



**KARNATAKA ANTIBIOTICS &  
PHARMACEUTICALS LIMITED**

(A Government of India Enterprise)

ENQUIRY REF. No.	KAPL/QAD/020/0847
DATE	11/07/2024
DUE DATE	16/07/2024 (13.00HRS)

Dear Sir,

Please submit your lowest and competitive offer in a SEALED ENVELOPE, DULY SUPERSCRIBING OUR ABOVE ENQUIRY REF. NO., DATE and DUE DATE on it/ OR MAIL, with other details of F.O.R terms, Taxes, Credit period, Delivery offered, Name of the Make, Detailed Specification etc., for below mentioned material/s

SL. NO.	ITEM CODE	ITEM DESCRIPTION	UOM	QTY
01	QSPHPL421	HPLC COLUMN 25CM X 4.6MM,ODS,5 $\mu$ (SYMMETRY C18)	NOS	01
02	QSPHPL423	HPLC COLUMN 15CM X 4.6MM,C8,5 $\mu$ (SYMMETRY C8)	NOS	01
03	QSPHPL415	HPLC COLUMN 15CM X 4.6 MM,ODS,5 $\mu$ ( X-TERRA RP 18)	NOS	01

**OTHER TERMS:**

- |                                 |                  |
|---------------------------------|------------------|
| 1. F.O.R TERMS                  | : DOOR DELIVERY  |
| 2. GST %                        | : PLEASE SPECIFY |
| 3. PACKING & FORWARDING CHARGES | : NOT APPLICABLE |
| 4. CREDIT PERIOD                | : 30 DAYS        |
| 5. DELIVERY OFFERED             | :                |

NOTE: IN CASE YOU ARE NOT QUOTING PLEASE SEND THE REGRET LETTER.

Thanking you,

Yours faithfully,  
For KARNATAKA ANTIBIOTICS  
& PHARMACEUTICALS LIMITED

  
YUVARAJA M  
DEPUTY MANAGER PURCHASE DEPT

**User Requirement specifications****Material Description** : HPLC COLUMN 15cm x 4.6mm, ODS, 5u**URS Number**: QC/URS/001/0724

## 1. Description and Quantity:

Material Description	15cm x 4.6mm, ODS, 5u
Item code	QSPHPL415
Quantity/ Box	1

## 2. User Specifications:

#	Requirement	Specification
1	Brand Name	15cm x 4.6mm, ODS, 5u (such as X-Terra RP 18)
2	Make	Waters
3	Brand	X-Terra
4	Part Number	186000492
5	Matrix active group	Silica
6	Particle size	5u
7	Length (mm)	150
8	Internal Diameter (I.D.)	4.6 mm
9	Particle Substrate	Hybrid
10	Particle Shape	Spherical
11	External Construction Materials	Stainless Steel
12	Endcapped	Yes
13	Endfitting Type	Waters
14	USP Classification	L1
15	Separation Mode	Reverse phase
16	P <sup>H</sup> Range	2-12
17	Maximum Pressure	6000 psi (415 Bar)
18	Pore Size	125 °A

**User Requirement specifications****Material Description** : HPLC COLUMN 15cm x 4.6mm, C8, 5u**URS Number**: QC/URS/002/0724**1. Description and Quantity:**

Material Description	15cm x 4.6mm, C8, 5u
Item code	QSPHPL423
Quantity/ Box	1

**2. User Specifications:**

#	Requirement	Specification
1	Brand Name	15cm x 4.6mm, C8, 5u (Symmetry C8)
2	Make	Waters
3	Brand	Symmetry
4	Part Number	WAT045995
5	Matrix active group	Silica
6	Particle size	5u
7	Length (mm)	150
8	Internal Diameter (I.D.)	4.6 mm
9	Particle Substrate	Silica
10	Particle Shape	Spherical
11	External Construction Materials	Stainless Steel
12	Endcapped	Yes
13	Endfitting Type	Waters
14	USP Classification	L7
15	Separation Mode	Reverse phase
16	P <sup>H</sup> Range	2-8
17	Maximum Pressure	6000 psi (415 Bar)
18	Pore Size	100 °A

**User Requirement specifications****Material Description** : HPLC COLUMN 25cm x 4.6mm, C18, 5u**URS Number**: QC/URS/003/0724**1. Description and Quantity:**

Material Description	25cm x 4.6mm, C18, 5u
Item code	QSPHPL421
Quantity/ Box	1

**2. User Specifications:**

#	Requirement	Specification
1	Brand Name	25cm x 4.6mm, C18, 5u (Symmetry C18)
2	Make	Waters
3	Brand	Symmetry
4	Part Number	WAT054275
5	Matrix active group	Silica
6	Particle size	5u
7	Length (mm)	250
8	Internal Diameter (I.D.)	4.6 mm
9	Particle Substrate	Silica
10	Particle Shape	Spherical
11	External Construction Materials	Stainless Steel
12	Endcapped	Yes
13	Endfitting Type	Waters
14	USP Classification	L1
15	Separation Mode	Reverse phase
16	P <sup>H</sup> Range	2-8
17	Maximum Pressure	6000 psi (415 Bar)
18	Pore Size	100 °A

**Capsules.** Page 1297**Soft Gelatin Capsules****Disintegration.** Line 5

Change from: 60 minutes

to: 30 minutes

**NOTE** — This change shall be applicable for all soft gelatin capsules including any three or more components of vitamins, minerals, amino acids, fatty acids, trace elements etc.

**Abacavir Sulphate.** Page 1355**Specific optical rotation.** Delete the requirement.Insert before **Heavy metals****Enantiomeric purity.** Determine by liquid chromatography (2.4.14).

**Solvent mixture.** A 0.5 per cent v/v solution of trifluoroacetic acid in methanol.

**Test solution.** Dissolve 4 mg of the substance under examination in 3 ml of the solvent mixture, with the aid of ultrasound, add 3 ml of 2-propanol, mix and dilute to 10.0 ml with heptane.

**Reference solution.** A solution containing 0.04 per cent w/v of abacavir stereoisomers mixture IPRS in the solvent mixture (30 per cent of the final volume) and disperse with the aid of ultrasound. Add 2-propanol (30 per cent of the final volume), mix and dilute to volume with heptane.

**Chromatographic system**

- a stainless steel column 25 cm x 4.6 mm, packed with amylose tris-3,5-dimethylphenylcarbamate coated to porous spherical silica particles (10 µm) (Such as Chiralpak AD),
- mobile phase: A. a mixture of 85 volumes of heptane, 15 volumes of 2-propanol and 0.1 volume of diethylamine,  
B. a mixture of 50 volumes of heptane and 50 volumes of 2-propanol,
- a gradient programme using the conditions given below,
- spectrophotometer set at 286 nm,
- injection volume: 20 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)	Flow rate (ml/min)
0	100	0	1.0
25	100	0	1.0
27	0	100	0.8
37	0	100	0.8
39	100	0	1.0
55	100	0	1.0

Name	Relative retention time
<i>trans</i> -abacavir <sup>1</sup>	0.8
Abacavir enantiomer	0.9
Abacavir	1.0

<sup>1</sup>{(1*R*,4*R*)-4-[2-Amino-6-(cyclopropylamino)-9*H*-purin-9-yl]-cyclopent-2-enyl}methanol.

Inject the reference solution. The test is not valid unless the resolution between the peaks due to *trans*-abacavir and abacavir enantiomer is not less than 1.0 and abacavir enantiomer and abacavir is not less than 1.5.

Inject the test solution. The area of any peak due to abacavir enantiomer is not more than 0.3 per cent, calculated by area normalization.

**Water.** Change to:**Water** (2.3.43). Not more than 0.5 per cent, determined on 0.5 g.**Sulphated ash**

Change from: 0.3 per cent.

to: 0.2 per cent.

**Aceclofenac and Paracetamol Tablets**

Aceclofenac and Paracetamol Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of aceclofenac, C<sub>16</sub>H<sub>13</sub>C<sub>12</sub>NO<sub>4</sub> and paracetamol, C<sub>8</sub>H<sub>9</sub>NO<sub>2</sub>.

**Usual strength.** Aceclofenac 100 mg and Paracetamol 325 mg.**Identification**

In the Assay, the principal peaks in the chromatogram obtained with the test solution correspond to the principal peaks in the chromatogram obtained with reference solution (c).

**Tests****Dissolution** (2.5.2).

Apparatus No. 2 (Paddle),

Medium. 900 ml of phosphate buffer pH 6.8, prepared by dissolving 6.8 g of potassium dihydrogen orthophosphate in 1000 ml of water, adjusted to pH 6.8 with dilute sodium hydroxide,

Speed and time. 75 rpm and 45 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

*solution.* Use the filtrate, dilute if necessary, with the dissolution medium.

*Reference solution.* Dissolve 11 mg of *aceclofenac IPRS* and 36 mg of *paracetamol IPRS* in 5 ml of *acetonitrile* and dilute to 100.0 ml with the dissolution medium.

**Chromatographic system**

- a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as X-Terra RP 18),
- mobile phase: A. a mixture of 90 volumes of 0.005 M disodium hydrogen phosphate, adjusted to pH 8.0 with dilute orthophosphoric acid, 9 volumes of acetonitrile and 1 volume of methanol,

B. a mixture of 90 volumes of acetonitrile and 10 volumes of methanol,

- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 280 nm,
- injection volume: 10 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	95	5
10	35	65
11	95	5
15	95	5

Inject the reference solution. The test is not valid unless the column efficiency is not less than 1500 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent, for both the peaks.

Inject the reference solution and the test solution.

Calculate the content of C<sub>16</sub>H<sub>13</sub>C<sub>12</sub>NO<sub>4</sub> and C<sub>8</sub>H<sub>9</sub>NO<sub>2</sub> in the medium.

Q. Not less than 70 per cent of the stated amount of C<sub>16</sub>H<sub>13</sub>C<sub>12</sub>NO<sub>4</sub> and C<sub>8</sub>H<sub>9</sub>NO<sub>2</sub>.

**Related substances.** Determine by liquid chromatography (2.4.14).

*Solvent mixture.* Equal volumes of acetonitrile and water.

*Test solution.* Disperse a quantity of the powdered tablets containing 325 mg of Paracetamol in the solvent mixture, with the aid of ultrasound for 10 minutes with intermittent shaking and dilute to 100.0 ml with the solvent mixture, filter.

*Reference solution.* A solution containing 0.01624 per cent w/v of paracetamol IPRS and 0.005 per cent w/v of aceclofenac IPRS in the solvent mixture. Dilute 1.0 ml of the solution to 10.0 ml with the solvent mixture.

**Chromatographic system**

- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Symmetry C18),

- column temperature: 40°,
- mobile phase: A. a buffer solution prepared by dissolving 1 g of 1-octane sulphonic acid sodium salt anhydrous and 2 g of sodium dihydrogen orthophosphate anhydrous in 1000 ml of water, adjusted to pH 3.5 with dilute orthophosphoric acid,

B. a mixture of 90 volumes of acetonitrile and 10 volumes of water,

- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 220 nm,
- injection volume: 10 µl.

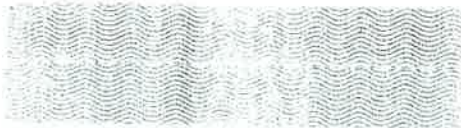
Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	95	5
3	95	5
8	80	20
42	20	80
50	20	80
52	95	5
60	95	5

Name	Relative retention time	Correction factor
Paracetamol	0.27	---
4-aminophenol	0.43	0.62
4-chloroacetanilide	0.69	1.52
Aceclofenac (Retention time: about 31 minutes)	1.0	---
Aceclofenac impurity A <sup>1</sup>	1.1	0.89

<sup>1</sup>[2-[(2,6-dichlorophenyl)amino] phenyl]acetic acid.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 1500 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 5.0 per cent for both the peaks.

Inject the reference solution and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to aceclofenac impurity A is not more than 10 times the area of the aceclofenac peak in the chromatogram obtained with the reference solution (5.0 per cent), the area of any peak corresponding to 4-aminophenol is not more than 0.2 times the area of the paracetamol peak in the chromatogram obtained with the reference solution (0.1 per cent), the area of any peak corresponding to 4-chloroacetanilide is not more than 0.1 times the area of the paracetamol peak in the chromatogram obtained with the reference solution (0.05 per cent), the area of any other secondary peak is not more than the area of the aceclofenac peak in the chromatogram obtained with the reference



solution (0.5 per cent) and the sum of areas of all the secondary peaks, excluding aceclofenac impurity A is not more than 4 times the area of the aceclofenac peak in the chromatogram obtained with the reference solution (2.0 per cent).

**Other tests.** Comply with the tests stated under Tablets.

**Assay.** Determine by liquid chromatography (2.4.14).

*NOTE* — Use freshly prepared solutions.

**Solvent mixture.** 40 volumes of acetonitrile and 60 volumes of water.

**Test solution.** Weigh and powder 20 tablets. Disperse a quantity of the powder containing 325 mg of Paracetamol in 40 ml of acetonitrile, with the aid of ultrasound with intermittent shaking. Add 100 ml of the solvent mixture and sonicate for 15 minutes with intermittent shaking, dilute to 200.0 ml with the solvent mixture. Dilute 5.0 ml of the solution to 50.0 ml with the solvent mixture.

**Reference solution (a).** Dissolve 32.5 mg of paracetamol IPRS in 5 ml of acetonitrile, with the aid of ultrasound for 5 minutes and dilute to 20.0 ml with the solvent mixture.

**Reference solution (b).** Dissolve 25 mg of aceclofenac IPRS in 10 ml of acetonitrile, with the aid of ultrasound for 5 minutes and dilute to 50.0 ml with the solvent mixture.

**Reference solution (c).** Transfer 5.0 ml, each of, reference solution (a) and reference solution (b) to a 50- ml volumetric flask. Add 10 ml of acetonitrile and dilute to 50.0 ml with the solvent mixture.

**Chromatographic system**

- a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as X-Terra RP 18),
- mobile phase: A. a mixture of 90 volumes of 0.005 M disodium hydrogen phosphate, adjusted to pH 8.0 with dilute orthophosphoric acid, 9 volumes of acetonitrile and 1 volume of methanol,  
B. a mixture of 90 volumes of acetonitrile and 10 volumes of methanol,
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 280 nm,
- injection volume: 10 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	95	5
10	35	65
11	95	5
15	95	5

The elution order is paracetamol followed by aceclofenac peak.

Inject reference solution (c). The test is not valid unless the column efficiency is not less than 1500 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 5.0 per cent, for both the peaks.

Inject reference solution (c) and the test solution.

Calculate the content of C<sub>16</sub>H<sub>13</sub>C<sub>12</sub>NO<sub>4</sub> and C<sub>8</sub>H<sub>9</sub>NO<sub>2</sub> in the tablets.

**Storage.** Store protected from moisture, at a temperature not exceeding 30°.

**Alprazolam.** Page 1402

**Related substances.** Change to:

**Related substances.** Determine by liquid chromatography (2.4.14).

*NOTE*—Use freshly prepared solution and carry out the test protected from light.

**Solvent mixture.** Equal volumes of acetonitrile and water.

**Test solution.** Dissolve 25 mg of the substance under examination in the solvent mixture and dilute to 100.0 ml with the solvent mixture.

**Reference solution (a).** A 0.0025 per cent w/v solution of alprazolam IPRS in the solvent mixture. Dilute 1.0 ml of the solution to 100.0 ml with the solvent mixture.

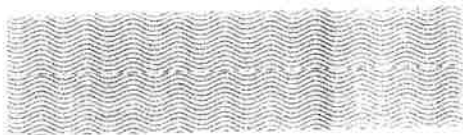
**Reference solution (b).** A solution containing 0.002 per cent w/v, each of, alprazolam IPRS, alprazolam related compound A IPRS and 2-amino-5-chlorobenzophenone IPRS in the solvent mixture.

**Chromatographic system**

- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as purospher star RP 18e),
- column temperature: 40°,
- mobile phase: a mixture of 50 volumes of acetonitrile and 50 volumes of a buffer solution prepared by dissolving 1.4 g of monobasic potassium phosphate in 1000 ml of water,
- flow rate: 1 ml per minute,
- spectrophotometer set at 231 nm,
- injection volume: 20 µl.

Name	Relative retention time	Correction factor
Alprazolam related compound A <sup>1</sup>	0.8	1.32
Alprazolam	1.0	---
2-Amino-5- chloro benzophenone <sup>2</sup>	4.0	---

<sup>1</sup>2-(2-Acetylhydrazino)-7-chloro-5-phenyl-3H-1,4-benzodiazepine.



compound A, pantoprazole related compound D and F\*, each of, is not more than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent), the area of any peak corresponding to pantoprazole related compound B is not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent), the area of any other secondary peak is not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent) and the sum of the areas of all the secondary peaks is not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.0 per cent). Ignore any peak with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent).

## Paracetamol and Tramadol Tablets N

### Paracetamol and Tramadol Hydrochloride Tablets

Paracetamol and Tramadol Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of paracetamol,  $C_8H_9NO_2$  and tramadol hydrochloride,  $C_{16}H_{25}NO_2 \cdot HCl$ .

**Usual strength.** Paracetamol 325 mg and Tramadol Hydrochloride 37.5 mg.

### Identification

In the Assay, the principal peaks in the chromatogram obtained with test solution (b) and (c) correspond to the principal peaks in the chromatogram obtained with the reference solution.

### Tests

#### Dissolution (2.5.2).

Apparatus No. 2 (Paddle),

Medium. 900 ml of 0.1 M hydrochloric acid,

Speed and time. 50 rpm and 30 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

**Test solution.** Use the filtrate, dilute if necessary, with the dissolution medium.

**Reference solution.** A solution containing 0.036 per cent w/v of paracetamol IPRS and 0.004 per cent w/v of tramadol hydrochloride IPRS in the dissolution medium.

#### Chromatographic system

- a stainless steel column 15 cm x 4.6 mm, packed with octylsilane bonded to porous silica (5  $\mu$ m),
- column temperature: 30°,

- mobile phase: a mixture of 80 volumes of a buffer solution prepared by dissolving 6.8 g of potassium dihydrogen orthophosphate in 1000 ml of water, adjusted to pH 2.5 with orthophosphoric acid and 20 volumes of acetonitrile,
- flow rate: 1 ml per minute,
- spectrophotometer set at 272 nm,
- injection volume: 25  $\mu$ l.

The relative retention time with reference to tramadol for paracetamol is about 0.5.

Inject the reference solution. The test is not valid unless the resolution between the peaks due to paracetamol and tramadol is not less than 5.0, the relative standard deviation for replicate injections for both the peaks is not more than 2.0 per cent.

Inject the reference solution and the test solution. Run the chromatogram twice the retention time of the tramadol.

Calculate the content of  $C_8H_9NO_2$  and  $C_{16}H_{25}NO_2 \cdot HCl$  in the medium.

Q. Not less than 80 per cent of the stated amount of  $C_8H_9NO_2$  and  $C_{16}H_{25}NO_2 \cdot HCl$ .

**4-Aminophenol.** Not more than 0.15 per cent.

Determine by liquid chromatography (2.4.14).

**NOTE** — Prepare the solutions immediately before use and protect from light.

**Solvent mixture.** 90 volumes of a buffer solution prepared by dissolving 4.0 g of sodium citrate dihydrate and 1.5 g of anhydrous citric acid in 1000 ml of water and 10 volumes of acetonitrile.

**Test solution (a).** Disperse a quantity of powdered tablets containing 1 g of Paracetamol in the solvent mixture and dilute to 100.0 ml with the solvent mixture.

**Test solution (b).** Dilute 10.0 ml of test solution (a) to 20.0 ml with the solvent mixture.

**Reference solution (a).** A 0.0025 per cent w/v solution of 4-aminophenol IPRS in the solvent mixture.

**Reference solution (b).** Dilute 25.0 ml of test solution (a) and 15.0 ml of reference solution (a) to 50.0 ml with the solvent mixture

**Reference solution (c).** Dilute 5.0 ml of reference solution (a) to 50.0 ml with the solvent mixture

#### Chromatographic system

- a stainless steel column 15 cm x 4.6 mm, packed with octylsilane consists of both reversed-phase (an alkyl chain longer than C8) and weak cation-exchange (carboxyl groups) functional groups bonded to porous or nonporous silica (5  $\mu$ m),



the phase: A. 0.01M phosphate buffer prepared by dissolving 0.6 g of *potassium dihydrogen orthophosphate* and 0.82 g of *disodium hydrogen orthophosphate anhydrous* in 1000 ml of water, adjusted to pH 7.0,

B. water,

C. acetonitrile,

- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 300 nm,
- injection volume: 10  $\mu$ l.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)	Mobile phase C (per cent v/v)
0	90	5	5
5	90	5	5
7	10	10	80
7.1	90	5	5
10	90	5	5

NOTE — The retention time for 4-aminophenol is about 4.2 to 5.3.

Inject reference solution (b) and (c). The test is not valid unless the resolution between the peaks due to 4-aminophenol and nearest peak is not less than 1.0, the tailing factor is not more than 1.5 for 4-aminophenol peak and the relative standard deviation for replicate injections is not more than 5.0 per cent in the chromatogram obtained with reference solution (b) and the signal-to-noise ratio is not less than 20 in the chromatogram obtained with reference solution (c).

Inject reference solution (b) and test solution (b).

Calculate the percentage of 4-aminophenol ( $C_6H_7NO$ ) relative to paracetamol, using following expression:

$$\text{4-Aminophenol} = \left[ \frac{r_u}{(r_s - r_u)} \right] \times \left[ \frac{W_s}{W_u} \right] \times 100$$

where,  $r_u$  = peak response of 4-aminophenol from test solution (b),

$r_s$  = peak response of 4-aminophenol from reference solution (b),

$W_s$  = amount of 4-aminophenol IPRS added to reference solution (b) (mg),

$W_u$  = amount of paracetamol in test solution (b) (mg).

**Related substances.** Determine by liquid chromatography (2.4.14).

**Solvent mixture.** 10 volumes of *methanol* and 90 volumes of *water*.

**Test solution.** Disperse a quantity of the powdered tablets containing 37.5 mg of *tramadol hydrochloride* in 30 ml of the solvent mixture, with the aid of ultrasound for 30 minutes with intermittent shaking and dilute to 50.0 ml with the solvent mixture. Centrifuge the solution and use the supernatant liquid, filter.

**Reference solution.** A solution containing 0.0075 per cent w/v, each of, *tramadol hydrochloride IPRS* and *tramadol related compound A IPRS* in the solvent mixture. Dilute 1.0 ml of the solution to 100.0 ml with the solvent mixture

**Chromatographic system**

- a stainless steel column 15 cm x 4.6 mm, packed with phenyl group bonded to porous silica (5  $\mu$ m),
- column temperature: 50°,
- mobile phase: a mixture of 92 volumes of *water*, 8 volumes of *tetrahydrofuran*, 0.1 volume of *triethylamine* and 0.1 volume of *trifluoroacetic acid*, adjusted to pH 2.3,
- flow rate: 1 ml per minute,
- spectrophotometer set at 216 nm,
- injection volume: 30  $\mu$ l.

Name	Relative retention time
Paracetamol	0.38
O-desmethyl-tramadol <sup>1</sup>	0.6
Tramadol related compound A <sup>2</sup>	0.8
Tramadol	1.0

<sup>1</sup>3-[(1*R*,2*R*)-2-[(Dimethylamino)methyl]-1-hydroxycyclohexyl]phenol,  
<sup>2</sup>*R*,*S*,*S**R*-1-(3-Methoxyphenyl)-2-(dimethylaminomethyl)cyclohexanol hydrochloride.

Inject the reference solution. The test is not valid unless the resolution between the peaks due to tramadol related compound A and tramadol hydrochloride is not less than 2.0 and the relative standard deviation for replicate injections is not more than 6.0 per cent for tramadol peak.

Inject the reference solution and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to o-desmethyl-tramadol and tramadol related compound A, each of, is not more than twice the area of the principal peak in the chromatogram obtained with the reference solution (0.2 per cent), the area of any other secondary peak is not more than twice the area of the principal peak in the chromatogram obtained with the reference solution (0.2 per cent) and the sum of areas of all the secondary peaks is not more than 8 times the area of the principal peak in the chromatogram obtained with the reference solution (0.8 per cent). Ignore the peaks due to paracetamol and 4-aminophenol.

**Uniformity of content.** Complies with the test stated under Tablets.

Analyse by liquid chromatography (2.4.14), as described under Assay with the following modification.

**Test solution.** Disperse one tablet in 30 ml of the solvent mixture, with the aid of ultrasound for 30 minutes with intermittent shaking and dilute to 50.0 ml with the solvent mixture, centrifuge. Dilute 1.0 ml of the supernatant liquid to 10.0 ml with the solvent mixture.

Inject the reference solution and the test solution. Run the chromatogram 4 times the retention time of the paracetamol peak.

Calculate the content of the  $C_{16}H_{25}NO_2 \cdot HCl$  in the tablet.

**Other tests.** Comply with the tests stated under Tablets.

**Assay.** Determine by liquid chromatography (2.4.14).

**Solvent mixture.** 10 volumes of *methanol* and 90 volumes of *water*.

**Test solution (a).** Weigh and powder 20 tablets. Disperse a quantity of the powder containing 325 mg of Paracetamol in 30 ml of the solvent mixture, with the aid of ultrasound for 30 minutes with intermittent shaking and dilute to 50.0 ml with the solvent mixture. Centrifuge and use the supernatant liquid.

**Test solution (b).** Dilute 1.0 ml of test solution (a) to 100.0 ml with the solvent mixture.

**Test solution (c).** Dilute 5.0 ml of test solution (a) to 50.0 ml with the solvent mixture.

**Reference solution.** A solution containing 0.0065 per cent w/v of *paracetamol* IPRS and 0.0075 per cent w/v of *tramadol hydrochloride* IPRS in the solvent mixture.

Use the chromatographic system as described under Related substances with the following modification.

- spectrophotometer set at 216 nm (for tramadol hydrochloride) and 249 nm (for paracetamol),
- injection volume: 20  $\mu$ l.

Inject the reference solution. The test is not valid unless the resolution between the peaks due to paracetamol and tramadol hydrochloride is not less than 10.0, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent for both the peaks.

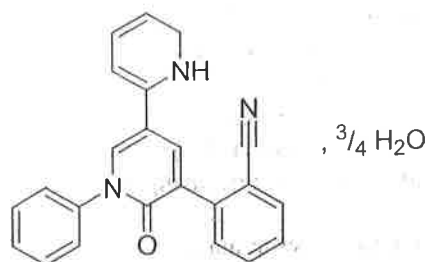
Inject the reference solution, test solution (b) (for paracetamol) and test solution (c) (for tramadol hydrochloride). Run the chromatogram 4 times the retention time of the paracetamol peak.

Calculate the content of  $C_8H_9NO_2$  and  $C_{16}H_{25}NO_2 \cdot HCl$  in the tablets.

**Storage.** Store protected from moisture, at a temperature not exceeding 30°.

## Perampanel

**N**



$C_{23}H_{15}N_3O \cdot \frac{3}{4}H_2O$

Mol. Wt. 362.9

Perampanel is 2-(2-oxo-1-phenyl-5-pyridin-2-yl-1,2-dihydropyridin-3-yl)benzotrile hydrate (4:3).

Perampanel contains not less than 98.0 per cent and not more than 102.0 per cent of  $C_{23}H_{15}N_3O$ , calculated on the anhydrous basis.

**Category.** Antiepileptic.

**Description.** A white to yellowish white powder.

### Identification

A. Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *perampanel* IPRS or with the reference spectrum of perampanel.

B. In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with reference solution (b).

### Tests

**Related substances.** Determine by liquid chromatography (2.4.14).

**Solvent mixture.** 40 volumes of *acetonitrile* and 60 volumes of *water*.

**Test solution.** Dissolve 100 mg of the substance under examination in the mobile phase B and dilute to 50.0 ml with the mobile phase B. Dilute 1.0 ml of the solution to 10.0 ml with the solvent mixture.

**Reference solution (a).** A 0.2 per cent w/v solution of *perampanel* IPRS in mobile phase B.

**Reference solution (b).** Dilute 1.0 ml of reference solution (a) to 10.0 ml with the solvent mixture.

**Reference solution (c).** Dilute 1.0 ml of reference solution (b) to 100.0 ml with the solvent mixture.

**Reference solution (d).** A 0.01 per cent w/v solution of *perampanel* impurity F IPRS (*methyl 2-(2-oxo-1-phenyl-5-pyridin-2-yl-1,2-dihydropyridin-3-yl)benzoate*) in mobile phase B. Transfer 1.0 ml of the solution to a 50-ml volumetric

