DUODOPA® Healthcare Professional Guide

(Levodopa/Carbidopa Intestinal Gel)

Educational Material for Risk Minimization
(Risk Management Plan)

abbvie

Duodopa®
LEVODOPA/CARBIDOPA INTESTINAL GEL

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About this Guide

This guide is an educational material as part of the additional risk minimization program for Duodopa®. This guide is intended to inform gastroenterologists, neurologists and other healthcare professionals (HCPs) with recommended measures to minimize gastrointestinal, gastrointestinal device, and gastrointestinal procedure related events.

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About Duodopa®

Duodopa® is indicated for the treatment of advanced levodopa-responsive Parkinson's disease with severe motor fluctuations and hyperkinesia or dyskinesia when available combinations of Parkinson medicinal products have not given satisfactory results.

Duodopa® is an intestinal gel which contains a combination of carbidopa and levodopa.

Duodopa® is administered into the jejunum through a percutaneous endoscopic gastrostomy (PEG) with a jejunal tube (AbbVie® PEG and J) using a pump.

Please read your current and locally available Duodopa® Prescribing Information and Summary of product characteristic for comprehensive safety information.

Duodopa® Pump System

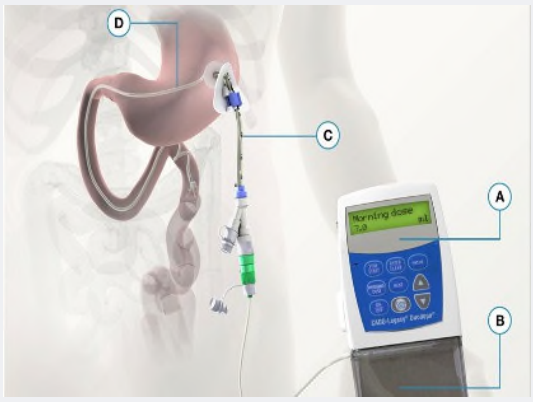


Figure 1.

Duodopa® Pump System:

A) Pump

B) Duodopa® cassette

C) PEG

D) Intestinal tube

Important Risk Information

The selected important safety risks below are associated with the PEG-J procedure or PEG-J tube (device) and are targeted for additional risk minimization:

Very Common
- Postoperative wound infection

Common
- Device dislocation
- Device occlusion
- Peritonitis
- Pneumoperitoneum
- Pneumonia/Aspiration pneumonia

Uncommon
- Bezoar
- Gastrointestinal obstruction
- Intussusception
- Large intestine perforation
- Pancreatitis
- Postoperative abscess
- Small intestinal hemorrhage

Frequency Unknown
- Implant site erosion/ulcer
- Sepsis
- Small intestinal perforation

Note: Some of these risks may result in serious outcomes such as the need for surgery.

Please read your current and locally available Duodopa® Prescribing Information for comprehensive safety information or Instruction for Use (IFU) for AbbVie® PEG and J Tube information. If you have questions about the pump, please refer to the pump manual.

Gastroenterologist

This guide is intended to provide approaches to minimize gastrointestinal (GI) safety risks from the PEG-J procedure and device. For complete step-by-step PEG-J procedural instructions, please refer to AbbVie® PEG PERCUTANEOUS ENDOSCOPIC GASTROSTOMY KIT 15 FR / 20 FR IFU and AbbVie® J INTESTINAL TUBE 9 FR for PEG 15 and 20 FR IFU.

Important Pre-Procedure Steps to Minimize Risks

In addition to the general preoperative procedures and institutional protocols, also follow the recommended contraindications criteria to ensure proper patient selection for the PEG-J procedure and minimize the safety risks (Table 1).

Table 1. Contraindications*
Known or suspected intestinal obstruction
Serious coagulation disorders (INR >1.5, Quick <50%, PTT >50s, platelets <50,000/mm)++
Sepsis
Active peritonitis
Lack of transillumination and positive needle aspiration test are an absolute contraindication for AbbVie® PEG insertion
Relative contraindications include ascites and neoplastic, inflammatory, and infiltrative diseases of the gastric and abdominal walls

Additional Pre-Procedure Steps include:

Prior to the procedure, the patient should be:

1. Fasting for at least 8 hours.
2. Provided with oral hygiene.
3. Given antibiotic prophylaxis as per institutional protocol.
4. Placed in a supine position for the procedure.
5. Managing their anti-coagulation as per institutional protocol.
6. Confirmed to be in stable medical condition, no recent infection, and reasonable nutritional status (albumin > 30g/L).

On the morning of the procedure, the patient should:

1. Continue their current Parkinson's disease medications to prevent stiffness during the procedure.
2. Drink clear fluids only, up to 2 hours prior to the PEG-J procedure.

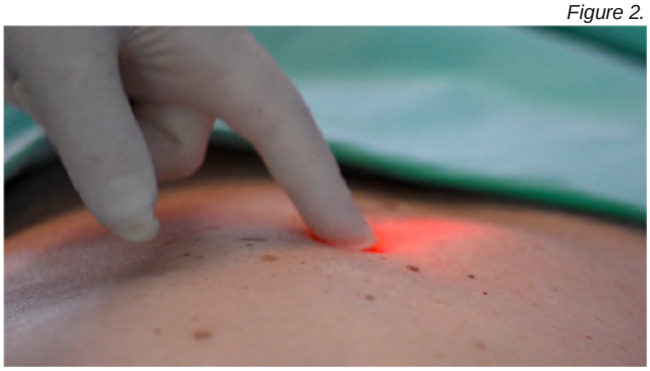
* Source: Instructions for Use for AbbVie® PEG Percutaneous Endoscopic Gastrostomy Kit 15 FR / 20 FR and AbbVie® J Intestinal Tube 9 FR for PEG 15 and 20 FR.
++ = Löser C, Aschl G, Hebutérne, et al. ESPEN guidelines on artificial enteral nutrition – Percutaneous endoscopic gastrostomy (PEG). Clinical Nutrition 2005;24:848-861.

Important PEG-J Placement Steps to Minimize Risks

A. Identification of Puncture Site

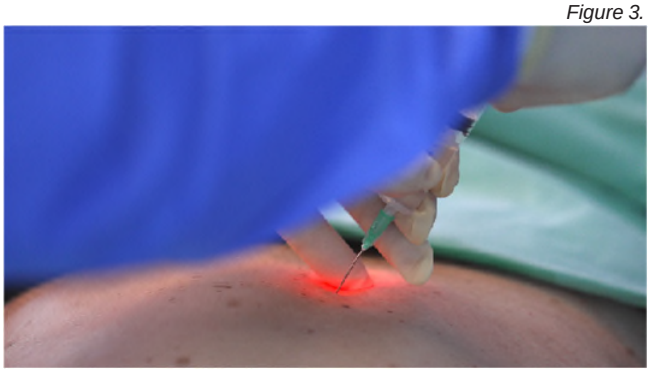
1. Transillumination and Indentation: Carefully locate the correct puncture site - it should give a sharp impression from the pointing finger and good transillumination of the abdominal wall. This limits potential injury to the intra-abdominal organs from puncture.
2. Needle Aspiration: A safe track to the stomach is confirmed by slow insertion of the needle using aspiration to ensure no air or feces are encountered prior to entering the stomach cavity.
3. Try to avoid areas of scar, hernia, or expected locations of major abdominal wall vessels (superior and inferior epigastric artery).

Figure 2.



Carefully locate the puncture site through good transillumination of the abdominal wall.

Figure 3.

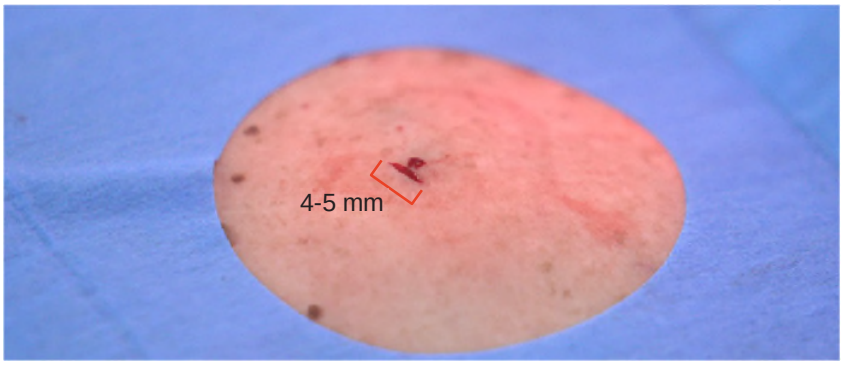


Perform slow insertion of the needle using aspiration.

B. Stomach Puncture and Thread Placement

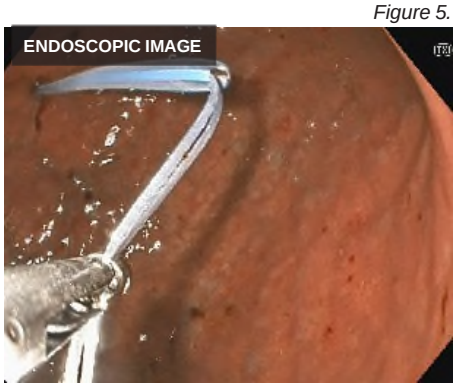
1. Patients with advanced Parkinson's disease tend to be thin. To avoid incising the stomach, be careful not to make skin incisions too deeply. Cutting after making a wheal of local anesthesia facilitates this.
2. The skin incision should be just large enough to accommodate the PEG tube (4-5 mm for AbbVie® PEG 15 FR or 6-7 mm for AbbVie® PEG 20 FR).
3. Angle the puncture cannula toward the pylorus to enable direct access of the inner intestinal tube to the pylorus.
4. Complete the puncture of the stomach under endoscopic control, as per standard procedure.
5. Insert the thread, draw it out through the mouth and affix to the fixation loop on the AbbVie® PEG.

Figure 4.



Skin incision should be approximately 4-5 mm for AbbVie® PEG 15 FR.

Figure 5.

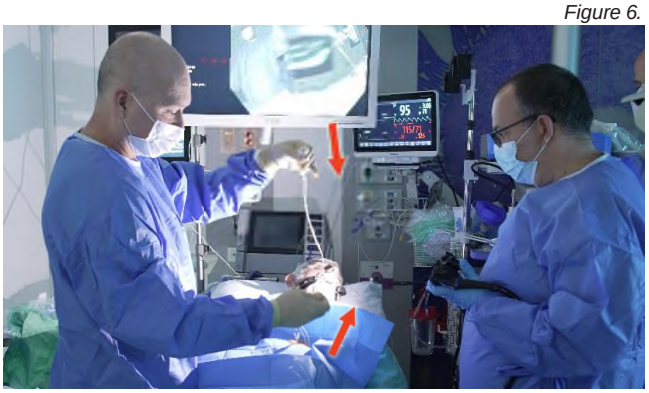


Draw the thread out through the mouth.

C. Pull Insertion Technique

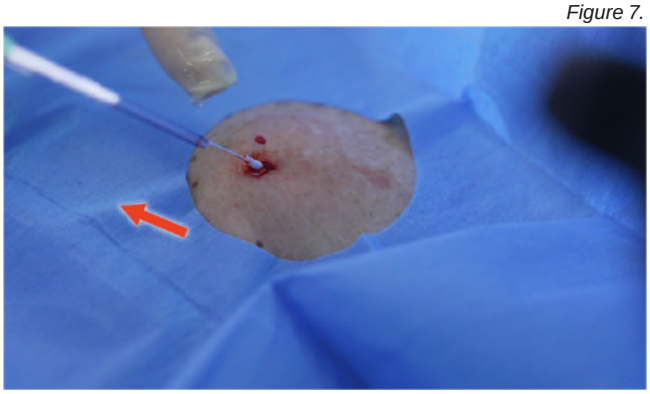
1. Position the AbbVie® PEG Tube in the stomach by slowly pulling on the distal end of the thread until slight resistance is felt when the tip of the PEG tube enters the puncture cannula.
2. Pull the AbbVie® PEG Tube and the puncture cannula out through the abdominal wall until the internal retention plate is in direct opposition to the inner gastric wall. Note that the AbbVie® PEGs are not traction removable, so there is low risk of inadvertent PEG dislodgement during the procedure.
3. PEG length should be approximately 20 cm. After placement of the PEG, make a straight cut 20 cm outside of the body.

Figure 6.



Pulling on the distal end of the thread while inserting the PEG tube into the mouth.

Figure 7.



Puncture cannula leaving the body as the PEG tube is being pulled out.

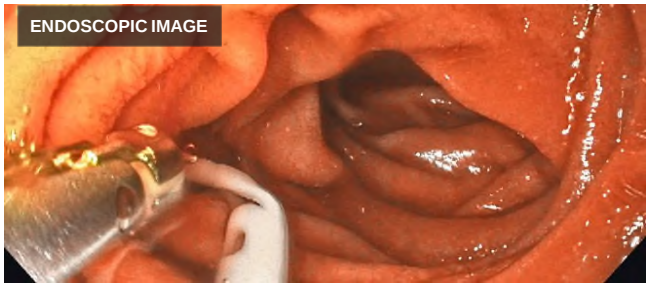
D. Insertion of Intestinal Tube - Key Safety Highlights

1. The intestinal tube should be placed using an endoscope long enough (i.e., standard gastroscope in most cases) to reach the ligament of Treitz. Proper straightening of the tube after passage of the pylorus is essential.
2. To avoid intestinal perforation, make sure to lock the guidewire inside the intestinal tube before insertion.
3. To avoid tube dislocation, grasp the ball at the tip of the J tube with biopsy forceps and insert it back into the working channel of the scope, advance forceps gently and avoid resistance while backing away with the endoscope.
4. Advance the endoscope and the distal end of the intestinal tube under observation until it has safely passed the ligament of Treitz. This step minimizes the risk of dislocation of the tube back into the gastric lumen.
5. According to institutional protocol, confirm via X-ray that the distal end of the intestinal tube is located beyond the ligament of Treitz.

Figure 8.

J tube passing through PEG tube into the stomach.

Figure 9.

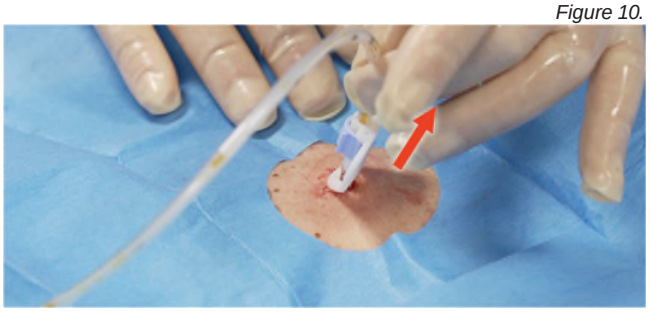


Ball at the tip of the J tube being advanced under direct visualization into the intestine.

E. Securing the PEG Tube

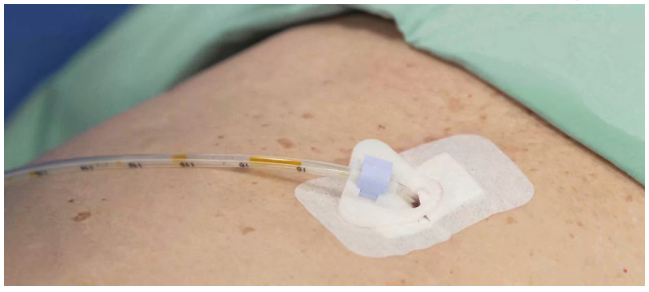
1. Pull Tension: Avoid pulling the AbbVie® PEG Tube too hard to prevent ischemia and necrosis.
2. PEG Tube Tension (24-72 hours or as per institutional protocol): The PEG tube should remain under moderate tension for 24-72 hours to promote good adherence of the stomach wall to the inner abdominal wall and avoid leakage.
3. PEG System Hygiene: Clean and dry the puncture site, fixation site, and PEG tube to avoid inflammation and infection.

Figure 10.



PEG tube should initially be placed under moderate tension.

Figure 11.



External fixation plate secured in place.

F. Final Assembly of the PEG-J Connectors

For further guidance on assembly of the PEG-J connectors illustrated below, refer to the AbbVie® J IFU for a step-by-step guide.

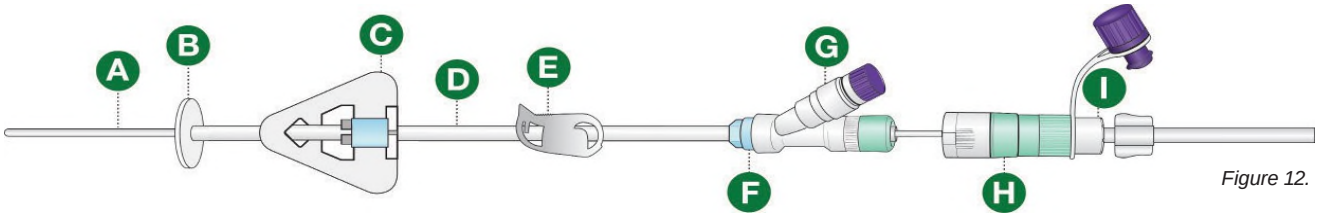


Figure 12.

A. Intestinal tube
B. Internal retention plate
C. External fixation plate with tube clip
D. PEG tube
E. Tube clamp
F. Fixation screw
G. Y-connector
H. Click adaptor
I. Click adaptor cap

Post Procedure Care to Minimize Risks

1. PEG Tube Tension Post 72 hours: Ensure the fixation plate has been loosened to leave 5-10 mm of free play between the outer stomach wall and fixation plate to prevent inflammation and subsequent buried bumper syndrome.
2. Stoma Assessment: Check the stoma site for any signs of inflammation, infection, or leakage and treat accordingly.
3. Stoma Hygiene: Remind the patient to maintain stoma hygiene and to keep the fixation plate clean and dry.

Refer the patient to the ‘Post-Procedure Care Routine’ found in the ‘Patient Guide’.

Neurologist

After the patient has gone through the pre-procedure and procedure phases, it is critical to observe the patient's stoma for signs of inflammation or infection. The sections below provide Neurology HCPs resources:

- to identify GI complications following the PEG-J procedure and long-term use of PEG-J tube
- to enable appropriate clinical interventions to minimize risks

The guide is divided into:

- Post-Procedure Care: focused on ensuring stoma healing and proper tube management.
- Long-Term Care: focused on maintaining a healthy stoma and proper tube management.

Post-Procedure Care

If the patient is within the post-procedure phase (until the stoma is fully healed - approximately 10 days):

- Remind the patient not to touch the bandage for 48 hours after the procedure
- Remind the patient not to move the tube for at least 72 hours after the procedure, or as advised by the gastroenterologist
- Ensure the patient has access to the 'Patient Guide'
- Remind the patient to follow the 'Post Procedure Care Routine' in the 'Patient Guide'

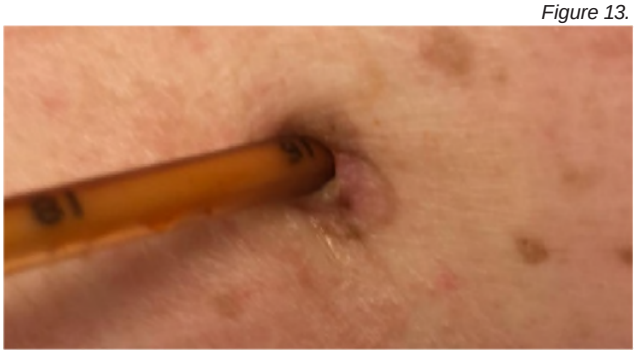
Stoma

Stoma Assessment: Check the stoma site for any signs of inflammation, infection, or leakage and treat accordingly. For identification and recommended follow up care of stoma complications, refer to the 'Stoma Visual Identification and Care' section.

While the stoma is healing, your patient may experience some symptoms which are normal and should resolve spontaneously:

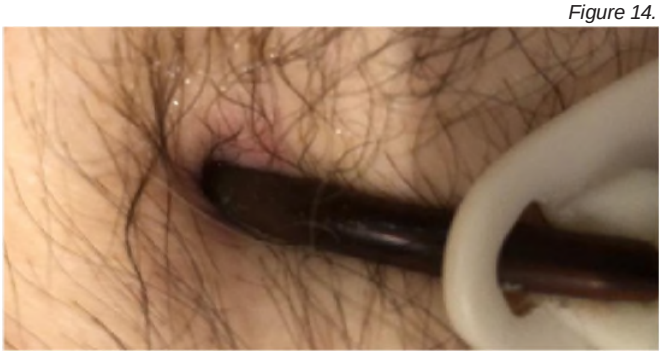
- some stomach pain or soreness at the procedure site
- up to 5 mm of redness of skin around the stoma
- a small amount of mucus from the stoma

Figure 13.



An example of a healthy stoma approximately 1 month post procedure.

Figure 14.



A healthy stoma approximately 18 months post procedure.

PEG Tube

1. PEG Tube Tension: The PEG tube should remain under moderate tension for 24-72 hours. After 72 hours, the fixation plate should be loosened to leave 5-10 mm of free play between the outer stomach wall and fixation plate to prevent inflammation and subsequent buried bumper syndrome.
2. PEG Tube Movement: Recommended to initiate tube mobilization only after the stoma site has healed or otherwise follow institutional protocol.
3. PEG Tube Function: Confirm that tube can be flushed.
4. PEG Tube Leakage: Confirm that tube is not leaking.

Important follow-up considerations:

- Check stoma healing and signs of infection
- Check PEG-J connectors and tube functioning
- Counsel patients not to use petroleum-based lubricants (e.g., baby oil, petroleum jelly) on the tube and stoma

Long-Term Care

If the patient is within the long-term care phase (beginning when the stoma is fully healed - approximately 10 days after the procedure):

- Ensure the patient has access to the ‘Patient Guide’
- Remind the patient to follow the ‘Long Term Care Routine’ in the ‘Patient Guide’

Stoma

Stoma Assessment: Check the stoma site for any signs of inflammation, infection, or leakage and treat accordingly. For identification and recommended follow up care of stoma complications, refer to the ‘Stoma Visual Identification and Care’ section.

PEG Tube

1. PEG Tube Tension: Counsel patient to continue to secure the external fixation plate to leave 5-10 mm of free play between the outer stomach wall and the fixation plate.
2. PEG Tube Movement: Once the stoma is healed, instruct the patient to mobilize the PEG tube each day to prevent Buried Bumper Syndrome. Carefully, push the PEG tube 3-4 cm into the stoma, then gently pull the PEG tube until resistance is felt. The tube should not be turned or rotated under any circumstances.
3. PEG Tube Function: Confirm that the tube is being flushed daily.
4. PEG Tube Leakage: Confirm that the tube is not leaking.

Figure 15.

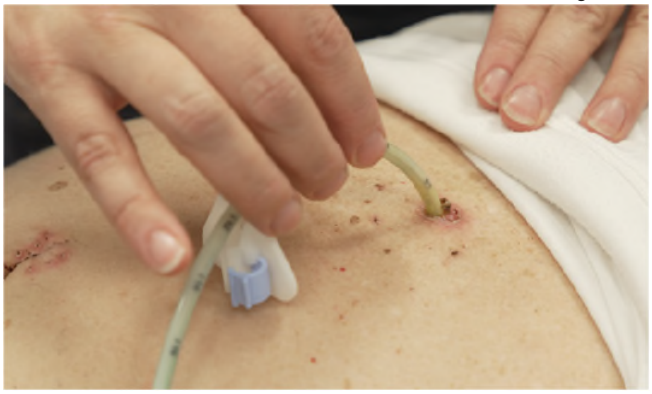
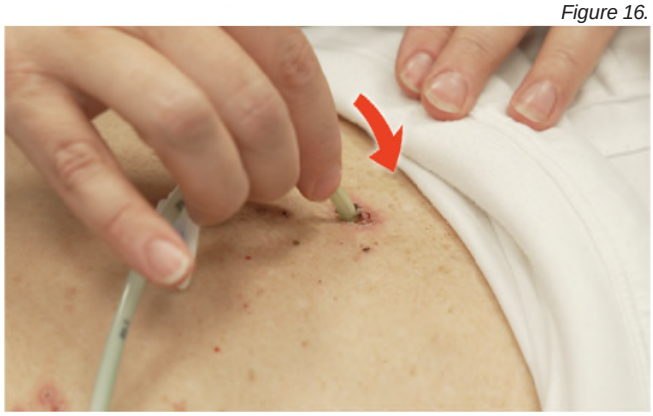


Figure 16.



Demonstration of PEG tube movement from instructional video.

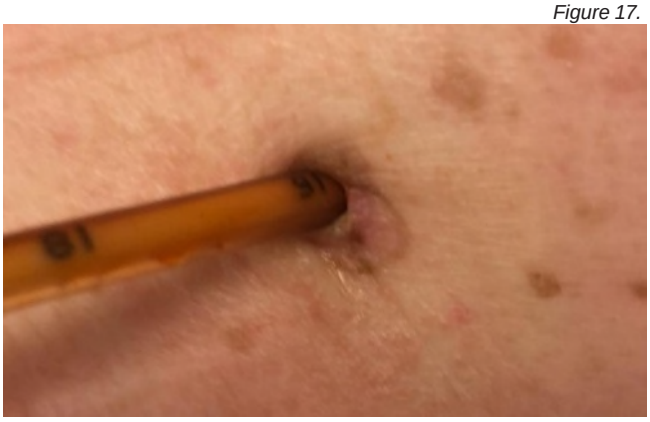
Buried Bumper Syndrome (BBS)

A severe complication in which the internal fixation device migrates alongside the tract of the stoma outside to the stomach.[1] The device can end up anywhere between the stomach mucosa and the surface of the skin.[2] BBS is primarily due to excessive compression of tissue between the internal and external fixation bumpers.[3] This is an uncommon severe complication after long-term PEG-J placement and can be prevented by proper tube movement and proper tube tension. Refer to the 'Stoma Visual Identification and Care' section for further details.

Stoma Visual Identification and Care

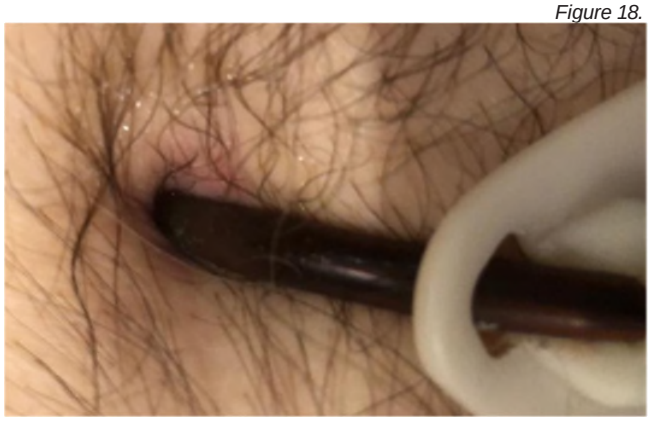
Healthy Stoma Examples

Figure 17.



Approximately 1 month post procedure.

Figure 18.



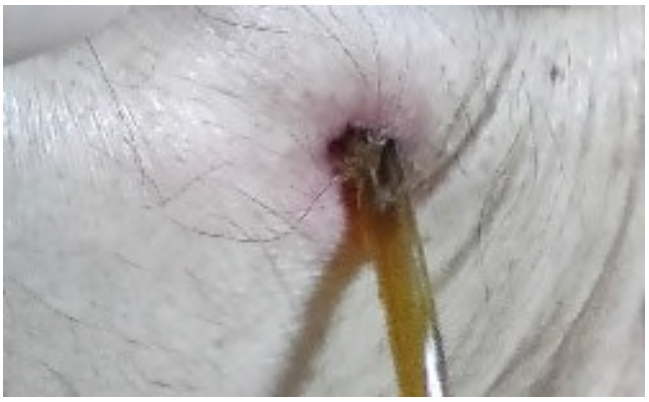
Approximately 18 months post procedure.

Stoma Complications with Recommended Follow Up Care

The following are examples of stoma complications with recommended follow up care.
Please consult with a gastroenterologist or appropriate specialist as needed for the appropriate patient care.

Infection

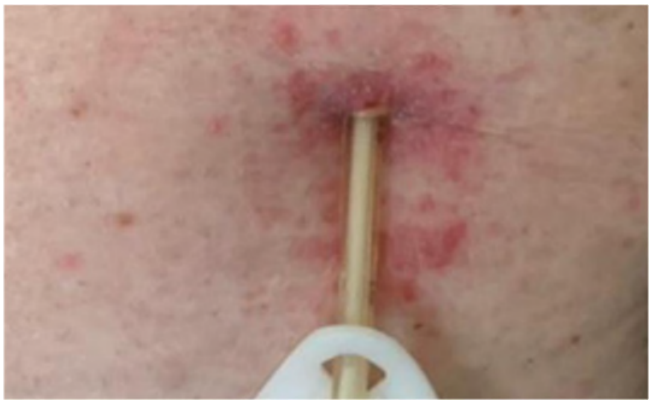
Figure 19.



Possible Bacterial Infection

Recommended intervention: Hygiene, culture, and broad-spectrum antibiotic cream.

Figure 20.

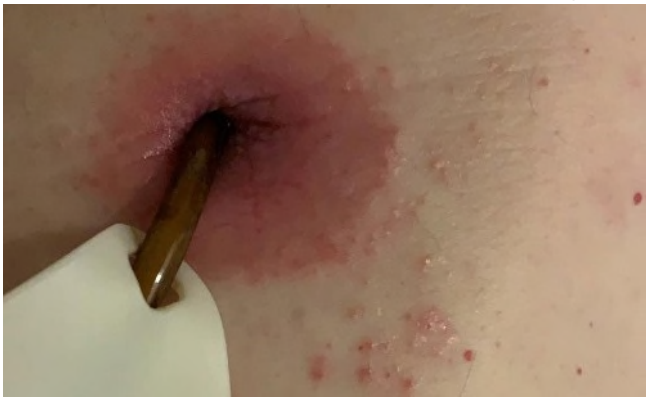


Possible Fungal Infection

Recommended intervention: Topical antifungals.

Infection

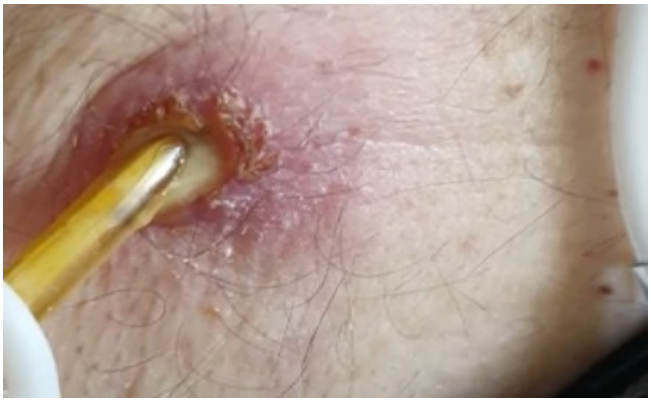
Figure 21.



Infection

Recommended intervention: Topical antibiotic/anti-fungal, and if no improvement, oral antibiotics.

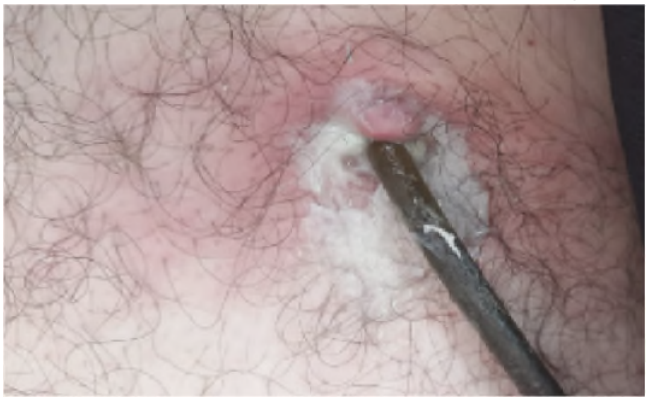
Figure 22.



Cellulitis, Purulent Discharge

Recommended intervention: Culture, topical antibiotics

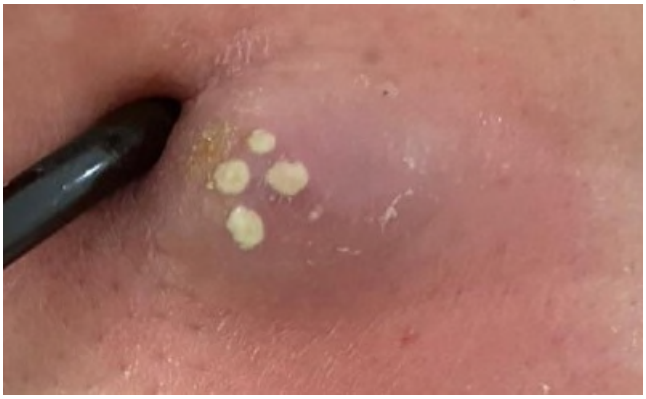
Figure 23.



Cellulitis and Granulation Tissue

Recommended intervention: Topical antibiotics and local therapy for granulation with low potency steroid cream and topical antibiotics.

Figure 24.

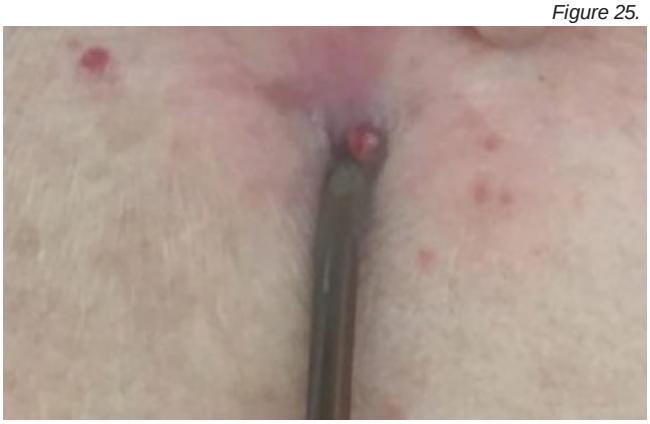


Abscess

Recommended intervention: Incision, drainage and antibiotics.

Granulation

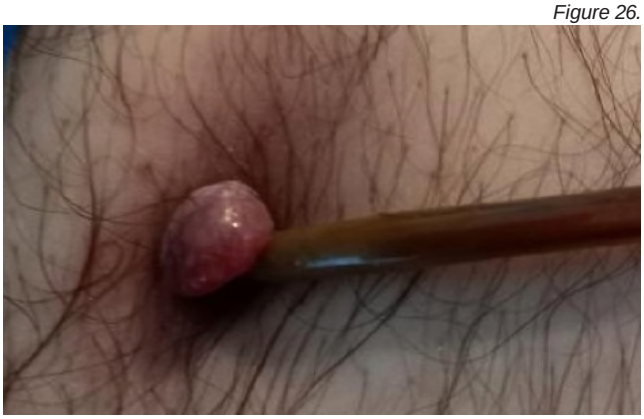
Figure 25.



Granulation Tissue

Recommended intervention: No intervention or low potency steroid and antibiotic cream. If not responsive, consider chemical ablation with silver nitrate applicator.

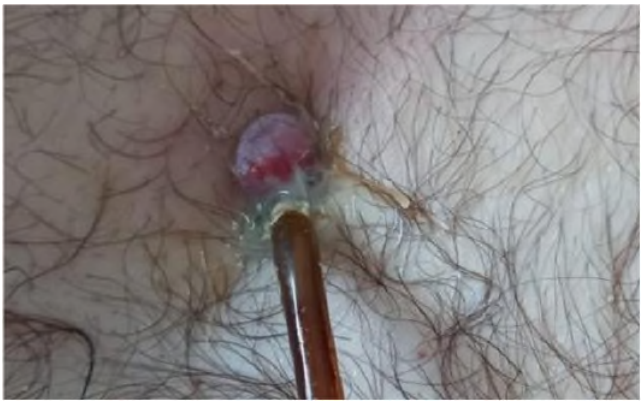
Figure 26.



Granulation Tissue

Recommended intervention: Topical steroid, antibiotic, and chemical ablation (silver nitrate). If epithelialized, it might not respond and will need plastic surgeon consultation.

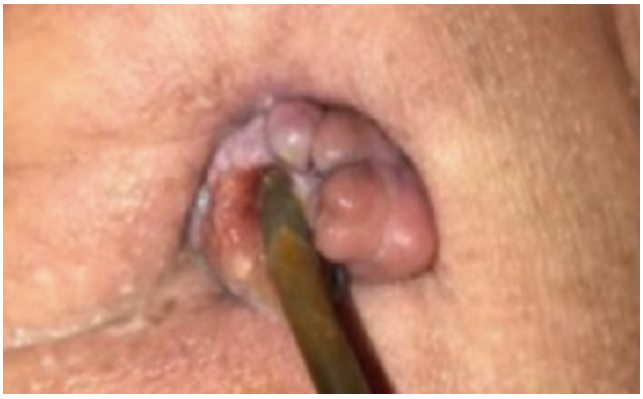
Figure 27.



Granulation Tissue

Recommended intervention: Topical steroid, antibiotic, and chemical cauterization with silver nitrate.

Figure 28.

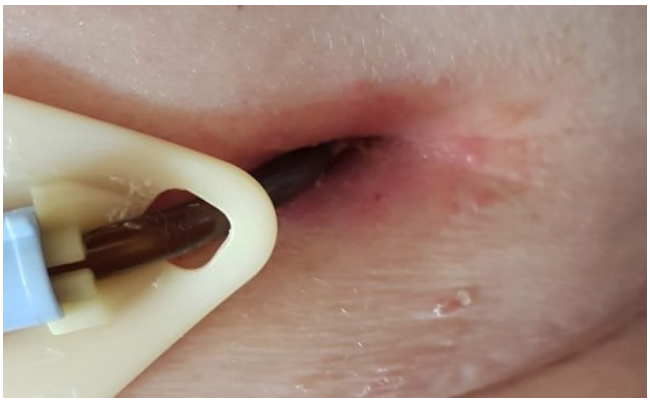


Extreme Hypergranulation

Recommended intervention: Trial of topical low potency steroid and antibiotic cream, chemical ablation (silver nitrate applicator). Consider surgical excision if no response.

Other

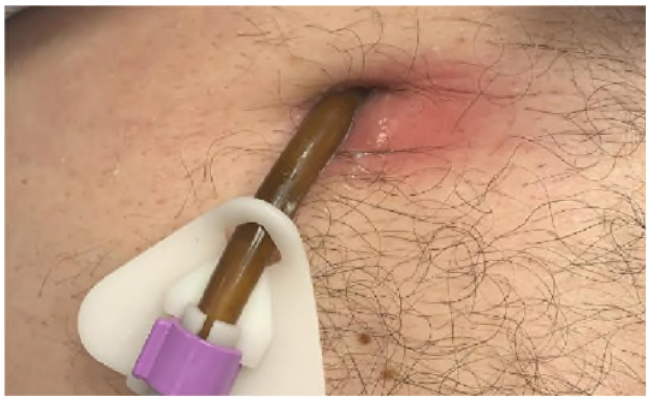
Figure 29.



Chemical Irritation

Recommended intervention: Due to leaking stoma, possibly intercurrent infection. Attempt to tighten bumper, meticulous hygiene, culture of discharge, possible antibiotics.

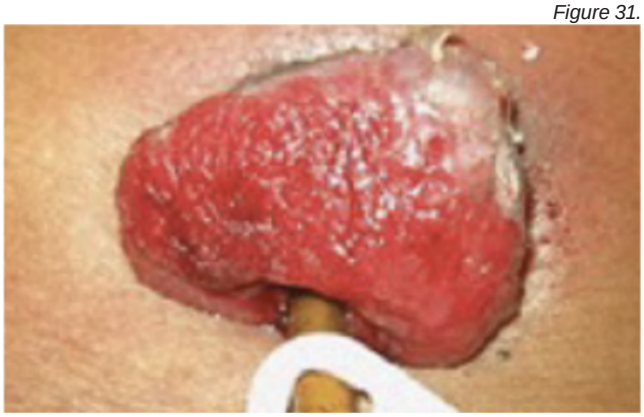
Figure 30.



Chemical Irritation (possible contact irritation from tube)

Recommended intervention: Alternate the tube positioning and use barrier cream.

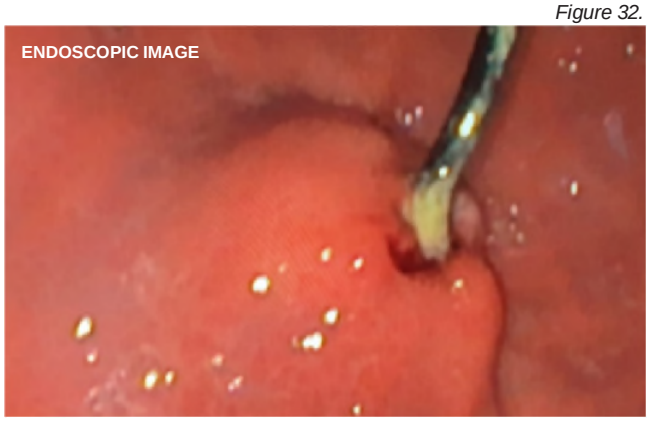
Figure 31.



Prolapse of Gastric Mucosa

Recommended intervention: Usually non-urgent surgical intervention.

Figure 32.



Buried Bumper Syndrome (BBS)

Recommended prevention: Upon healing of the stoma, move the tube 3-4 cm in and out daily. When securing the tube, allow 5-10 mm between the skin and the fixation plate. See Patient Guide for details (Long-Term Care Steps 4 and 5).

Recommendation intervention: Consultation with a specialist.

Frequently Asked Questions

PEG-J Placement

Q. To prevent the formation of loops, kinking, or knotting of the tube in the intestine after PEG-J placement, which actions are recommended?

A.
- Do not turn or rotate the AbbVie® PEG Tube under any circumstances to prevent the formation of loops and dislocation of the AbbVie® J tube.
- Do not rotate the AbbVie® J Tube or click adapter cap as kinking or knotting may occur.

Please refer to AbbVie® PEG and AbbVie® J IFUs for additional details.

Q. How does the gastroenterologist verify proper tube placement in the jejunum during the PEG-J placement procedure?

A. Endoscopic placement/replacement of the AbbVie® J should be with direct visualization of the tip of the tube as it is advanced. Blind advancement of the tube by pushing with the grasping forceps is to be absolutely avoided. Confirm via X-ray or other techniques (fluoroscopy) that distal tip is beyond the ligament of Treitz.

Please refer to the AbbVie® J IFU for additional details.

Q. What are the unique connectors or adapters of the PEG-J tube for a patient with advanced Parkinson's disease undergoing a gastrostomy for Duodopa® therapy?

A. The Duodopa® administration system utilizes reverse Luer connectors. These are Luer connectors that are reversed in orientation compared to an IV set. The AbbVie® PEG-J tubing and the Duodopa® cassettes both utilize this configuration.

Please refer to the AbbVie® J IFU for additional details.

Stoma Care

Q. Following PEG-J placement, patients can experience leaking of liquid, blood, or colored fluid from the stoma site. What steps should be taken to minimize the leaks from the stoma site?

A. Leaks are usually a complication of suboptimal healing of the stoma tract due to infection or ischemia. Promptly treat infection if present.

If the leak is from the space between the tube and the stoma within the first 72 hours after PEG-J placement, verify that the tube tension is appropriate given the length of time in place.

- The AbbVie® PEG Tube should remain under moderate tension for 24-72 hours to promote good adherence of the stomach wall to the inner abdominal wall.
- Avoid in/out movement of the AbbVie® PEG Tube within 72 hours post placement.

If the leak is from the space between the tube and the stoma after the first 72 hours after PEG-J placement:

- The tube clip should be opened and the fixation plate loosened. For long term maintenance, leave 5-10 mm free play between the outer stomach wall and the fixation plate.

Leaks may also occur if the connectors are loose or damaged. Follow up with an AbbVie® Duodopa® Specialist or a gastroenterologist as needed, to check the tightness and correct accordingly.

Q. Buried bumper syndrome is a potential and serious long-term complication after PEG-J placement in Duodopa® patients. Which actions should be taken to minimize this syndrome?

A. Proper tensioning of the external fixation plate and regular movement of the tube are critical to prevent buried bumper syndrome.

- The PEG tube should remain under moderate tension for 24-72 hours after the procedure. After 72 hours, the fixation plate should be loosened to leave 5-10 mm of free play between the outer stomach wall and fixation plate.
- Following gastroenterologist guidance or once the stoma has healed, move the tube once each day. Carefully push the tube 3-4 cm into the stomach and gently pull back until you feel resistance of the internal retention plate. Do not twist the tube.

Please refer to AbbVie® PEG and AbbVie® J IFUs for additional details or consult with your gastroenterology team for any stoma, tube evaluation, or complications.

Q. What are the recommendations for proper stoma care to prevent stoma complications after gastrostomy?

A.
1. Wound dressing should be performed under good aseptic conditions once a day, for the first 7-10 days.
2. Disinfect hands and put on disposable gloves.
3. Remove the dressing, open the fixation plate tube clip and release the tube from the plate.
4. Clean (aseptic technique) and disinfect the wound.
5. Always keep the stoma clean and as dry as possible.
6. Never apply an ointment on a PEG stoma or an inflamed PEG wound.
7. Starting 72 hours after the procedure, the fixation plate should be loosened to leave 5-10 mm of free play between the outer stomach wall and fixation plate to prevent inflammation and subsequent BBS.

Post-Procedure Care

Q. What are the recommended standards to flush AbbVie® PEG-J Tube?

A.
- Flush the AbbVie® PEG Tube (via white, blue, or violet "g" port) with at least 20 ml room temperature tap or drinking water daily and after it has been used for feeding. Failure to adequately flush the AbbVie® PEG Tube may result in occlusion or blockage.
- Flush the AbbVie® J Tube (via green "i" port) with at least 20 ml room temperature tap or drinking water daily after administration of Duodopa®. Failure to adequately flush the AbbVie® J may result in occlusion or blockage.
- Do not flush the lumen of the AbbVie® J Tube using force or unblock using a wire. There is the risk of AbbVie® J Tube disconnection or tube perforation. Check for patency of the tube. If the tube becomes occluded, replace with new tube.

Q. What are the recommended practices to minimize the risk of bezoars in patients with advanced Parkinson's disease using Duodopa®?

A. HCPs should advise their patients to avoid high fiber foods (such as celery, asparagus, sunflower seeds) while on the Duodopa® system.

Q. Sometimes the patient's Y-connector from the PEG-J is dislocated after the procedure. Which steps should be taken to properly restore the Y-connector?

A. To properly connect the PEG tube to the Y-Connector, follow the instructions in the IFU. Specifically note the following steps:

1. Ensure that the PEG tube is cut perpendicular (90-degree angle) to the tube and not on a diagonal.
2. Push the PEG tube fully onto the Y-Connector prior to fastening the fixation screw. Visually verify the tubing has been pushed all the way onto the pin of the Y-Connector.
3. Tighten the fixation screw onto the Y-Connector. Confirm there is no space between the fixation screw and the Y-Connector.

Please refer to the AbbVie® J IFU for additional details.

References

1. Bischoff, S. C, Austin, P, Boeykens, K, Chourdakis, M, Cuerda, C, Jonkers-Schuitema, C, et al.. ESPEN guideline on home enteral nutrition. Clinical Nutrition 2020;39: 5-22.
2. Cyrany J, Rejchrt S, Kopacova M, Bures J. Buried bumper syndrome: a complication of percutaneous endoscopic gastrostomy. World J Gastroenterol 2016;22:618-27.
3. Faris M.F., Blatnik J. (2016). Chronic Complications of PEG. In M.E. Pauli (Ed.). M.J Marks (Ed.). Percutaneous Endoscopic Gastrostomy (PEG): Techniques, Effectiveness and Potential Complications (pp 245-259). New York: Nova Science Publishers.

Further Information

- As a healthcare professional, it is important that you report any suspected adverse reactions. See Summary of the product characteristics (SPC) approved by SFDA for how to report adverse reactions.
- Please contact AbbVie medical information at medinfo_saudi@abbvie.com if you have any questions.
- Please contact AbbVie Pharmacovigilance at PV.MEA@abbvie.com if require additional copies of the Patient Guide.
- For more details on prescribing Duodopa®, please refer to the Summary of the product characteristics (SPC) approved by SFDA.

- Report side effects directly to AbbVie Biopharmaceuticals GmbH via Email: PV.MEA@abbvie.com , Hotline: 00966 55 828 2010 and National Pharmacovigilance Center Saudi Food and Drug Authority via SFDA Unified Call Center: 19999, E-mail: npc.drug@sfda.gov.sa , Website: https://ade.sfda.gov.sa/

This material was developed by AbbVie® as part of Duodopa® Risk Management Plan.

This document is approved by The Executive Directorate of Pharmacovigilance, at SFDA.