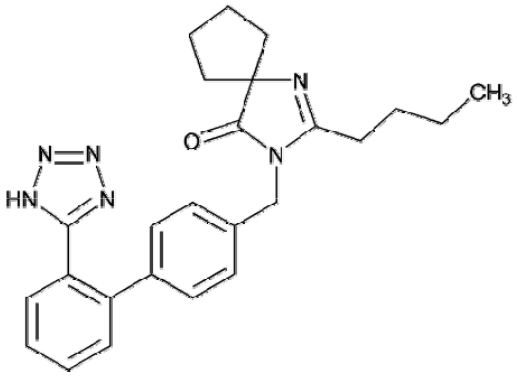
# Irbesartan

## USP Method Irbesartan Assay




**Original Manufacturer:** Sanofi-Aventis (patent expire March 2012)

**Original Brand Name:** Avapro, Aprovel, Karvea

**Combination Drugs:** Irda, CoIrda, CoAprovel, Karvezide, Avalide, Avapro HCT (Irbesartan and Hydrochlorothiazide)

Irbesartan is an angiotensin II receptor antagonist used mainly for the treatment of hypertension. It is jointly marketed by Sanofi-Aventis and Bristol-Myers Squibb.

Irbesartan is also available in a combination formulation with a low dose thiazide diuretic, invariably hydrochlorothiazide, to achieve an additive antihypertensive effect.

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# Irbesartan

## USP34 – NF29 S1

### USP Columns:

Nucleosil C18 Assay and Related Compounds 4.0 mm x 25 cm, 7 µm, Macherey-Nagel.

### Equivalent Column:

Purospher®STAR RP-18 endcapped (5 µm) 250x4.0 mm (1.50252.0001)

### Optional Scaled Column 1:

Purospher®STAR RP-18 endcapped (5 µm) 250x3.0 mm (1.50254.0001)

### Optional Scaled Column 2:

Purospher®STAR RP-18 endcapped (3 µm) 125x3.0 mm (1.50175.0001)

### Recommended Solvents and Reagents:

**Methanol** for liquid chromatography LiChrosolv® (1.06018)

**Acetonitrile** isocratic grade for liquid chromatography LiChrosolv® (1.14291)

**Water** Water for chromatography LiChrosolv® (1.15333)
or freshly purified water from Milli-Q water purification system

**Triethylamine** Use a suitable grade with a content of not less than 99.5%. (8.45061)
**Phosphoric Acid** Use ACS reagent grade

### USP Standards

| | | |
|---|---|---|
| Irbesartan (200 mg) | USP Product Number: | 1347700 |
| Irbesartan Related Compound A (25 mg) | USP Product Number: | 1347711 |

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# USP Method Irbesartan Assay

## pH 3.2 Phosphate buffer
Mix 5.5 mL of phosphoric acid with about 950 mL of water, and adjust pH to 3.2 with triethylamine.

## Mobile phase
Prepare a filtered and degassed mixture of pH 3.2 phosphate buffer and acetonitrile (67:33).
Make adjustments if necessary (*see System Suitability under Chromatography 621*).

## System suitability solution
Dissolve accurately weighed quantities of USP Irbesartan RS and USP Irbesartan Related Compound A RS in methanol to obtain a solution having a known concentration of about 0.05 mg per mL of each USP Reference Standard.

## Standard preparation
Dissolve an accurately weighed quantity of USP Irbesartan RS in methanol to obtain a solution having a known concentration of about 0.5 mg per mL.

## Assay preparation
Transfer about 50 mg of Irbesartan, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with methanol to volume, and mix.

## Chromatographic system (*see Chromatography 621*)
The liquid chromatograph is equipped with a 220-nm detector and a 4.0-mm × 25-cm column that contains packing L1. The flow rate is about 1.0 mL per minute. Chromatograph the System suitability solution, and record the peak responses as directed for Procedure:

the relative retention times are about 0.8 for Irbesartan related compound A and 1.0 for Irbesartan
the resolution, R, between Irbesartan and Irbesartan related compound A is not less than 2.0.

Chromatograph the Standard preparation, and record the peak response as directed for Procedure: the standard deviation for replicate injections is not more than 1.0%.

## Procedure
Separately inject equal volumes (about 10 µL) of the Standard preparation and the Assay preparation into the chromatograph, record the chromatograms, and measure the responses for all the peaks. Calculate the quantity, in mg, of $C_{25}H_{28}N_6O$ in the portion of Irbesartan taken by the formula:

$100C(r_U/r_S)$

in which C is the concentration, in mg per mL, of USP Irbesartan RS in the Standard preparation; and $r_U$ and $r_S$ are the peak responses obtained from the Assay preparation and the Standard preparation, respectively.

# USP Method Irbesartan RS

## pH 3.2 Phosphate buffer and Mobile phase (*Proceed as directed in the Assay.*)

## Standard solution
Prepare as directed for the System suitability solution in the Assay.

## Test solution
Dissolve an accurately weighed quantity of Irbesartan in methanol to obtain a solution having a known concentration of about 1 mg per mL.

## Chromatographic system *(see Chromatography 621)*
Proceed as directed in the Assay. Chromatograph the Standard solution and record the peak responses as directed for Procedure: the relative standard deviation for replicate injections is not more than 2.0%.

## Procedure
Separately inject equal volumes (about 10 µL) of the Standard solution and the Test solution into the chromatograph, record the chromatograms, and measure the area for the Irbesartan related compound A peak. Calculate the percentage of Irbesartan related compound A in the portion of Irbesartan taken by the formula:

$$100(C_S/C_T)(r_U/r_S)$$

in which $C_S$ is the concentration, in mg per mL, of USP Irbesartan Related Compound A RS in the Standard solution; $C_T$ is the concentration, in mg per mL, of Irbesartan in the Test solution; $r_U$ is the peak response for Irbesartan related compound A obtained from the Test solution; and $r_S$ is the peak response for Irbesartan related compound A obtained from the Standard solution.

Calculate the percentage of other impurities in the portion of Irbesartan taken by the formula:

$$100(C_S/C_T)(r_U/r_S)$$

in which $C_S$ is the concentration, in mg per mL, of USP Irbesartan RS in the Standard solution; $C_T$ is the concentration, in mg per mL, of Irbesartan in the Test solution; and $r_U$ and $r_S$ are the peak responses for each of the other impurities and USP Irbesartan RS obtained from the Test solution and the Standard solution, respectively:

- not more than 0.2% of Irbesartan related compound A is found
- not more than 0.1% of any other impurity is found
- not more than 0.5% of total impurities is found

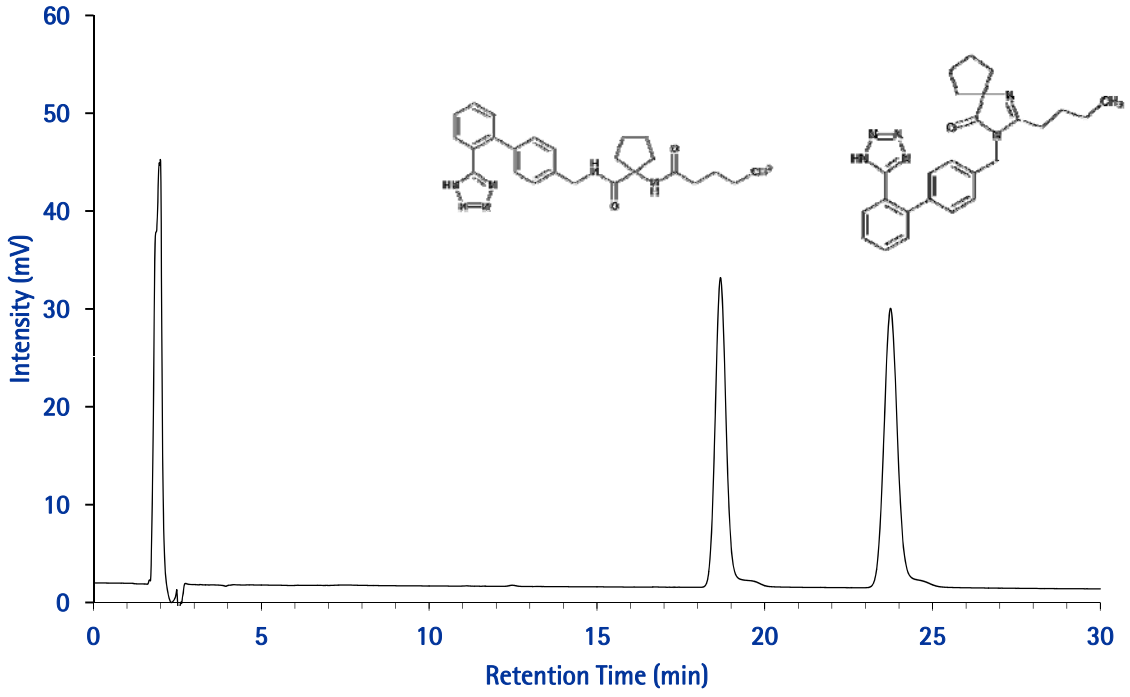
HPLC Application note 2034
*USP Method Irbesartan Assay – scaled to narrow id column*

# USP Method for Irbesartan Assay

## Purospher®STAR RP-18 endcapped

### Chromatographic Conditions

| | | |
|---|---|---|
| Column: | Purospher®STAR RP-18 endcapped (5 µm) 250x3.0 mm | 1.50254.0001 |
| Injection: | 6 µL | |
| Detection: | Shimadzu Prominence 2010, UV 220 nm | |
| Cell: | semi-micro cell 2.5 µL | |
| Flow Rate: | 0.6 mL/min | |
| Mobile Phase (v/v): | Buffer: Mix 5.5 mL of phosphoric acid with about 950 mL of water, and adjust pH to 3.2 with triethylamine. Prepare a filtered and degassed mixture of pH 3.2 phosphate buffer and acetonitrile (67:33). | |
| Temperature: | Ambient | |
| Diluent | Methanol | |
| Sample: | 50 ppm (0.05 mg/mL) of each Irbesartan and Irbesartan RS A (SST solution) | |
| Pressure Drop: | 184 Bar (2650 psi) | |




### Chromatographic Data

| No. | Compound | Time (min) | Resolution | Relative Retention Time (RRT) | Tailing Factor ($T_{USP}$) |
|---|---|---|---|---|---|
| 1 | Irbesartan RS A | 18.7 | - | 0.8 | 1.12 |
| 2 | Irbesartan | 23.7 | 7.6 | 1.0 | 1.13 |

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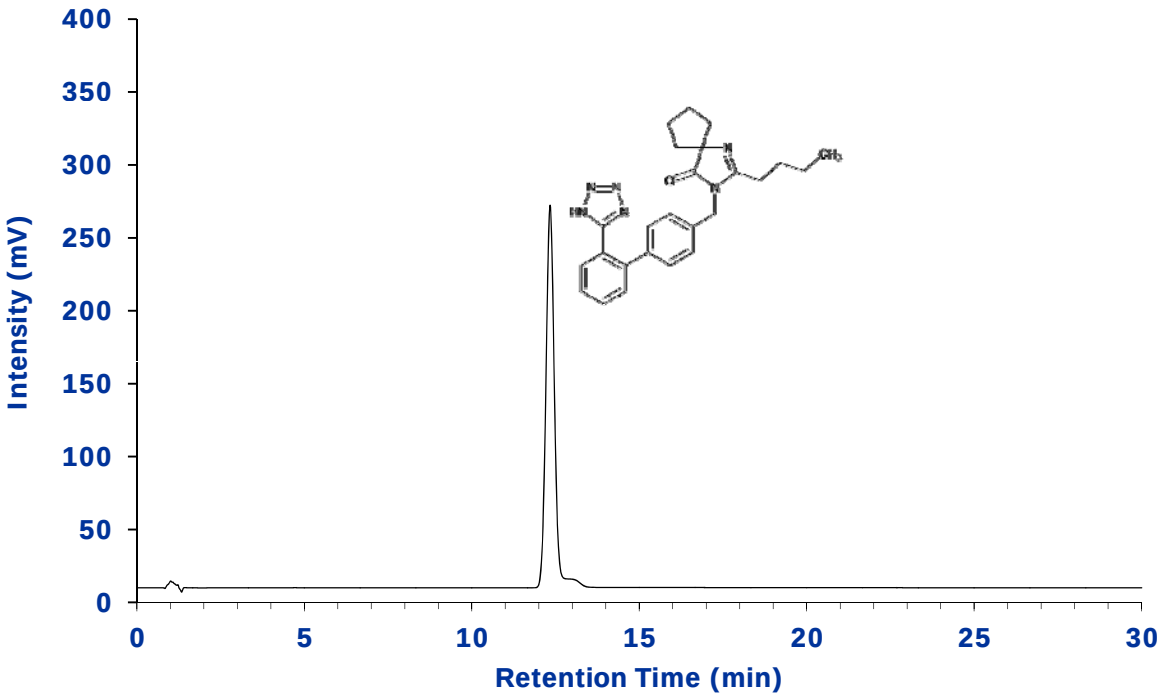
# USP Method for Irbesartan Assay

## Purospher®STAR RP-18 endcapped

### Chromatographic Conditions

| | | |
|---|---|---|
| Column: | Purospher®STAR RP-18 endcapped (3 µm) 125x3.0 mm | 1.50175.0001 |
| Injection: | 3 µL | |
| Detection: | Shimadzu Prominence 2010, UV 220 nm | |
| Cell: | semi-micro cell 2.5 µL | |
| Flow Rate: | 0.6 mL/min | |
| Mobile Phase (v/v): | Buffer: Mix 5.5 mL of phosphoric acid with about 950 mL of water, and adjust pH to 3.2 with triethylamine. Prepare a filtered and degassed mixture of pH 3.2 phosphate buffer and acetonitrile (67:33). | |
| Temperature: | Ambient | |
| Diluent | methanol | |
| Sample: | 500 ppm (0.05 mg/mL) of Irbesartan (Assay solution) | |
| Pressure Drop: | 204 Bar (2938 psi) | |




### Chromatographic Data

| No. | Compound | Time (min) | Resolution | Relative Retention Time (RRT) | Tailing Factor ($T_{USP}$) |
|---|---|---|---|---|---|
| 1 | Irbesartan RS A | - | - | - | - |
| 2 | Irbesartan | 12.3 | - | 1.0 | 1.08 |

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