Part VI: Summary of the risk management plan

Summary of risk management plan for Zambon oral acetylcysteine

This is a summary of the risk management plan (RMP) for all Zambon oral acetylcysteine containing products.

Authorized brand names at EEA level are:

Fluimucil, Fluimucil Long, Fluimucil oral, Fluimucil oral Infantil, Fluimucil Hustenlöser Akut, Fluimucil A, Fluimucil D, Fluimucil N, Fluimucil Forte, Fluimucil 100, Fluimucil 200, Fluimucil 600, Fluimucil Erkältungshusten, Fluimucil Bruis, Fluimucil Mucolitico, Fluimucil expectorant acetylcysteine, Fluimucil Muko, Fluimucil Muko Junior, Fluimucil Sugar, Fluimucil Junior, Fluimucil Pediatric, Fluimucil Kindersaft, Fluimucil Drank, Dynamucil, Lysomucil, Lysomucil Junior, Flumil, Flumil Infantil, Fluimusil, Flumilexa, Acetylcïsteine Zambon, Acetylcysteine Imphos

The RMP details important risks, how these risks can be minimised, and how more information will be obtained about product's risks and uncertainties (missing information).

Acetylcysteina Zambon, Acetylcysteine Imphos, Fluimucil, Fluimucil Expectorant Acetylcysteine, Fluimucil Forte, Fluimucil Mucolitico, Fluimucil Muko, Fluimucil Muko Junior, Flumil, Flumil Infantil, Lysomucil, Lysomucil Junior, Fluimucil long, Fluimucil Junior, Fluimucil szirup's summary of product characteristics (SmPC) and package leaflets give essential information to healthcare professionals and patients on how the product should be used.

I. The medicine and what it is used for

NAC oral acetylcysteine is authorized within EEA for:

Respiratory conditions associated with excessive mucus production
NAC is a mucolytic agent that reduces the viscosity of secretions, making mucus more fluid and consequently more easily eliminated by the mucociliary mechanism. The use of NAC as a mucolytic is justified by statistically and clinically significant results from a number of studies examining its efficacy in the treatment of a variety of respiratory diseases.

Acetaminophen poisoning
NAC has been used for several decades and has proven to be the antidote of choice in treating acetaminophen-induced hepatotoxicity. Acetylcysteine plays its primary importance role by maintaining of adequate glutathione levels, thus contributing to the cellular protection.

Iso- and cyclophosphamide uropathy
NAC has been used both in vitro and in vivo and has proven to be the prophylactic strategy of choice in preventing iso- and cyclophosphamide uropathy. Acetylcysteine plays its primary importance role by maintaining of adequate glutathione levels, thus contributing to the cellular protection.

Approved route of administration and strengths are:
Capsule, hard 200 mg; Effervescent tablet 200 mg; Effervescent tablet 600 mg; Tablet 600 mg; Film-coated tablets 200mg; Film-coated tablets 600mg; Orodispersible tablet 200 mg; Granules for oral

solution 100 mg; Granules for oral solution 200 mg; Granules for oral solution 600 mg; Oral solution 2%; Oral solution 4%.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of acetylcysteine oral, together with measures to minimise such risks and the proposed studies for learning more about oral acetylcsyteine's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of acetylcysteine oral is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of oral acetylcysteine are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of oral acetylcysteine. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

List of important risks and missing information	
Important identified risks	• Increased risk of respiratory obstruction in children aged < 2 years • Severe hypersensitivity reactions including anaphylactic shock
Important potential risks	• Severe skin reactions (incl SJS and TEN)

List of important risks and missing information	
	• Clinical effects resulting from anticoagulants and platelet-inhibiting properties of acetylcysteine • High-dose NAC-induced gastrolesivity
Missing information	• Use in pregnant and lactating women

II.B Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

Important identified risks: increased risk of respiratory obstruction in children aged < 2 years	
Evidence for linking the risk to the medicine	Published literature, post-marketing experience, CMDh website (www.hma.eu/464.html).
Risk factors and risk groups	Children under 2 years of age
Risk minimisation measures	Routine risk minimization measures: SmPC sections 4.3, 4.4 and 4.8 and corresponding sections of PIL.

Important identified risks: Severe hypersensitivity reactions including anaphylactic shock	
Evidence for linking the risk to the medicine	Published literature, post-marketing experience, CMDh website (www.hma.eu/464.html).
Risk factors and risk groups	Patients with a known hypersensitivity to acetylcysteine or any of its excipients.
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3, 4.4 and 4.8 and corresponding sections of PIL.

Important potential risks: Severe skin reactions (incl SJS and TEN)	
Evidence for linking the risk	Published literature, post-marketing experience, CMDh

to the medicine	website (www.hma.eu/464.html).
Risk factors and risk groups	In general, risk factors that increase the risk of developing severe skin reaction include viral infection, history of Stevens-Johnson syndrome (including family history), compromised immune system and genetyc predisposition.
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.4 or 4.8 and corresponding sections of PIL.

Important potential risks: Clinical effects resulting from anticoagulants and platelet-inhibiting properties of acetylcysteine	
Evidence for linking the risk to the medicine	Published literature, post-marketing experience, CMDh website (www.hma.eu/464.html).
Risk factors and risk groups	Not known. The clinical significance has not yet been established.
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.8 and corresponding section of PIL.

Important potential risk: High-dose NAC-induced gastro-lesivity	
Evidence for linking the risk to the medicine	Preclinical data.
Risk factors and risk groups	Patients with peptic ulcer or history of it, or concomitantly on other medicines with a known irritating effect on the gastric mucosa.
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 and corresponding section of PIL.

Missing information: Use in pregnant and lactating women	
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.6 and 5.3 and corresponding sections of PIL

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of oral acetylcysteine.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for oral acetylcysteine.