PACLITAXEL-ELUTING CORONARY STENT PREMOUNTED ON TWO RAPID EXCHANGE DELIVERY SYSTEMS FOR BIFURCATION LESIONS TREATMENT

STERILE, SINGLE USE ONLY. Sterilized with ethylene oxide gas. Non pyrogenic. Do not resterilize. Do not use opened or damaged packages. Destroy product after use. Store in a dry place between 0°- 40° C, keep away from light. Read instructions prior to use.

1 Description

The **Nile *PAX*®** intracoronary stent system is composed of two parallel rapid exchange catheters with a premounted L605 alloy (cobalt chromium) Paclitaxel coated stent crimped on the balloon of the Main Branch Catheter (MBC) and the tip of the Side Branch Catheter (SBC). Both Main Branch Catheter (MBC) and Side Branch Catheter (SBC) shafts are joined together through an auto-release sheath, which peels off progressively when passing through the valve of the "Y" access system.

The **Nile *PAX*®** is a stent fitted with the PAX technology: an abluminal polymer-free Paclitaxel coating intended to release within a 45 days period. Paclitaxel is an antiproliferative agent that reduces neointimal hyperplasia associated with smooth muscle cell proliferation and cellular migration.

The amount of Paclitaxel loaded onto the **Nile *PAX*®** is specified in the table hereafter:

Stent Length [mm]	Main branch balloon diameter [mm]	Side branch balloon diameter [mm]	Paclitaxel loading [µg/stent]
18	2.50	2.00	54
	2.50	2.50	
	3.00	2.00	68
	3.00	2.50	
	3.00	3.00	
	3.50	2.50	
	3.50	3.00	
24	2.50	2.00	69
	2.50	2.50	
	3.00	2.00	88
	3.00	2.50	
	3.00	3.00	
	3.50	2.50	
	3.50	3.00	

The three radiopaque markers on the Main Branch Catheter (MBC) and two radiopaque markers on the Side Branch Catheter (SBC), aid in the accurate placement of the stent in the vessel.
Once both Main Branch Catheter (MBC) and Side Branch Catheter (SBC) have reached the bifurcation site and after stent deployment, both catheters can be manipulated separately and independently.

The distal shafts of both Main Branch Catheter (MBC) and Side Branch Catheter (SBC) comprise two lumens, one is used for inflation of the balloon and the other permits the use of a guide wire (0.014" max.) to enable advancement of the catheter to and through the stenosis to be stented.

The balloons provide an expandable segment of known diameter at specific pressure. The proximal cone of the SBC balloon is lengthened in order to prevent an over-dilatation of the artery proximal to the carina in case of simultaneous MBC and SBC inflation (kissing) for post-dilatation. MBC and SBC shafts are made of a stainless steel hypotube. Proximal visual markers located approximately 90 cm and 100 cm from the distal tips aid catheter positioning without fluoroscopy assistance.

2 Indications

The **Nile *PAX*®** intracoronary stent system is exclusively and specifically intended for use in the treatment of patients with clinical symptoms of myocardial ischemia related to the pathological condition of *de novo* coronary arteries lesions located on bifurcation sites, excluding left main trunk.
It is indicated for improving coronary artery luminal diameter, while simultaneously maintaining side branch access.

3 Warning

- PTCA procedures should only be performed in hospitals where emergency coronary artery bypass graft surgery can be immediately performed in the event of potentially injurious or life threatening complications.
- Only physicians trained in PTCA and stent implantations should use this device. The physician should consult current peer-reviewed publications on the interventional cardiology techniques.
- Ensure that the medical team is trained on the products and their reference system to avoid any error in choosing equipment.
- PTCA in patients who are not acceptable candidates for coronary artery bypass graft surgery requires careful consideration, including possible haemodynamic support during the procedure, as treatment of this patient population carries special risk.
- In order to minimise the risk of stent migration or healing, Magnetic Resonance Imaging (MRI) should not be performed until the stent has been completely endothelialised. The stent may cause artefacts in MRI scans due to distortion of the magnetic field.
- Appropriate anticoagulant and vasodilator therapy should be administrated before insertion of the catheter.
- The **Nile *PAX*®** should not be in contact with another drug eluting stent other than PAX technology devices. Potential interactions of the **Nile *PAX*®** stent with other drug-eluting stents have not been evaluated and should be avoided.
- If the **Nile *PAX*®** is in contact with another stent, this other stent should be of identical metal.

- Always predilate the lesion.
- Not approved for direct stenting procedures.
- Verify that the internal diameter of the guiding catheter is equal or higher than the value indicated on labelling.
- It is not recommended to use the **Nile *PAX*®** with the 0.014 PT Graphix™ (Boston Scientific Corporation).
- Clearly identify the two guide wires and the two rapid exchange catheters, respectively placed into the main branch (Main Branch Catheter MBC - blue strain relief) and into the side branch (Side Branch Catheter SBC - white strain relief) of the lesion.
- In case of any possible guide wires twisting, withdraw one of the two, by gently pulling either the Main Branch or Side Branch guide wire back into the system.
- Never continue to advance the **Nile *PAX*®** if a resistance is felt. One of the causes might be the twisting of the guide wires within or outside the guiding catheter.
- Never continue to advance the **Nile *PAX*®** intracoronary stent system when guide wires are twisted.
- Never advance the auto-release sheath through and into the “Y” access system.
- Never manually peel off the auto-release sheath.
- Never separate the two catheters before reaching the targeted lesion. The two catheters must remain perfectly parallel until the stent has been expanded.
- Do not dilate the stent prior to checking the correct positioning of the PTCA rapid exchange catheters Main Branch Catheter (MBC) and Side Branch Catheter (SBC), aligning the middle marker placed on the Main Branch Catheter (MBC) with the aperture of the Side branch vessel.

4 Precautions

- The **Nile *PAX*®** intracoronary stent system is designed and intended for single use. In case of re-use, device sterility shall be lost and performances altered. Do not resterilise or reuse it. Use prior to “use before” date noted on the packaging. Do not use opened or damaged packages.
- When the stent delivery system is exposed to the vasculature, and more specifically the bifurcation locations, it should be manipulated while under high-quality fluoroscopic observation. If resistance is met during manipulation, determine the cause of the resistance before proceeding. Applying excessive push or pull force to the stent delivery system can potentially result in loss or damage to the stent and delivery system components. In case of complete removal of the system, please refer to Chapter 10 of the instructions for use: removal of an unexpanded stent.
- Do not attempt to pull back an unexpanded stent through the guiding catheter as dislodgement of the stent may result. The entire system (guiding catheter and delivery system) should be removed and replaced.
- Inspect the delivery system entirely prior to use for any kinks, curves or potential catheters damage, which could alter the **Nile *PAX*®** intracoronary stent system performances.
- Do not “roll” the mounted stent with your fingers, as this action may loosen the stent from the delivery balloons.
- Do not wipe, rub or handle the **Nile *PAX*®** stent before insertion into the guiding catheter to avoid any damage to the Paclitaxel coating.
- **Nile *PAX*®** stent contact with any fluid is not recommended to avoid any premature drug release. If required, limited contact time with saline solution is possible.

- Do not expose the **Nile *PAX*®** to organic solvents.
- Do not attempt to reposition the stent on the delivery system. Care must be taken not to handle or in any way disrupt the delicate placement of the stent. This is most important during **Nile *PAX*®** intracoronary stent system removal from the dispenser, placement over guide wires and advancement through the "Y" access system and guiding catheter hub.
- Expansion of the stent should not be undertaken if the stent is approximately positioned in the vessel – i.e. the middle marker placed on the Main Branch Catheter (MBC) aligned with the aperture of the Side branch vessel. If the position of the stent is not optimal, it should not be expanded (See Chapter 10 of the instructions for use: removal of an unexpanded stent).
- Do not attempt to reposition a fully or partially inflated balloon. Attempting repositioning may result in severe vessel damage.
- Do not use, or try to straighten bent or kinked catheters; not following these instructions could result in the shaft rupture. In case of defective product, use another **Nile *PAX*®** intracoronary stent system.
- Balloon pressure should be monitored via an indeflator during inflation. Balloon inflation pressure should not exceed the Rated Burst Pressure (RBP; see labelling). To reduce the potential for damage, the inflated diameter of the balloons should approximate the diameter of the main and side vessel proximal and distal to the stenosis.
- Use only diluted contrast medium to inflate the balloons. Do not use air or any gaseous medium.
- Do not preinflate the balloons prior to stent deployment. Use the balloons purging technique described in the Instructions for use chapter 8.
- Subsequent restenosis may require repeated dilatation of the arterial segment containing the stent. The long-term outcome following repeated dilatation of endothelialized **Nile *PAX*®** intracoronary stents is unknown at present.
- Great care must be exercised when crossing a newly deployed stent with a coronary guide wire or balloon catheter to avoid disrupting the stent geometry.

4.1 Guiding catheter and Guide wire selection

- Only guiding catheters and guide wires indicated for use in coronary angioplasty should be used. See labelling for guiding catheter compatibility (minimum internal diameter).
- Guide wire diameter recommended with the **Nile *PAX*®** intracoronary stent system is 0.014''. It is not recommended to use the **Nile *PAX*®** with the 0.014 PT Graphix™ (Boston Scientific Corporation).

4.2 Stent selection

Careful stent sizing is important for successful stenting. In general, the stent size should match the diameter of the reference vessel, and the length of the lesion to be stented. The diameter of the expanded delivery system must not be superior to the segment diameter, proximal and distal to the lesions.

5 Contra-indications

Related to the patient:

- Patients who are judged not to be candidates for coronary artery bypass surgery,
- Patients with totally obstructed coronary arteries,
- Arterial spasm,
- Patients with allergies to procedural medications, to anticoagulation and/or antiplatelet therapy, to L605 cobalt chromium alloy, to contrast media, to Paclitaxel or any drugs in similar class,
- Patients with an ejection fraction < 30 %,

- Patients having experienced recent acute myocardial infarction (<72 hours),
- Patients having experienced cardiogenic shock,
- Patients with bleeding diathesis or other disorder eg. Peptic ulceration or recent cerebrovascular accident, limiting the use of antiplatelet and/or anticoagulation therapy,
- Pregnant women or women of child bearing potential,

Conditions related to the lesion:

- Lesion not located on coronary bifurcation sites,
- Lesion of the left main trunk bifurcation,
- Side branch artery takeoff angle > 90°
- Severe stenosis of the unprotected left main coronary artery,
- Reference vessel diameter of the main branch of the bifurcation lesion out of the available **Nile PAX®** products range (MBC diameter),
- Reference vessel diameter of the side branch of the bifurcation lesion out of the available **Nile PAX®** products range (SBC diameter),
- Heavily calcified lesion or diffuse lesion longer than the longest **Nile PAX®** reference available,
- Presence of definite or probable intra-luminal thrombus in the target vessel,
- Stenosis which can not be predilated with an angioplasty balloon to a mean luminal diameter of 2.50 mm on the main branch of the bifurcation lesion site,
- Vessels where an untreated lesion of > 50% diameter would remain after the planned intervention,
- Target lesions distal to a 50% or greater stenosis, which cannot be pre-dilated or target lesions proximal to untreatable areas of significant flow compromising disease.

6 Adverse events

6.1 Short and medium term

- Nausea and vomiting
- Arterial fistula
- Dissection or perforation of the coronary artery
- Injury or rupture of the coronary artery
- Total occlusion
- Thrombosis
- Arterial spasm
- Ventricular fibrillation
- Disturbance of cardiac conductibility
- Bradycardia
- Embolism
- Side branch occlusion
- Entry site complications

➔ These complications can directly result in the patient's death.

6.2 Long term

- Emergency or non emergent Coronary Artery Bypass Graft Surgery
- Restenosis of the dilated artery
- Unstable angina
- Ischemia

- Acute myocardial infarction
- Disturbance of cardiac conductibility
- Bleeding complications

➔ These complications can directly result in the patient's death.

7 Individualization of treatment

The risks and benefits described in this notice should be considered for each patient before use of the **Nile *PAX*®** intracoronary stent system. Patient selection factors to be assessed should include a judgement regarding risk of anti-platelet therapy. Special consideration should be given to those patients with recently active gastritis or peptic ulcer disease.
Physicians should use their best judgement in determining the need and duration of antiplatelet therapy when using the **Nile *PAX*®**. Please refer to ACC/AHA most recent Guidelines for Percutaneous Coronary Intervention.
Premorbid conditions that increase the risk of poor initial results or the risks of emergency referral for bypass surgery (diabetes mellitus, renal failure and severe obesity) should be reviewed.
Thrombosis following stent implantation is affected by several baseline angiographic and procedural factors. These include vessel diameter less than 3.00 mm, intra-procedural thrombus, or poor distal runoff and/or dissection following stent implantation. In patients who have undergone coronary stenting, the persistence of a thrombus or dissection should be considered a maker for subsequent thrombotic occlusion. These patients should be monitored very carefully during the first month after stent implantation.

8 Instructions for use

The following instructions for use provide guidance but do not obviate the necessity for appropriate training.

The stenting procedure should be done according to standard PTCA guidelines.

8.1 Delivery system preparation

Check before use that the packaging has not been damaged in a way that might have rendered the product unsterile.
Prepare the inflation devices according to the manufacturer's instructions. Prepare diluted contrast medium and sterile saline solution. Fill a 10 or 20 cc syringe with sterile saline solution.
Remove the **Nile *PAX*®** intracoronary stent system from its dispenser; remove carefully the distal protective sleeve from the system, the stylet placed in each of the two balloons.
Prepare the device according to standard techniques. Flush the guide wires lumen according to routine procedure. Inspect the stent to ensure that it has not been damaged.
Purge the Main Branch Catheter (MBC) and Side Branch Catheter (SBC) balloons according to standard recommended techniques.
Connect the inflation systems with the utmost care to avoid air bubbles entering the system.

Note: Do not apply positive or negative pressure after purging and before final positioning of the **Nile *PAX*®** intracoronary stent system.

8.2 Implantation procedure

The **Nile *PAX*®** intracoronary stent system is designed for use as a unit. Prepare the **Nile *PAX*®** intracoronary stent system according to standard techniques, placing an appropriately sized introducer sheath, guiding catheter and guide wires to be employed during use with the **Nile *PAX*®** intracoronary stent system. A guiding catheter with a minimum lumen diameter as per indicated on labelling and 0.014" guide wires to be positioned in the main and side branch should be used.

Insert the main vessel guide wire and the side branch guide wire (0.014'' max) into the guiding catheter and advance them through to the target bifurcation lesion site. To avoid movement of the guide wires, tighten the "Y" access system, so that the guide wires are firmly rounded in the "Y" access system.

8.2.1 Predilatation

Always predilate the main and the side branches using PTCA catheters approved for coronary dilatation selecting a length and diameter corresponding to the lesion to be treated. For predilatation, please follow the manufacturer's instructions for use for preparation and utilisation of the predilatation catheter. Withdraw the catheters after predilatation.

Never consider a non predilatation (Direct Stenting) technique.

8.2.2 Stent placement

The stent is not to be removed from its delivery balloons. The stent is not to be crimped onto another balloon. Removing the stent from its delivery system can cause damage to the stent, lead to stent embolisation or make positioning of the side aperture / branch unreliable.
Special care must be taken when handling the stent, so as not to disrupt the stent position on the delivery device. This will cause possible marker misalignment. This is most important during catheter removal from packaging, placement over guide wire, and advancement through the "Y" access system and guiding catheter hub.
Excessive manipulation, e.g. rolling the mounted stent, may cause dislodgement of the stent from the delivery balloons, or misalign the positioning markers.

Carefully place the stent and its delivery system between thumb and finger with the side branch tip in the upright position. Gently and securely back-load the 1st guide wire into the distal tip of the **Nile *PAX*®** Main Branch Catheter (MBC) - blue strain relief - ensuring that it exits through the notch located approximately 25 cm proximal to the dilatation catheter tip. Gently and securely back-load the 2nd guide wire into the distal tip of the **Nile *PAX*®** Side Branch Catheter (SBC) - white strain relief - ensuring that it exits through the notch located approximately 27 cm proximal to the dilatation catheter tip. Open the "Y" access system and advance the **Nile *PAX*®** intracoronary stent system to the distal end of the guiding catheter. Never advance the auto-release sheath into the valve of the "Y" access system. The auto-release sheath progressively peels off when passing the **Nile *PAX*®** intracoronary stent system through the valve of the access system.

Caution: Never remove the auto-release sheath manually.

Ensure that the two catheters (Main Branch Catheter and Side Branch Catheter) are always kept perfectly parallel until the stent has reached its correct positioning at the lesion site.

Note: Only the two markers located on the proximal part of the shaft of the Main Branch Catheter (MBC) may be used to estimate when the **Nile *PAX*®** intracoronary stent system has reached the distal end of the guiding catheter (depending on whether the approach is brachial or femoral).

Caution: Incorrect placement of the stent has the potential to compromise side branch patency.

If resistance is felt, use fluoroscopy to determine the cause of resistance before proceeding.
Do not advance the system if a resistance is felt. This resistance could be due to guide wire twisting within or outside the guiding catheter. Untwist the guide wires before further advancing the system by retracting either the guide wire of the Main Branch Catheter into the catheter or the guide wire of the Side Branch Catheter into the catheter or both consecutively.

Confirm stent position using main branch and side branch markers under standard angiographic techniques. For optimal results the entire stenosed arterial segment should be covered by the stent. Visually confirm that the marker indicating side branch aperture is correctly aligned with the ostium of the side branch vessel.

Caution: Expansion of the stent should not be undertaken if the stent is not properly positioned in the stenotic segment of the vessel. If the position of the stent is not optimal, it should be repositioned or removed. (See Chapter 10 of the instructions for use: removal of an unexpanded stent).

Inflate the Main Branch Catheter (MBC) balloon to a minimum pressure of 8 bar in order to deploy the stent. The inflation pressure should not exceed the Rated Burst Pressure (RBP; see labelling).
All efforts should be taken to ensure that the stent is not underdilated, and that apart from the ostium of the side branch, the stent is in full contact with the arterial wall upon deflation of the delivery balloon.

At this stage, the physician will have the possibility to treat the side branch. The Side Branch Catheter (SBC) will be positioned in the side branch.

If the stent expansion requires optimisation, readvance the **Nile PAX®** delivery balloons or another balloon catheter of the appropriate size to the stented area using standard angioplasty techniques.
Align the proximal marker of the Side Branch Catheter balloon with the middle marker of the Main Branch Catheter balloon.
Inflate the balloons to the desired pressure while observing under fluoroscopy. Deflate the balloons.
Note: Both Main Branch Catheter (MBC) and Side Branch Catheter (SBC) can be inflated simultaneously (kissing) if required or one after each other.
Reconfirm stent deployment and angiographic result. Repeat inflations until the desired result is achieved.
After deflation, slowly withdraw the balloon catheter(s), guide wires and guiding catheter.

Visual observation should be used to determine proper stent deployment. The final stent internal diameter should match the size of the reference vessel diameter.

8.2.3 System removal procedure
Ensure balloons are fully deflated.
Fully open the “Y” access system.
While maintaining guide wires position and negative pressure on inflation devices, withdraw the **Nile *PAX*®** intracoronary stent system.

Note: Should unusual resistance be felt at any time during the removal of the **Nile *PAX*®** intracoronary stent system, the entire system including guiding catheter and guide wires should be removed as a single unit, *see Chapter 10 of the instructions for use: removal of an unexpanded stent.*

Tighten the “Y” access system.
Repeat angiography to assess stented area. If necessary, post dilate within stent. Balloon inflations should incorporate balloon size closely matching vessel.
Final stent diameter should match reference vessel. Assure stent is not underdilated.

9 Compliance chart, Inflation pressure, Sterilisation and Storage conditions

Refer to labelling.

10 Removal of an unexpanded stent

Remove the **Nile *PAX*®** intracoronary stent system as a single unit.
Do not retract the **Nile *PAX*®** intracoronary stent system into the guiding catheter.
Position the proximal balloon markers (SBC) just distal to the tip of the guiding catheter.
Advance the guidewires into the coronary anatomy as far distally as safely possible.
Tighten the “Y” access system to secure the **Nile *PAX*®** intracoronary stent system to the guiding catheter; then remove the guiding catheter, the guide wires and the **Nile *PAX*®** system as a single unit.

Failure to follow these steps and/or applying excessive push or pull force to the **Nile *PAX*®** intracoronary stent system can potentially result in loss or damage to the stent and/or the **Nile *PAX*®** system components.
Stent retrieval methods (use of additional wires, snares and or forceps) may result in additional trauma to the coronary vasculature and/or the vascular access site. Complications may include bleeding, hematoma or pseudoaneurysm.

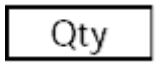
11 Liability

Minvasys has endeavoured to ensure that the products comply with all relevant standards and regulations currently in force and to ensure that the quality of the products meets the requirements of the above mentioned standards and regulations for a period ending upon the indicated expiry date. The above statement does not apply when the products are used for a purpose other than its intended purpose. Where any loss or damage is caused (other than death or personal injury) due to a defective product, Minvasys shall not be liable for such loss or damage.

12 Conversion Chart

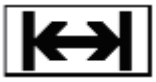
1cc	1 mL		
1 French	0.0131"	0.33 mm	
1 bar	1.02 atm	14.5 PSI	10^5 Pa

13 Symbols meaning



Quantity per box

Balloon diameter



Length

Nominal Pressure

Rated Burst Pressure

Minimum guiding catheter inner diameter

Maximum guidewire outer diameter

Do not use damaged packaging

Do not resterilize

Note: If reporting the **Nile *PAX*** ® intracoronary stent system lot number, please only refer to the lot number indicated on the pouch label or on the detachable labels placed on the box.
Never refer to the lot numbers indicated on the MBC or SBC hub.

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