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Abstract: In 2016, the FDA approved several new drugs for use in primary care. These drugs include amphetamine extended-release orally disintegrating tablets (Adzenys XR-ODT), elbasvir and grazoprevir (Zepatier), emtricitabine and tenofovir alafenamide (Descovy), glycopyrrolate and formoterol (Bevespi Aerosphere), insulin degludec injection (Tresiba), and ixekizumab (Taltz).

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▼ ADHD

Amphetamine extended-release orally disintegrating tablets (Adzenys XR-ODT)

Attention-deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental childhood disorders, often continuing through adolescence and adulthood.[1] The first central nervous system (CNS) stimulant and amphetamine of its kind, Adzenys XR-ODT is an extended-release orally disintegrating tablet (XR-ODT) that received FDA-approval in January 2016.[2,3] This Schedule II drug is manufactured by Neos Therapeutics, Inc.[3]

Indications

Adzenys XR-ODT is indicated in patients age 6 and older for the treatment of ADHD.[3]

Mechanism of action

Adzenys XR-ODT contains immediate-release and delayed-release amphetamine. Amphetamines are sympa-

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thomimetic amines that stimulate the CNS by increasing the amount of norepinephrine and dopamine within the neurons.[3]

Dosing and administration

The recommended adult dose is 12.5 mg once daily. The initial recommended dose in pediatric patients is 6.3 mg once in the morning. The dose may be increased at weekly intervals by 3.1 mg or 6.3 mg, if needed. For patients ages 6 to 12, the maximum dose is 18.8 mg daily. For patients ages 13 to 17, the maximum dose is 12.5 mg daily.[3] Adzenys XR-ODT cannot be substituted on a mg-per-mg basis with other amphetamine products. However, the package insert provides recommendations for equivalent doses between Adzenys XR-ODT and Adderall XR.[3]

Contraindications

Adzenys XR-ODT is contraindicated in patients with known hypersensitivity to amphetamines. Additionally, concomitant therapy with monoamine oxidase inhibitors (MAOIs) or within 14 days after discontinuation of MAOI treatment is contraindicated due to increased risk of hypertensive crisis.[3]

Warnings and precautions

Adzenys XR-ODT has a black box warning for increased potential for abuse and dependence. Prior to prescribing, risk of abuse should be assessed. If prescribed, signs of abuse and dependence should be monitored closely.[3] CNS stimulants can increase heart rate and BP. Serious cardiovascular events, such as myocardial infarction, stroke, and sudden death, have occurred in patients treated with CNS stimulants (even at recommended doses). Do not use Adzenys XR-ODT in patients with structural cardiac abnormalities, coronary artery disease, cardiomyopathy, or cardiac dysrhythmias.[3] Psychiatric reactions (psychosis and manic symptoms) have been documented in patients taking CNS stimulants. Dependent on patient-specific factors, if psychiatric symptoms occur, discontinuation of Adzenys XR-ODT should be considered.[3] Postmarketing cases of peripheral vasculopathy, including Raynaud syndrome, have occurred in patients taking stimulants. Symptoms typically resolve after dose reduction or discontinuation of the stimulant.[3]

Amphetamines are known to speed up metabolism, causing weight loss and growth rate suppression in pediatric patients. Weight and growth of pediatric patients receiving Adzenys XR-ODT should be monitored closely.[3]

Adverse reactions

Common adverse reactions associated with Adzenys XR-ODT include nausea, vomiting, diarrhea, dizziness, anxiety, nervousness, restlessness, and emotional lability.[3]

Pharmacokinetics

Adzenys XR-ODT absorption is not affected by food; however, alcohol can potentially increase amphetamine release. Metabolism occurs in the liver, whereas 30% to 40% of the drug appears in the urine unchanged. Adzenys XR-ODT has an elimination half-life of approximately 12 hours. When combined with medications that alter urinary pH (acidifying or alkalinizing agents), amphetamine concentration blood levels can be altered. Patients treated with tricyclic antidepressants or proton pump inhibitors with Adzenys XR-ODT should be closely monitored, as an interaction exists between these agents.[3]

Clinical pearls

- No dosage adjustments for renal or hepatic insufficiency are provided in the manufacturer's labeling.[3]
- Adzenys XR-ODT is a pregnancy category C drug.[3]
- The drug is not recommended in women who are breastfeeding.[3]
- Alcohol avoidance is advised due to increased levels of amphetamine concentration.[3]
- Do not substitute Adzenys XR-ODT on a mg-per-mg basis for other amphetamine products.[3]

REFERENCES

1. Centers for Disease Control and Prevention. Facts about ADHD. 2016. www.cdc.gov/ncbddd/adhd/facts.html.
2. Neos Therapeutics, Inc. Neos Therapeutics announces FDA approval of Adzenys XR-ODT™ (amphetamine extended-release orally disintegrating tablet) for the treatment of ADHD in patients 6 years and older. 2016. http://investors.neostx.com/phoenix.zhtml?c=254075&p=RssLanding&cat=news&id=2132931.
3. ADZENYS XR-ODT [package insert]. Grand Prairie, TX: Neos Therapeutics, Inc.; 2016.

▼ Hepatitis C

Elbasvir and grazoprevir (Zepatier)

Zepatier is an oral tablet containing elbasvir and grazoprevir, inhibiting hepatitis C virus (HCV) viral replication through two different mechanisms. Zepatier is manufactured by Merck and Co. Inc. and was approved by the FDA in January 2016.[1,2] According to the new 2016 American Association for the Study of Liver Diseases and the Infectious Diseases Society of America Recommendations for Testing, Managing and Treating Hepatitis C Guidelines, Zepatier is recommended as a first-line treatment option for genotype 1a/1b HCV and is an additional treatment option for genotype 4 HCV.[3]

Indications

Zepatier is indicated for adults in the treatment of chronic HCV genotypes 1 or 4, with or without the use of ribavirin.[1]

Mechanism of action

Zepatier contains elbasvir, an inhibitor of HCV NS5A, and grazoprevir, an inhibitor of HCV NS3/4A protease, hindering HCV viral replication.[1,3]

Dosing and administration

Zepatier contains 50 mg of elbasvir and 100 mg of grazoprevir; it is to be taken once daily by mouth, regardless of food. Hepatic lab testing is recommended before and during Zepatier treatment. NS5A resistance testing is recommended in patients with HCV genotype 1a infection, prior to initiation of Zepatier to determine the appropriate treatment regimen.

Dependent upon HCV genotype, previous treatment for HCV, and genetic polymorphisms, certain populations are recommended to take Zepatier with ribavirin (RBV). If RBV is warranted, the dose is weight and kidney function specific, taken in two divided doses with food. To determine treatment regimen specific to the patient population and genotype for patients with or without cirrhosis, see the prescribing information.[1-4]

Contraindications

Zepatier is contraindicated in moderate-to-severe liver impairment (Child-Pugh score B or C); concurrent use of organic anion transporting polypeptides 1B1/3 inhibitors (atazanavir, darunavir, lopinavir, saquinavir, tipranavir, and cyclosporine); strong cytochrome P450 CYP3A inducers (rifampin, phenytoin, carbamazepine, and St. John's wort); and efavirenz. If RBV is added to the Zepatier treatment regimen, contraindications to RBV must be considered.[1]

Warnings and precautions

During phase III clinical trials, 1% of patients experienced alanine aminotransferase (ALT) levels greater than five times the upper limit of normal (ULN). ALT elevations were typically asymptomatic and resolved with ongoing or completion of therapy. If elevations in ALT remain continually greater than 10 times ULN, discontinue Zepatier. Prior to initiation of therapy, hepatic lab testing should be performed at week 8 of treatment and week 12 if receiving 16 weeks of therapy. Advise patients to contact their healthcare provider immediately if they develop fatigue, weakness, lack of appetite, discolored feces, nausea, or vomiting.

Consider discontinuing Zepatier if signs and symptoms of liver inflammation or an increase in alkaline phosphatase, conjugated bilirubin, or international normalized ratio occur. In combination with RBV, the warnings and precautions of RBV, including pregnancy avoidance, should be followed. Refer to RBV prescribing information for full list of warnings and precautions.[1-4]

Adverse reactions

In phase II and III clinical trials, the most common adverse reactions reported included headache, fatigue, and nausea.[1,2]

Pharmacokinetics

After the first dose, Zepatier reaches a maximum concentration in approximately 2 to 3 hours and steady state in approximately 6 days. Zepatier is greater than 99% protein bound and distributes into most tissues (predominately liver tissue). Zepatier is primarily metabolized by CYP3A. The elimination half-life is 24 to 31 hours and primarily excreted in feces.[1]

Clinical pearls

- No renal dosage adjustments are needed unless RBV is included in the treatment.
- No dosage adjustments are needed in patients with mild hepatic impairment (Child-Pugh score A).[1]
- Prior to initiation of Zepatier, test for NS5A resistance-associated polymorphisms and conduct hepatic lab tests.[1]
- Zepatier has not been studied in pregnancy and lacation.[1,2] Ribavirin is contraindicated in women who are pregnant and in men whose female partners are pregnant. Therefore, treatment of Zepatier with ribavirin is contraindicated in these patients.[1,2]
- HCV/HIV-1 coinfection patients are recommended to follow the same dosing and duration as non-HCV/HIV-1 coinfected patients.[1]
- The safety and efficacy of Zepatier have not been established in patients under age 18.[1]

REFERENCES

1. ZEPATIER (elbasvir + grazoprevir). [package insert]. Whitehouse Station, NJ; Merck; 2016.
2. U.S. Food and Drug Administration. FDA approves Zepatier for treatment of chronic hepatitis C genotypes 1 and 4. 2016. www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm483828.htm.
3. American Association for the Study of Liver Diseases/Infection Diseases Society of America. Recommendations for testing, managing, and treating hepatitis C. 2016. www.hcvguidelines.org.
4. Zeuzem S, Ghalib R, Reddy KR, et al. Grazoprevir-elbasvir combination therapy for treatment-naive cirrhotic and noncirrhotic patients with chronic hepatitis C virus genotype 1, 4, or 6 infection: a randomized trial. *Ann Intern Med*. 2015;163(1):1-13.

▼ HIV-1 infection

Emtricitabine and tenofovir alafenamide (Descovy)

Descovy is a fixed-dose combination tablet containing the nucleoside analogue reverse transcriptase inhibitors emtricitabine and tenofovir alafenamide.[1] Tenofovir alafenamide,

the novel prodrug of tenofovir, has a dose smaller than one-tenth of previous tenofovir formulations, demonstrating similar antiviral efficacy with fewer kidney and bone adverse reactions.[2,3] Descovy was approved by the FDA in April 2016 and is manufactured by Gilead Sciences, Inc.[1]

Indications

Descovy is indicated in patients age 12 and older for HIV-1 infection treatment in combination with other antiretroviral agents.[1]

Mechanism of action

Emtricitabine is a cytidine nucleoside analogue that becomes emtricitabine 5'-triphosphate following phosphorylation by intracellular enzymes.[1] Tenofovir alafenamide is converted intracellularly to tenofovir by hydrolysis and then becomes phosphorylated to tenofovir diphosphate. Both active metabolites then inhibit HIV-1 replication after viral DNA incorporation, resulting in chain termination.[1]

Dosing and administration

Descovy contains 200 mg of emtricitabine and 25 mg of tenofovir alafenamide and is taken once daily by mouth, regardless of food. Descovy is not recommended in patients with creatinine clearances less than 30 mL/minute. Studies have not evaluated the use of Descovy in patients with Child-Pugh score C hepatic impairment. However, in patients with Child-Pugh score A or B hepatic impairment, dosage adjustments are not offered.[1]

Contraindications

No contraindications are provided in the manufacturer's labeling.[1]

Warnings and precautions

Descovy has a black box warning for posttreatment hepatitis B virus (HBV) acute exacerbations, warranting hepatic monitoring and possibly adding concomitant antihepatitis B medications if Descovy initiation is implemented in this patient population.[1] The drug also has a black box warning for lactic acidosis and severe hepatomegaly with steatosis, warranting precaution in patients with liver disease risk factors.[1]

Efficacy and safety of Descovy in patients with concurrent HIV-1 and HBV coinfection have not been established. Practitioners should ensure patients are first tested for the presence of HBV infection before starting Descovy.[1] In clinical trials, worsening or new kidney dysfunction have been observed in patients taking Descovy, warranting additional caution in patients receiving concomitant nephrotoxic agents. Monitoring of creatinine clearance, urine protein, and urine glucose should be implemented prior to initiation and periodically throughout treatment.[1,3]

Mineralization defects and decrease in bone mineral density have been observed in patients receiving Descovy.[1,3] Emtricitabine has been reported to cause immune reconstitution syndrome in combination with additional antiretrovirals. This syndrome can result in opportunistic infections, including *Pneumocystis jirovecii* pneumonia and *Mycobacterium avium* infection.[1]

Fat redistribution has been reported in patients receiving antiretroviral treatment, including central obesity, enlargement of breasts, and "buffalo hump."[1]

Adverse reactions

Pooled analysis of two phase III clinical trials involving 866 patients who received therapy with emtricitabine plus tenofovir alafenamide with elvitegravir plus cobicistat demonstrated diarrhea and nausea as the most common adverse reactions (approximately 15%), with a discontinuation rate of approximately 0.9%.[2,3]

Pharmacokinetics

Less than 4% of emtricitabine and approximately 80% of tenofovir alafenamide bind to plasma proteins.[1] Emtricitabine is not metabolized to a significant extent, while tenofovir alafenamide is metabolized by peripheral blood mononuclear cells and the liver. Emtricitabine is eliminated primarily through urine, while approximately one-third of tenofovir alafenamide is eliminated in the feces.[1]

Tenofovir alafenamide is a P-glycoprotein (P-gp) substrate, whereby strong P-gp inducers (rifampin, St. John's wort, protease inhibitors, phenytoin, phenobarbital, carbamazepine, and oxcarbazepine) can reduce the concentration of tenofovir alafenamide. Drugs that are eliminated by the kidney can increase the concentrations of Descovy, increasing the risk of adverse reactions.[1]

Clinical pearls

- Insufficient data exist to determine the safety of Descovy use during pregnancy.[1]
- To reduce postnatal transmission of HIV, the CDC recommends HIV-positive mothers avoid breastfeeding.[4]
- Calcium and vitamin D supplementation may be beneficial for patients receiving Descovy to prevent bone demineralization.[1]
- Descovy is not indicated as a preexposure prophylaxis agent to decrease the risk of sexually transmitted HIV-1 in high-risk adults.

REFERENCES

1. Descovy [package insert]. Foster City, CA: Gilead Sciences, Inc.; 2016.

2. Gilead Sciences, Inc. 2016. www.gilead.com/NEWS/PRESS-RELEASES/2016/4/US-FOOD-AND-DRUG-ADMINISTRATION-APPROVES-DESCOVY-EMTRICITABINE-TENOFOVIR-ALAFENAMIDE-GILEADS-THIRD-TAFBASED-HIV-THERAPY.
3. Sax PE, Wohl D, Yin MT, et al. Tenofovir alafenamide versus tenofovir disoproxil fumarate, coformulated with elvitegravir, cobicistat, and emtricitabine, for initial treatment of HIV-1 infection: two randomised, double-blind, phase 3, non-inferiority trials. *Lancet*. 2015;385(9987):2606-2615.
4. Centers for Disease Control and Prevention. HIV in the United States: at a glance. 2016. www.cdc.gov/hiv/statistics/overview/ataglance.html.

▼ COPD

Glycopyrrolate and formoterol fumarate (Bevespi Aerosphere)

Chronic obstructive pulmonary disease (COPD) remains one of the leading causes of death and results in significant morbidity.[1] Bevespi Aerosphere is a metered-dose inhaler approved in April 2016 by the FDA for the maintenance treatment of COPD.[2] The drug is formulated with two long-acting bronchodilating agents, glycopyrrolate and formoterol, administered as an aerosolized fixed dose and manufactured by AstraZeneca Pharmaceuticals.[3]

Indications

Bevespi Aerosphere is an oral inhalation aerosol indicated for long-term maintenance treatment of airflow obstruction in patients with COPD.[3] It has not been approved for the treatment of asthma or for the relief of acute bronchospasm.[3]

Mechanism of action

Glycopyrrolate, an anticholinergic agent, is an antagonist at the M3 (muscarinic) receptor within the airways, leading to bronchodilation. Formoterol fumarate is a highly selective long-acting beta-2 adrenergic agonist (LABA), which stimulates the beta-2 receptor, also leading to bronchodilation.[3]

Dosing and administration

Bevespi Aerosphere is only available in one strength (glycopyrrolate 9 mcg/formoterol 4.8 mcg per inhalation). It is administered as two inhalations twice daily, separating dosing by approximately 12 hours. It is necessary to prime the canister before using the inhaler for the first time, releasing four sprays into the air. Patients should shake the canister before each spray. If the inhaler has not been used for more than 7 consecutive days, it is necessary to reprime the inhaler by releasing two sprays into the air. The canister should be stored at room temperature.[3]

Contraindications

Bevespi Aerosphere is contraindicated in patients who have a hypersensitivity to any of the components. Additionally, a black box warning appears on the labeling, contraindicating its use in patients with asthma due to an increased risk of asthma-related death with LABA.[3]

Warnings and precautions

Paradoxical bronchospasm and immediate hypersensitivity reactions have occurred with Bevespi Aerosphere. If symptoms occur, discontinue use and provide immediate standard of care interventions.[3] Precautions associated with increased beta adrenergic activity include tachycardia, hypertension, and electrocardiographic changes, including QTc prolongation. Patients with cardiovascular diseases such as coronary artery disease, dysrhythmias, and hypertension should be closely monitored.[3]

Hyperthyroidism and seizure disorders may be worsened as a result of stimulation from beta-agonists. Additionally, beta-agonists may cause hypokalemia or hyperglycemia. Bevespi Aerosphere should be used with caution in urinary retention or narrow-angle glaucoma due to anticholinergic effects.[3]

Adverse reactions

In clinical trials, cough and urinary tract infections were the most frequent adverse reactions.[3]

Pharmacokinetics

Peak time for Bevespi Aerosphere is 5 to 15 minutes with a half-life of approximately 12 hours. Drug interactions with Bevespi Aerosphere are not expected to occur due to inhaled route of administration; however, the use of Bevespi Aerosphere with other long-acting bronchodilators has not been evaluated and is considered inappropriate as a result of increased sympathomimetic activity, leading to unfortunate cardiovascular effects and death.[3] Anticholinergic medications, medications that cause hypokalemia, and beta-blockers may lead to additional adverse reactions when used with Bevespi Aerosphere.[3]

Clinical pearls

- Bevespi Aerosphere is a pregnancy category C drug; however, no adequate and well-controlled trials have been conducted on women during pregnancy or lactation.[3]
- The drug has not been adequately studied in patients with kidney or hepatic impairment.[3]
- Bevespi Aerosphere has not been evaluated in patients with acute worsening of COPD.[3]
- Patients should be counseled on appropriate inhaler technique and how to use the inhaler on a routine scheduled basis, not as rescue therapy.[2,3]

REFERENCES

1. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management and Prevention of COPD. 2016. www.goldcopd.org.

2. AstraZeneca Pharmaceuticals. Bevespi Aerosphere™ approved by the US FDA for patients with COPD. 2016. www.astrazeneca.com/media-centre/press-releases/2016/bevespi-aerosphere-approved-by-the-us-fda-for-patients-with-copd-25042016.html.

3. Bevespi Aerosphere [package insert]. Wilmington, Delaware: AstraZeneca Pharmaceuticals LP; 2016.

▼ Diabetes mellitus

Insulin degludec injection (Tresiba)

Since 2012, five new insulin formulations have been approved by the FDA.[1] Tresiba is a once-daily, ultra-long-acting basal insulin for adults with type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM). Tresiba was approved by the FDA in September 2015 and was made available in the United States during the first quarter of 2016. Tresiba is manufactured by Novo Nordisk.[2-4]

■ Indications

Tresiba is indicated for adults with T1DM and T2DM, either used alone or in combination with bolus insulin or oral medications, to provide glycemic control.[3-6]

■ Mechanism of action

Tresiba provides exogenous insulin to regulate glucose metabolism and lower blood glucose by inhibiting hepatic glucose production and stimulating peripheral glucose uptake in the skeletal muscle and adipose tissue. When injected, Tresiba forms multihexamers within the subcutaneous tissue, forming a depot. The extended action time of Tresiba is due to delayed absorption of the depot into the systemic circulation, where it binds with circulating albumin.[3,5]

■ Dosing and administration

Tresiba provides a duration of action beyond 42 hours and is administered subcutaneously once daily, allowing flexibility of dosing at any time of the day. It is injected into the abdomen, thigh, or upper arm, and injection sites should be rotated daily to reduce the risk of lipodystrophy. If a dose is missed, patients should dose during waking hours when they realize the dose is missed, ensuring at least 8 hours have lapsed between consecutive doses. Dosing of Tresiba will be individualized to the patient.[2,3,5]

Tresiba is available as U-100 (100 units/mL) or U-200 (200 units/mL) in 3 mL FlexTouch pens. Dose conversion is not recommended between U-100 or U-200 FlexTouch pens nor should it be transferred into a separate insulin syringe for administration. The markings on an insulin syringe do not match the FlexTouch pens, resulting in overdose and possibly severe hypoglycemia.[3,5] Tresiba FlexTouch pens can provide a single injection of 80 units and 160 units. When in use, the product can remain at room temperature for 8 weeks if away from direct heat and light.[3,5]

■ Contraindications

Tresiba is not to be used during episodes of hypoglycemia or if the patient has a hypersensitivity to any of Tresiba's excipients.[3,5]

■ Warnings and precautions

Tresiba should not be used to treat diabetic ketoacidosis.[2,3,5] Hypersensitivity reactions can be generalized, severe, life-threatening, or anaphylactic; discontinue if symptoms occur.[3,5] Hyperglycemia or hypoglycemia can result due to changes in insulin regimen. Instruct the patient to increase frequency of glucose monitoring with any changes to the following: insulin dose/regimen, concomitant oral antidiabetic medications, meal pattern, and/or physical activity.[3,5]

Patients at greater risk for hypoglycemia include those with kidney or hepatic impairment, long-standing diabetes mellitus, hypoglycemic unawareness, neuropathy, or those taking medications that block the sympathetic nervous system. Due to the risk of transmitting bloodborne pathogens, FlexTouch pens should never be shared, even if the needle is changed.[3,5]

Hypokalemia can occur due to insulin shifting potassium from extracellular to intracellular space. Untreated hypokalemia may be life-threatening and cause respiratory paralysis, ventricular dysrhythmias, and death. Monitor potassium levels in patients at risk; treat if indicated.[3,5] Fluid retention and heart failure can occur with insulin used in combination with thiazolidinediones (TZD). If signs or symptoms of heart failure occur, dose reduction or discontinuation of TZD must be considered.[3,5]

■ Adverse reactions

The most common adverse reactions of Tresiba in clinical trials were hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, pruritus, rash, edema, and weight gain.[4-6] In the BEGIN trial, a 25% reduction of nocturnal hypoglycemia was seen with Tresiba versus the competitor insulin.[6] However, overall, no clinically important differences in risk of hypoglycemia between Tresiba and other insulins were observed in clinical trials.[5]

■ Pharmacokinetics

After the first dose of Tresiba, onset of action is approximately 1 hour with time to peak approximately 9 hours. Steady state is achieved within 3 to 4 days of daily administration followed by a half-life elimination of approximately 25 hours independent of the dose. Similar to human insulin,

Tresiba is metabolized into inactive metabolites.[5] Tresiba is greater than 99% albumin bound. However, in vitro protein binding studies show no clinically relevant interaction with protein-bound drugs. Potential drug interactions include medications that affect glucose metabolism and antiadrenergic drugs; adjustment of insulin dosage with close glucose monitoring may be needed.[5]

Clinical pearls

- No dose adjustment is recommended in patients with kidney impairment or hepatic impairment. Recommendations are to monitor blood glucose closely in these patients, as insulin requirements may be reduced due to changes in insulin clearance or metabolism.
- Tresiba is a pregnancy category C drug. There have been no well-controlled clinical studies of the use of Tresiba in pregnant women.
- Caution should be used in breastfeeding women, with possible adjustment to the mother's insulin dose.
- Tresiba has greater variability within older adult patients.

REFERENCES

1. U.S. Food and Drug Administration. FDA-approved diabetes medicines. 2016. www.fda.gov/ForPatients/Illness/Diabetes/ucm408682.htm.
2. U.S. Food and Drug Administration. FDA approves two new drug treatments for diabetes mellitus. 2015. www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm464321.htm.
3. Novo Nordisk. Novo Nordisk receives FDA approval for Tresiba® (insulin degludec injection) for adults with type 1 and type 2 diabetes. 2015. http://press.novonordisk-us.com/2015-09-25-Novo-Nordisk-Receives-FDA-Approval-for-Tresiba-insulin- degludec-injection-for-Adults-with-Type-1-and-Type-2-Diabetes.
4. Meneghini L, Atkin SL, Gough SC, et al. The efficacy and safety of insulin degludec given in variable once-daily dosing intervals compared with insulin glargine and insulin degludec dosed at the same time daily: a 26-week, open-label, parallel-group, treat-to-target trail in individuals with type 2 diabetes. *Diabetes Care.* 2013;36(4):858-864.
5. Tresiba [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; 2015.
6. Garber AJ, King AB, Del Prato S, et al. Insulin degludec, an ultra-long-acting basal insulin, versus insulin glargine in basal-bolus treatment with mealtime insulin aspart in type 2 diabetes (BEGIN Basal-Bolus Type 2): a phase 3, randomized, open-label, treat-to-target non-inferiority trial. *Lancet.* 2012;379(9825):1498-1507.

▼ Plaque psoriasis

Ixekizumab (Taltz)

Taltz is an anti-interleukin-17A monoclonal antibody used in the treatment of plaque psoriasis.[1] Taltz is a subcutaneous injection manufactured by Eli Lilly and Company and was approved by the FDA in March 2016.[1,2]

Indications

Taltz is indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy.[1,2]

Mechanism of action

Taltz is a humanized immunoglobulin G subclass 4 (IgG4) monoclonal antibody that binds with the cytokine interleukin-17A; it inhibits the release of proinflammatory cytokines and chemokines, and thereby, inhibits the inflammatory and immune response.[1]

Dosing and administration

Taltz is a subcutaneous injection containing 80 mg of ixekizumab supplied as an autoinjector and prefilled syringe for single use. The recommended dose is 160 mg (two 80 mg injections) at week 0, followed by 80 mg every 2 weeks until and including week 12, then a maintenance dose every 4 weeks.[1] Taltz should be stored in the refrigerator and removed prior to use, allowing the drug to reach room temperature 30 minutes prior to administration.

The full dose should be injected into adipose tissue of the abdomen, thigh, or the back of the arm, rotating injection sites from the previously administered site. Patients may self-inject after proper education and training from a healthcare provider regarding injection technique, sterile technique, administration, and disposal of the autoinjector or prefilled syringe.[1]

Contraindications

Taltz is contraindicated in individuals with serious hypersensitivity reactions to ixekizumab or any of its excipients.[1]

Warnings and precautions

Use of Taltz may increase the risk of infections. Educate patients to seek medical attention if they experience symptoms of an infection, are being treated for an infection, or have been in close contact with someone with tuberculosis (TB).[1,3] Patients must be evaluated for TB prior to initiation of Taltz.[1,3] Patients should not receive Taltz if they have an active TB infection.[1] Healthcare providers are advised to treat patients with latent TB prior to initiating Taltz. Patients should be monitored closely for signs and symptoms of TB during and after treatment with Taltz.[1]

Due to a high risk of infection, patients should complete all age-appropriate immunizations according to current immunization guidelines prior to starting Taltz and should avoid live vaccines during Taltz treatment.[1,3] Rare hypersensitivity reactions of angioedema or urticaria have occurred (0.1% or less).[3] Discontinue and seek medical attention if reaction occurs.[1,3]

Onset and disease exacerbations of inflammatory bowel disease (IBD) (Crohn disease and ulcerative colitis) have occurred during clinical trials. During treatment, patients with a history of IBD should be monitored closely for exacerbation, and all patients should be monitored for onset of IBD.[1]

Adverse reactions

Based on phase III clinical trials, the most common adverse reactions include injection site reactions, upper respiratory tract infections, nausea, and tinea infections.[1-3] Upper respiratory tract infections, oral candidiasis, conjunctivitis, and tinea infections occurred more frequently in patients taking Taltz compared with a placebo group (27% and 23%, respectively).[1,3]

Pharmacokinetics

Four days after 160 mg is administered, Taltz reaches peak concentration. Taltz bioavailability ranges from 60% to 81%, with thigh administration achieving higher bioavailability. Steady state is achieved approximately 10 weeks after the last dose of the recommended dosing regimen.[1] Taltz is estimated to be broken down into amino acids and small peptides via catabolic pathways, with an elimination half-life of 13 days.[1]

Clinical pearls

- Dose adjustments in individuals with renal or hepatic impairment have not been studied.[1,2]
- Currently, drug interaction studies have not been conducted with Taltz.[1]
- Avoid live vaccines during treatment with Taltz.[1]
- Taltz has not been studied in pregnancy or lactation.[1]
- Do not inject within 1 in (2.5 cm) of navel or in an area of skin that is tender, bruised, hard, or area of skin affected by psoriasis.[1]
- The safety and effectiveness of Taltz in patients under age 18 has not been evaluated.[1]

REFERENCES

1. TALTZ (ixekizumab). [package insert]. Indianapolis, IN; Eli Lilly and Company; 2016.
2. U.S. Food and Drug Administration. FDA approves new psoriasis drug Taltz. 2016. www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm491872.htm.
3. Armstrong AW, Lynde CW, McBride SR, et al. Effect of ixekizumab treatment on work productivity for patients with moderate-to-severe plaque psoriasis: analysis of results from 3 randomized phase 3 clinical trials. *JAMA Dermatol.* 2016;152(6):661-669.

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