Croscarmellose Sodium

1 Nonproprietary Names
BP: Croscarmellose Sodium
JP: Croscarmellose Sodium
PhEur: Croscarmellose Sodium
USP-NF: Croscarmellose Sodium

2 Synonyms
Ac-Di-Sol; carmellosum natricum conexum; crosslinked carboxymethylcellulose sodium; Explocel; modified cellulose gum; Nymcel ZSX; Pharmacel XL; Primellose; Solutab; Vivasol.

3 Chemical Name and CAS Registry Number
Cellulose, carboxymethyl ether, sodium salt, crosslinked [74811-65-7]

4 Empirical Formula and Molecular Weight
Croscarmellose sodium is a crosslinked polymer of carboxymethylcellulose sodium.
See Carboxymethylcellulose sodium.

5 Structural Formula
See Carboxymethylcellulose sodium.

6 Functional Category
Tablet and capsule disintegrant.

7 Applications in Pharmaceutical Formulation or Technology
Croscarmellose sodium is used in oral pharmaceutical formulations as a disintegrant for capsules,[1,2] tablets,[3–13] and granules.
In tablet formulations, croscarmellose sodium may be used in both direct-compression and wet-granulation processes. When used in wet granulations, the croscarmellose sodium should be added in both the wet and dry stages of the process (intra- and extra-granularly) so that the wicking and swelling ability of the disintegrant is best utilized.[11,12] Croscarmellose sodium at concentrations up to 5% w/w may be used as a tablet disintegrant, although normally 2% w/w is used in tablets prepared by direct compression and 3% w/w in tablets prepared by a wet-granulation process. See Table I.

<table>
<thead>
<tr>
<th>Use</th>
<th>Concentration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disintegrant in capsules</td>
<td>10–25</td>
</tr>
<tr>
<td>Disintegrant in tablets</td>
<td>0.5–5.0</td>
</tr>
</tbody>
</table>

8 Description
Croscarmellose sodium occurs as an odorless, white or grayish-white powder.

9 Pharmacopeial Specifications
See Table II. See also Section 18.

10 Typical Properties
Acidity/alkalinity p H = 5.0–7.0 in aqueous dispersions.
Bonding index 0.0456
Brittle fracture index 0.1000
Density (bulk) 0.529 g/cm³ for Ac-Di-Sol
11 Stability and Storage Conditions

Croscarmellose sodium is a stable though hygroscopic material.

A model tablet formulation prepared by direct compression, with croscarmellose sodium as a disintegrant, showed no significant difference in drug dissolution after storage at 30°C for 14 months.\(^{(9)}\)

Croscarmellose sodium should be stored in a well-closed container in a cool, dry place.

12 Incompatibilities

The efficacy of disintegrants, such as croscarmellose sodium, may be slightly reduced in tablet formulations prepared by either the wet-granulation or direct-compression process that contain hygroscopic excipients such as sorbitol.\(^{(10)}\)

Croscarmellose sodium is not compatible with strong acids or with soluble salts of iron and some other metals such as aluminum, mercuric, and zinc.

13 Method of Manufacture

Alkali cellulose is prepared by steeping cellulose, obtained from wood pulp or cotton fibers, in sodium hydroxide solution. The alkali cellulose is then reacted with sodium monochloroacetate to obtain carboxymethylcellulose sodium. After the substitution reaction is completed and all of the sodium hydroxide has been used, the excess sodium monochloroacetate slowly hydrolyzes to glycolic acid. The glycolic acid changes a few of the sodium carboxymethyl groups to the free acid and catalyzes the formation of crosslinks to produce croscarmellose sodium. The croscarmellose sodium is then extracted with aqueous alcohol and any remaining sodium chloride or sodium glycolate is removed. After purification, croscarmellose sodium of purity greater than 99.5% is obtained.\(^{(4)}\)

The croscarmellose sodium may be milled to break the polymer fibers into shorter lengths and hence improve its flow properties.

14 Safety

Croscarmellose sodium is mainly used as a disintegrant in oral pharmaceutical formulations and is generally regarded as an essentially nontoxic and nonirritant material. However, oral consumption of large amounts of croscarmellose sodium may have a laxative effect, although the quantities used in solid dosage formulations are unlikely to cause such problems.

In the UK, croscarmellose sodium is accepted for use in dietary supplements.

The WHO has not specified an acceptable daily intake for the related substance carboxymethylcellulose sodium, used as a food additive, since the levels necessary to achieve a desired effect were not considered sufficient to be a hazard to health.\(^{(14)}\)

See also Carboxymethylcellulose Sodium.

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Croscarmellose sodium may be irritant to the eyes; eye protection is recommended.

16 Regulatory Status

Included in the FDA Inactive Ingredients Database (oral capsules, granules, sublingual tablets, and tablets). Included in nonparenteral medicines licensed in the UK. Included in the Canadian List of Acceptable Non-medicinal Ingredients.

17 Related Substances

Carboxymethylcellulose calcium; carboxymethylcellulose sodium.

18 Comments

Croscarmellose sodium is one of the materials that have been selected for harmonization by the Pharmacopeial Discussion Group. For further information see the General Information Chapter \(<1196>\) in the USP32–NF27, the General Chapter 5.8 in PhEur 6.0, along with the ‘State of Work’ document on the PhEur EDQM website, and also the General Information Chapter 8 in the JP XV.

Typically, the degree of substitution (DS) for croscarmellose sodium is 0.7.

The EINECs number for croscarmellose sodium is 232-674-9.

19 Specific References

Crospovidone

1 Nonproprietary Names
BP: Crospovidone
PhEur: Crospovidone
USP-NF: Crospovidone

2 Synonyms
Crospovidonum; Crospopharm; crosslinked povidone; E1202; Kollidon CL; Kollidon CL-M; Polyplasdone XL; Polyplasdone XL-10; polyvinylpolypyrrolidone; PVPP; 1-vinyl-2-pyrrolidinone homopolymer.

3 Chemical Name and CAS Registry Number
1-Ethenyl-2-pyrrolidinone homopolymer [9003-39-8]

4 Empirical Formula and Molecular Weight
\((\text{C}_6\text{H}_9\text{NO})_n\)  >1 000 000

The USP32–NF27 describes crospovidone as a water-insoluble synthetic crosslinked homopolymer of N-vinyl-2-pyrrolidinone. An exact determination of the molecular weight has not been established because of the insolubility of the material.

5 Structural Formula
See Povidone.

6 Functional Category
Tablet disintegrant.

7 Applications in Pharmaceutical Formulation or Technology
Crospovidone is a water-insoluble tablet disintegrant and dissolution agent used at 2–5% concentration in tablets prepared by direct-compression or wet- and dry-granulation methods.\(^1\)–\(^6\) It rapidly exhibits high capillary activity and pronounced hydration capacity, with little tendency to form gels. Studies suggest that the particle size of crospovidone strongly influences disintegration of analgesic tablets.\(^7\) Larger particles provide a faster disintegration than smaller particles. Crospovidone can also be used as a solubility enhancer. With the technique of co-evaporation, crospovidone can be used to enhance the solubility of poorly soluble drugs. The drug is adsorbed on to crospovidone in the presence of a suitable solvent and the solvent is then evaporated. This technique results in faster dissolution rate.

8 Description
Crospovidone is a white to creamy-white, finely divided, free-flowing, practically tasteless, odorless or nearly odorless, hygroscopic powder.

9 Pharmacopeial Specifications
See Table I. See also Section 18.

10 Typical Properties
Acidity/alkalinity  \(\text{pH} = 5.0–8.0\) (1% w/v aqueous slurry)
Density  1.22 g/cm\(^3\)
Density (bulk)  see Table II.
Density (tapped)  see Table II.

20 General References

21 Author
RT Guest.

22 Date of Revision
6 February 2009.