

INDICATION: Treatment of adult patients with unstable angina/non- ST segment elevation myocardial infarction (UA/NSTEMI) planned for urgent or early intervention. 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.

PRE-CATH LAB (MEDICALLY MANAGED PATIENTS)

**BOLUS:
ALL PATIENTS**

**0.1
mg/kg**



**INFUSION:
ALL PATIENTS**
0.25 mg/kg/h
For up to 72 hours

If patient proceeds
to PCI or CABG
off-pump receiving
0.25 mg/kg/h
infusion

CATH LAB

**BOLUS: ALL PATIENTS
ALREADY RECEIVING
BIVALIRUDIN**

**0.5
mg/kg**



**INFUSION:
NORMAL RENAL
FUNCTION AND MILD
RENAL IMPAIRMENT**
1.75 mg/kg/h*

For at least the duration
of the PCI procedure



**INFUSION:
MODERATE RENAL
IMPAIRMENT**
1.4 mg/kg/h*

For at least the duration
of the PCI procedure

Volume (ml) of diluted solution (5mg/ml bivalirudin)	Volume (ml) of diluted solution (5mg/ml bivalirudin)
0.8	2
0.9	2.3
1	2.5
1.1	2.8
1.2	3
1.3	3.3
1.4	3.5
1.5	3.8
1.6	4
1.7	4.3
1.8	4.5
1.9	4.8
2	5
2.1	5.3
2.2	5.5
2.3	5.8
2.4	6
2.5	6.3
2.6	6.5
2.7	6.8
2.8	7
2.9	7.3
3	7.5
3.1	7.8
3.2	8

Patient weight (kg)
38 - 42
43 - 47
48 - 52
53 - 57
58 - 62
63 - 67
68 - 72
73 - 77
78 - 82
83 - 87
88 - 92
93 - 97
98 - 102
103 - 107
108 - 112
113 - 117
118 - 122
123 - 127
128 - 132
133 - 137
138 - 142
143 - 147
148 - 152
153 - 157
158 - 162

Volume (ml) of diluted solution (5mg/ml bivalirudin)
4
4.5
5
5.5
6
6.5
7
7.5
8
8.5
9
9.5
10
10.5
11
11.5
12
12.5
13
13.5
14
14.5
15
15.5
16

Volume (ml) of diluted solution (5mg/ml bivalirudin)	Volume (ml) of diluted solution (5mg/ml bivalirudin)
14	11
16	12.5
17.5	14
19	15.5
21	17
23	18
24.5	19.5
26	21
28	22.5
30	24
31.5	25
33	26.5
35	28
37	29.5
38.5	31
40	32
42	33.5
44	35
45.5	36.5
47	38
49	39
51	40.5
52.5	42
54	43.5
56	45

*Following PCI, the reduced infusion of 0.25 mg/kg/h may be resumed for 4–12 hours 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.

- Pre-Cath lab: no adjustment of infusion dose is required.
- Cath lab: 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.

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 SmPC¹ 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

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 haemo-dialysable. 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