com**

References:
1. Duvyzat Summary of Product Characteristics, MHRA, **https://www.medicines.org.uk/emc/product/100605/smpc**
2. Mercuri E, Vilchez JJ, Boespflug-Tanguy O, et al. Safety and efficacy of givinostat in boys with Duchenne muscular dystrophy (EPIDYS): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Neurol.* 2024; 23: 393-403.
3. Data on file – EPIDYS Study Protocol.
4. Arizona Center for Education and Research on Therapeutics. Available at: **www.CredibleMeds.org**
5. Stockley's Drug Interactions Available at: **www.medicinescomplete.com**

Date of preparation: February 2026. Job Code: UK-DVZ-25-00043 V2