IMPORTANT MEDICAL DEVICES SAFETY INFORMATION ON CYPHER™ CORONARY STENTS AND SUBACUTE THROMBOSIS

Cordis
a Johnson & Johnson company

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Dear Health Care Professional:

Subacute Thrombosis in Association with CYPHER™ Coronary Stents

In Canada, it is estimated that 900 CYPHER™ Sirolimus-eluting Coronary Stents have been implanted since November 2002, when the CYPHER™ Sirolimus-eluting Coronary Stent was granted a device licence for use in de novo coronary artery lesions with lengths that can be appropriately covered with a stent ≤ 18 mm and with a reference vessel diameter ≥ 2.5 mm and ≤ 3.5mm. **There have been no reports of subacute stent thrombosis**.

Since the introduction of the CYPHER™ Sirolimus-eluting Coronary Stent in the United States on April 24, 2003, it is estimated that well over 50,000 patients have received a CYPHER™ Stent. From the more than 50,000 patient procedures an adverse event report has been received for 47 stents (34 patients) due to stent thrombosis occurring at the time of implantation or within a few days of implantation. This is less than a 0.1% incidence rate. Some centers have reported multiple events.

Thrombosis is a rare complication of any coronary stenting procedure. In completed and ongoing clinical trials of the CYPHER™ Stent worldwide, the rate of stent thrombosis appears to have been similar to that of a bare metal stent. We are carefully reviewing the adverse event reports received from U.S. centers to try to determine if the thrombosis rate in current clinical experience differs from the rate in clinical studies completed pre-approval.

Based on the reports so far, factors impacting the rate of thrombosis may include failure to achieve adequate stent apposition (due to under-deployment) or suboptimal use of antiplatelet medication. In addition, Cordis Corporation has become aware that some interventionalists have been over-expanding smaller stents for use in larger diameter vessels. Overexpansion of stents beyond their intended diameter may negatively affect performance and is not advisable. Due to the extremely high demand for the CYPHER™ Stent, Cordis Corporation concentrated its manufacturing efforts on the 2.5 mm and 3.0 mm diameter CYPHER™ Stents to serve the patient populations with the greatest perceived potential benefit. We have recently started to introduce the 3.5 mm CYPHER™ Stents.

What You Should Do

1. Follow the Instructions for Use

To help ensure that your experience is similar to that observed in pre-approval clinical trials, we strongly advise you to use the product in accordance with the *Indications for Use* (IFU) and procedures contained in the package insert. Please take particular note of the following:

- *Select the appropriate stent size*

  We recommend that the stent size match the reference vessel diameter as closely as possible. The 2.5 mm and 3.0 mm diameter CYPHER™ Stents are based on a 6-cell design; the 3.5 mm diameter CYPHER™ Stent is based on a 7-cell design. Use of a CYPHER™ Stent in a vessel larger than the indicated stent diameter could adversely affect the stent's performance. Do not use the smaller stents for vessels larger than indicated in the IFU.

- *Select appropriate patients*

  The CYPHER™ stent is indicated for improving coronary luminal diameter in patients with symptomatic ischemic disease due to discrete *de novo* lesions of lengths $\leq$ 18 mm in native coronary arteries with reference vessel diameters of $\geq$ 2.5 mm to $\leq$ 3.5 mm. The CYPHER™ stent is NOT indicated for treatment of the following:

  - Restenosis
  - Acute myocardial infarction
  - Saphenous vein graft lesions
  - Bifurcation lesions

  The safety and effectiveness of the CYPHER™ stent have not been established for these situations. Off- label use is contraindicated as it may be associated with an increase in the rate of thrombosis.

- *Use an adequate antiplatelet regimen*

  In certain *in vitro* laboratory settings, sirolimus has been shown to potentiate the effect of some platelet agonists. While the clinical significance of the effect is unknown, it is advisable to be sure the patient is receiving a fully effective antiplatelet regimen, including an adequate pre-medication period or optimal loading dose. Administration of continued antiplatelet therapy for two (2) months post-stenting is considered critical.

- *Use the proper technique for stent deployment*

  - Be sure that the stent is fully deployed and in contact with the vessel wall. Poor stent apposition due to under-deployment is a factor that can increase the thrombosis risk for any coronary stent.
  - Predilate the lesion with a PTCA catheter. The CYPHER™ stent is not approved for direct stenting. The longitudinal length of pre-dilatation by the PTCA balloon should be limited to avoid creating a region of vessel injury that is outside the boundaries of the CYPHER™ stent upon deployment.

2. Report Your Experience

In most product development programs, rare side effects are difficult to detect, and their risks for special populations are difficult to assess. Therefore, as a matter of course, it is important for you to report any product complaints and adverse events directly to Cordis Canada, a Business unit of Johnson & Johnson Medical Products, division of Johnson & Johnson Inc by:

- **Telephone to Customer Service** 1 800 268 5577
- **Mail to the attention** of Product Quality Services, Johnson & Johnson Medical Products, 200 Whitehall Dr., Markham ON, L3R 0T5

Please feel free to contact Cordis Canada for any questions you may have on the subject matter of this letter. We, in cooperation with Health Canada, will continue to keep you updated with the latest information.

Sincerely,
original signed by

Dennis Donohoe, M.D.
Vice President, Therapeutics and Clinical Research
Cordis Corporation

Any suspected adverse incident can also be reported to:
Health Products & Food Branch Inspectorate
HEALTH CANADA
Address Locator: 3002C
OTTAWA, Ontario, K1A 0K9
Tel: The Medical Devices Hotline 1-800-267-9675