Resolute Integrity™ Zotarolimus-Eluting Coronary Stent System
Over the Wire Delivery System

INSTRUCTIONS FOR USE

CAUTION – Federal (USA) law restricts this device for sale by or on the order of a physician.
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THE COMPONENTS OF THE RESOLUTE INTEGRITY ZOTAROLIMUS-ELUTING CORONARY STENT SYSTEM ARE STERILE.

1 RESOLUTE INTEGRITY™ ZOTAROLIMUS ELUTING CORONARY STENT SYSTEM

The Medtronic Resolute Integrity™ Zotarolimus-Eluting Coronary Stent System (Resolute Integrity System) is a device/drug combination product comprised of the following device components: the Integrity Coronary Stent and MicroTrac delivery systems and a drug component (a formulation of zotarolimus in a polymer coating). The characteristics of the Resolute Integrity System are described in Table 1-1.

Table 1-1: Device Component Description and Nominal Dimensions

<table>
<thead>
<tr>
<th>Component</th>
<th>Resolute Integrity Zotarolimus-Eluting Coronary Stent System</th>
<th>Small Vessel</th>
<th>Medium/Large Vessel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Available Stent Diameters (mm):</td>
<td></td>
<td>2.25, 2.5, 2.75</td>
<td>3.0, 3.5, 4.0</td>
</tr>
<tr>
<td>Available Stent Lengths Unexpanded (mm):</td>
<td>8, 12, 14, 18, 22, 26, 30</td>
<td></td>
<td>9, 12, 15, 18, 22, 26, 30, 34, 38</td>
</tr>
<tr>
<td>Stent Material &amp; Geometry:</td>
<td>A cobalt-based alloy conforming to ASTM F562 and ISO 5832-6:1997; With 1.0 mm length elements, 7.5 alternating crowns and 0.0035” strut thickness; the stent utilizes a single helix fusion pattern. The coronary stent is formed from a single wire bent into a continuous sinusoid pattern and then laser fused back onto itself. The stents are provided in multiple lengths and diameters.</td>
<td>A cobalt-based alloy conforming to ASTM F562 and ISO 5832-6:1997; With 0.9 mm length elements, 9.5 alternating crowns and 0.0035” strut thickness; utilizes a helical u-joint fusion pattern. The coronary stent is formed from a single wire bent into a continuous sinusoid pattern and then laser fused back onto itself. The stents are provided in multiple lengths and diameters.</td>
<td></td>
</tr>
<tr>
<td>Drug Component:</td>
<td>A coating of polymers loaded with zotarolimus in a formulation applied to the entire surface of the stent at a dose of approximately 1.6 μg/mm² which results in a maximum nominal drug content of 380 μg on the largest stent (4.0 mm x 38 mm).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delivery System Working Length:</td>
<td>140 cm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delivery System Luer Adapter Ports:</td>
<td>Two-arm luer (side arm for access to balloon inflation/deflation lumen. Straight arm is continuous with shaft inner lumen). Designed for guidewire less than or equal to 0.36 mm (0.014 inch).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stent Delivery Balloon:</td>
<td>Single-layer Pebax balloon, wrapped over an inner member tubing with 2 radiopaque marker bands to locate the stent edges.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Balloon Inflation Pressure:</td>
<td>Nominal Pressure: 9 ATM (912 kPa)</td>
<td>Rated Burst Pressure: 16 ATM (1621 kPa) for 2.25 - 3.5 mm diameters 15 ATM (1520 kPa) for 4.0 mm diameter</td>
<td></td>
</tr>
<tr>
<td>Minimum Guide Catheter Inner Diameter:</td>
<td>≥ 5 F (1.42 mm, 0.056 inch)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Catheter Shaft Outer Diameter:</td>
<td>Proximal OD: 3.4 F (1.1 mm, 0.044 inch)</td>
<td>Distal Section OD: 2.7 F (0.91 mm, 0.036 inch)</td>
<td></td>
</tr>
</tbody>
</table>
1.1 Device Component Description

The Medtronic Resolute Integrity Zotarolimus-Eluting Coronary Stent System (Resolute Integrity System) consists of a balloon-expandable intracoronary drug-eluting stent pre-mounted on the MicroTrac Over the Wire (OTW) stent delivery system. The Resolute Integrity Stent is manufactured from a cobalt alloy and is formed from a single wire bent into a continuous sinusoid pattern and then laser fused back onto itself. The stents are available in multiple lengths and diameters. The delivery system has two radiopaque markers to aid in the placement of the stent during fluoroscopy and is compatible with 0.014 inch (0.36 mm) guidewires. The MicroTrac OTW delivery system (Figure 1-1) has an effective length of 140 cm.

![Figure 1-1: MicroTrac OTW Delivery System (with Stent)](image)

The stent is crimped on various size delivery catheter balloons, which are sized from 2.25 to 4.0 mm. The Resolute Integrity available stent sizes are listed in Table 1-2.

<table>
<thead>
<tr>
<th>Diameter (mm)</th>
<th>8</th>
<th>9</th>
<th>12</th>
<th>14</th>
<th>15</th>
<th>18</th>
<th>22</th>
<th>26</th>
<th>30</th>
<th>34</th>
<th>38</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.25</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>2.5</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>2.75</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>3.0</td>
<td>---</td>
<td>✓</td>
<td>✓</td>
<td>---</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>3.5</td>
<td>---</td>
<td>✓</td>
<td>✓</td>
<td>---</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>4.0</td>
<td>---</td>
<td>✓</td>
<td>✓</td>
<td>---</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

Note: "---" indicates sizes not offered; "✓" indicates sizes offered.
1.2 Drug Component Description

The drug coating of Resolute Integrity System consists of the drug zotarolimus (the active ingredient) and BioLinx polymer system (the inactive ingredient).

1.2.1 Zotarolimus

The active pharmaceutical ingredient utilized in the Resolute Integrity System is zotarolimus. It is a tetrazole-containing macrocyclic immunosuppressant.

The Chemical name of zotarolimus is:

\[
\]

The chemical structure of zotarolimus is shown in Figure 1-2:

![Zotarolimus Chemical Structure](image)

Zotarolimus has extremely low water solubility and is a lipophilic compound that is freely soluble in Propylene glycol, Acetone, Toluene, Acetonitrile, Ethanol, Benzyl alcohol and DMSO. The molecular formula of zotarolimus is C_{52}H_{79}N_{5}O_{12} and its molecular weight is 966.2.

Zotarolimus does not have any ionizable group(s) in the physiological pH range; therefore, its solubility is expected to be unaltered in this range.

1.2.2 Polymer System Description

The Resolute Integrity stent is comprised of a bare metal stent with a Parylene C primer coat and a coating that consists of a blend of the drug zotarolimus and the BioLinx polymer system. BioLinx is a blend of the Medtronic proprietary components C10 and C19, and PVP (polyvinyl pyrrolidone). The structural formula of the BioLinx polymer subunits are shown in Figure 1-3:

![Chemical Structure of the BioLinx Polymer Subunits](image)
1.2.3 Product Matrix and Zotarolimus Content

Table 1-3: Resolute Integrity Zotarolimus-Eluting Coronary Stent System Product Matrix and Nominal Zotarolimus Doses

<table>
<thead>
<tr>
<th>Product Number OTW</th>
<th>Nominal Expanded Stent ID (mm)</th>
<th>Nominal Unexpanded Stent Length (mm)</th>
<th>Nominal Zotarolimus Content (μg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RSINT22508W</td>
<td>2.25</td>
<td>8</td>
<td>59</td>
</tr>
<tr>
<td>RSINT25008W</td>
<td>2.5</td>
<td>8</td>
<td>59</td>
</tr>
<tr>
<td>RSINT27508W</td>
<td>2.75</td>
<td>8</td>
<td>59</td>
</tr>
<tr>
<td>RSINT30009W</td>
<td>3.0</td>
<td>9</td>
<td>90</td>
</tr>
<tr>
<td>RSINT35009W</td>
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<tr>
<td>RSINT40009W</td>
<td>4.0</td>
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<td>90</td>
</tr>
<tr>
<td>RSINT22512W</td>
<td>2.25</td>
<td>12</td>
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</tr>
<tr>
<td>RSINT25012W</td>
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<td>12</td>
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<tr>
<td>RSINT27512W</td>
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<td>12</td>
<td>85</td>
</tr>
<tr>
<td>RSINT30012W</td>
<td>3.0</td>
<td>12</td>
<td>120</td>
</tr>
<tr>
<td>RSINT35012W</td>
<td>3.5</td>
<td>12</td>
<td>120</td>
</tr>
<tr>
<td>RSINT40012W</td>
<td>4.0</td>
<td>12</td>
<td>120</td>
</tr>
<tr>
<td>RSINT22514W</td>
<td>2.25</td>
<td>14</td>
<td>102</td>
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<tr>
<td>RSINT25014W</td>
<td>2.5</td>
<td>14</td>
<td>102</td>
</tr>
<tr>
<td>RSINT27514W</td>
<td>2.75</td>
<td>14</td>
<td>102</td>
</tr>
<tr>
<td>RSINT30015W</td>
<td>3.0</td>
<td>15</td>
<td>150</td>
</tr>
<tr>
<td>RSINT35015W</td>
<td>3.5</td>
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<tr>
<td>RSINT40015W</td>
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<td>15</td>
<td>150</td>
</tr>
<tr>
<td>RSINT22518W</td>
<td>2.25</td>
<td>18</td>
<td>128</td>
</tr>
<tr>
<td>RSINT25018W</td>
<td>2.5</td>
<td>18</td>
<td>128</td>
</tr>
<tr>
<td>RSINT27518W</td>
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<td>18</td>
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<tr>
<td>RSINT30018W</td>
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<tr>
<td>RSINT35018W</td>
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<td>RSINT40018W</td>
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<td>180</td>
</tr>
<tr>
<td>RSINT22522W</td>
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<tr>
<td>RSINT25022W</td>
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<td>22</td>
<td>153</td>
</tr>
<tr>
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<td>22</td>
<td>153</td>
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<td>RSINT30022W</td>
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</tr>
<tr>
<td>RSINT35022W</td>
<td>3.5</td>
<td>22</td>
<td>220</td>
</tr>
<tr>
<td>RSINT40022W</td>
<td>4.0</td>
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</tr>
<tr>
<td>RSINT22526W</td>
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<td>188</td>
</tr>
<tr>
<td>RSINT25026W</td>
<td>2.5</td>
<td>26</td>
<td>188</td>
</tr>
<tr>
<td>RSINT27526W</td>
<td>2.75</td>
<td>26</td>
<td>188</td>
</tr>
<tr>
<td>RSINT30026W</td>
<td>3.0</td>
<td>26</td>
<td>260</td>
</tr>
<tr>
<td>RSINT35026W</td>
<td>3.5</td>
<td>26</td>
<td>260</td>
</tr>
<tr>
<td>RSINT40026W</td>
<td>4.0</td>
<td>26</td>
<td>260</td>
</tr>
<tr>
<td>RSINT22530W</td>
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<td>30</td>
<td>213</td>
</tr>
<tr>
<td>RSINT25030W</td>
<td>2.5</td>
<td>30</td>
<td>213</td>
</tr>
<tr>
<td>RSINT27530W</td>
<td>2.75</td>
<td>30</td>
<td>213</td>
</tr>
</tbody>
</table>
Table 1-3: Resolute Integrity Zotarolimus-Eluting Coronary Stent System Product Matrix and Nominal Zotarolimus Doses

<table>
<thead>
<tr>
<th>Product Number OTW</th>
<th>Nominal Expanded Stent ID (mm)</th>
<th>Nominal Unexpanded Stent Length (mm)</th>
<th>Nominal Zotarolimus Content (μg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RSINT30030W</td>
<td>3.0</td>
<td>30</td>
<td>300</td>
</tr>
<tr>
<td>RSINT35030W</td>
<td>3.5</td>
<td>30</td>
<td>300</td>
</tr>
<tr>
<td>RSINT40030W</td>
<td>4.0</td>
<td>30</td>
<td>300</td>
</tr>
<tr>
<td>RSINT30034W</td>
<td>3.0</td>
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<tr>
<td>RSINT35034W</td>
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<tr>
<td>RSINT40034W</td>
<td>4.0</td>
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<td>340</td>
</tr>
<tr>
<td>RSINT30038W</td>
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<td>38</td>
<td>380</td>
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<tr>
<td>RSINT35038W</td>
<td>3.5</td>
<td>38</td>
<td>380</td>
</tr>
<tr>
<td>RSINT40038W</td>
<td>4.0</td>
<td>38</td>
<td>380</td>
</tr>
</tbody>
</table>

2 INDICATIONS
The Resolute Integrity Zotarolimus-Eluting Coronary Stent System is indicated for improving coronary luminal diameters in patients, including those with diabetes mellitus, with symptomatic ischemic heart disease due to de novo lesions of length ≤ 35 mm in native coronary arteries with reference vessel diameters of 2.25 to 4.2 mm.

3 CONTRAINDICATIONS
The Resolute Integrity System is contraindicated for use in:
- Patients with known hypersensitivity or allergies to aspirin, heparin, bivalirudin, clopidogrel, prasugrel, ticagrelor, ticlopidine, drugs such as zotarolimus, tacrolimus, sirolimus, everolimus, or similar drugs or any other analogue or derivative.
- Patients with a known hypersensitivity to the cobalt-based alloy (cobalt, nickel, chromium, and molybdenum).
- Patients with a known hypersensitivity to the BioLinx polymer or its individual components (see details in Section 1.2.2 – Polymer System Description).

Coronary artery stenting is contraindicated for use in:
- Patients in whom anti-platelet and/or anticoagulation therapy is contraindicated.
- Patients who are judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or stent delivery system.

4 WARNINGS
- Please ensure that the inner package has not been opened or damaged as this would indicate the sterile barrier has been breached.
- The use of this product carries the same risks associated with coronary artery stent implantation procedures which include subacute and late vessel thrombosis, vascular complications, and/or bleeding events.
- This product should not be used in patients who are not likely to comply with the recommended antiplatelet therapy.

5 PRECAUTIONS
- Only physicians who have received adequate training should perform implantation of the stent.
- Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed.
- Subsequent stent restenosis or occlusion may require repeat catheter-based treatments (including balloon dilatation) of the arterial segment containing the stent. The long term outcome following repeat catheter-based treatments of previously implanted stents is not well characterized.
- The risks and benefits of stent implantation should be assessed for patients with a history of severe reaction to contrast agents.
• Do not expose or wipe the product with organic solvents such as alcohol.
• When Drug Eluting Stents (DES) are used outside the specified Indications for Use, patient outcomes may differ from the results observed in the RESOLUTE pivotal clinical trials.
• Compared to use within the specified Indications for Use, the use of DES in patients and lesions outside of the labeled indications, including more tortuous anatomy, may have an increased risk of adverse events, including stent thrombosis, stent embolization, MI, or death.
• Care should be taken to control the position of the guide catheter tip during stent delivery, deployment, and balloon withdrawal. Before withdrawing the stent delivery system, visually confirm complete balloon deflation by fluoroscopy to avoid guiding catheter movement into the vessel and subsequent arterial damage.
• Stent thrombosis is a low-frequency event that is frequently associated with myocardial infarction (MI) or death. Data from the RESOLUTE clinical trials have been prospectively evaluated and adjudicated using the definition developed by the Academic Research Consortium (ARC) (see Section 9.8 – Pooled Results of the Global RESOLUTE Clinical Trial Program (RESOLUTE FIM, RESOLUTE US, RESOLUTE AC, RESOLUTE Int, RESOLUTE Japan) for more information).

5.1 Pre- and Post-Procedure Antiplatelet Regimen

In the Medtronic RESOLUTE US Clinical Trial, RESOLUTE AC Clinical Trial, RESOLUTE International Study, RESOLUTE First-In-Man (FIM) Clinical Trial and RESOLUTE Japan Clinical Trial, the protocol specified administration of clopidogrel or ticlopidine prior to the procedure and for a period of at least 6 months post-procedure. Aspirin was administered prior to the procedure concomitantly with clopidogrel or ticlopidine and then continued indefinitely to reduce the risk of thrombosis. In the Medtronic RESOLUTE US Primary Enrollment Group, 95.9%, 93.8% and 46.6% of the patients remained on dual antiplatelet therapy at 6 months, 12 months and 60 months, respectively. In the RESOLUTE AC Clinical Trial, 93.1%, 84.2% and 11.0% of the patients remained on dual antiplatelet therapy at 6 months, 12 months and 60 months, respectively. In the RESOLUTE International Study, 95.9%, 91.1% and 34.6% of the patients remained on dual antiplatelet therapy at 6 months, 12 months and 36 months, respectively. In the RESOLUTE FIM Clinical Trial, 79.1%, 58.1% and 39.4% of the patients remained on dual antiplatelet therapy at 6 months, 12 months and 60 months, respectively. In the RESOLUTE Japan Clinical Trial, 99.0%, 94.9% and 62.5% of the patients remained on dual antiplatelet therapy at 6 months, 12 months and 60 months, respectively. In the RESOLUTE 38 mm Length Group, 92.8%, 91.3% and 63.7% of the patients remained on dual antiplatelet therapy at 6 months, 12 months and 48 months, respectively. See Section 9 - CLINICAL STUDIES, for more information.

5.1.1 Oral Antiplatelet Therapy

The optimal duration of dual antiplatelet therapy following DES implantation is unknown, and DES thrombosis may still occur despite continued therapy. Continuation of combination treatment with aspirin and a P2Y12 platelet inhibitor after percutaneous coronary intervention (PCI) appears to reduce major adverse cardiac events. On the basis of randomized clinical trial protocols, and expert consensus opinion, aspirin 81 mg daily should be given indefinitely after PCI. Likewise, a P2Y12 platelet inhibitor should be given daily for at least 12 months in patients who are not at high risk of bleeding.

It is very important that the patient is compliant with the post-procedural antiplatelet recommendations. Early discontinuation of prescribed antiplatelet medication could result in a higher risk of stent thrombosis, MI or death. Prior to PCI, if a surgical or dental procedure is anticipated that requires early discontinuation of antiplatelet therapy, the interventional cardiologist and patient should carefully consider whether a DES and its associated recommended antiplatelet therapy is the appropriate PCI choice. Following PCI, should a surgical or dental procedure be recommended, the risks and benefits of the procedure should be weighed against the possible risk associated with early discontinuation of antiplatelet therapy. Patients who require early discontinuation of antiplatelet therapy (e.g., secondary to active bleeding) should be monitored carefully for cardiac events. At the discretion of the patient’s treating physicians, the antiplatelet therapy should be restarted as soon as possible.

For full oral antiplatelet guidelines, please refer to the following website:
http://content.onlinejacc.org/cgi/content/full/j.jacc.2011.08.007v1

http://content.onlinejacc.org/cgi/content/full/j.jacc.2011.08.007v1
5.2 Use of Multiple Stents
The long-term effects of zotarolimus are currently unknown. The extent of the patient’s exposure to zotarolimus drug and the stent and polymer coating is directly related to the number of stents and total stent length implanted.

When multiple stents are required, stent materials should be of similar composition. Placing multiple stents of different materials in contact with each other may increase potential for corrosion. To avoid the possibility of dissimilar metal corrosion, do not implant stents of different materials in tandem where overlap or contact is possible.

Potential interactions of the Resolute Integrity stent with other drug-eluting or coated stents have not been evaluated and should be avoided whenever possible.

When using two wires, care should be taken when introducing, torquing and removing one or both guidewires to avoid entanglement. In this situation, it is recommended that one guidewire be completely withdrawn from the patient before removing any additional equipment.

5.3 Use in Conjunction with Other Procedures
The safety and effectiveness of using mechanical atherectomy devices (directional atherectomy catheters, rotational atherectomy catheters) or laser angioplasty catheters in conjunction with Resolute Integrity stent implantation have not been established.

5.4 Brachytherapy
The safety and effectiveness of the Resolute Integrity stent in target lesions treated patients with prior brachytherapy, or the use of brachytherapy to treat in-stent restenosis of a Resolute Integrity stent, have not been established.

5.5 Use in Special Populations
Information on use of the Resolute Integrity stent in certain special patient populations is derived from clinical studies of the Resolute stent system, which uses the same drug (zotarolimus) – see Section 7 OVERVIEW OF CLINICAL TRIALS for a description of the other features of the Resolute Stent System compared to the Resolute Integrity Stent System.

5.5.1 Pregnancy
Pregnancy Category C. See Section 6.6 Pregnancy under Drug Information. There are no well-controlled studies in pregnant women or men intending to father children. The Resolute Integrity stent should be used during pregnancy only if the potential benefit outweighs the potential risk to the embryo or fetus. Effective contraception should be initiated before implanting a Resolute Integrity stent and for 1 year after implantation.

5.5.2 Lactation
It is not known whether zotarolimus is excreted in human milk. The pharmacokinetic and safety profiles of zotarolimus in infants are not known. Because many drugs are excreted in human milk and because of the potential for adverse reactions in nursing infants from zotarolimus, a decision should be made whether to discontinue nursing or to implant a Resolute Integrity stent, taking into account the importance of the stent to the mother. See Section 6.7 – Lactation under Drug Information.

5.5.3 Gender
Clinical studies of the Resolute stent did not suggest any significant differences in safety and effectiveness for male and female patients. See Section 9.8.1 – Gender Analysis from the RESOLUTE Pooled On-label Dataset.

5.5.4 Ethnicity
Clinical studies of the Resolute stent did not include sufficient numbers of patients to assess for differences in safety and effectiveness due to ethnicity.

5.5.5 Pediatric Use
The safety and effectiveness of the Resolute Integrity stent in patients below the age of 18 years have not been established.
5.5.6 Geriatric Use

Clinical studies of the Resolute stent did not have an upper age limit. Among the 1242 patients treated with the Resolute stent in the Resolute US Main Study that included 2.25 - 3.5 mm stents, 617 patients were age 65 or older and 88 patients were age 80 or older. A post hoc analysis of patients treated with the Resolute stent showed no significant differences in rates of cardiac death, target vessel MI, target lesion revascularization, ARC definite or probable stent thrombosis, or target lesion failure at 12 months. The rate of all-cause death at 12 months was 0.3% in patients under age 65 vs. 1.8% in patients age 65 or older.

5.5.7 Lesion/Vessel Characteristics

The safety and effectiveness of the Resolute Integrity stent have not been established in the cerebral, carotid, or peripheral vasculature or in the following coronary disease patient populations:

- Patients with coronary artery reference vessel diameters < 2.25 mm or > 4.2 mm.
- Patients with coronary artery lesions longer than 35 mm or requiring more than one Resolute Integrity stent.
- Patients with evidence of an acute MI within 72 hours of intended stent implantation.
- Patients with vessel thrombus at the lesion site.
- Patients with lesions located in a saphenous vein graft, in the left main coronary artery, ostial lesions, or bifurcation lesions.
- Patients with diffuse disease or poor flow distal to identified lesions.
- Patients with tortuous vessels in the region of the target vessel or proximal to the lesion.
- Patients with in-stent restenosis.
- Patients with moderate or severe lesion calcification at the target lesion.
- Patients with occluded target lesions including chronic total occlusions.
- Patients with 3 vessel disease.
- Patients with a left ventricular ejection fraction of < 30%.
- Patients with a serum creatinine of > 2.5 mg/dl.
- Patients with longer than 24 months of follow-up.

5.6 Drug Interactions

The effect of potential drug interactions on the safety or effectiveness of the Resolute Integrity stent has not been investigated. While no specific clinical data are available, drugs, like sirolimus, that act through the same binding protein (FKBP12) may interfere with the efficacy of zotarolimus. Zotarolimus is metabolized by CYP3A4, a human cytochrome P450 enzyme. When administered concomitantly with 200 mg ketoconazole bid, a strong inhibitor of CYP3A4, zotarolimus produces less than a 2-fold increase in AUC0-inf with no effect on Cmax. Therefore, consideration should be given to the potential for drug interactions when deciding to place a Resolute Integrity stent in a patient who is taking drugs that are known substrates or inhibitors of the cytochrome P450 isoenzyme CYP3A4. Systemic exposure of zotarolimus should also be taken into consideration if the patient is treated concomitantly with systemic immunosuppressive therapy.

Formal drug interaction studies have not been conducted with the Resolute Integrity stent.

5.7 Magnetic Resonance Imaging (MRI)

Non-clinical testing has demonstrated the Resolute Integrity Stent up to a total length of 120 mm is MR Conditional. It can be scanned safely under the following conditions:

- Static magnetic field of 1.5 and 3 Tesla.
- Spatial gradient field of 1000 G/cm or less
- Maximum whole body averaged specific absorption rate (SAR) of 2.0 W/kg or less under normal operating mode only, for 15 minutes of scanning.
1.5 T
Based on non-clinical testing and modeling, a 38 mm Resolute Integrity Stent was calculated to produce an in-vivo temperature rise of less than 2.35°C, and overlapped stents with a maximum length of 120 mm were calculated to produce an in-vivo temperature rise of less than 3.87°C at a maximum whole body averaged specific absorption rate (SAR) of 2.0 W/kg for 15 minutes of MR scanning per sequence in a 64 MHz whole body transmit coil, which corresponds to a static field of 1.5 Tesla. These calculations do not take into consideration the cooling effects of perfusion and blood flow. The maximum whole body averaged specific absorption rate (SAR) was derived by calculation.

3 T
Based on non-clinical testing and modeling, a 38 mm Resolute Integrity Stent was calculated to produce an in-vivo temperature rise of less than 3.29°C and overlapped stents with a maximum length of 120 mm were calculated to produce an in-vivo temperature rise of less than 3.95°C at a maximum whole body averaged specific absorption rate (SAR) of 2.0 W/kg for 15 minutes of MR scanning per sequence in a 3 T GE SIGNA HDx with software version 14\LX\MR release 14.0.M5A.0828.b. These calculations do not take into consideration the cooling effects of perfusion and blood flow. The maximum whole body averaged specific absorption rate (SAR) was derived by calculation.

1.5 T and 3 T
The Resolute Integrity Stent should not move or migrate when exposed to MR scanning immediately post-implantation. MRI at 3 Tesla and 1.5 Tesla may be performed immediately following the implantation of the stent. Non-clinical testing at field strength greater than 3 Tesla has not been performed to evaluate stent migration and heating. MR image quality may be compromised if the area of interest is in the same area or relatively close to the position of the device. Therefore, it may be necessary to optimize MR imaging parameters for the presence of the stent. The image artifact extends approximately 1 cm from the device, both inside and outside the device lumen when scanned in non-clinical testing using the spin echo and gradient echo sequences specified in ASTM F2119-01; the device lumen was always observed during scanning. This testing was completed using a GE SIGNA HDx with software version 14\LX\MR release 14.0.M5A.0828.b.

5.8 Stent Handling Precautions
- For single use only. The Resolute Integrity System is provided sterile. Do not resterilize or reuse this product. Note the “Use By” date on the product label. Do not use if package or product has been opened or damaged.
- Only the contents of the pouch should be considered sterile. The outside surface of the pouch is not sterile.
- Do not remove the contents of the pouch until the device will be used immediately.
- Do not remove the stent from the delivery balloon; removal may damage the stent and polymer coating and/or lead to stent embolization. The Resolute Integrity System is intended to perform as a system. The stent is not designed to be crimped onto another delivery device.
- Special care must be taken not to handle or in any way disrupt the stent on the balloon. This is most important while removing the catheter from the packaging, placing it over the guidewire, and advancing it through the rotating hemostatic valve and guide catheter hub.
- Do not try to straighten a kinked shaft or hypotube. Straightening a kinked metal shaft may result in breakage of the shaft.
- Stent manipulation (e.g., rolling the mounted stent with your fingers) may cause coating damage, contamination or dislodgement of the stent from the delivery system balloon.
- The Resolute Integrity System must not be exposed to any direct handling or contact with liquids prior to preparation and delivery as the coating may be susceptible to damage or premature drug elution.
- Use only the appropriate balloon inflation media. Do not use air or any gaseous medium to inflate the balloon as this may cause uneven expansion and difficulty in deployment of the stent.
- The Resolute Integrity stent delivery system should not be used in conjunction with any other stents or for post-dilatation.