Download our final edition of **Postpartum Haemorrhage and Synthetic Oxytocin Dilutions in Labour** with **Preface** and **Postscript**, with illustrations embedded at oxytocinmeasures.com/publications

Figures, Graphics and Tables below showing the 'recommended dosage range' (Novartis 1977)

In 2015 we approached Novartis with a question.

If - as is being practised - it is safe to use Syntocinon in an unlicensed manner, why has the licence not been updated to reflect this?

After a few infrequent exchanges we asked Novartis for a statement.

Novartis replied 16 January 2018 and gave us permission to quote:

'Novartis only recommend use of the licensed dosage and method of administration, as detailed in the Syntocinon Summary of Product Characteristics (SmPC). We cannot advocate and do not recommend use of any product in an unlicensed manner.'

During this period, Novartis negotiated with Mylan to take over the brand 'Syntocinon' in 2019.

https://www.medicines.org.uk/emc/product/9736/smpc Patient Information Leaflet by Mylan (April 2022) https://www.medicines.org.uk/emc/files/pil.9735.pdf

6.1 List of excipients: Sodium acetate tri-hydrate, acetic acid, <u>chlorobutanol</u>, <u>ethanol</u> and water for injections.

We are to assume that in the licensed dilutions, the negative effects of chlorobutanol (aka chlorbutol) and ethanol are sufficiently mitigated.

All other manufacturers of synthetic oxytocin for intravenous infusion contain no chlorobutanol and no ethanol. The instructions for use in induction of labour are the same in all the SmPC leaflets.

11 June 2022



Induction with oxytocin

- Treatment regimes:
 milliunits per minute not
 millilitres per minute
- 30 iu in 500 ml normal saline
- 1 millilitres/hr = 1 milliunits/minute
- Deliver via either syringe driver or infusion pump with non-return valve
- Oxytocin performance optimised with ruptured membranes

Oxytocin (in the presence of ruptured membranes)

Time after starting (minutes)	Dose delivery (milliunits/ minute)
0	1
30	2
60	4
90	8
120	12
150	16
180	20
210	24
240	28
270	32

- Most women should have adequate contractions at 12 milliunits per minute
- Trials have used doses up to 32 milliunits per minute
- Maximum licensed dose is 20 milliunits per minute
- **②** If regular contraction not established after TOTAL of 5 iu (five hours on suggested regimen) then induction should be stopped

Induction of Labour RCOG - June 2001 (advice)

http://www.perinatal.sld.cu/docs/guiasclinicas/inductionoflabour.pdf

Figure A

5 IU synthetic oxytocin in 500 ml THE LICENSED DILUTION

Figure B

Full licensed dosage range: mIU / minute 0.5 1 1.5 2.5 3 3.5 4 2

8 4.5 5 5.5 6 7 7.5 6.5

12

16

20

24

28

32

10 8.5 9 9.5 11 10.5 11.5 15 15.5

12.5 13 13.5 14 14.5

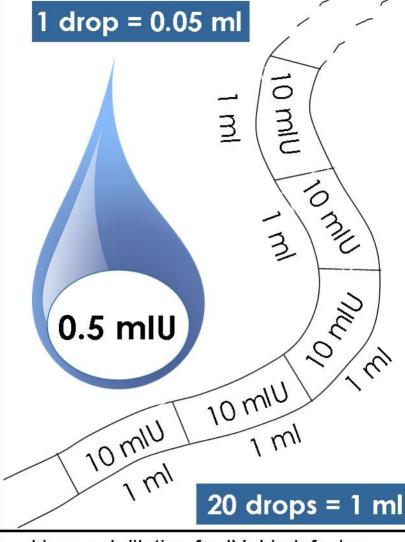
16.5 17 17.5 18 18.5 19 19.5

Maximum licensed rate = 20 mlU / min

The RCOG's regime is highlighted in blue showing all rates omitted by it and unlicensed increments of 4 mIU at a time, up to 32 mIU.

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Figure C (Table 1)



Licensed dilution for IV drip infusion, volumetric pump (and syringe driver)



for drip infusion or volumetric pump VOLUMETRIC

0.5 mlU / 0.05 ml

(0.05 ml = 1 drop)

(Figure C) Table 2 Synthetic Oxytocin 5 IU in 500 ml

10 mlL Licensed dilution via volumetric pump. Fine-tune 10 mIU / 1 ml over 20 minutes.

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10 mlU

10 mll

<u>3</u>

PUMP

In the table below drops match mIU location and mI location. KEY to Numbers in bold have no additional therapeutic meaning. synthetic milliunits (mIU) / minute Volume (ml) / minute oxytocin 0.1 0.15 0.5 0.05 0.2 drip 10.5 12 1.05 1.1 1.15 1.2 infusion and for 1.85 1.9 2.0 18.5 19.5 20 1.95 volumetric Rate changes of 0.5 mIU / minute x 20 minutes = 10 mIU (more, or less) pump NOTE: volume variations will depend on the dilution being infused.

5 IU Synthetic Oxytocin in 500 ml for drip infusion (10 mU / ml) 0.5 mIU / drop Total mIU / no of drops Volume (0.05 ml / drop) Α 3 4 0.5 1.5 2 0.05 0.1 0.15 0.2 5 6 8 2.5 3 3.5 0.25 0.3 0.35 4 0.4

5.5

7.5

9.5

11.5

13.5

15.5

17.5

19.5

Synthetic Oxytocin in drops / minute, mIU / drops and mI / no of drops

A 1 drop - 20 drops / minute B 21 drops - 40 drops / minute

6

8

10

12

14

16

18

20

0.45

0.65

0.85

1.05

1.25

1.45

1.65

1.85

0.5

0.7

0.9

1.1

1.3

1.5

1.7

1.9

Oxy tocin Measures 0.55

0.75

0.95

1.15

1.35

1.55

1.75

1.95

0.6

0.8

1.0

1.2

1.4

1.6

1.8

2.0

Table 1 (drop / mIU / ml)

A

В

9

13

17

21

25

29

33

37

10

14

18

22

26

30

34

38

11

15

19

23

27

31

35

39

12

16

20

24

28

32

36

40

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4.5

6.5

8.5

10.5

12.5

14.5

16.5

18.5

5

9

11

13

15

17

19

LICENSED DILUTION - 5 IU Synthetic Oxytocin in 500 ml for Drip Infusion, Volumetric Pump or Syringe Driver mIU / minute mIU / 20 minutes ml / 20 minutes 0.515 2 10 20 30 40 3

Table 2

(mIU / 1 and 20 minutes / 20 minute VTBI ml)

	0.0	500	1.0	_	10	20	00	10	- 1	_	9	7.5
	2.5	3	3.5	4	50	60	70	80	5	6	7	8
	4.5	5	5.5	6	90	100	110	120	9	10	11	12
	6.5	7	7.5	8	130	140	150	160	13	14	15	16
	8.5	9	9.5	10	170	180	190	200	17	18	19	20
В	10.5	11	11.5	12	210	220	230	240	21	22	23	24
	12.5	13	13.5	14	250	260	270	280	25	26	27	28
	14.5	15	15.5	16	290	300	310	320	29	30	31	32
	16.5	17	17.5	18	330	340	350	360	33	34	35	36
	18.5	19	19.5	20	370	380	390	400	37	38	39	40

Volumes containing the recommended dosage range for 1 and 20 minutes. A Start rates for augmentation. Maximum start for induction = 4 mIU / minute

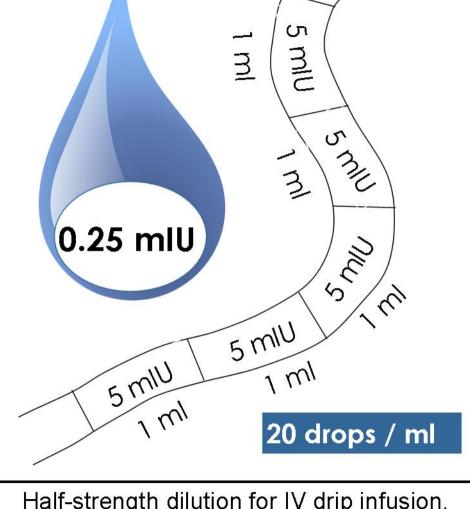
<10 mIU / minute = average rate; B upper range to maximum 20 mIU / minute.

Oxy TOCIT

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Synthetic Oxytocin 2.5 IU in 500 ml

Figure F (Table 3)



Half-strength dilution for IV drip infusion, volumetric pump and syringe driver



Table 3
2.5 IU Synthetic Oxytocin in 500 ml for drip infusion (5 mlU / ml)

0.2	25 ml	U / di	rop	Total m	of drop	Volu	me (0.	05 ml / (drop)		
1	2	3	4	0.25	0.5	0.75	1	0.05	0.1	0.15	0.2
5	6	7	8	1.25	1.5	1.75	2	0.25	0.3	0.35	0.4
9	10	11	12	2.25	2.5	2.75	3	0.45	0.5	0.55	0.6
13	14	15	16	3.25	3.5	3.75	4	0.65	0.7	0.75	8.0
17	18	19	20	4.25	4.5	4.75	5	0.85	0.9	0.95	1.0
21	22	23	24	5.25	5.5	5.75	6	1.05	1.1	1.15	1.2
25	26	27	28	6.25	6.5	6.75	7	1.25	1.3	1.35	1.4
29	30	31	32	7.25	7.5	7.75	8	1.45	1.5	1.55	1.6
33	34	35	36	8.25	8.5	8.75	9	1.65	1.7	1.75	1.8
37	38	39	40	9.25	9.5	9.75	10	1.85	1.9	1.95	2.0

Half-strength standard dilution in drops / mIU / mI / minute.

If IVI >10 mIU / minute, when 500 ml ends, go to 5 IU in 500 ml.

2.5 IU Synthetic Oxytocin in 500 ml for volumetric pump

n	nIU / m	ninute		m	IU / 20) minut	tes	m	l / 20 i	minute	es
0.25	0.5	0.75	1	5	10	15	20	1	2	3	4
1.25	1.5	1.75	2	25	30	35	40	5	6	7	8
2.25	2.5	2.75	3	45	50	55	60	9	10	11	12
3.25	3.5	3.75	4	65	70	75	80	13	14	15	16
4.25	4.5	4.75	5	85	90	95	100	17	18	19	20
5.25	5.5	5.75	6	105	110	115	120	21	22	23	24
6.25	6.5	6.75	7	125	130	135	140	25	26	27	28
7.25	7.5	7.75	8	145	150	155	160	29	30	31	32
8.25	8.5	8.75	9	165	170	175	180	33	34	35	36
9.25	9.5	9.75	10	185	190	195	200	37	38	39	40

Half-strength standard dilution mIU / mI / 20 minutes.

To reduce rate by 0.25 mIU / minute slow pump by 5 mIU in 1.0 mI over 20 minutes.



dilution NOT for drip infusion SYRINGE DRIVER 1 ml

Figure D (Table 4)
Synthetic Oxytocin 10 IU in 50 ml

10.0 mIU / 0.05 ml

= unlicensed

3

At this dilution a syringe driver is essential to control speed of infusion

200ml



10 IU synthetic oxytocin in 50 ml diluent for Syringe Driver mIU / minute ml / minute 0.5 1 1.5 2 0.0025 0.005

10

12

14

16

18

20

40

80

120

160

200

240

280

320

360

400

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8.5

10.5

12.5

14.5

16.5

18.5

10

50

90

130

170

210

250

290

330

370

9

11

13

15

17

19

20

60

100

140

180

220

260

300

340

380

9.5

11.5

13.5

15.5

17.5

19.5

30

70

110

150

190

230

270

310

350

390

mIU / 20 minutes

2.5	3	3.5	4	0.0125	0.015	0.0175
4.5	5	5.5	6	0.0225	0.025	0.0275
6.5	7	7.5	8	0.0325	0.035	0.0375

Table 4

0.0425

0.0525

0.0625

0.0725

0.0825

0.0925

0.05

0.25

0.45

0.65

0.85

1.05

1.25

1.45

1.65

1.85

To reduce rate by 0.5 mIU / minute, slow pump by 10 mIU in 0.05 mI over 20 minutes

0.045

0.055

0.065

0.075

0.085

0.095

0.1

0.3

0.5

0.7

0.9

1.1

1.3

1.5

1.7

1.9

ml / 20 minutes

0.0075

0.0475

0.0575

0.0675

0.0775

0.0875

0.0975

0.15

0.35

0.55

0.75

0.95

1.15

1.35

1.55

1.75

1.95

Oxy tocir

0.01

0.02

0.03

0.04

0.05

0.06

0.07

0.08

0.09

0.1

0.2

0.4

0.6

0.8

1.0

1.2

1.4

1.6

1.8

2.0

Figure E		<u>Dilutions</u> sed diluti		exytocin fo	Licensed dilutions	
Method	Diluent (ml)	IU <u>added</u>	Milliunits (mIU)	mIU /ml	Information	Tables and Figures
Volumetric	500	5	5,000	10	Licensed dilution	Table 2 - Figure C
Volumetric	500	2.5	2,500	5	Half-strength	Table 3 - Figure F

500 2.5 2.500 5

20

20

20

60

200

100

50

Syringe Driver (Table 4) for 10 IU in 50 ml shows VTBI volumes / 30 minutes cannot be logged accurately. Do not round up incomplete numbers. Rather, drop the 3rd decimal digit, or use 20 minute VTBI settings.

5 IU in 50 ml and 2.5 IU in 50 ml offer closer 0.5mIU fine-tuning over 20 minute VTBIs.

RCOG regime

RCOG regime

RCOG regime

RCOG regime

0.5 mIU/0.0025 ml

0.5 mIU/0.005 ml

0.5 mIU/0.01 ml

oxy tocir

Figure A

Figure B

Note: volumes as Table 1 and 2

+ mIU doubled.

Low rate = f error factor

Table 4 - Figure D

Table 5 - Figure G

Table 6 - Figure H

Drip Infusion Half-strength Table 3 - Figure F 500 5.000 10 Licensed dilution **Drip Infusion** 5 Table 1 - Figure C **Drip Infusion** 1,000 10 10.000 10 Licensed dilution Table 1 - Figure C

IMPORTANT NOTE - 20 mU / ml (next below) is licensed ONLY for after intrauterine death.

20,000

10.000

10,000

30.000

10,000

5.000

2.500

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The RCOG's advice for live pregnancies includes this and allows for other irregular dilutions.

Drip Infusion

Drip Infusion

Volumetric

Volumetric

Syringe Driver

Syringe Driver

Syringe Driver

1,000

500

500

500

49

49

49.5

10 x 2

10

10

10 x 3

10

5

2.5

5.0 mlU / 0.05 ml = unlicensed dilution **NOT for drip** infusion SYRINGE DRIVER

Figure G (Table 5) Synthetic Oxytocin 5 IU in 50 ml

100 mIU | 100 mIL mIU / 0.01 ml At this dilution a syringe driver is

essential to control speed of infusion



5 IU synthetic oxytocin in 50 ml for Syringe Driver (100 mIU per ml for administration of the licensed dosage range) mIU / minute ml / minute 0.5 1.5 0.01 0.015 0.02 1 2 0.005 2.5 3 3.5 4 0.025 0.03 0.035 0.04 4.5 5 5.5 6 0.045 0.05 0.055 0.06

0.065

0.085

0.105

0.125

0.145

0.165

0.185

0.1

0.5

0.9

1.3

1.7

2.1

2.5

2.9

3.3

3.7

To reduce rate by 0.5 mIU / min, slow pump by 10 mIU in 0.1 ml over 20 minutes.

40

80

120

160

200

240

280

320

360

400

0.07

0.09

0.11

0.13

0.15

0.17

0.19

0.075

0.095

0.115

0.135

0.155

0.175

0.195

0.3

0.7

1.1

1.5

1.9

2.3

2.7

3.1

3.5

3.9

ml / 20 minute

0.2

0.6

1.0

1.4

1.8

2.2

2.6

3.0

3.4

3.8

0.08

0.1

0.12

0.14

0.16

0.18

0.2

0.4

0.8

1.2

1.6

2.0

2.4

2.8

3.2

3.6

4.0

Oxy tocin Measures

6.5

8.5

10.5

12.5

14.5

16.5

18.5

10

50

90

130

170

210

250

290

330

370

7

9

11

13

15

17

19

20

60

100

140

180

220

260

300

340

380

7.5

9.5

11.5

13.5

15.5

17.5

19.5

mIU / 20 minute

8

10

12

14

16

18

20

30

70

110

150

190

230

270

310

350

390

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Table 5

50 mIU = unlicensed dilution 50 mlU **NOT for drip** 3 infusion SYRINGE DRIVER

Figure H (Table 6) Synthetic Oxytocin 2.5 IU in 50 ml

2.5 mlU / 0.05 ml

3

50 mIU 0.5 mlU / 0.01 ml At this dilution a syringe driver is essential to control speed of infusion

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(50 mIU per ml for administration of the licensed dosage range) mIU / minute ml / minute 0.5 1.5 2 0.01 0.02 0.04 1 0.03 2.5 4 0.05 3 3.5 0.06 0.07 0.08 4.5 5 5.5 6 0.09 0.1 0.11 0.12

0.21

0.25

0.29

0.33

0.37

0.2

1.0

1.8

2.6

3.4

4.2

5.0

5.8

6.6

7.4

To reduce rate by 0.5 mIU / min, slow pump by 10 mIU in 0.2 ml over 20 minutes.

40

80

120

160

200

240

280

320

360

400

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0.14

0.18

0.22

0.26

0.34

0.38

0.3

0.15

0.99

0.23

0.27

0.31

0.35

0.39

0.6

1.4

2.2

3.0

3.8

4.6

5.4

6.2

7.0

7.8

Oxy tocin Measure

ml / 20 minute

0.4

1.2

2.0

2.8

3.6

4.4

5.2

6.0

6.8

7.6

0.16

0.2

0.24

0.28

0.32

0.36

0.4

8.0

1.6

2.4

3.2

4.0

4.8

5.6

6.4

7.2

8.0

Table 6

2.5 IU synthetic oxytocin in 50 ml for Syringe Driver

 5
 5.5
 6
 0.09

 7
 7.5
 8
 0.13

 9
 9.5
 10
 0.17

12

14

16

18

20

30

70

110

150

190

230

270

310

350

390

11.5

13.5

15.5

17.5

19.5

mIU / 20 minute

6.5

8.5

10.5

12.5

14.5

16.5

18.5

10

50

90

130

170

210

250

290

330

370

11

13

15

17

19

20

60

100

140

180

220

260

300

340

380