Technical Information

November 2015
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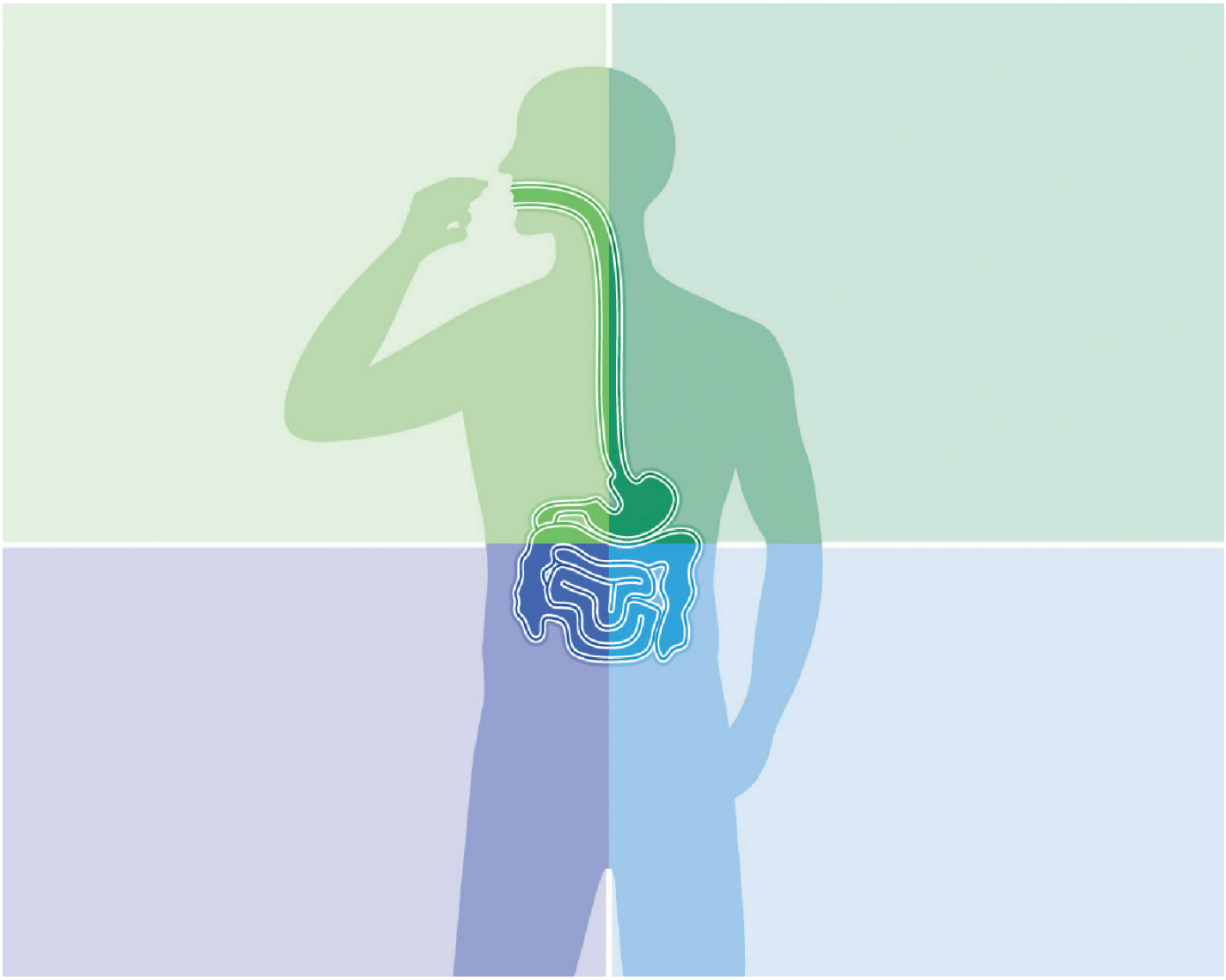
Kollicoat® IR

® = Registered trademark of BASF in many countries.

Ethylene Glycol and Vinyl Alcohol Graft Copolymer for instant-release coatings and for use as wet-binder



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Contents

1. Introduction

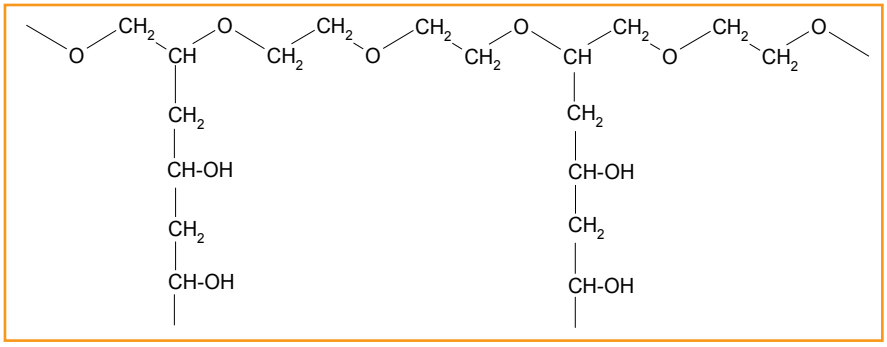
1.1 General

Kollicoat® IR is a polyethylene glycol- polyvinyl alcohol graft copolymer that is very readily soluble in water. It iwas initially designed for the application as a polymer for instant-release coating of tablets but in addition to that proofed its functionality as wet binder, too.

Due to its property not to form peroxides Kollicaot® IR can be posititioned as wet-binder for oxygen-sensitve API solid dosage which is superior to binder polymers of other chemistry.

When tested even under accelerated storage conditions in stabililty testing Kollicoat® IR in contrast to some of these standard wet-binder polymers does not form detectable levels of peroxides.

1.2 Structural formula



1.3 Physical form

Kollicoat® IR is a white to faintly yellow, free-flowing, spray-dried powder.

2. Specification and properties

2.1 Chemical nature

The polymer consists of 75% polyvinyl alcohol units and 25% polyethylene glycol units. The product also contains approx. 0.3% colloidal silica to improve its flow properties.

2.2 Physicochemical properties

In contrast to polyvinyl alcohol, the polymer dissolves very fast in acidic, neutral and alkaline aqueous media. Aqueous solutions have a comparatively low viscosity.

Molecular weight

approx. 45,000 AMU

Solubility

Solutions of Kollicoat® IR with concentrations of up to 40% can be prepared in water and aqueous systems, e.g. weak acids or alkalis. Solutions of up to 25% can be prepared in a 1:1 ethanol-water mixture.

The polymer is insoluble in organic solvents.

Viscosity

The viscosity of a 20% solution is determined according to EN ISO 2555 at 23°C and a shear rate of 100 rpm.

Film formation

An aqueous solution is cast onto a smooth surface. When the water has evaporated, a clear, colourless, flexible film remains.

Microbial status

See specification limits

2.3 Specification

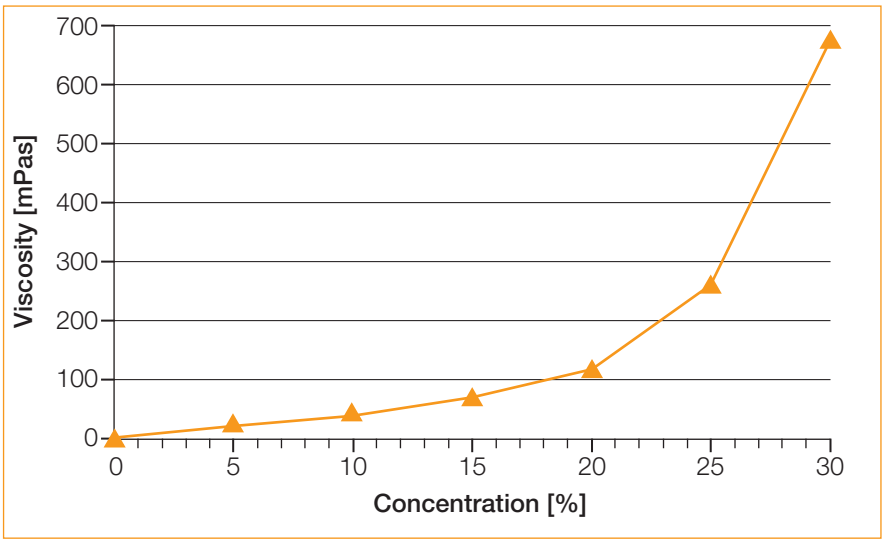
See separate document: “Standard Specification (not for regulatory purposes)“ available via BASF’s WorldAccount: https://worldaccount.basf.com (registered access).

2.4 Properties of aqueous solutions

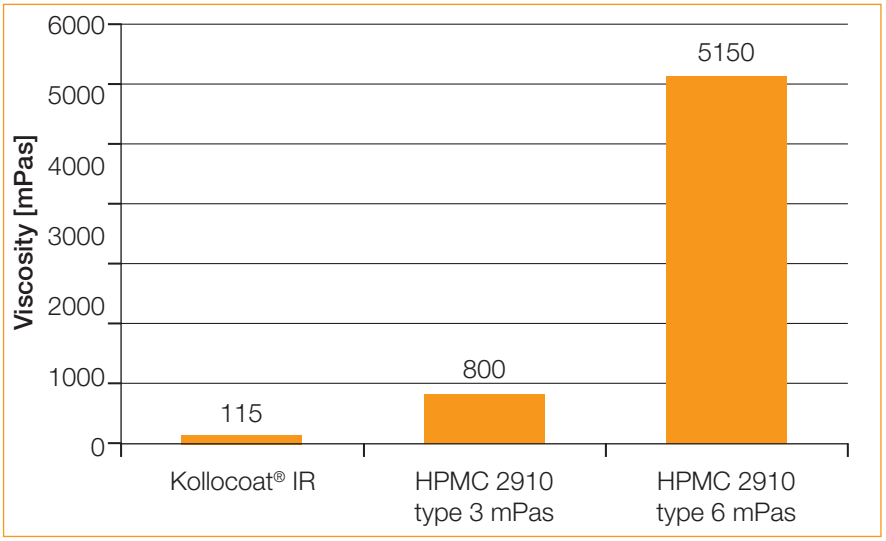
Viscosity

Kollicoat® IR dissolves rapidly in water. It is though the viscosity of aqueous solutions of Kollicoat® IR increases with the polymer concentration, however remains much lower than that of equivalent solutions of, for instance, cellulose derivatives.

Viscosity of aqueous Kollicoat® IR solutions as a function of polymer concentration:



Viscosity of polymer solutions (20% w/w):



Surface Tension

Kollicoat® IR reduces the surface tension of water. This makes aqueous solutions easy to spray, and the spray droplets exhibit good wetting behavior on the tablet surface.

2.5 Peroxide Formation

Peroxide levels, expressed in meq/kg, are at levels below the detection limit of 1 meq/kg. Even when stored under accelerated storage conditions at 40 °C/ 75% r.h. the peroxide levels do not exeed 1 meq/kg after 30 months.

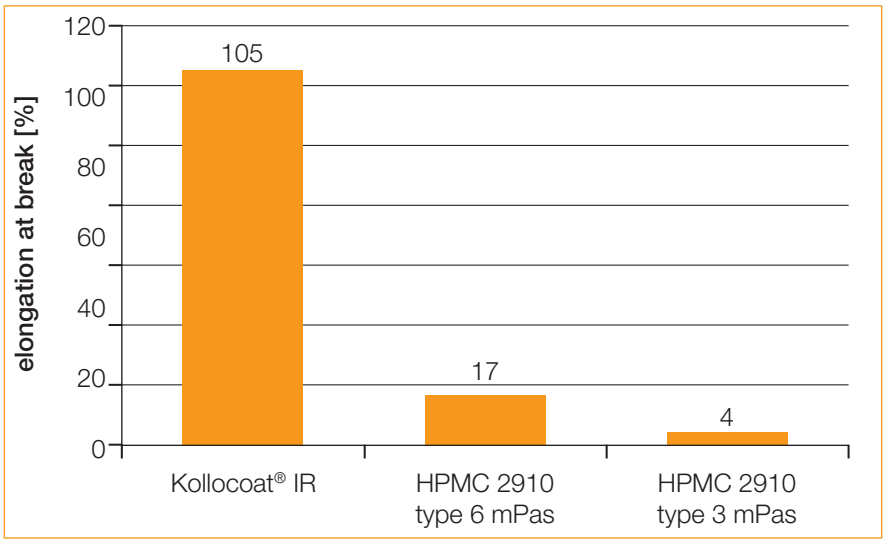
Months at 40°C/75% r.h.	Peroxide level, meq/kg*
0 month	<1
3 months	< 1
6 months	< 1
12 months	1
18 months	1
30 months	1

2.6 Film properties

Kollicoat® IR forms clear, colorless films that are enormously flexible and dissolve very rapidly in water. Kollicoat IR films are not tacky, have a high pigment binding capacity and can easily be imprinted.

Kollicoat® IR has a much higher elongation at break than cellulose derivatives.

Elongation at break of various instant release polymers (54% r. h.)



2.7 Properties as wet-binder

The low viscosity allows even concentrated aqueous solutions to be applied in standard wet-granution equipment such as high-shear blenders or fluid-bed granulators. Alternatively powder blends containing Kollicoat® IR can be granulated using water as solvent for the binder.

3. Processing and Application in Film-Coatings

3.1 Applications

Kollicoat® IR can be used for all applications for which a water-soluble flexible polymer is required.

- **Instant release coating**
  - Improves appearance, makes tablets easier to swallow, gives a distinctive appearance, protects sensitive active ingredients and protects against unpleasant taste or odour.
- **Pore former in sustained-release coatings**
  - To control drug release rate
- **Film former in sprays and transdermal therapeutic systems**
- **Suspension and emulsion stabiliser**
- **Protective colloid**

The special advantages of Kollicoat® IR are reflected in its enormous flexibility, low viscosity and fast dissolution.

Kollicoat® IR solutions for spraying onto tablets can be applied with a high solids content, which greatly reduces the coating time and minimises costs.

3.2 Processing notes

Because of the high flexibility of Kollicoat® IR films, it is not necessary to add a plasticiser.

A spray suspension is best prepared as follows:

Dissolve Kollicoat® IR in water and stir in the previously homogenised pigment suspension. The other water-soluble ingredients can be dissolved together with the Kollicoat® IR. The speed of the stirrer should be set such that little or no foam is produced.

As spray suspensions of Kollicoat® IR have a lower viscosity than those of other instant release polymers, they can have a much higher concentration. This greatly shortens the spraying and processing time in the manufacture of film-coated tablets. Polymer concentrations of 15 – 25% can be used, giving a total solids concentration of 20 – 35%, depending on the quantity of pigments.

Since Kollicoat® IR has surfactant properties and can act as a protective colloid, it prevents the aggregation of the pigment particles and ensures that the pigment is evenly distributed over the tablet core.

The great elasticity of Kollicoat® IR ensures that it does not crack on the tablets when they are exposed to different humidity conditions in storage, even when the cores contain powerful swelling agents such as HPMC, xanthan or alginate which are frequently used in sustained release tablets.

The coating can be applied in all the usual coaters. e.g. horizontal drum coaters, fluidised bed coaters, immersion sword coaters, and coating pans under the usual conditions for aqueous solutions.

The following conditions have been used successfully in numerous trials:

Inlet air temperature:	60 – 80 °C
Outlet air temperature:	30 – 50 °C
Atomizing pressure:	3 – 6 bar

The product can very easily be cleaned off the equipment with warm or cold water.

4. Typical formulations for Instant Release Coating

4.1 Propranolol instant-release film-coated tablets

Composition of the tablets

40 mg propranolol HCl; 97.5 mg Ludipress®; 12.5 mg Kollidon® VA 64; 2.5 mg magnesium stearate; 97.5 mg Avicel PH 102

Composition of the spray suspension

The formulation is designed for 250 kg of tablets (tablet weight 250 mg; diameter 9 mm)

	Weight [g]	Proportion [%]
Polymer solution		
Kollicoat® IR	6.080	16.0
Water	24.320	64.0
Pigment suspension		
Talc	1.710	4.5
Titanium dioxide	1.140	3.0
Sicovit Red 30	570	1.5
Water	4.180	11.0
	38.000	**100.0**

Preparation of the spray suspension

Polymer solution:

Stir the Kollicoat® IR into the specified quantity of water until it has dissolved.

Pigment suspension:

Vigorously stir talc, Sicovit Red 30 and titanium dioxide into the specified quantity of water and homogenise in a carborundum disk mill.

Spray suspension:

Stir the pigment suspension into the polymer solution. To avoid sedimentation during the spraying process, the mixture must be continuously stirred.

Machine parameters

Coating equipment	Driacoater type 900, perforated drum coater
Batch size	250 kg
Inlet air temperature	70 °C
Outlet air temperature	48 °C
Product temperature	50 °C
Air flow	4400 m^3/h
Atomizing pressure	6 bar
Number of spray nozzles	6
Spraying rate	700 g/min
Spraying time	55 min
Final drying	60 °C/5 min
Quantity applied	3.8%

Tablet properties

	Core	Film-coated tablet
Appearance	White	Red
Hardness	93 N	109 N
Friability	0%	0%
Disintegration time	5:53 [min:s]	5:47 [min:s]
Drug release	10 min: 49% 20 min: 98%	10 min: 54% 20 min: 99%

4.2 Caffeine instant-release tablets

Composition of the tablets

50 mg caffeine; 229 mg Ludipress®; 10 mg Kollidon® CL;
1 mg magnesium stearate; 40 mg Avicel PH 101

Composition of the spray solution

The formulation is designed for 5 kg of tablets (weight 330 mg; diameter 9 mm)

	Weight [g]	Proportion [%]
Polymer solution		
Kollicoat® IR	108.2	20.8
Water	286.0	55.0
Pigment suspension		
Talc	40.0	7.7
Titanium dioxide	20.8	4.0
Water	65.0	12.5
	520.0	**100**

Preparation of the spray suspension

Polymer solution:
Stir the Kollicoat® IR into the specified quantity of water until it has dissolved.

Pigment suspension:
Vigorously stir talc and titanium dioxide into the specified quantity of water and homogenise in a carborundum disk mill.

Spray suspension:
Stir the pigment suspension into the polymer solution. To avoid sedimentation during the spraying process, the mixture must be continuously stirred.

Machine parameters

Coater	Accela-Cota 24“, perforated drum coater
Batch size	5 kg
Inlet air temperature	60 °C
Outlet air temperature	39 °C
Product temperature	35 °C
Air flow	180 m^3/h
Atomizing pressure	3 bar
Number of spray nozzles	1
Spraying rate	30 g/min
Spraying time	18 min
Final drying	60 °C/4 min
Quantity applied	3 mg/cm^2 polymer

Tablet properties

	Uncoated Core	Film-coated tablet
Appearance	White	White
Hardness	116 N	119 N
Friability	0%	0%
Disintegration time	0:58 [min:s]	0:51 [min:s]
Drug release	10 min: 93% 20 min: 98%	10 min: 92% 20 min: 98%

5. Processing and Application as Wet-Binder

5.1 Applications

Kollicoat® IR can be used for all applications for which a water-soluble binder polymer is required .

The special advantages of Kollicoat IR when used as wet-binder next to its low viscosity, fast dissolution and high binding power in granulation processes is its property that no peroxides become detectale. Due to this propertiy even very oxygen sensitive APIs such as hormones can be formulated with Kollicoat® IR in wet binder applications.

5.2 Processing Notes

Standard equipment such as high-shear mixer or fluid-bed granulators can be applied.

Kollicoat® IR can be incorporated into formulations in two ways.

Either the blended components are granulated using a Kollicoat® IR binder solution of appropriate concentration in order to achieve binder concentrations of 3% to 10%.

Alternatively water can be used as granulation fluid in cases where the polymer is already part of the tableting mixture.

6. Typical Applications as Wet-Binder

6.1 Acetaminophen instant granules

Composition of the powder mixture

49% acetaminophen, fine powder; 49% sorbitol; 2% aspartame; 0.06% aroma

Composition of the binder solution

The formulation is designed for 1 kg of powder mixture

	Weight [g]	Proportion [%]
Granulating solution		
Kollicoat® IR	27.0	15.0
Water	153.0	85.0
	180.0	**100.0**

Preparation of the binder solution

Kollicoat® IR is dissolved in the specified quantity of water under thorough stirring.

Manufacture of the granules

Mix the components of the powder mixture for 10 min using a Stephan mixer Type UMC 5 Electronic.

Apply the Kollicoat ®IR solution in a fine spray, keeping the mixture in motion. First the moist mass is passed through a 3-mm sieve, then through a 1-mm sieve.

Dry the moist granules and repass them through a 1-mm sieve.

Properties of the granules

The granules dissolve in water within 1 min.

6.2 Instant-release Ibuprofen tablets : 600mg/tablet

Composition of the powder mixture

	Weight [g]	Proportion [%]
Ibuprofen	700.0	100.0

Composition of the binder solution

	Weight [g]	Proportion [%]
Kollicoat® IR	35.0	18.9
Water	150.0	81.1
Weight	185.0	100.0

The binder solution is suited for 0.7 kg of Ibuprofen 25

Manufacture of the granules

The granulation is performed in a Diosna P1/6 with a 3L Container. The Ibuprofen is mixed for 3 min, the granulation fluid is dosed within 2 minutes. After dosing the binder solution the granulation is performed for additionally 3 minutes with a stirrer speed fo 250 rpm and the chopper set to 2,200 rpm.

Wet Sieving	Glatt GS 100 screen	1.500 µm sieve grater screen 500 rpm with mixer insert # 6
Drying	The granules were dried in a Glatt GPCG 3 at 50 °C in a 5 L container at an air rate of 66 m³/h. Drying time: 16 min	

Tableting mixture

Ibuprofen granules	79.50%
Avicel PH-102	15.00%
Aerosil 200	1.00%
Ac-Di-Sol	4.00%
Mg-Stearat	0.50%

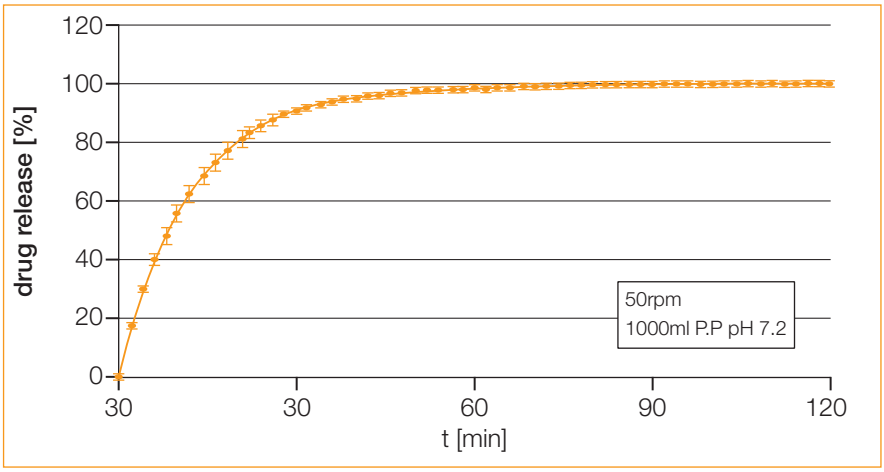
The components except the Mg-stearate were mixed in a Turbala mixer for 5 minutes and sieved using a 800 µm sieve. Finally the Mg-stearate was added and the blend again Turbula-mixed for 1 minute.

This tableting mixture was compressed on a Korsch XL 100.

Tableting Parameters

Weight	802 mg
Formate	footballshaped 9.00*8.50
Speed	20 rpm
Compression force	10 kN

Release testing for tablets with 5% Kollicoat® IR as binder and compressed with 10kN



6.3 Instant-release Raloxifen-HCl tablets: 300mg

Composition of the powder mixture

	Weight [g]	Proportion [%]
Raloxifen-HCl	300.0	31.9
Di-calcium phosphate	640.0	64.9
Aerosil 200	20.0	2.1
Mg-Stearate	10.0	1.1
	970.0	**100**

Composition of the binder solution

The formulation is designed for 0.97 kg of powder mixture

	Weight [g]	Proportion [%]
Granulating solution		
Kollicoat® IR	30.0	17.1
Water	145.0	82.9
	175.0	**100.0**

Preparation of the binder solution

Kollicoat IR is dissolved in the specified quantity of water under thorough stirring.

Manufacture of the granules

Mix the components of the powder mixture for 10 min (Stephan mixer Type UMC 5 Electronic).

Apply the Kollicoat IR solution in a fine spray, keeping the mixture in motion. The moist mass is passed through a 800 µm sieve. The moist granules are dried in a vaccum-dryer to a final water content of around 1 – 1.2%.

Tableting Parameters

Karnavati (India) 8 station rotary press

Tablet diameter	mm	7
Tablet shape		circular, concave
Compression force	kg	900
Hardness	N	150
Friability	%	<0.05

Stability Testing

When stored under accelerated conditions at 45 °C, 75% r.h. the degradation product raloxifen-N-oxide could not be detected after 6 months.

7. Storage conditions

Below 30 °C.

8. Stability

At least 2 years in the original sealed containers at room temperature.

9. Toxicology

Comprehensive toxicological studies are compiled in a Tox-Abstract
Individual reports are available on request and can be provided under CDA.

10. Product Number

PRD: 30132288
ART: 55554797

11. Packaging

PE-drum, 20 kg capacity with sealed, 0.100 mm PE-inner liner.

Disclaimer

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