Annex III

Amendments to relevant sections of the Product Information

Note:

These amendments to the relevant sections of the Product Information are the outcome of the referral procedure.

The product information may be subsequently updated by the Member State competent authorities, in liaison with the Reference Member State, as appropriate, in accordance with the procedures laid down in Chapter 4 of Title III of Directive 2001/83/EC.

Amendments to relevant sections of the Product Information

The existing product information shall be amended (insertion, replacement or deletion of the text as appropriate) to reflect the agreed wording as provided below.

A. Summary of Product Characteristics

[…]

4.8 Undesirable effects

[…]

[Information in this section before information on the reporting of suspected adverse reactions should be replaced by the following one]

Summary of the safety profile

No serious adverse events have been reported in the clinical studies with the combination of paracetamol and methocarbamol published in literature.

The most frequent adverse reaction reported after methocarbamol is headache. The most frequently reported adverse reactions during the use of paracetamol are hepatotoxicity, renal toxicity, blood disorders, hypoglycaemia and allergic dermatitis.

Tabulated list of adverse reactions

The adverse reactions observed with the combination of paracetamol and methocarbamol are represented in the table below. They are listed by MedDRA system organ class (SOC) and frequency: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (frequency cannot be estimated from available data).

System organ class	**Frequency**		
	Rare (≥1/10,000 to <1/1,000)	Very rare (<1/10,000)	Unknown
Blood and lymphatic system disorders		Thrombocytopenia[b], agranulocytosis[b], leukopenia[b], neutropenia[b], pancytopenia[b], haemolytic anaemia[b]	Leukopenia[a],
Immune system disorders		Anaphylactic reaction[a], hypersensitivity reactions ranging from a simple skin eruption (rash) or urticaria to angioedema and anaphylactic shock[b]	
Metabolism and nutrition disorders		Hypoglycaemia[b]	
Psychiatric disorders		Nervousness[a], anxiety[a], confusion[a]	
Nervous system disorders	Headache[a], dizziness (or light headedness)[a]	Syncope[a], nystagmus[a], tremor[a], seizures (including grand mal)[a], somnolence[a]	Muscle incoordination[a], amnesia[a], insomnia[a], vertigo[a]
Eye disorders	Conjunctivitis[a]	Blurred vision[a]	Diplopia[a]
Cardiac disorders		Bradycardia[a]	

Vascular disorders	Hypotension[c]	Flushing[a]	
Respiratory, thoracic and mediastinal disorders	Nasal congestion[a]	Bronchospasm[b]	
Gastrointestinal disorders	Dysgeusia (metallic taste)[a]	Nausea[a], vomiting[a]	Dyspepsia[a], dry mouth[a], diarrhoea[c]
Hepatobiliary disorders	Increased hepatic transaminase levels[b]	Hepatotoxicity (jaundice)[b]	Jaundice (including cholestatic jaundice)[a]
Skin and subcutaneous tissue disorders	Angioedema[a], pruritus[a], rash[a], urticaria[a]	Allergic dermatitis[b], severe skin reactions (including Stevens-Johnson syndrome, toxic epidermal necrolysis)[b]	
Renal and urinary disorders		Sterile pyuria (cloudy urine)[b], adverse renal disorders[b], especially in overdose	
General disorders	Fever[a], malaise[b]		Fatigue[a]

[a] Usually attributable to Methocarbamol
[b] Usually attributable to Paracetamol
[c] Usually attributable to Methocarbamol and Paracetamol

Reporting of suspected adverse reactions

[…]

C. Package Leaflet

[…]

[The content of this section before the usual information on Reporting of side effects should be replaced by the below]

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If any of the following reactions occur, stop the treatment and notify your doctor immediately:
- Allergic reactions ranging from simple skin eruption or urticaria to more severe reactions such as anaphylactic reaction or angioedema (rash, itching, swelling of extremities, face, lips, mouth or throat that may cause you difficulty swallowing or breathing) or severe skin reactions;
- Jaundice (yellowing of skin and whites of the eyes), indicative of a liver problem;
- If you experience an infection with symptoms such as fever and pain call your doctor immediately, since it may be indicative of an alteration of white blood cells or platelets in blood, decreasing its resistance to infections;
- Convulsions or fainting (syncope).

The following adverse effect may occur rarely (may affect up to 1 in 1,000 people):
- Headache, dizziness or light-headedness;
- Conjunctivitis with nasal congestion;
- Decrease in blood pressure, metallic taste, increase in hepatic transaminases;
- Fever, malaise.

The following adverse effects may occur very rarely (may affect up to 1 in 10,000 people):
- Nausea, vomiting;
- Nervousness, anxiety, confusion, tremor, drowsiness, blurred vision, nystagmus (rapid and involuntary eye movements);
- Low blood sugar levels, decrease in the frequency of heartbeat, reddening of the skin (flushing);

- Renal toxicity (dark urine);
- Difficulty breathing.

The following adverse effects have been reported but the frequency cannot be estimated from available data:

- Slight muscular incoordination, loss of memory, vertigo, insomnia, double vision;
- Heartburn, dry mouth, fatigue, diarrhoea.

Reporting of side effects

[…]