University HOSPITAL
Newark, NJ

Pharmacy News

Third Quarter 2022
Vol. XV, Issue 3

Special Points of Interest:

- Hepatitis B Treatment Strategies after Liver Transplantation at University Hospital
- Tenecteplase Medication Guide
- Peanut oral immunotherapy
- Novel Once Weekly Tirzepatide in the Treatment of Type 2 Diabetes

P&T Update

Formulary Additions

1. *Empagliflozin*
   Empagliflozin is FDA approved for the reduction of cardiovascular death and reduction of heart failure hospitalizations in adults with heart failure. – Formulary Addition Approved

2. *PCV20*
   Formulary addition request for PCV20 reviewed; Submitted by division of Infectious Disease PCV20 is FDA approved for the prevention of invasive disease and pneumonia caused by Streptococcus pneumoniae in adults ≥ 18 years of age.

   On October 21, 2021, the ACIP recommended use of PCV20 alone or PCV15 in series with PPSV23 for all adults aged ≥65 years, and for adults aged 19–64 years with certain underlying medical conditions or other risk factors, who have not previously received a pneumococcal conjugate vaccine or whose previous vaccination history is unknown.

   PCV20 data suggests comparable immunogenicity and safety outcomes compared to PCV13 alone or in combination with PPSV23.

   Cost-effectiveness studies demonstrated that use of PCV20 alone for adults at or greater than 65 years of age was associated with cost-savings.

Formulary Deletions

1. *Dapagliflozin*
   Empagliflozin being utilized for aforementioned indication along with existing FDA approved use for T2DM; redundancy exists with 2 SGLT2-inhibitor class agents with no additional quality benefit for medical care. – Formulary Deletion Approved

Formulary Line Extensions

Policies and Procedures/Floorstocks

Autotherapeutic exchange revisions policy
Autotherapeutic exchange policy was reviewed for revisions.
Dapagliflozin will be auto substituted with empagliflozin and approved by endocrinology division chief.

Infectious disease related medications have been removed due to active updates in EPIC orders. Other updates are being built in Epic – Revisions Approved

Resuscitation Equipment/ Code carts/ Emergency boxes
Reviewed and validated inventory on crash carts and emergency boxes in different locations.
Revised list of clinics for crash carts/ emergency boxes.
Approximately 9 additional boxes since the last inventory due to clinics opening and mobile clinics. Removed tubing associated with older IV pump.

Medication Sample Addition Request

N/A

Continued on Page 2

University HOSPITAL Newark, NJ

Pharmacy News

P&T Update

Continued from Page 1

Medication/Clinical Guidelines

ED Guideline on Outpatient COVID-19 Treatment
Updated ED Guideline on Outpatient COVID-19 Treatment was reviewed & discussed. Approved

University Hospital Adult Emergency Medicine Treatment of Acute Pain Guideline
Updated University Hospital Adult Emergency Medicine Treatment of Acute Pain Guideline was reviewed & discussed. – Approved

Hepatitis B Treatment Strategies after Liver Transplantation at University Hospital

One of the indications for liver transplant is Hepatitis B Liver Cirrhosis. Despite advances in Hepatitis B treatment, liver transplantation is a life-saving surgical intervention to many with decompensated liver cirrhosis due to Hepatitis B. Initially, liver transplantations due to Hepatitis B were largely unsuccessful due to the graft high re-infection rates.[1,2] Since the late 1980s, the introduction of various treatment strategies with Hepatitis B Immune Globulin and nucleoside/nucleotide analogues has led to significantly improved overall survival.[3] In this article, we will review our transplant center's protocol.

Dosing of Hepatitis B Immune globulin (HBIG) is 20,000 units based on the stamped potency on each vial (550 units/mL or higher) or 10,000 units based on the minimum assured potency (312 units/mL).[4-7] At University Hospital, HBIG is dosed at 9,360 units per dose based on the minimum assured potency of 312 units/mL. This is rounded down from 10,000 units, so 30 mL is the volume being dispensed as opposed to 32 mL. This avoids an additional vial being partially used, thus leading to cost savings. Though protocols may differ from center to center, many transplant centers use this strategy to minimize workload of staff pharmacists so they do not have to calculate 20,000 units dosing from the varying stamped potency in each vial.

Donor Liver	Recipient	Peri-Transplant	Anti-Viral ^^	Post transplant HBIG	Laboratory monitoring
---	HBV VL (-) but HepB surface antigen (sAg) positive	Hepatitis B Immune Globulin (HBIG) ^ • HBIG 10,000 units (30 mL HepaGam) IV x 1 dose (during anhepatic phase in OR)	Yes- life long Start on POD 1	POD 1-6: HBIG 10,000 units (30 mL) IV once daily. Stop when HBV PCR is negative and HBsAb > 500 IU/L	POD 2: HBV PCR, HbsAg, HbsAb quantitative POD 6: HbsAb quantitative Monthly therafter
---	HBV VL positive			POD 1-6: HBIG 10,000 units (30 mL) IV once daily. Stop when HBV PCR is negative and HBsAb > 500 IU/L	See above AND POD 6: HBV PCR and HbsAg Monthly thereafter Further HBIG doses will be determined based on out-patient serial HBV DNA monitoring
HB coreAb (+)	HBV VL/ sAg (-)	---	Yes – life long	n/a	
HB core Ab (-)	HB core Ab (+),sAg (-), sAb (-)	---	Yes- life long	n/a	

Based on donor and recipient serologies, patient may receive HBIG and antiviral therapy. Patients that have a Hepatitis B viral load and/or are positive for Hepatitis B surface antigens will receive 30 mL of HBIG in the OR during the anhepatic phase. This dose is continued POD 1-6 until HBV PCR is negative AND HbsAB > 500 IU/L. Patient with positive viral load will most likely need all 7 days from the perioperative period to day 6 post-transplant and may need additional doses based on Hepatitis B PCR and serology. These patients need to be continually monitored in regards to their Hepatitis B PCR and the Hepatitis B surface antibodies to determine their course of therapy. These patients are also treated with antivirals for the rest of their lives. Patients that receive HBcoreAb positive organs or are coreAB positive are placed on an antiviral and do not need HBIG.

Historically, due to risk of graft loss due to Hepatitis B recurrence and antivirals prone to high resistance, HBIG remained a mainstay treatment to maintain graft and patient survival. Lamivudine, a nucleoside analogue, is not utilized in the transplant setting due to the high risk of resistance.[8] Adefovir, a nucleotide analogue, also is no longer recommended due to resistance and nephrotoxicity.[9] Fortunately, there are potent antivirals such as entecavir, tenofovir disoproxil fumarate (tenofovir DF) and tenofovir alefenamide (tenofovir AF) that have led to decreased need for doses of HBIG and are all considered first line in treating Hepatitis B.[10-12] Tenofovir AF, the newest Hepatitis B antiviral on the market, has less renal toxicity and is an alternative for patients with or at risk for renal impairment, although the data in the transplant setting is limited. There is ongoing research to treat Hepatitis B with several agents in the pipeline. With advancing treatment options and higher vaccination rates, the hope is to be able to cure and eliminate Hepatitis B.

References:

1. O'Grady JG et al. Hepatitis B virus reinfection after orthotopic liver transplantation. Serological and clinical implications. J Hepatol. 1992;14(1):104.
2. Lucey MR et al. Recurrence of hepatitis B and delta hepatitis after orthotopic liver transplantation.Gut. 1992;33(10):1390.
3. Kim WR at al. Outcome of liver transplantation for hepatitis B in the United States. Liver Transpl. 2004;10(8):968.
4. HepaGam B (hepatitis B immune globulin intravenous [human]) [prescribing information]. Roswell, GA: Saol Therapeutics Inc; March 2021.
5. Nabi-HB (hepatitis B immune globulin intravenous [human]) [prescribing information]. Boca Raton, FL: ADMA Biologics; October 2019.
6. Dickson RC, Terrault NA, Ishitani M, et al, "Protective Antibody Levels and Dose Requirements for IV 5% Nabi Hepatitis B Immune Globulin Combined With Lamivudine in Liver Transplantation for Hepatitis B-Induced End Stage Liver Disease," Liver Transpl, 2006, 12(1):124-33.
7. Terrault NA et al. Prophylaxis in liver transplant recipients using a fixed dosing schedule of hepatitis B immunoglobulin. Hepatology. 1996;24(6):1327.
8. Bartholomew MM, et al. Hepatitis-B-virus resistance to lamivudine given for recurrent infection after orthotopic liver transplantation. Lancet. 1997;349(9044):20.
9. Lim YS et al. Monotherapy with tenofovir disoproxil fumarate for adefovir-resistant vs. entecavir-resistant chronic hepatitis B: A 5-year clinical trial. J Hepatol. 2019;71(1):35.
10. Entecavir. In: Lexi-Drugs [database on the Internet]. Hudson, Ohio: Hudson, Ohio: Wolters Kluwer UpToDate, Inc.; [updated 2022 Apr 21, cited 2022 Apr 28].
11. Tenofovir Disoproxil Fumarate. In: Lexi-Drugs [database on the Internet]. Hudson, Ohio: Hudson, Ohio: Wolters Kluwer UpToDate, Inc.;[updated 2022 Apr 19, cited 2022 Apr 28].
12. Tenofovir Alefenamide. In: Lexi-Drugs [database on the Internet]. Hudson, Ohio: Hudson, Ohio: Wolters Kluwer UpToDate, Inc.; [updated 2022 Apr 19, cited 2022 Apr 28].

Contributed by Liver Transplant Clinical Pharmacists:
Brielle Okulicz PharmD, BCPS
Merlin Punnoose PharmD, BCPS

University HOSPITAL Newark, NJ
Pharmacy News

Tenecteplase Medication Guide

Tenecteplase Indication	Tenecteplase Dose
Acute Ischemic Stroke (AIS) within 4.5 hours of last known well – *off label*	0.25 mg/kg, maximum 25 mg
Massive pulmonary embolism – *off label*	< 60 kg: 30 mg ≥ 60 to < 70 kg: 35 mg ≥ 70 to < 80 kg: 40 mg ≥ 80 to < 90 kg: 45 mg ≥ 90 kg: 50 mg
Cardiac arrest secondary to pulmonary embolism – *off label*	
STEMI	

Mechanism of Action/Kinetics:
Tenecteplase binds to fibrin and converts plasminogen to plasmin. Tenecteplase is essentially alteplase with the exception of 3 point mutations and is more fibrin specific, more resistant to plasminogen activator inhibitor -1 (PAI-1), with a longer duration of action compared to alteplase

Comparison of Thrombolytic Agents

Thrombolytic	Infusion time	Generation	Direct plasminogen activator?	Half-life, min	Fibrin selectivity	PAI resistance*	FDA Indication	Formulary?
Alteplase	120 min (PE), 60 min (stroke), 1 min (cardiac arrest)	Second	Yes	4-8	++	++	PE, AIS, STEMI	Yes
Tenecteplase	5-10 seconds	Third	Yes	20-24 (initial), 90-130 (terminal)	+++	+++	STEMI	Yes

**PAI is a 52-kDa circulating glycoprotein that is the primary native of plasminogen-activating enzymes, and greater PAI resistance confers a longer duration of fibrinolysis*

Preparation & Administration **(see page 4)**
- Remove the tenecteplase 50mg/10mL kit after the order is placed in Epic
- Remove shield assembly from supplied 10 mL syringe
- Withdraw 10 mL of Sterile Water for Injection (SWFI) from the supplied diluent vial. Note: Do not use Bacteriostatic Water for Injection
- Inject 10 mL of SWFI into the tenecteplase vial directing the diluent stream into the powder, slight foaming is common
- Gently swirl until contents are completely dissolved (usually ~ 1 minute), DO NOT SHAKE
  - o **Reconstituted preparation contains tenecteplase 5 mg/mL**
- Inspect the solution for particulate matter or discoloration (should be a colorless to pale yellow solution)
- Withdraw the appropriate volume of solution
- Administer as an IV bolus over 5 to 10 seconds using a peripheral vein
- Flush a dextrose-containing line with a saline-containing solution prior to and following administration (precipitation may occur when tenecteplase is administered in an IV line containing dextrose).

Contraindications:
- Overall, tenecteplase has similar contraindications to other thrombolytics, and should be used with caution in patients who are at high risk of bleeding. See *Stroke Toolkit* on *UH Clinical Links* site for more detailed list of contraindications.

Recommended Monitoring:
A neurological assessment and vital signs (BP, HR, RR, SpO2) is recommended for 24 hours from the time thrombolysis is given: every 15 minutes for 2 hours (8 times), every 30 minutes for 6 hour (12 times), every 60 minutes for 16 hours (16 times), for a total of 24 hours.

Reversal Recommendations:
- *See UH Anticoagulation Reversal Guidelines for recommendations*

Patient deemed **thrombolysis candidate** by Neurology BAT Team

Contraindication to fibrinolysis?
(See *Stroke Toolkit* on clinical links for more detailed list of contraindications)

this list of contraindications is a guideline and a physician experienced in the treatment of acute stroke may modify the list on a case by case basis

Exclusion Criteria

- Current or history of intracranial hemorrhage
- Ischemic stroke within 3 months
- Symptoms suggestive of SAH
- Arterial puncture in non-compressible site within 7 days
- Intracranial or spinal surgery within 3 months
- Recent significant head trauma within 3 months
- Known structural intracranial cerebrovascular disease
- Known malignant intracranial neoplasm
- Blood pressure SBP > 185 mmHg or DBP > 110 mmHg
- Active internal bleeding
- Bleeding diathesis: platelets <100,000 mm3, aPTT> 40s, PT > 15 s, INR >1.7
- Anticoagulation contraindications (last dose within):
  - Apixiban (Eliquis®) within 48 hours**
  - Dabigatran (Pradaxa®) within 72 hours**
  - Enoxaparin (Lovenox®) therapeutic dose within 24 hours**
  - Heparin therapeutic dose and aPTT > ULN**
  - Rivaroxaban (Xarelto®) within 48 hours**
  - Warfarin (Coumadin®) and INR> 1.7

  *** for patients with normal renal function, activity may be prolonged in patients with renal impairment*
- Blood glucose <50 mg/dL or > 400 mg/dL
- CT shows frank hypo-density or extensive hypo-attenuation
- Symptoms consistent with infective endocarditis
- Known or suspected aortic arch dissection
- Gastrointestinal hemorrhage within previous 21 days
- Gastrointestinal malignancy

Additional Exclusion Criteria for Onset 3-4.5 Hours

- Imaging evidence of ischemic injury involving more than 1/3 middle cerebral artery territory

Relative Exclusion Criteria

- Major surgery/serious trauma within previous 14 days
- Lumbar or arterial puncture in previous 7 days
- Recent or active menorrhagia
- Pregnancy or post-partum (<14 days)
- Hemorrhagic ophthalmic condition
- Acute myocardial infarction within 3 months
- Other cardiac condition: acute pericarditis, known LV thrombus, cardiac myxoma, papillary fibroelastoma
- Intracranial arterial dissection
- Large burden of cerebral micro-bleed on MRI
- Current systemic malignancy

Consider risk vs. benefit:

- Only minor, non-disabling symptoms; or rapidly improving stroke symptoms (clearing spontaneously)
- Seizure at onset of symptoms, only if residual symptoms are thought to be post-ictal etiology

Relative Exclusion Criteria for Onset 3-4.5 hours

- NIHSS score ≥ 25

Consider risk vs. benefit:

- Oral anticoagulant use
- History of prior stroke AND diabetes mellitus

No Contraindication to fibrinolysis

Wake-up stroke

MRI

Refer to Neurology for thrombolytic recommendation

Last known well within 4.5 hours

Time out by Neurology MD to review patient criteria, inclusion/exclusion criteria, and dosing

Contraindication to fibrinolysis

Refer to Stroke Team or Emergency Medicine team for alternative therapy

Tenecteplase (TNK): 0.25 mg/kg (max 25 mg/5ml)
Administration: single IV push over 5-10 seconds given by Neurology MD, refer to page 4 for preparation instructions

Endovascular intervention if applicable

This guidance is intended to be flexible. They serve as reference points or recommendations, not rigid criteria. Guidelines should be followed in most cases, but there is an understanding that, depending on the patient, setting, circumstances or factors, guidelines can and should be tailored to fit individual needs.

August 2022

Continued on Page 6

Tenecteplase Medication Guide

Continued from Page 5

Pulmonary Embolism Thrombolysis Guideline

Assess risk of an **acute pulmonary embolism**

CARDIAC ARREST due to fulminant PE

HEMODYNAMIC INSTABILITY

HIGH RISK PE

Weigh risk/benefit of thrombolysis (See thrombolysis considerations in **table 1**)

1. Clinical signs of PE severity or serious comorbidity
   - PESI Class III-IV or sPESI ≥ 1
   - ≥ 1 Hestia criteria of PE severity of comorbidity fulfilled
2. RV dysfunction on TTE or CTPA

1 or 2 present

Troponin (+)

INTERMEDIATE- HIGH RISK

Start anticoagulation with **heparin infusion**

Consult **cardiology** and consider early **interventional radiology** notification to assess for possible surgical embolectomy or percutaneous catheter directed treatment

Further decompensation?

YES

Joint decision to weigh risk/benefit of thrombolysis (See thrombolysis considerations in **table 2**)

NO

Joint decision made to go to IR

Continue **heparin infusion**

Troponin (-)

INTERMEDIATE- LOW RISK

Neither 1 nor 2 present

LOW RISK PE

Anticoagulation*: Heparin, LMWH, apixaban, or rivaroxaban

**See UH VTE Anticoagulation Guidelines for guidance*

Continue anticoagulation with close monitoring

Decision made to administer thrombolysis

Discontinue heparin (if started) while fibrinolytic is being administered

Tenecteplase (TNK)

Single IV push over 5-10 seconds

< 60 kg	30 mg
≥60 to <70 kg	35 mg
≥70 to <80 kg	40 mg
≥80 to < 90 kg	45 mg
≥90 kg	50 mg

aPTT should be measured 60-90 minutes after TNK, resume heparin when aPTT is < 2x upper limit of normal

***Alteplase** (alternative thrombolytic) may not be readily available in your unit. If alteplase is desired instead of TNK, consider picking up from pharmacy*

Recommendations adapted from: 2019 ESC for the Diagnosis and Management of Acute Pulmonary Embolism. Eur Heart J 2019;Aug 31

This guidance is intended to be flexible. They serve as reference points or recommendations, not rigid criteria. Guidelines should be followed in most cases, but there is an understanding that, depending on the patient, setting, circumstances or factors, guidelines can and should be tailored to fit individual needs.

August 2022

Tenecteplase Medication Guide

TABLE 1. HIGH RISK PULMONARY EMBOLISM THROMBOLYSIS CONSIDERATIONS

Major Contraindications (high risk PE)	Relative Contraindications (high risk PE)
Active internal bleeding Recent ICH	Structural intracranial disease Previous ICH Ischemic stroke within 3 months Recent brain/spinal surgery Bleeding diathesis

TABLE 2. INTERMEDIATE - HIGH RISK PULMONARY EMBOLISM THROMBOLYSIS CONSIDERATIONS

Major Contraindications (intermediate-high risk PE)	Relative Contraindications (intermediate-high risk PE)
Structural intracranial disease Previous ICH Ischemic stroke within 3 months Recent brain surgery or spinal surgery Recent head trauma Bleeding Diathesis	SBP > 180, DBP > 110 Recent bleeding, surgery, or invasive procedure Ischemic stroke > 3 months ago Anticoagulation Traumatic CPR Pericarditis or pericardial fluid Pregnant >75 years old < 60 kg Female gender Black race

Exclusion criteria directly from CHEST Guideline: *Kearon C, et al. Antithrombotic Therapy for VTE Disease: CHEST Guideline and Expert Panel Report. Chest. 2016 Feb;149(2):315-352.*

This guidance is intended to be flexible. They serve as reference points or recommendations, not rigid criteria. Guidelines should be followed in most cases, but there is an understanding that, depending on the patient, setting, circumstances or factors, guidelines can and should be tailored to fit individual needs.

August 2022

Continued on Page 8

Tenecteplase Medication Guide

Continued from Page 7

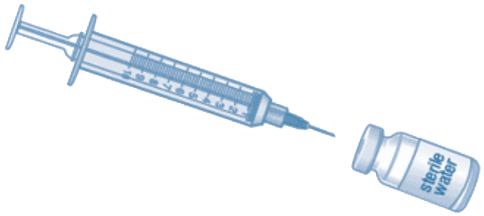
Tenecteplase Medication Guide

Preparation for Tenecteplase Administration

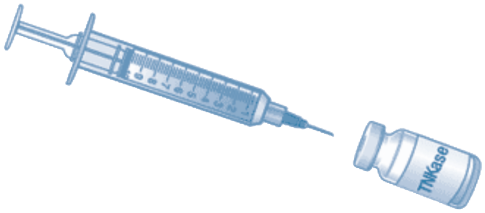
Full instructions on reconstitution and administration
Full video on dosing and administration

Step 1: Remove the shield assembly from the supplied B-D 10 mL syringe with TwinPak™ Dual Cannula Device.

Step 2: Aseptically WITHDRAW 10 mL of Sterile Water for Injection, USP, using the B-D 10 mL syringe with TwinPak™ Dual Cannula Device included in the kit. Do not use Bacteriostatic Water for Injection, USP.

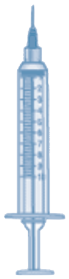


Step 3: INJECT entire contents (10 mL) into the TNKase vial, directing the diluent into the powder. Slight foaming upon reconstitution is not unusual; any large bubbles will dissipate if the product is allowed to stand undisturbed for several minutes. **Final concentration is 50 mg/10mL (5mg/mL)**

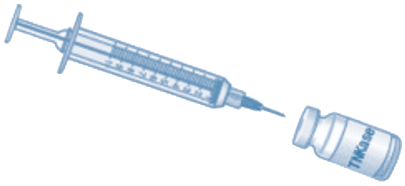


Step 4: GENTLY SWIRL until contents are completely dissolved. DO NOT SHAKE. Solution should be colorless or pale yellow and transparent. Once the appropriate dose of TNKase is drawn into the syringe, stand the shield vertically and recap the red tab cannula.

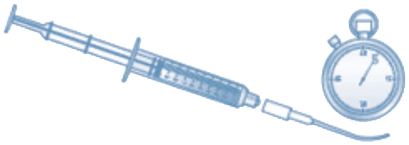
Step 5: Determine the correct dose of TNKase based on patient weight. TNKase is for IV administration only.



Step 6: WITHDRAW the appropriate volume of solution based on patient weight. **The recommended total dose should not exceed 25 mg for stroke, 50 mg for all other indications. Discard solution remaining in the vial.**



Step 7: FLUSH a dextrose-containing line with a saline-containing solution prior to and following administration (precipitation may occur when TNKase is administered in an IV line containing dextrose). **ADMINISTER as an IV BOLUS over 5 seconds.**



Contributed by:

ED Clinical Pharmacy Team: Jaclyn Scalgione, PharmD, BCPS; Joseph Plott, PharmD; Irene Yang, PharmD

This guidance is intended to be flexible. They serve as reference points or recommendations, not rigid criteria. Guidelines should be followed in most cases, but there is an understanding that, depending on the patient, setting, circumstances or factors, guidelines can and should be tailored to fit individual needs.

August 2022

Peanut Oral Immunotherapy

The objective of oral peanut immunotherapy is to build tolerance to peanuts. Oral immunotherapy (Palforzia) makes the body less sensitive to the allergen. According to research, gradually increasing the patient's peanut exposure can desensitize them to high quantities of peanut protein[1]. Peanut allergy is one of the most common food allergies in some people, and it can be fatal in others. In order to desensitize people to peanuts, this entails feeding them progressively higher doses of peanuts over time.[3] It may be more effective to change a child's immune response to peanuts early in childhood when the immune system is still developing than to wait until later. Immunotherapy for peanut allergy is a kind of management, not a cure. It is intended to reduce allergic reactions' frequency and severity. This includes potentially fatal anaphylaxis in kids aged 4 to 17 who unintentionally eat peanuts. In the United States, about 1 in 50 kids suffers from a peanut allergy. Your immune system wrongly interprets the proteins in peanuts as dangerous when you have a peanut allergy. The following symptoms of a peanut allergy, which can range in severity from mild to severe, are: diarrhea, breathing difficulties, hives or skin rashes, nausea and vomiting, stomach cramps, and swelling, generally in the lips or tongue. Anaphylaxis may result from a peanut allergy[3]. Breathing can be difficult or impossible during anaphylaxis. Keeping track of allergic reactions can aid in a precise diagnosis by your doctor. A blood test may be used by your doctor to identify a peanut allergy. Also, a skin test may be used by your doctor to detect or rule out other allergies. An allergic reaction is indicated by red, itchy skin patches. Your healthcare provider can use these details to identify allergies by your healthcare provider. A challenge with oral food may also exist for you. At an oral food challenge, you consume a peanut-based product in your doctor's office in tiny, increasing amounts. In the event that you experience an allergic reaction, your healthcare practitioner has equipment and emergency medications on hand[2].

The goal of peanut oral immunotherapy is to increase the amount of peanuts required to elicit an allergic reaction. Nearly 75-80% of children over the age of four who receive peanut oral immunotherapy become desensitized, but few experience long-term protection (such as remission) after discontinuing the oral immunotherapy[5]. A significant area of research in the management of food allergies is oral immunotherapy (OIT). However, research has not yet shown that food allergies may be cured (and induce true tolerance). In addition, patients on OIT are more likely to experience allergic reactions to the drug than people who avoid it. The justification for employing the oral route is that ingesting a food antigen by a person who is not allergic to that food results in a preferentially active immune system response that does not cause an allergic reaction to that antigen. In the clinical trials that are currently available, peanut OIT repeatedly raised the rate of allergic responses, including anaphylaxis that requires epinephrine therapy.

Continued on Page 10

Peanut Oral Immunotherapy

Continued from Page 9

Trial:

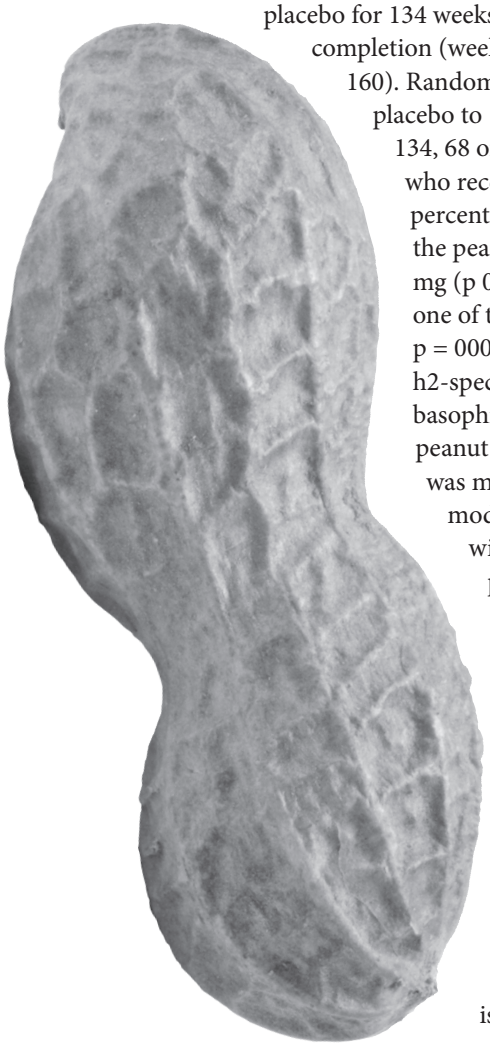
- A double-blind, randomized, placebo-controlled study

Inclusion Criteria:

- Children who were sensitive to 500 mg or less of peanut protein between the ages of 12 and less than 48 months.
- Clinical history of peanut allergy or avoidance without ever having eaten peanuts.
- Skin prick test (SPT) peanut-specific IgE levels of 5 kUA/L or higher, saline control by 3 mm or more.
- Positive reaction to a cumulative dose of 500 mg or less of peanut.

Exclusion Criteria:

- A history of severe anaphylaxis with hypotension to peanuts, more than mild asthma or uncontrolled asthma, uncontrolled atopic dermatitis, and eosinophilic gastrointestinal disease.



In a 2:1 allocation ratio, participants were randomly assigned to undergo oral immunotherapy with peanuts or a placebo for 134 weeks (2000 mg of peanut protein per day), followed by 26 weeks of avoidance. At treatment's completion (week 134), desensitization and remission following avoidance were the main results (week 160). Random assignments were made to give peanut oral immunotherapy (96 participants) or a placebo to 146 children with a median age of 39 months (IQR 30.8-44.7). (50 participants). At week 134, 68 of the 96 patients who received peanut oral immunotherapy and one of the 50 participants who received a placebo achieved the primary objective of desensitization (risk difference: 69 percent, 95 percent confidence interval: 59-79; p 0.0001). In comparison to 5 mg of a placebo, the peanut oral immunotherapy's median cumulative tolerated dose during week 134 was 5005 mg (p 0.0001)8. Following avoidance, 20 of the 96 recipients of peanut oral immunotherapy and one of the 50 recipients of a placebo met the remission criteria (RD 19%, 95 percent CI 10-28; p = 00021). At weeks 134 and 160, peanut oral immunotherapy raised peanut-specific and Ara h2-specific IgG4 while decreasing peanut-specific and Ara h2-specific IgE, skin prick test, and basophil activation compared to placebo. Most individuals (80% with placebo vs. 98% with peanut oral immunotherapy) experienced at least one oral immunotherapy dose reaction, which was more common in those receiving peanut oral immunotherapy and was typically mild to moderate in severity[4]. Epinephrine was used to treat 35 oral immunotherapy dose events with mild symptoms in 21 patients undergoing peanut oral immunotherapy[7]. Starting peanut oral immunotherapy before the age of four in children with a peanut allergy has been linked to faster desensitization and remission. Immunological biomarkers and remission development were associated. The findings imply that there is a window of opportunity for intervention to cause peanut allergy to remit when children are young.

Desensitization:

There are 3 types of peanut allergy immunotherapy available, Epicutaneous immunotherapy (EPIT) called viaskin peanut, also called the “peanut patch”, Sublingual immunotherapy (SLIT) SLIT is another form of peanut allergy treatment. SLIT involves placing drops of a peanut protein extract under the tongue for 2 minutes before swallowing, and oral immunotherapy called Palforzia is a capsule manufactured by Aimmune Therapeutics that contains a calculated amount of peanut powder and is taken as directed by a board-certified allergist. It is only available right now to kids

between the ages of 4 and 17. Patients get the powder in progressively larger doses until a tolerance level is reached, at which point they continue receiving that dose indefinitely[5]. The United States Food and Drug Administration has approved Palforzia as the first therapy for peanut allergy (FDA). A non-pharmaceutical grade peanut product is carefully prepared and administered using predetermined protocols by an allergist who specializes in peanut allergy desensitization. Although these commercial solutions are not FDA-approved for the treatment of food allergies, thousands of individuals have seen success with them. In addition to OIT, other peanut allergy immunotherapy products and techniques are being researched but have not yet received FDA approval or are not yet available as treatments. Therefore, an unintentional encounter won't result in a significant allergic reaction. Patients must keep away from anything containing peanuts. Even when a certain tolerance threshold has been reached, they could still need to undergo OIT. The palforiza is given orally, made up of capsules containing peanut powder. It will be necessary to break the capsules and combine the peanut powder with semi solid meals (e.g. apple sauce, yogurt). Patients will need to take each dose according to your allergist's recommendations. The goal is to reach a daily dose that will shield you from unintentional exposure[5]. Most patients (but not all) will be able to take higher doses of the allergic food after some time (often months) of ongoing (daily) treatment. To sustain desensitization, one must consume the daily maintenance dose. The main advantage of Food OIT is protection from unintentional exposure. Research investigations have also observed an improvement in quality of life5. Food OIT necessitates numerous hospital visits and a considerable time commitment. For Peanut specifically, OIT with Palforzia will entail a minimum of 11 up-dosing visits (for regular dose increases every two weeks), as well as an initial visit for assessment (to make sure it is safe to undergo treatment with the drug), a visit for rapid initial dose escalation, and a visit for rapid initial dose escalation.

References:

1. U.S. Department of Health and Human Services. (2022, January 20). Oral immunotherapy induces remission of peanut allergy in some young children. National Institutes of Health. Retrieved July 25, 2022, from https://www.nih.gov/news-events/news-releases/oral-immunotherapy-induces-remission- peanut-allergy-some-young-children
2. Define_me. (n.d.). Retrieved July 25, 2022, from https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02390-4/fulltext#sec cesectitle
3. Matthew Greenhawt, Marcus Shaker, Elissa M Abrams, Peanut oral immunotherapy in very young children,The Lancet,Volume 399, Issue 10322,2022,Pages 336-337,ISSN 0140-6736,https://doi.org/10.1016/S0140-6736(22)00088-5.(https://www.sciencedirect.c om/science/article/pii/S0140673622000885)
4. Oral immunotherapy induces remission of peanut allergy in some young children. (2022, January 20). Oral Immunotherapy Induces Remission of Peanut Allergy in Some Young Children.https://www.nih.gov/news-events/news-releases/oral-immunotherapy-induces-re mission-peanut-allergy-some-young-children
5. Peanut Allergy Treatment. (2021, January 21). Peanut Allergy Treatment. httpsU.S. Department of Health and Human Services. (2022, January 20). Oral immunotherapy induces remission of peanut allergy in some young children. National Institutes of Health. Retrieved July 25, 2022, from https://www.nih.gov/news-events/news-releases/oral-immunotherapy-induces-remission- peanut-allergy-some-young-children
6. Define_me. (n.d.). Retrieved July 25, 2022, from https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00088-5/fulltext
7. Define_me. (n.d.). Retrieved July 25, 2022, from https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02390-4/fulltext#sec cesectitle1://allergyasthmanetwork.org/health-a-z/immunotherapy/peanut-allergy-treatme nt/[az1]

Contributed by:
Eriny Morgan, Pharm. D. Candidate
FDU Class of 2023

University HOSPITAL Newark, NJ
Pharmacy News

Novel Once Weekly Tirzepatide in the Treatment of Type 2 Diabetes

Type 2 diabetes is characterized by relative insulin deficiency caused by pancreatic β-cell dysfunction and insulin resistance in target organs. Over 34 million Americans have diabetes, and approximately 90-95% of diabetics have type 2 diabetes[2]. The disease most often develops in people >45 years old. However, there is an increasing number of children, teens, and young adults that are developing type 2 diabetes[2].

The current pharmacological standard of care for the treatment of Type 2 diabetes is Metformin, which is first-line, Insulin and sulfonylureas, which are second-line and glitazones, which are third-line. Tirzepatide is a dual glucose-dependent insulinotropic polypeptide and glucagonlike peptide-1 (GLP-1) receptor agonist which is hypothesized to act centrally to potentiate a GLP-1–induced reduction in food intake. It functions to increase glucose-dependent insulin secretion, decrease inappropriate glucagon secretion, and slow gastric emptying, allowing it to potentially become an ideal treatment option for type 2 diabetic patients.

Tirzepatide was compared to semeglutide in an open-labeled, double-blinded phase 3 clinical trial which hypothesized that in patients with type 2 diabetes, a single molecule combining the glucose-dependent insulinotropic polypeptide receptor and GLP-1 receptor agonism (tirzepatide) may have a greater effect on glucose levels and weight control than selective GLP-1 receptor agonists (semeglutide), allowing greater glycemic control.

The primary end point of this study was a Change in glycated hemoglobin level from baseline to week 40. The secondary endpoints were a change in body weight from baseline to week 40 and attainment of glycated hemoglobin level targets of > 7.0% and > 5.7%. Finally, the safety endpoints were adverse events, Discontinuation of tirzepatide or semaglutide because of adverse events, adjudicated pancreatic adverse events, incidence of hypersensitivity reactions, mean changes from baseline in pulse rate and systolic and diastolic blood pressure and the occurrence of hypoglycemic events. 2,526 patients were screened for trial eligibility and 1,879 patients were enrolled and underwent randomization. 1,878 patients participated in the trial and received at least one dose of tirzepatide or semaglutide. The trial was conducted in 128 sites in the United States, Argentina, Australia, Brazil, Canada, Israel, Mexico, and the United Kingdom.

The authors of this study concluded that in patients with type 2 diabetes who were receiving metformin, novel once weekly tirzepatide was noninferior and superior to semaglutide with respect to the mean change in the glycated hemoglobin level from baseline to 40 weeks. All tirzepatide doses achieved larger reductions in the fasting serum glucose level than with semaglutide. Tirzepatide treatment achieved a glycated hemoglobin level target of less than 5.7% without an increase in hypoglycemia, which has not been attainable by current treatment options. The dual agonism (glucose-dependent insulinotropic polypeptide receptor and GLP-1 receptor) of Tirzepatide may allow some patients to reach near-normal glycemia with potential long-term benefits.

Citations:

1. Juan FP, Davies MJ, Rosenstock J, et al. Tirzepatide versus semaglutide once weekly in patients with type 2 diabetes. N Engl J Med. 2021;385(6):503-515
2. Centers for Disease Control and Prevention. (2021, August 10). Type 2 diabetes. Centers for Disease Control and Prevention. Retrieved November 16, 2021, from https://www.cdc.gov/diabetes/basics/type2.html.

Contributed by:
Sarah Elkamhway, Pharm. D. Candidate
Class of 2024
Rutgers Ernest School of Pharmacy