ANGIOX®
250 mg
(bivalirudin)[1]

DOSING AND ADMINISTRATION INSTRUCTIONS FOR PCI AND PRIMARY PCI

Angiox® bivalirudin

INDICATION: ANGIOX is indicated for use as an anticoagulant in adult patients undergoing percutaneous coronary intervention (PCI), including patients with ST segment elevation myocardial infarction (STEMI) undergoing primary PCI. ANGIOX should be administered with acetylsalicylic acid and clopidogrel.

IMPORTANT: ANGIOX must be administered as a bolus dose followed immediately by an intravenous infusion, even if a short PCI procedure is planned. Do not use without dilution.

DOSE RECOMMENDED	BOLUS: ALL PATIENTS		INFUSION: NORMAL RENAL FUNCTION AND MILD RENAL IMPAIRMENT		INFUSION: MODERATE RENAL IMPAIRMENT
	0.75 mg/kg	+	1.75 mg/kg/h For at least the duration of the PCI procedure	OR	1.4 mg/kg/h For at least the duration of the PCI procedure

Patient weight (kg)	Volume (ml) of diluted solution (5mg/ml bivalirudin)	Volume (ml) of diluted solution (5mg/ml bivalirudin)	Volume (ml) of diluted solution (5mg/ml bivalirudin)
38 - 42	6	14	11
43 - 47	7	16	12.5
48 - 52	7.5	17.5	14
53 - 57	8	19	15.5
58 - 62	9	21	17
63 - 67	10	23	18
68 - 72	10.5	24.5	19.5
73 - 77	11	26	21
78 - 82	12	28	22.5
83 - 87	13	30	24
88 - 92	13.5	31.5	25
93 - 97	14	33	26.5
98 - 102	15	35	28
103 - 107	16	37	29.5
108 - 112	16.5	38.5	31
113 - 117	17	40	32
118 - 122	18	42	33.5
123 - 127	19	44	35
128 - 132	19.5	45.5	36.5
133 - 137	20	47	38
138 - 142	21	49	39
143 - 147	22	51	40.5
148 - 152	22.5	52.5	42
153 - 157	23	54	43.5
158 - 162	24	56	45

Incompatibilities with ANGIOX:

IV line incompatibilities: alteplase, amiodarone HCl, amphotericin B, chlorpromazine HCl, diazepam, prochlorperazine edisylate, reteplase, streptokinase, vancomycin HCl.

Incompatible with ANGIOX at higher concentrations: dobutamine HCl, famotidine, haloperidol lactate, labetalol HCl, lorazepam, promethazine HCl : refer to SmPC[1] for more information.

Switching from heparin to ANGIOX:

0:30 MIN

FROM UNFRACTIONATED HEPARIN (UFH) TO ANGIOX
Discontinue UFH given intravenously for **30 MINUTES** before starting ANGIOX

8:00 H

FROM LOW MOLECULAR WEIGHT HEPARIN (LMWH) TO ANGIOX
Discontinue LMWH given subcutaneously for **8 HOURS** before starting ANGIOX

Dosing Instructions Following PCI:

The infusion of 1.75 mg/kg/h may be continued for up to 4 h post-PCI and at a reduced dose of 0.25 mg/kg/h for an additional 4–12 h as clinically necessary.

In **STEMI** patients the infusion of 1.75 mg/kg/h **should** be continued for up to 4 h post-PCI and continued at a reduced dose of 0.25 mg/kg/h for an additional 4–12 h as clinically necessary.

RENAL IMPAIRMENT

Angiox is contraindicated in patients with **severe** renal impairment (GFR <30ml/min) and also in dialysis dependent patients.

In **moderate** renal impairment (GFR 30-59 ml/min) there is no adjustment to the bolus dose. It remains at 0.75 mg/kg. The infusion rate **should** be reduced to 1.4 mg/kg/h.

Administration Instructions:

1. RECONSTITUTION

ADD 5 ml of water for injections to the vial.
SWIRL gently until all material is dissolved. After reconstitution, 1 ml contains 50 mg bivalirudin.

2. DILUTION

WITHDRAW the contents of the vial.
DILUTE in a total volume of 50 ml of 5% glucose in water or 0.9% (9 mg/mL) sodium chloride for injection. Solutions containing particulate matter should not be used. After dilution, 1 ml contains 5 mg bivalirudin.

3. ADMINISTRATION

REMOVE the bolus dose from the IV bag and administer the bolus dose via rapid IV push prior to procedure start, ensure IV lines are primed and then initiate and continue the infusion immediately after the bolus dose to ensure continuity of drug delivery to the patient.

The Medicines Company

[1] ANGIOX Summary of Product Characteristics 10/2016

To request medical or pharmacovigilance information call toll-free: +353 1800812065 or +353 (0)19075583
Or send an email to: medical.information@themedco.com

NAME OF THE MEDICINAL PRODUCT: ANGIOX 250 mg powder for concentrate for solution for injection or infusion. QUALITATIVE AND QUANTITATIVE COMPOSITION: Each vial contains 250 mg bivalirudin. After reconstitution 1 mL contains 50 mg bivalirudin. After dilution 1 mL contains 5 mg bivalirudin. For a full list of excipients, see the section "List of excipients". PHARMACEUTICAL FORM: Powder for concentrate for solution for injection or infusion. White to off-white lyophilized powder.

AX/IE/102016/04

Abbreviated Prescribing Information for ANGIOX® (bivalirudin) 250mg powder for concentrate for solution for injection or infusion

Please refer to the full Summary of Product Characteristics when prescribing Angiox®.

Legal classification: Medicinal product subject to restricted medical prescription **Presentation:** Each vial contains 250mg bivalirudin, mannitol and sodium hydroxide. **Indications:** An anticoagulant in adult patients undergoing percutaneous coronary intervention (PCI) including patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary PCI and patients with unstable angina/non-STEMI planned for urgent or early intervention. Angiox should be administered with acetylsalicylic acid and clopidogrel. **Dose and administration:** For intravenous (IV) use, should be administered by a physician experienced in either acute coronary care or in coronary intervention procedures. *Adults/Elderly:* Increased awareness due to high bleeding risk should be exercised in the elderly because of decrease in renal function. *PCI/ including patients with STEMI undergoing primary PCI:* Initial IV bolus of 0.75 mg/kg body weight followed immediately by IV infusion of 1.75 mg/kg body weight/hour for at least the duration of the procedure or continued for up to 4 hours post-procedure and at a reduced infusion dose of 0.25 mg/kg body weight/hour for an additional 4 – 12 hours as clinically necessary. In STEMI patients the infusion should be continued after the procedure for up to 4 hours at the PCI dose. If clinically necessary further continued for 4-12 hours at the reduced dose of 0.25 mg/kg body weight/hour. *Acute coronary syndromes (ACS):* Starting dose for medically managed patients is an IV bolus of 0.1 mg/kg followed by an IV infusion of 0.25 mg/kg/h. Medically managed patients may continue the infusion of 0.25 mg/kg/h for up to 72 hours. If proceeding to PCI, an additional bolus of 0.5 mg/kg should be administered before the procedure and the infusion increased to 1.75 mg/kg/h for PCI duration. Following PCI, the 0.25 mg/kg/h IV infusion may be resumed for 4 to 12 hours. For patients who proceed to CABG refer to the full prescribing information. **The safety and efficacy of a bolus dose of Angiox without the subsequent infusion has not been evaluated and is not recommended even if a short PCI procedure is planned.** Refer to full prescribing information for instructions regarding method of administration and ACT monitoring. **Use with other anticoagulant therapy:** Start Angiox 30 minutes after discontinuation of UFH, or 8 hours after LMWH given subcutaneously. When combining anticoagulants, clinical and biological parameters of haemostasis should be regularly monitored. *Hepatic impairment:* No dose adjustment needed. *Renal insufficiency:* Refer to the full prescribing information and see contraindications if GFR<30ml/min and dialysis-dependent patients. Monitoring of clinical signs of bleeding and dose adjustments are recommended in this group. *Children and adolescents:* No indication. **Contraindications:** In patients with: a known hypersensitivity to bivalirudin, the excipients, or to hirudins; active/increased risk of bleeding; severe uncontrolled hypertension; subacute bacterial endocarditis; severe renal impairment (GFR<30ml/min) and dialysis-dependent patients. **Special Warnings and Precautions for Use:** *Haemorrhage:* Observe patients for bleeding, stop treatment if bleeding is observed or suspected. Consider INR monitoring in patients taking warfarin. *Hypersensitivity:* Anaphylaxis, including anaphylactic shock with fatal outcome has been reported very rarely in post-marketing experience. Caution in patients who have developed lepirudin antibodies. *Acute stent thrombosis* has been observed in patients with STEMI undergoing primary PCI. This increased risk of stent thrombosis was observed during the first 4 hours post procedure among patients who either discontinued the infusion of bivalirudin at the end of the procedure or continued with a reduced dose infusion. The majority of these cases were non-fatal. Patients should remain for at least 24 hours in a facility capable of managing ischaemic complications and should be carefully monitored following primary PCI for signs and symptoms consistent with myocardial ischaemia. Refer to the SmPC for full list of Warnings and Precautions. **Undesirable effects** (including reports with fatal outcome): Major and minor bleeding at any site, haemoglobin decrease, access site haemorrhage, vessel puncture site haematoma and ecchymosis are the most common adverse reactions; thrombosis (including coronary artery thrombosis, stent thrombosis and catheter thrombosis) has been reported rarely. In patients receiving warfarin, INR is increased by administration of bivalirudin (rare). Refer to full SmPC for complete information on other side effects. **Overdose:** Discontinue treatment immediately and monitor patient for signs of bleeding. There is no antidote to bivalirudin; however it is haemodialysable. Bleeding has been observed in some reports of overdose. **Pack size:** 10 vials. **Cost:** € 4200 for pack of 10. **Legal category:** POM. **Marketing authorisation number:** EU/1/04/289/001. **Marketing authorisation holder:** The Medicines Company UK Ltd., 115L Milton Park, Abingdon, Oxfordshire, OX14 4SA, UK. **Date of latest revision of abbreviated prescribing information:** October 2016.

Adverse events should be reported.

Healthcare professionals are asked to report any suspected adverse reactions via:
HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2
Tel: +353 1 6764971, Fax: +353 1 6762517,
Website: www.hpra.ie; email: medsafety@hpra.ie

Adverse events should be reported to: The Medicines Company, **Tel:** +353 1800812065 or +353 (0)19075583; **Email:** medical.information@themedco.com