

Annex I

**Scientific conclusions and grounds for the variation to the terms of the
Marketing Authorisation(s)**

Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for polystyrene sulfonate, the scientific conclusions are as follows:

In view of available data on gastrointestinal serious reactions from the literature and spontaneous reports including cases where the gastrointestinal damage was accompanied by presence of polystyrene sulfonate crystals in biopsy samples, the PRAC considers a causal relationship between polystyrene sulfonate administered without sorbitol and gastrointestinal stenosis and ischaemia is at least a reasonable possibility. The PRAC concluded that the product information of products containing polystyrene sulfonate should be amended accordingly.

The CMDh agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the Marketing Authorisation(s)

On the basis of the scientific conclusions for polystyrene sulfonate the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing polystyrene sulfonate is unchanged subject to the proposed changes to the product information.

The CMDh reaches the position that the marketing authorisation(s) of products in the scope of this single PSUR assessment should be varied. To the extent that additional medicinal products containing polystyrene sulfonate are currently authorised in the EU or are subject to future authorisation procedures in the EU, the CMDh recommends that the concerned Member States and applicant/marketing authorisation holders take due consideration of this CMDh position.

Annex II

**Amendments to the product information of the nationally authorised
medicinal product(s)**

Amendments to be included in the relevant sections of the Product Information (new text **underlined and in bold**, deleted text ~~strike through~~). The term "calcium" or "sodium" should be selected according to medicinal product composition.

Summary of Product Characteristics

- Section 4.4

~~Sorbitol:~~ **Gastrointestinal stenosis and ischaemia**

Gastrointestinal stenosis, intestinal ischemia and its complications (necrosis and perforation), **some of them fatal, were reported** in patients treated with polystyrene sulfonate **alone or in combination with**, especially in patients using sorbitol. Therefore, **Concomitant use of sorbitol with polystyrene sulfonate is not recommended. See 4.5**

Patients should be advised to seek prompt medical advice in case of newly developed severe abdominal pain, nausea and vomiting, stomach distension and rectal bleeding

Lesions seen in polystyrene sulfonate-induced gastrointestinal damage may overlap with those seen in inflammatory bowel disease, ischemic colitis, infectious colitis, and microscopic colitis.

- Section 4.8

Gastrointestinal ischemia, ischemic colitis, gastro-intestinal tract ulceration or necrosis which could lead to intestinal perforation have been reported which is sometimes fatal. ~~Most cases have been reported with concomitant use of sorbitol.~~

Package Leaflet

Package leaflet should include at least following minimum information, information that gastrointestinal ischaemia and stenosis were observed mostly with concomitantly administered sorbitol should be deleted.

4. Possible side effects

Talk to your doctor or nurse straight away if you notice any of the following serious side effects

- **Severe stomach pain, rectal pain**
- **Bloating, severe constipation**
- **Severe nausea and vomiting**
- **Black, bloody or tarry stools, coughing up blood or vomit that looks like coffee grounds.**

Annex III

Timetable for the implementation of this position

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Adoption of CMDh position:	June 2021 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position :	08 August 2021
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	07 October 2021