Revive Tablets

ری وائیو ٹیبلٹس

COMPOSITION: ***Each tablet contains:*** Clopidogrel (as Hydrogen Sulphate).....75 mg

DESCRIPTION: Clopidogrel is an inhibitor of ADP-induced platelet aggregation. Chemically it is methyl (+)-(*S*)-alpha-(2-chlorophenyl)-6,7-dihydrothieno[3,2-c]pyridine-5(4*H*)-acetate sulfate (1:1). The empirical formula of Clopidogrel Hydrogen Sulphate is C16H16ClNO2S•H2SO4 and its molecular weight is 419.9.

PHARMACOLOGY: ***Pharmacodynamics:*** Clopidogrel selectively inhibits the binding of adenosine diphosphate (ADP) to its platelet receptor and the subsequent ADP-mediated activation of the glycoprotein GPIIb/IIIa complex, thereby inhibiting platelet aggregation. ***Pharmacokinetics:*** Clopidogrel is rapidly absorbed after oral administration of repeated doses of 75 mg Clopidogrel (base), with peak plasma levels ($\cong$3 mg/L) of the main circulating metabolite occurring approximately 1 hour after dosing. Clopidogrel is extensively metabolized by the liver. The main circulating metabolite is the carboxylic acid derivative, and it has no effect on platelet aggregation. It represents about 85% of the circulating drug-related compounds in plasma. Clopidogrel and the main circulating metabolite bind reversibly *in vitro* to human plasma proteins (98% and 94%, respectively). Following an oral dose of ^{14}C-labeled Clopidogrel in humans, approximately 50% was excreted in the urine and approximately 46% in the feces in 5 days after dosing. The elimination half-life of the main circulating metabolite is 8 hours after single and repeated administration.

INDICATIONS: REVIVE (Clopidogrel) is indicated for the reduction of atherothrombotic events as follows:

1) **Recent MI, Recent Stroke, or Established Peripheral Arterial Disease:** For patients with a history of recent myocardial infarction (MI), recent stroke, or established peripheral arterial disease, REVIVE has been shown to reduce the rate of a combined endpoint of new ischemic stroke (fatal or not), new MI (fatal or not), and other vascular death.

2) **Acute Coronary Syndrome:**

   √ For patients with non-ST-segment elevation acute coronary syndrome (unstable angina/non-Q-wave MI) including patients who are to be managed medically and those who are to be managed with percutaneous coronary intervention (with or without stent) or CABG, REVIVE has been shown to decrease the rate of a combined endpoint of cardiovascular death, MI, or stroke as well as the rate of a combined endpoint of cardiovascular death, MI, stroke, or refractory ischemia.

   √ For patients with ST-segment elevation acute myocardial infarction, REVIVE has been shown to reduce the rate of death from any cause and the rate of a combined endpoint of death, re-infarction or stroke. This benefit is not known to pertain to patients who receive primary angioplasty.

CONTRAINDICATIONS: The use of Clopidogrel is contraindicated in the following conditions:

- Hypersensitivity to the drug substance or any component of the product.
- Active pathological bleeding such as peptic ulcer or intracranial hemorrhage.

POSSIBLE ADVERSE EFFECTS: The major side effects include gastrointestinal ulceration & hemorrhage and intracranial bleeding. Other side effects which may be encountered are dizziness, headache, hypertension, abdominal pain, diarrhea, dyspepsia, nausea, elevation of liver enzymes, prolonged bleeding time, neutropenia, pruritus and skin rash.

DRUG INTERACTIONS: ***Nonsteroidal Anti-Inflammatory Drugs (NSAIDs):*** In healthy volunteers receiving naproxen, concomitant administration of Clopidogrel was associated with increased occult gastrointestinal blood loss. NSAIDs and Clopidogrel should be co-administered with caution. ***Warfarin:*** Because of the increased risk of bleeding, the concomitant administration of warfarin with Clopidogrel should be undertaken with caution. Clopidogrel may interfere with the metabolism of phenytoin, tamoxifen, tolbutamide, warfarin, torsemide, fluvastatin, and many non-steroidal anti-inflammatory agents as Clopidogrel inhibits P450 (2C9) *in vitro* at high concentrations. Caution should be used when any of these drugs is coadministered with Clopidogrel.

WARNINGS: ***Thrombotic Thrombocytopenic Purpura (TTP):*** TTP has been reported rarely following use of Clopidogrel, sometimes after a short exposure (<2 weeks). TTP is a serious condition and requires prompt treatment. ***General:*** Clopidogrel prolongs the bleeding time and therefore should be used with caution in patients who may be at risk of increased bleeding from trauma, surgery, or other pathological conditions (particularly gastrointestinal and intraocular). If a patient is to undergo elective surgery and an antiplatelet effect is not desired, Clopidogrel should be discontinued 5 days prior to surgery. ***GI Bleeding:***

Clopidogrel should be used with caution in patients who have lesions with a propensity to bleed (such as ulcers). ***Use in Hepatically & Renally Impaired Patients:*** Clopidogrel should be used with caution in such patients. ***Pregnancy:*** There are no adequate and well-controlled studies in pregnant women. Therefore it should be used during pregnancy only if clearly needed. ***Lactation:*** Since many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the nursing woman. ***Pediatric Use:*** Safety and effectiveness in the pediatric population have not been established.

DOSAGE & ADMINISTRATION:

√ **Recent MI, Recent Stroke, or Established Peripheral Arterial Disease:**
The recommended daily dose of REVIVE Tablets is 75 mg once-daily.

√ **Acute Coronary Syndrome:**
For patients with acute coronary syndrome (unstable angina/non-Q-wave MI), REVIVE Tablets should be initiated with a single 300 mg loading dose (4 tablets of REVIVE) and then continued at 75 mg once-daily. Aspirin should be initiated and continued in combination with REVIVE Tablets.

For patients with ST-segment elevation acute myocardial infarction, the recommended dose of REVIVE Tablets is 75 mg once-daily, administered in combination with aspirin, with or without thrombolytics. REVIVE Tablets may be initiated with or without a loading dose.

REVIVE Tablets can be administered with or without food. No dosage adjustment is necessary for elderly patients or patients with renal disease.

SPECIAL INSTRUCTION TO THE PHYSICIAN: Overdosage following Clopidogrel administration may lead to prolonged bleeding time and subsequent bleeding complications. Based on biological plausibility, platelet transfusion may be appropriate to reverse the pharmacological effects of Clopidogrel if quick reversal is required.

STORAGE/PRECAUTIONS: Store in a cool, dry and dark place below 25 °C. Keep all medicines out of the children's reach.

PRESENTATION: REVIVE Tablets are available in packing containing 10 & 28 tablets, respectively.

عمومی خوراک: حالیہ مایئوکارڈیل انفارکشن، حالیہ فالج یا **Established Peripheral Arterial Disease**: ری وائیوٹیبلٹس کی تجویز کردہ خوراک 75 ملی گرام روزانہ ہے۔ شدید کرونری سنڈروم (**Unstable Angina/non-Q-wave MI**): 300 ملی گرام (4 ری وائیوٹیبلٹس) یکمشت ایک مرتبہ سے علاج شروع کرنا چاہئے اور پھر 75 ملی گرام روزانہ جاری رکھنا چاہئے۔ ری وائیوٹیبلٹس کے ہمراہ اسپرین کو شروع اور جاری رکھنا چاہئے۔ **ST-Segment Elevation Acute Myocardial Infarction**: اسپرین کے ہمراہ تجویز کردہ خوراک 75 ملی گرام روزانہ ہے جو کہ Thrombolytics کے ساتھ ملا کر یا اُن کے بغیر بھی دی جاسکتی ہے۔ ری وائیوٹیبلٹس زیادہ خوراک (Loading Dose) کے ساتھ یا اُس کے بغیر شروع کی جاسکتی ہیں۔ عمر رسیدہ مریض اور گردوں کی خرابی: ان مریضوں میں خوراک کو تبدیل کرنے کی ضرورت نہیں ہوتی۔ ری وائیوٹیبلٹس کو کھانے کے ہمراہ یا اُس کے بغیر استعمال کیا جاسکتا ہے۔

احتیاط: ☆ دوا صرف معتمد ڈاکٹر کے زیر ہدایت استعمال کریں۔ ☆ روشنی، نمی اور گرمی سے بچائیں۔
☆ 25 ڈگری سینٹی گریڈ سے کم درجہ حرارت پر محفوظ کریں۔ ☆ تمام ادویات بچوں کی پہنچ سے دور رکھیں۔

Complete Medical Information available only for doctors on request.

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5-D, I-10/3 Industrial Area, Islamabad-Pakistan.
www.scotmann.com