Training for AbbVie Duodopa® Specialist LCIG System, PEG-J Placement, Aftercare and Minimisation of Procedure Complications

Duodopa® (levodopa – carbidopa Intestinal gel)

Duodopa: Important Additional Risk Minimisation Information for Healthcare Providers

- The information presented in these slides is provided as part of additional Risk Minimisation Program for Duodopa targeted to minimize:
  - Gastrointestinal (GI) events
  - Device-related risks
  - Procedure-related risks associated with the LCIG system
- The information does not include a complete list of all risks or safety information on GI or device related procedure events associated with PEG-J: Percutaneous Endoscopic Gastrostomy (PEG) and Jejunal Tube (J) or Duodopa use
- Please carefully read your current and locally available Duodopa Prescribing Information and Patient Leaflet Information for comprehensive safety information on Duodopa or Instruction for Use (IFU) for PEG-J

Outline

- Goals for additional Risk Minimisation program
- Duodopa (LCIG system)
- PEG-J
  - Preparation of the patient
  - Placement
  - Aftercare
- Procedure complications and actions to take

Goals: Additional Risk Minimisation Program

- To inform Healthcare Providers (HCPs) and patients about the Gastrointestinal (GI), Gastrointestinal Device and Procedure-related risks associated with the LCIG system
- Educate HCPs on PEG-J and NJ (Naso-jejunal tube) insertion procedures
- Inform HCPs and patients about aftercare for long-term PEG-J placement in patients using the LCIG system

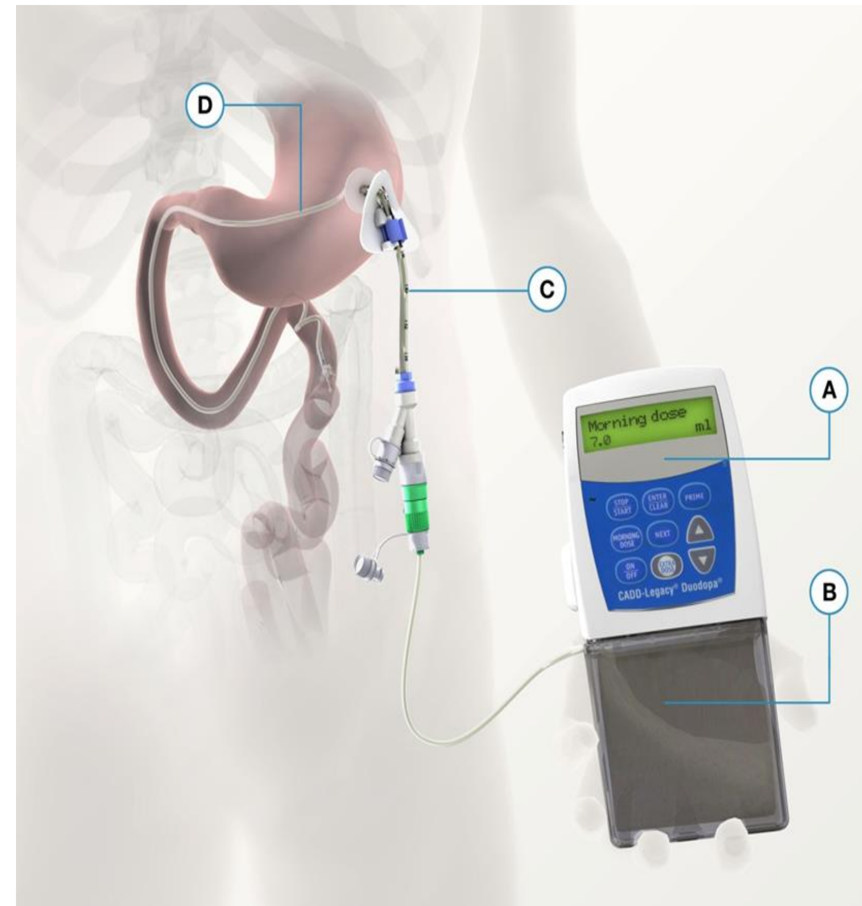
Target Population to Inform and Educate

Healthcare Providers

- Neurologists
- Gastroenterologist/Gastroenterology surgeon
- Center nurses
- Home care nurses
- AbbVie Duodopa Specialists

Duodopa (levodopa – carbidopa intestinal gel)

Indication: Treatment of advanced levodopa-responsive Parkinson’s disease with severe motor fluctuations and hyper-/dyskinesia when available combinations of Parkinson medicinal products have not given satisfactory results

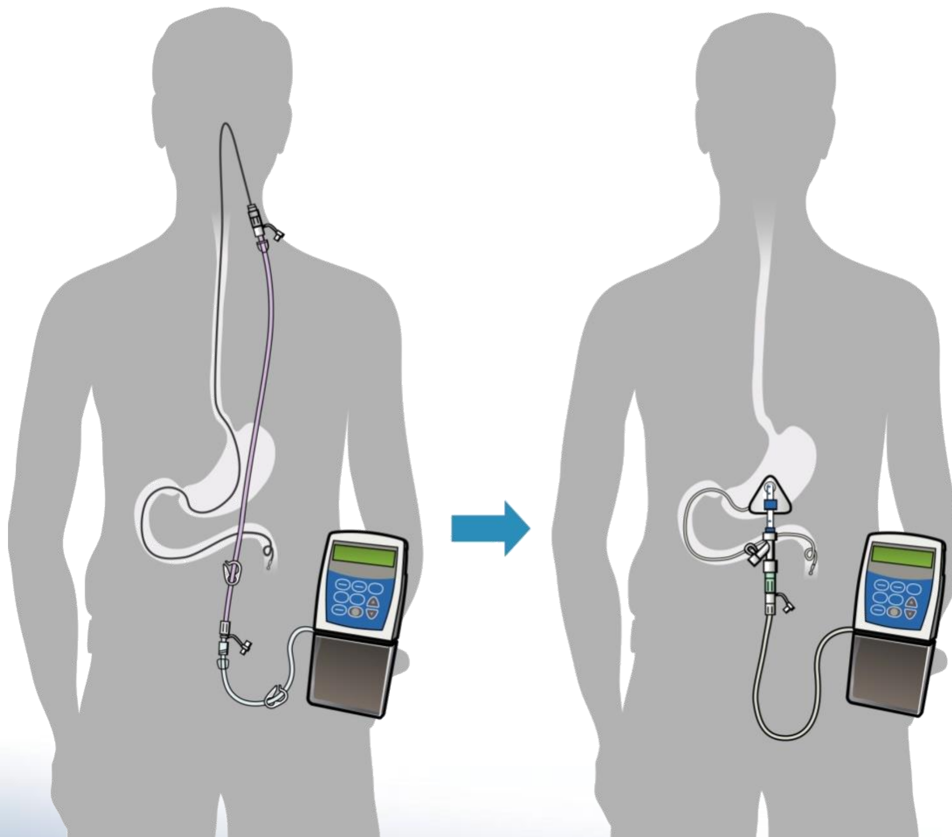


A. Pump
B. Duodopa cassette
C. PEG
D. Intestinal tube

Reference: Instruction for Use, Duodopa SmPC January 2021.

Duodopa: Levodopa and Carbidopa Intestinal Gel System

NJ Tube **PEG-J Tube**



Long administration of Duodopa uses the PEG-J delivery system.

A temporary NJ may be used to determine if the patient responds favorably before a permanent PEG-J is placed.

Reference: Instruction for Use, Duodopa SmPC January 2021.

Duodopa Safety

Contraindications: Duodopa

- Hypersensitivity to levodopa, carbidopa or to any of the excipients
- Narrow-angle glaucoma
- Severe heart failure
- Severe cardiac arrhythmia
- Acute stroke
- Non-selective MAO inhibitors and selective MAO type A inhibitors
- Conditions in which adrenergics are contraindicated (e.g., pheochromocytoma, hyperthyroidism and Cushing’s syndrome)
- Suspicious undiagnosed skin lesions or a history of melanoma

Reference: Instruction for Use, Duodopa SmPC January 2021.

Additional Device Complications

- Dislocation of the intestinal tube backward into the stomach leads to reappearance of motor fluctuations (due to erratic gastric emptying of Duodopa into the small intestine)
- Occlusion, kinks, or knots of the intestinal tube lead to high pressure signals from the pump. Should complete failure of the intestinal tube or pump occur, the patient must be treated with oral levodopa/carbidopa until the problem is solved.
- Abdominal pain, infection and leakage of gastric fluid may occur after surgery
- Local infections around the stoma should be treated conservatively with a disinfectant. If local infection continues, then antibiotics may be needed.

Reference: Instruction for Use, Duodopa SmPC January 2021.

PEG-J Device and Procedure Related Adverse Reactions

MedDRA System Organ Class	Very Common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1,000 to < 1/100)	Post-Marketing Events (frequency unknown)
Infections and infestations	Postoperative wound infection	Incision site cellulitis, Post procedural infection	Postoperative abscess	
Gastrointestinal disorders	Abdominal pain	Abdominal discomfort, Abdominal pain upper, Peritonitis, Pneumo-peritoneum	Bezoar, Colitis ischaemic, Gastrointestinal ischaemia, Gastrointestinal obstruction, Intussusception, Pancreatitis Small intestinal haemorrhage, Small intestinal ulcer, Large intestine perforation	Gastric perforation, Gastro-intestinal perforation, Small intestinal ischaemia, Small intestinal perforation
Skin and subcutaneous tissue disorders	Excessive granulation tissue			
General disorders and administration site conditions	Complications of device insertion[d]	Device dislocation, Device occlusion		
Injury, poisoning and procedural complications	Incision site erythema, Post procedural discharge, Procedural pain, Procedural site reaction	Gastrointestinal stoma complication, Incision site pain, Postoperative Ileus, Post procedural complication, Post procedural discomfort, Post procedural haemorrhage		

Reference: Instruction for Use, Duodopa SmPC January 2021.

Complications of NJ Device Insertion

Reported Adverse Reactions for Naso-Jejunal Tube (NJ)

- Oropharyngeal pain
- Abdominal distention, abdominal pain, abdominal discomfort, pain, throat irritation
- Gastrointestinal injury, esophageal haemorrhage
- Anxiety, dysphagia, and vomiting

Reference: Instruction for Use, Duodopa SmPC January 2021.

Travelling with CADD-Legacy® Duodopa Pump

- The pump conforms to the immunity requirements of RTCA DO-160C 12.89 (Section 21 – Radiated Emissions Only). The pump will not cause an interference with the aircraft's electronic equipment.
- The airplane will not interfere with the operation of the pump. The programmed accuracy of drug delivery using CADD pumps is not affected by airplane travel in pressurized cabins.
- The pump may or may not set off the metal detector. The sensitivity of metal detectors varies. The metal detector should not adversely affect the CADD pump. The pump may also be put through the x-ray machine without any adverse effect to the pump.

Reference: Instruction for Use, Duodopa SmPC January 2021.

Device: Special Warnings and Precautions for Use

Previous Surgery in Upper Abdomen	May lead to difficulty in performing gastrostomy or jejunostomy
Reduced Ability to Handle the System* Can Lead to Complications *Pump, tube connections	In such patients a caregiver (e.g., nurse, assistant nurse, or close relative) should assist the patient
Sudden or Gradual Worsening of Bradykinesia	May indicate an obstruction or other issue with the device and needs to be evaluated

Reference: Instruction for Use, Duodopa SmPC January 2021.

Device: Special Warnings and Precautions for Use (cont.)

Reported Complications	Bezoar, ileus, implant site erosion/ulcer, intestinal haemorrhage, intestinal ischaemia, intestinal obstruction, intestinal perforation, intussusception, pancreatitis, peritonitis, pneumoperitoneum and post-operative wound infection • A bezoar around the tip of the jejunal tube may function as a lead point for intestinal obstruction or the formation of intussusception • Abdominal pain may be a symptom of the above listed complications • Potential serious outcomes, such as surgery and/or death may occur with these complications • Patients should be advised to notify their physician if they experience any of the symptoms associated with the above events

Reference: Instruction for Use, Duodopa SmPC January 2021.

Starting a Patient

Logistic Flow:

- Preparations
- Tube insertions
- Calculation
- Titration

Starting a New Duodopa Patient in a Clinic with an NJ Tube

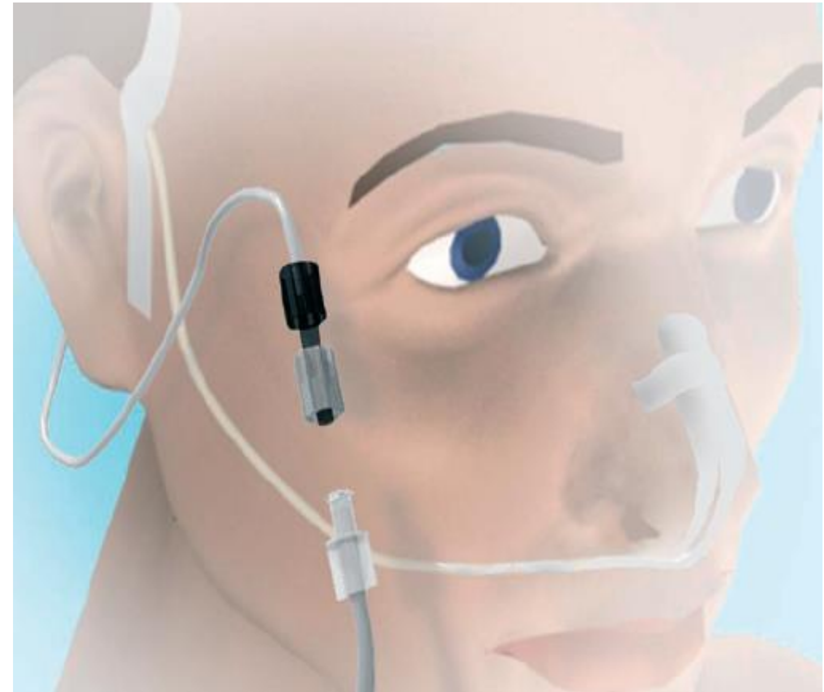
1. Naso-Jejunal Tube insertion
2. Duodopa dose calculation and pump programming
3. Titration period
4. PEG-J placement

AbbVie Nasogastric Tube

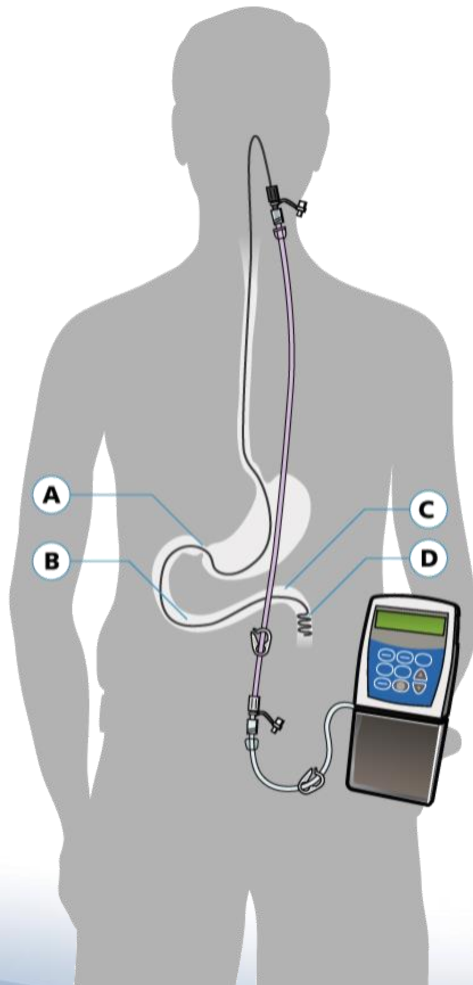
Test Phase: Naso-Jejunal Tube

Material:

- Naso-intestinal tube CH 10, 145 cm, holds 7 ml
- Extension tube 50 cm
- Tape for naso-intestinal tube fixation



Insertion of the Naso-Jejunal Tube



There are three options for placing the naso-jejunal intestinal tube:

1. **Endoscopic placement**
   Gastroscopy: force pylorus using guide wire and a grasping forceps/antenna
2. **Fluoroscopic control**
   Radiologist: Force pylorus using guide wire and fluoroscope
3. **Passive method**
   The tube is placed in the stomach (+30 cm) and the pigtail follow the peristaltic through pylorus. X-ray check needed to ensure a proper position before starting the infusion – prepare to force pylorus if the tube is not in place.

A. Pylorus
B. Duodenum
C. Treitz´ ligament
D. Jejunum

Critical Aspects of PEG-J Preparation, Placement and Aftercare

Administration of Duodopa

SHORT-TERM TEMPORARY THERAPY

(Prior to PEG-J tube placement)

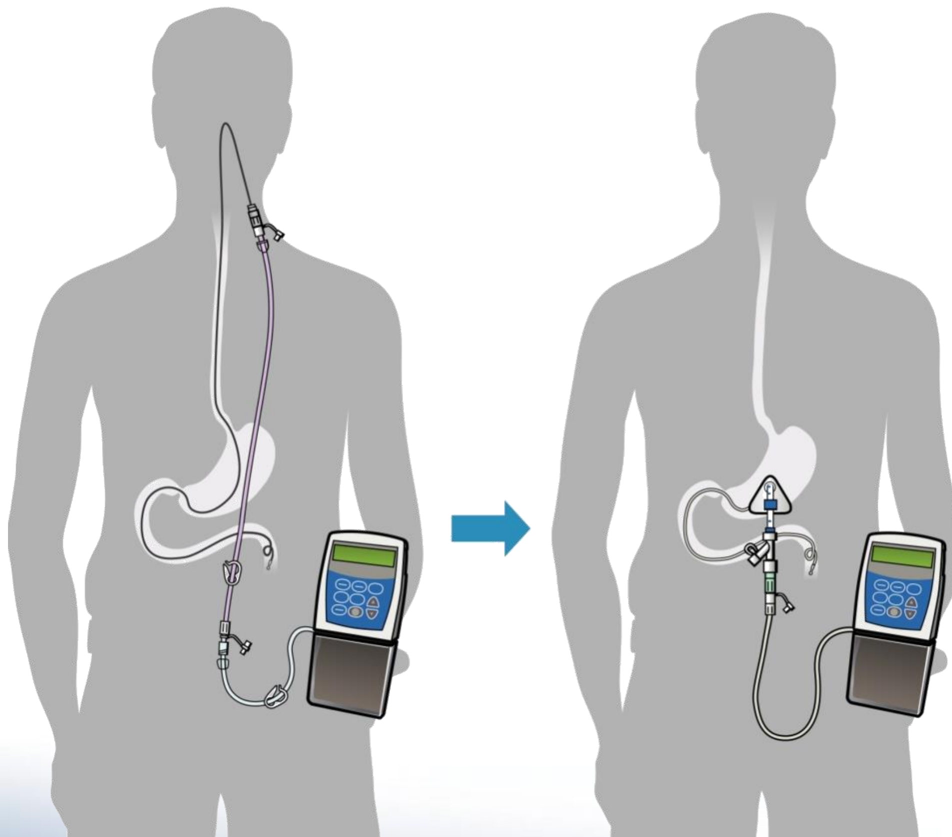
- Treatment may be initiated by a Naso-jejunal (NJ) tube with observation of the patient's clinical response

LONG-TERM THERAPY

(Requires placement of a PEG trans-abdominal tube and inner jejunal tube by percutaneous endoscopic gastrostomy)

- Duodopa is dispensed from medication cassette specifically designed to be connected to only a CADD-Legacy® 1400 pump
- PEG-J insertion and placement should be performed by a gastroenterologist or other healthcare provider experienced in this procedure

Duodopa: Levodopa and Carbidopa Intestinal Gel System



Long-term administration of Duodopa uses the PEG-J delivery system.

A temporary NJ tube may be used to determine if the patient responds favorably before a permanent PEG-J is placed.

Contraindications:* PEG Insertion

Lack of trans-illumination and positive needle aspiration test are an absolute contraindication for PEG insertion

Known or suspected intestinal obstruction

Serious coagulation disorders: ESPEN guideline++: (INR > 1.5, PTT > 50 s, platelets $< 50{,}000/mm^3$)

Sepsis

Active peritonitis

Relative contraindication includes ascites, and neoplastic, inflammatory, and infiltrative diseases of the gastric and abdominal walls

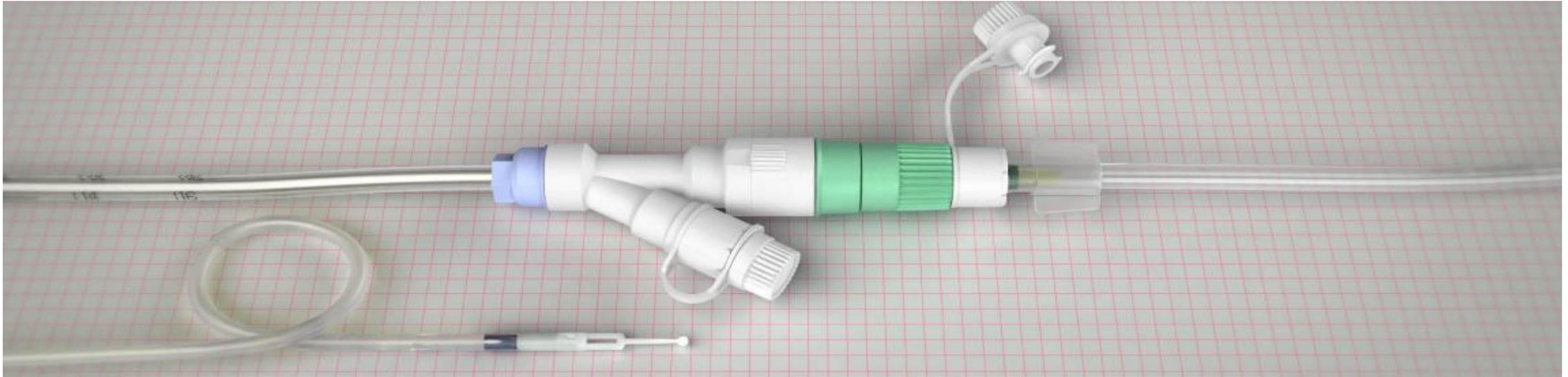
Interposed organs (e.g., liver, colon), marked peritoneal carcinomatosis, severe ascites, anorexia nervosa, severe psychosis and a clearly limited life expectancy++

PEG-J: Preparation, Placement and Aftercare

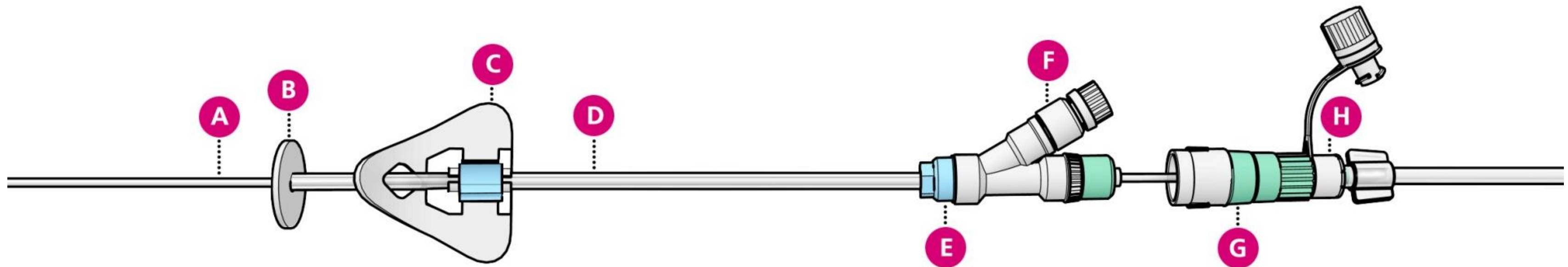
Educate HCPs on PEG-J and NJ tube insertion procedures through “Critical Aspects of PEG-J”:

- Materials to be used
- Preparation of the patient
- Placement
- Aftercare

Material to be Used:
PEG-J System – Assembled



Material to be Used: PEG-J System – Components



A. Intestinal tube
B. Internal retention plate
C. External retention plate
D. PEG tube
E. Fixation screw
F. Y-connector
G. Click connector
H. Luer Lock connector

Materials to be Used: PEG 15 FR – Kit Contents

1. PEG tube, polyurethane, FR 15
2. Puncture cannula with safety (air) valve
3. Disposable scalpel
4. Reel of thread with double thread and 4.1 introducer device
5. Universal funnel adapter for Luer and catheter tip syringe
6. Tube clamp

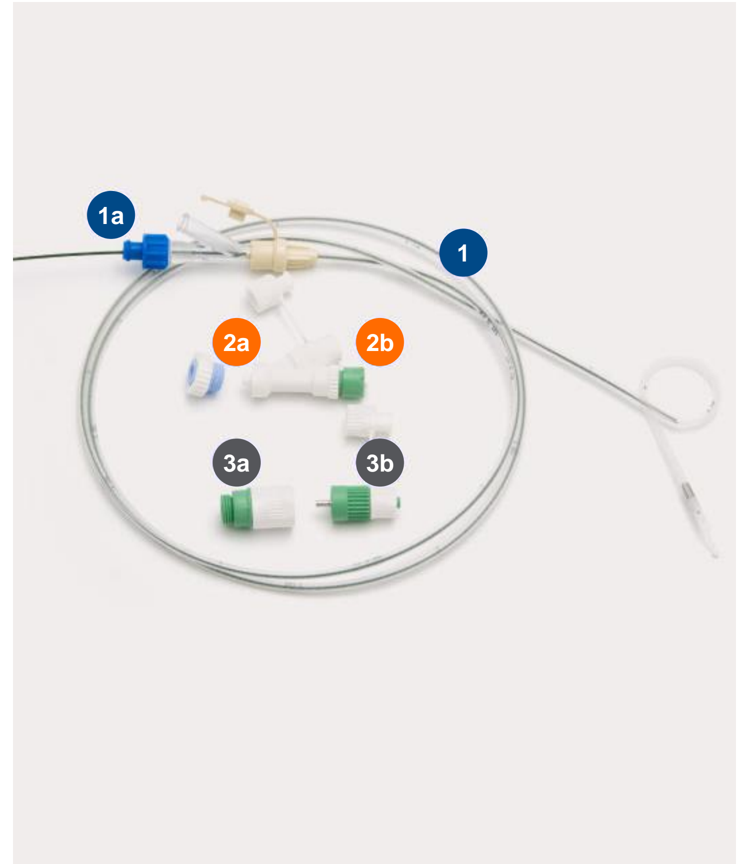
7a. Fixing screw for the Luer lock connector

7b. Luer lock connector

8. Silicone external fixation plate, radio-opaque

Materials to be Used:
Intestinal Tube 9 FR for PEG 15 FR Kit Components

1. Intestinal tube, polyurethane, 9 FR, 120 cm
   - 1a Integrated Teflon-coated guide wire with fitted Y-piece and blue transparent fixation screw
2. Y-connector for PEG 15 FR for simultaneous gastric and intestinal access consisting of:
   - 2a Fixation screw (blue-white)
   - 2b Y-connector with two positive Luer lock access points
3. Click adaptor 9 FR consisting of:
   - 3a Click connector
   - 3b Luer lock connector (with metal pin)



Preparation of the Patient: PEG-J Placement

Prior to the procedure the patient should be:

- Fasting overnight, at least 8 hours
- Provided with oral hygiene
- Given antibiotic prophylaxis per institutional protocol
- Current coagulation status per local guideline. ESP advised:
  - ESPEN guideline++: INR < 1.5, PTT < 50 s, platelets > 450,000/mm^{3}++
- Placed in a supine position for the procedure
- Placement of tube system under sterile surgical conditions
- On the morning of the procedure the patient should take their oral Parkinson's disease medications to prevent stiffness during the procedure

WARNING: Lack of trans-illumination and positive needle aspiration tests are an absolute contraindication for AbbVie™ PEG insertion.

PEG Placement: Important Highlights

The PEG tube should be placed according to standard procedure as published in the ESPEN-Guidelines and recommended by the tube manufacturer.

Reserve at least 40 minutes for the PEG-J procedure; it is essential to reserve enough time for the whole procedure.

The standard PEG pull-through method takes approx.12 minutes; intestinal tube insertion generally requires 10 to 30 minutes.

The skin incision at the puncture site should be slightly larger than the PEG tube.

Parkinson's patients tend to be thin. Be careful not to make skin incisions too deeply into their skin.

Angle the PEG toward the pylorus to enable direct access of the inner intestinal tube to pylorus.

PEG length: 20 cm

After placement of the PEG, make a straight cut 20 cm outside of the body.

Before connector assembly, ensure parts are dry and connectors are engaged.

Intestinal Tube Placement; Endoscopic Insertion

The intestinal tube can in general be placed in two different ways: endoscopic insertion or interventional radiology using standard equipment.

- **Endoscopic insertion:**
  - **Long enough endoscope;** the Intestinal tube is placed by using an endoscope long enough to reach the ligament of Treitz
  - **Avoid intestinal perforation;** make sure to lock the guide wire inside the intestinal tube before insertion

✓ **Confirm with X-ray that the distal end of the intestinal tube is located beyond ligament of Treitz**

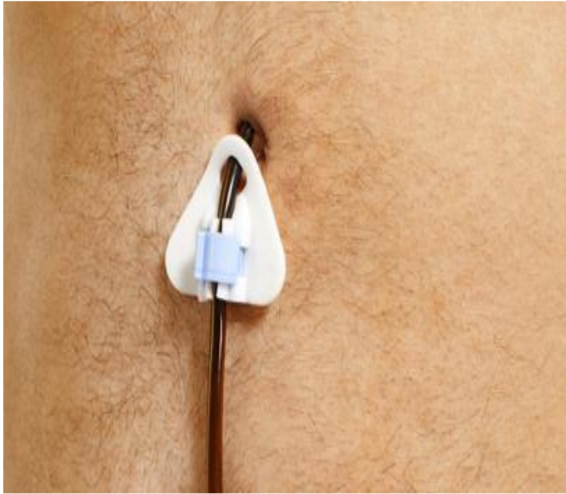
Intestinal Tube Placement; Endoscopic Insertion

- Endoscopic instruments to be used; grip the distal end of the intestinal tube using one of the following instruments:
  - The foreign body forceps, 2:1 teeth
  - The two-arm gripper or
  - The three-arm polyp gripper
- Distal end of intestinal tube beyond ligament of Treitz:
  - Advance the endoscope and the distal end of the intestinal tube under observation until it has safely passed the ligament of Treitz to reduce risk of dislocation of the tube back into the gastric lumen

Aftercare: Day of Placement, Day of Surgery (< 24 Hours After PEG-J Placement)

- The Duodopa treatment can normally be initiated directly following an uncomplicated PEG-J placement, after consultation with the gastroenterologist
- Oral feeding might be possible after 2 hours but it is preferred to wait until the next morning
- Do not change the dressing during the first 24 hours unless necessary
- Observe for signs of complications such as pain and bleeding
- GI or specialist should examine the patient before discharge

Aftercare: Day 1–10 (After PEG-J Placement)



Healthy PEG-J Stoma:
No redness, swelling, drainage, or crust at stoma site

The stoma site should be cleansed daily and kept dry at all times

- Wound dressing should be performed under good aseptic conditions once a day, for the first 7–10 days
- Disinfect hands and put on disposable gloves. Remove the dressing, open the retention plate and release the tube from the plate.
- Dispose the gloves, disinfect hands and put on new gloves
- Inspect the wound area (bleeding, erythema, secretion, induration, allergic skin reaction)
- Clean, disinfect, dry completely and redress the wound
- If there are any signs of complications, inform a physician

Aftercare: After Initial Wound Healing

After initial wound healing (24–72 hours, after initial PEG-J insertion), this procedure should be performed every 2–3 days to prevent **buried bumper syndrome**

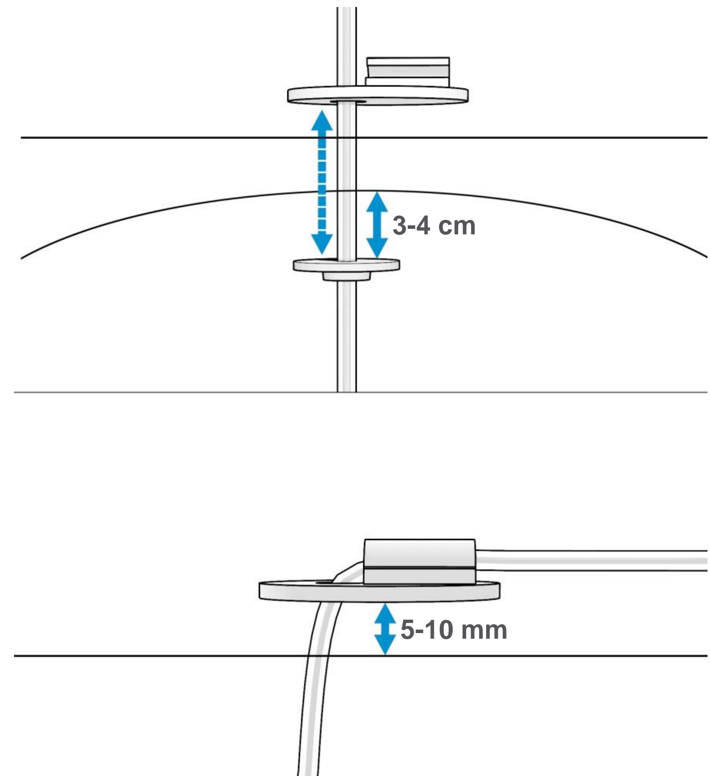
Remove the dressing and release the external retention plate to allow free movement of the PEG-J tube.

- Carefully push the tube 3-4 cm into the stomach and gently pull back until you feel resistance of the internal retention plate into the stoma and move the tube in a bi-directional motion (in and out) every time the dressing is changed
- The PEG tube should remain under moderate tension for 24 to 72 hours to promote good adherence of the stomach wall to the inner abdominal wall
- Avoid in/out movement of the PEG tube within 72 hours post placement,

Do not twist or rotate the PEG tube. It is important for the tube to move freely in the stoma to prevent the inner retention plate becoming embedded ("buried bumper syndrome").

Replace the retention plate allowing free movement of 5–10 mm. Apply sterile Y-compress under the tube.

- A plaster fixation is recommended for agitated patients



Aftercare: Tube Care

- Flush the AbbVie™ PEG tube daily with room temperature tap or drinking water (via the Flush Port)
- Flush the AbbVie™ J-tube and PEG daily with room temperature tap or drinking water
- Failure to adequately flush the PEG tube may result in occlusion or blockage
- The stoma area should be cleansed using an aseptic technique or refer to facility procedures for stoma care
- The gastric PEG tube should be carefully moved in and out slightly in the stoma every 2–3 days once the site has healed
- The stoma site should be clean and dry at all times

PEG-J: Precautions

Disinfectants such as
Povidone-Iodine (PVP-I; e.g., Iso-Betadine®, Braunol®) and
Octenidindihydrochlorid-Phenoxyethanol (e.g., Octanosept®)
should not be used; it might negatively affect the
physical/mechanical properties of the tube.

NOTE: Washing or showering with regular soap and water is possible two weeks after insertion of PEG. Always leave the area clean and dry.

Bathing and swimming (after complete initial wound healing) is possible. Fix tube securely with transparent adhesive dressing. Always leave the area clean and dry.

Aftercare: Some Complications and Action to Take

General:

- Circular erythema < 5 mm around the outer stoma canal is frequent and not a sign of wound infection
  - Carefully observe the reddening of the wound during initial wound dressing
  - **Never apply an ointment** on a PEG stoma nor an inflamed PEG wound
- Encrusted dressing → remove with 0.9% saline solution
- Signs of inflammation → twice daily sterile change of dressing with regular wound inspection, swab if prescribed by a doctor
  - Severe cases: systemic antibiotic treatment

Aftercare: Some Complications and Action to Take

- Severe discharge → keep the wound as dry as possible, change the dressing several times daily and place multiple Y- sterile compresses
- Over granulation tissue → remove granulation tissue only if there are complications (either by surgery or cauterization: Silver Nitrate)
- Residual tape → remove with disinfection spray (in special cases with surgical spirit – on intact skin only)
- Although rare serious abdominal complications have been reported with the AbbVie PEG-J system
  - All PEG-J patients and their caregivers should be informed to immediately contact their HCPs if they develop abdominal pain, abdominal bleeding, or signs of abdominal obstruction

Patient Aftercare: Discharging From the Hospital

Hospital Discharge Checklist

Provide the patient with the following material:

- For daily tube flushing
  - Syringes, 20 ml
  - Female/female connectors
- For stoma care
  - Dressings until the stoma has properly healed
  - Saline solution for stoma cleaning
  - Tape to fix the dressings around the stoma

Hospital Discharge Checklist (cont.)

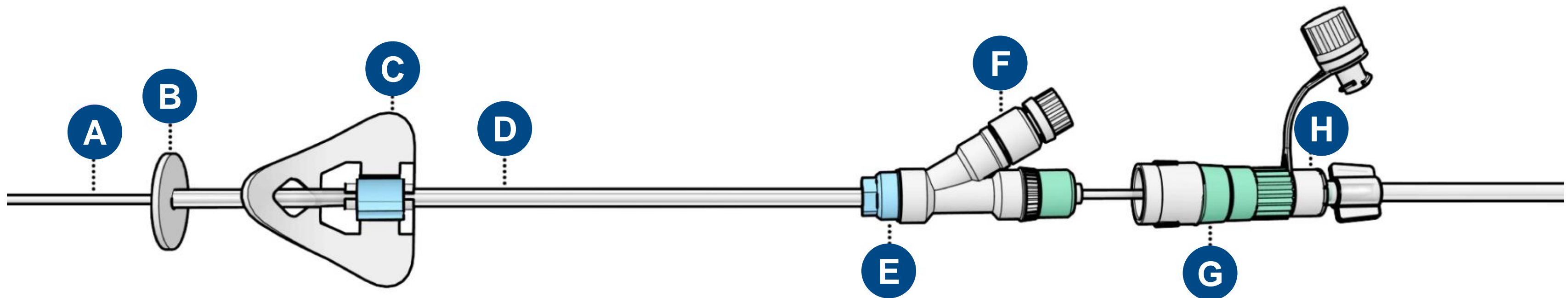
Information material

- Patient's pocket guide
- Relevant instruction for daily procedure
- CADD-Legacy® Duodopa patient pump manual
- Treatment certificate, filled out and stamped (optional)
- PEG-J aftercare guideline

Practical Handling of Duodopa: Changing the PEG-J Connector, AbbVie

Equipment

Scissors, two haemostatic forceps (or one haemostatic forceps and one tissue forceps), compress, gloves and AbbVie connectors for PEG FR 15/9.

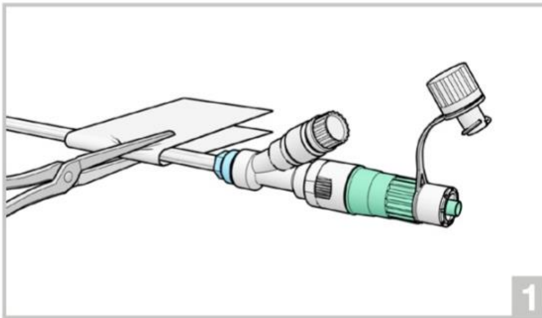


AbbVie PEG-J Tube

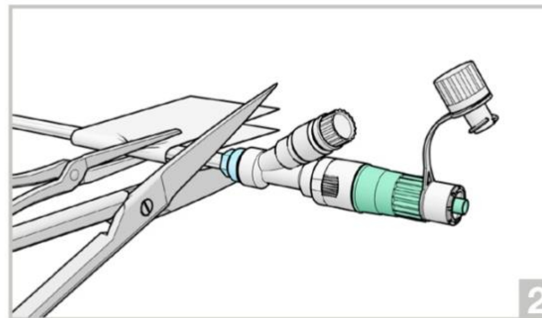
A. Intestinal tube **B.** Internal retention plate **C.** External retention plate **D.** PEG tube **E.** Fixation screw **F.** Y-connector **G.** Click connector **H.** Luer Lock connector

Practical Handling of Duodopa: Changing the PEG-J Connector, AbbVie

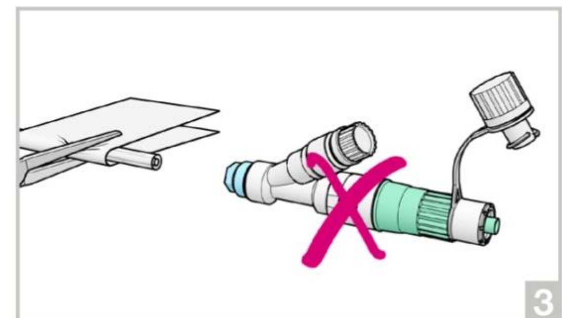
Remove the Old Connector



Fix the intestinal tube by locking the haemostatic forceps and then compress tightly on the PEG.



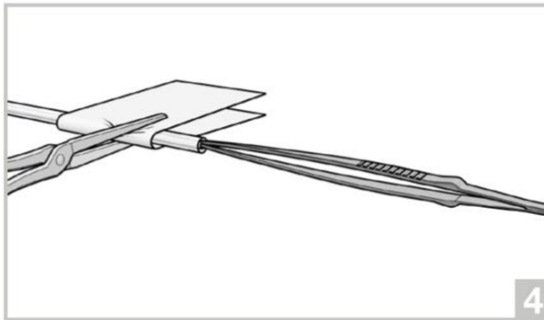
Make a straight cut through the PEG tube and intestinal tube close to the old connector.



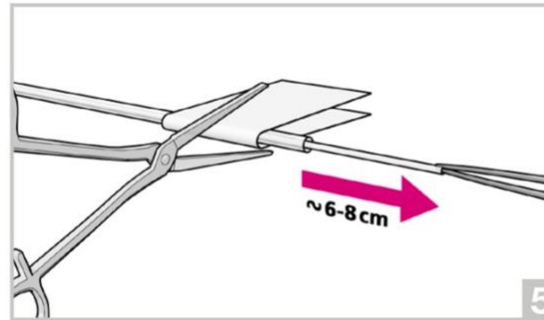
Discard the old connector.

Practical Handling of Duodopa: Changing the PEG-J Connector, AbbVie

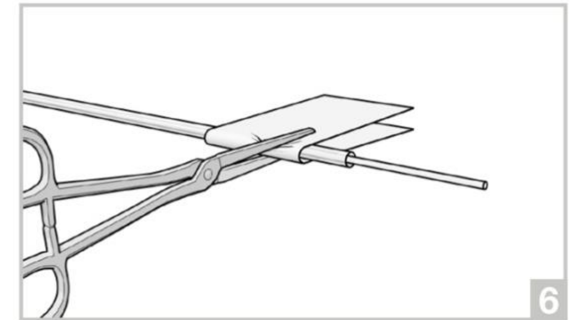
Prepare the Intestinal Tube



Grip the intestinal tube with the second tissue forceps (or another suitable forceps).



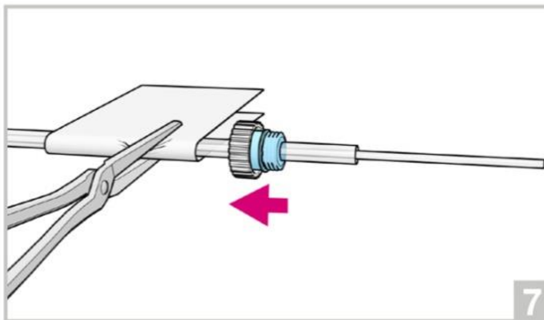
Carefully release the haemostatic forceps on the PEG and pull the intestinal tube out by approximately 6-8 cm.



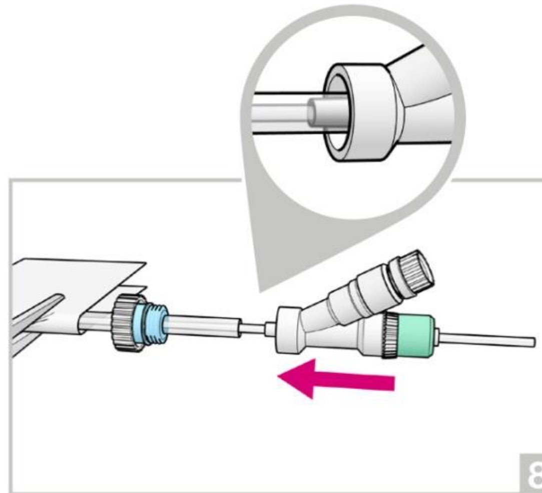
Place and lock the haemostatic forceps and the compress back on the PEG to fix the intestinal tube in position.

Practical Handling of Duodopa: Changing the PEG-J Connector, AbbVie

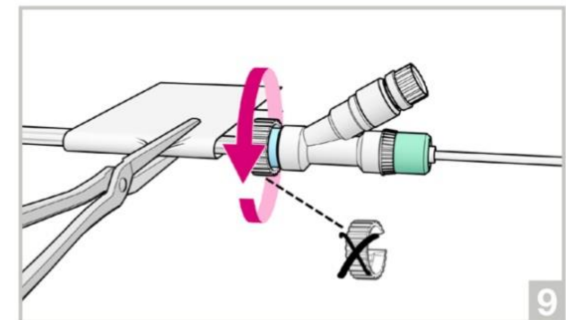
Assemble the New Connector



Push the blue and white fixation screw onto the PEG tube.



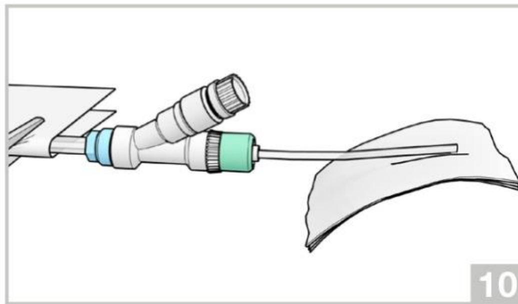
Push the white pin of the Y-connector onto the PEG tube as deep as possible. Before assembly, make sure the parts are dry.



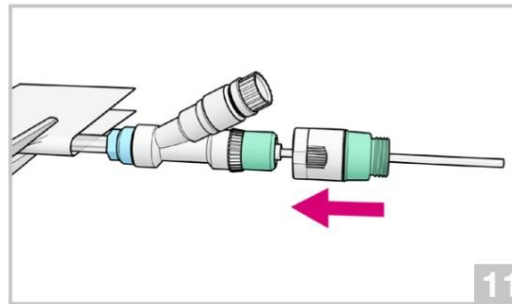
Screw the fixation screw onto the Y-connector all the way through. Thereafter pull off the screwing aid (outer white ring).

Practical Handling of Duodopa: Changing the PEG-J Connector, AbbVie

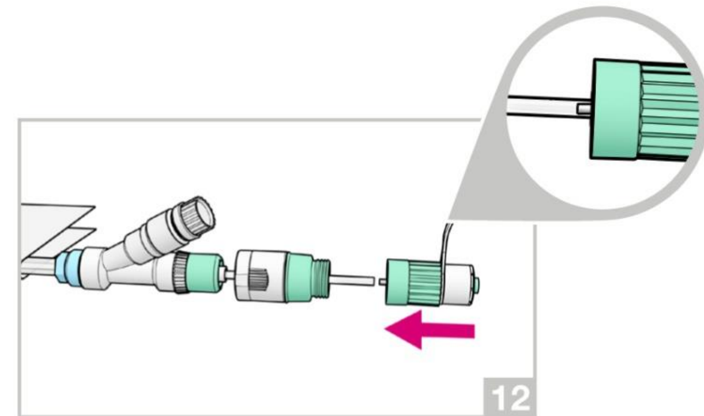
Assemble the New Connector



Dry the intestinal tube.



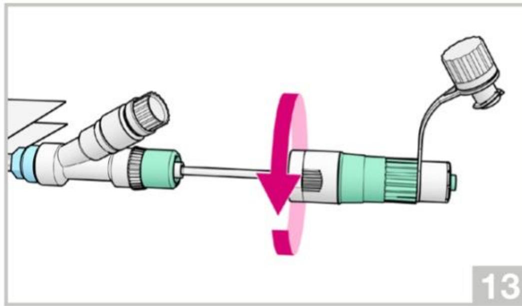
Push the green/white click connector onto the intestinal tube, leaving a small gap between the Y-connector and the click connector.



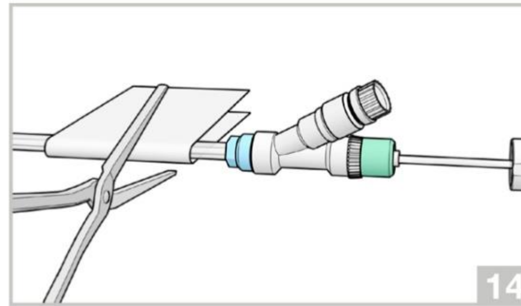
Make sure the metal pin is dry. Push the Luer Lock connector all the way into the intestinal tube.

Practical Handling of Duodopa: Changing the PEG-J Connector, AbbVie

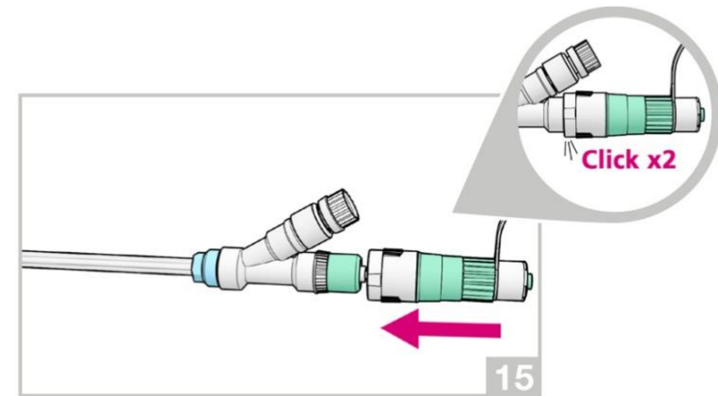
Assemble the New Connector



Screw the click connector tightly onto the Luer Lock connector. Do not twist the tube.



Release the forceps.

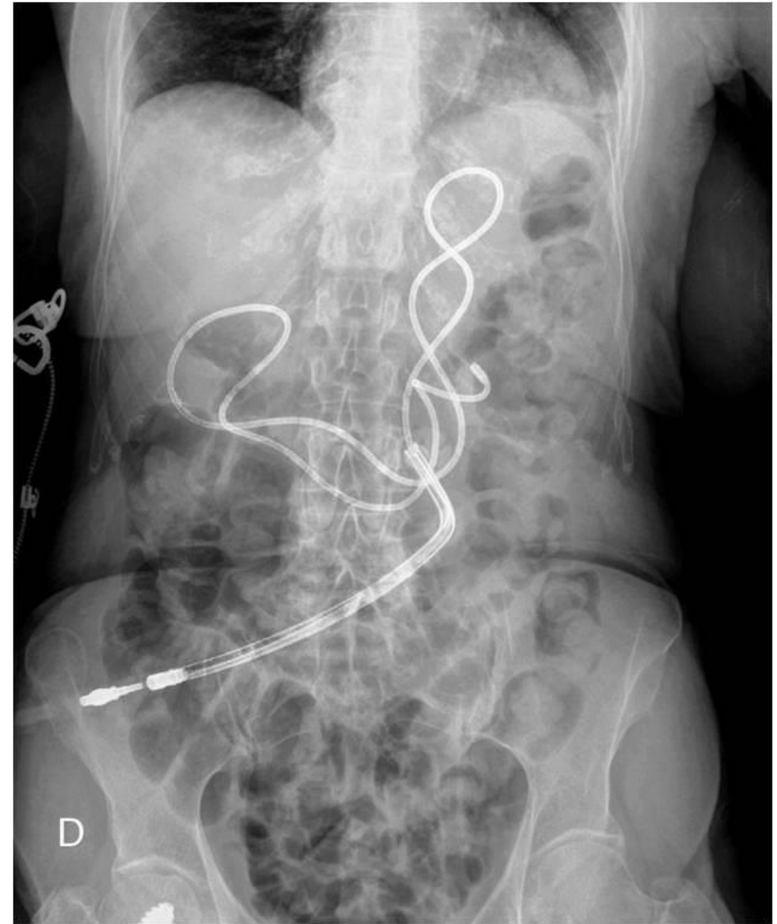


Push the two parts together firmly until a double click is heard, without twisting the tube. **Orientate the grip markers according to the image.**

Potential Issue During Aftercare: Loops

Action:

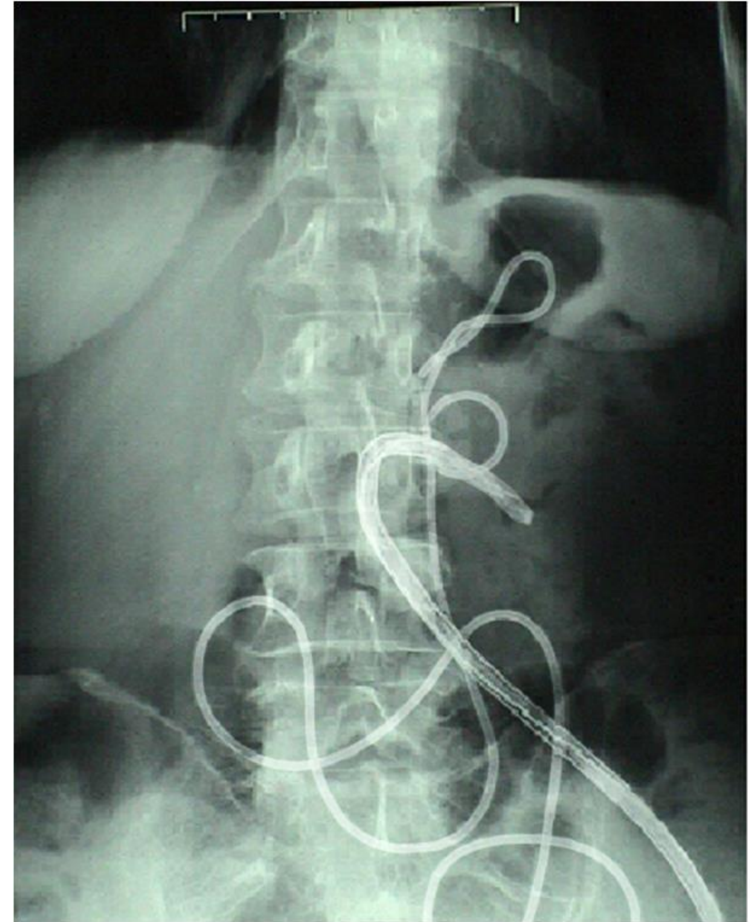
1. Place PEG-J straight down as far as possible into the intestine using fluoroscopy and guide wire
2. Shorten the intestinal tube if necessary to avoid loops in the stomach



Potential Issue During Aftercare: Kinks – Occlusion

Action:

1. Try to flush (carefully)
2. Fluoroscopy
   a) Turn around the inner tube
   b) Place it straight down as far as possible – use fluoroscopy and a guide wire
   c) Shorten the inner tube if necessary to avoid loops in the stomach



Potential Issue During Aftercare: Knots – Occlusion

Action:

1. Try to flush (carefully)
2. Fluoroscopy – knots
3. Gastroscopy – cut the inner tube and take it out. Do not leave it in the intestine, as it might cause ileus

In Summary

- The neurologist should work with a gastroenterologist who is experienced in PEG-J placement
- The gastroenterologist should examine patient for GI-related complications following PEG-J insertion procedure, long-term use of the PEG-J and associated tubing
- Follow proper PEG-J aftercare procedures to promote appropriate fistula tract formation for the PEG-J and to avoid potential complications, including peritonitis and postoperative wound infections
- Local care of the stoma site following PEG-J placement is important; carefully examine the stoma site at each visit and at any time the patient or caregiver is concerned about the site
- For more information on specific recommendations for PEG-J procedure and stoma care, please refer to PEG-J insertion video and aftercare materials