

Public Assessment Report

Name of the Product:

**ASA Health-Med 75 mg gastro-resistant tablets
ASA Health-Med 100 mg gastro-resistant tablets**

(acetylsalicylic acid)

Procedure number: HU/H/0693/001-002/DC

Marketing authorisation holder: Health-Med Sp. z o.o. sp.j.

Date: 19. 11. 2021.

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LAY SUMMARY

After careful assessment of its quality and therapeutic benefit/risk ratio, the member states have granted the marketing authorisation of the ASA Health-Med 75 mg and 100 mg gastro-resistant tablets. The holder of the marketing authorisation is Health-Med Sp. z o.o. sp.j.

The active substance is acetylsalicylic acid.

- ASA Health-Med 75 mg gastro-resistant tablets: each gastro-resistant tablet contains 75 mg acetylsalicylic acid.
- ASA Health-Med 100 mg gastro-resistant tablets: each gastro-resistant tablet contains 100 mg acetylsalicylic acid.

The other ingredients are:

- tablet core: microcrystalline cellulose; maize starch; silica, colloidal anhydrous; stearic acid;
- film-coating: methacrylic acid – ethyl acrylate copolymer (1:1) dispersion 30%; poly-sorbate 80; sodium laurilsulfate; triethyl citrate; talc.

The appearance of the tablets is:

- The 75 mg gastro-resistant tablets are white, oval, biconvex gastro-resistant tablets, 9.2 × 5.2 mm.
- The 100 mg gastro-resistant tablets are white, round, biconvex gastro-resistant tablets with a diameter of 7.2 mm.

The gastro-resistant tablets are available in packs in blisters.

ASA Health-Med contains acetylsalicylic acid, which in low doses belong to a group of medicines called anti-platelet agents. Platelets are tiny cells in the blood that cause the blood to clot and are involved in thrombosis. When a blood clot occurs in an artery it stops the blood flowing and cuts off the oxygen supply. When this happens in the heart it can cause a heart attack or angina; in the brain it can cause a stroke.

ASA Health-Med is taken to reduce the risk of blood clots forming and thereby prevent further:

- heart attacks (in patients that have had a previous heart attack),
- stroke (in patients that have had a previous stroke),
- cardiovascular problems in patients who suffer from stable or unstable angina (a type of chest pain), with the exception of the acute (recent onset) phase.

ASA Health-Med is also used to prevent the formation of blood clots after certain types of heart surgery in order to widen or to unblock the blood vessels.

This medicinal product is not recommended for emergencies. It can only be used as a preventive treatment.

What patients need to know before using ASA Health-Med

Patients must not take ASA Health-Med if they

- are allergic to acetylsalicylic acid (e.g. certain asthma patients who may suffer an attack or faint) or any of the ingredients of this medicine;
- currently have, or have ever had an ulcer in their stomach or small intestine;
- have, or ever had, a bleed in their stomach or intestines or any other type of bleeding like cerebrovascular hemorrhages;
- have ever had the problem of their blood not clotting properly;
- have severe liver or kidney problems;
- have gout (a condition that causes pain, inflammation and swelling in one or more of the joints);
- have severe cardiac insufficiency;
- are in their last 3 months of pregnancy; they must not use higher doses than 100 mg per day;
- are taking a medicine called methotrexate (e.g. for cancer or rheumatoid arthritis) in doses higher than 15 mg per week;
- are under 16 years old, unless their doctor tells them to.

Warnings and precautions

Before taking ASA Health-Med patients should talk to their doctor or pharmacist if they:

- have problems with their kidneys, liver or heart;
- have or have ever had problems with their stomach or small intestine;
- have high blood pressure;
- are asthmatic, are allergic to other drugs, especially other salicylates or non-steroidal anti-inflammatory drugs (NSAID), have hay fever, nasal polyps or other chronic respiratory diseases; acetylsalicylic acid may induce an asthma attack;
- have a condition called glucose-6-phosphate dehydrogenase deficiency;
- have ever had gout;
- are elderly (doctor may want to monitor them closely);
- have heavy menstrual periods;
- are pregnant or breast feeding.

Immediate medical care is advised, if symptoms get worse or if patients experience severe or unexpected side effects e.g. unusual bleeding symptoms, serious skin reactions or any other sign of serious allergy.

If patients experience unusual bleeding, such as coughing up blood, blood in their vomit or urine, or black stools they should immediately stop using ASA Health-Med and contact their doctor.

Doctor should be informed if they are planning to have an operation (even a minor one, such as tooth extraction) since acetylsalicylic acid is blood-thinning there may be an increased risk of bleeding.

Patients should take care not to become dehydrated (they may feel thirsty with a dry mouth) since the use of acetylsalicylic acid at the same time may result in deterioration of kidney function.

This medicinal product is not suitable as a pain killer or fever reducer.

Children and adolescents

Acetylsalicylic acid may cause Reye's syndrome when given to children. Reye's syndrome is a very rare disease which affects the brain and liver and can be life-threatening. For this reason, ASA Health-Med should not be given to children aged under 16 years, unless on the advice of a doctor.

Other medicines and ASA Health-Med

Those who are taking, have recently taken or might take any other medicines, must consult their doctor.

The effect of treatment may be influenced if acetylsalicylic acid is taken at the same time as some other medicines for:

- thinning of the blood/prevention of clots (e.g. warfarin, heparin, coumarin, clopidogrel, dipyridamole, phenindione);
- prevention of organ rejection after transplantation (cyclosporine, tacrolimus);
- high blood pressure (e.g. diuretics, ACE-inhibitors or beta blockers);
- regulation of the heart beat (digoxin);
- manic-depressive illness (lithium);
- pain and inflammation, e.g. NSAIDs such as ibuprofen, or metamizole, or steroids. Metamizole (substance to decrease pain and fever) may reduce the effect of acetylsalicylic acid on platelet aggregation (blood cells sticking together and forming a blood clot), when taken concomitantly. Therefore, this combination should be used with caution in patients taking low dose acetylsalicylic acid for cardioprotection;
- gout (e.g. probenecid, sulfinpyrazone);
- epilepsy (valproate, phenytoin);
- glaucoma (acetazolamide);
- cancer or rheumatoid arthritis (methotrexate; in doses lower than 15 mg per week);
- diabetes (e.g. glibenclamide, glipizide, insulin);
- infections - sulphonamide antibiotics (e.g. co-trimoxazole);
- depression (selective serotonin re-uptake inhibitors (SSRIs) such as sertraline or paroxetine);
- antacids (for indigestion) or adsorbents (e.g. kaolin for diarrhoea);
- zafirlukast (for asthma);

- use as hormone replacement therapy when the adrenal glands or pituitary gland have been destroyed or removed, or to treat inflammation, including rheumatic diseases and inflammation of the intestines (corticosteroids).

ASA Health-Med may affect the results of thyroid function tests. Taking this medicine should be told to the doctor or nurse.

ASA Health-Med with food, drink and alcohol

The gastro-resistant tablets can be taken with or without food. Drinking alcohol may possibly increase the risk of gastrointestinal bleeding and prolong bleeding time.

Pregnancy and breast-feeding

If patients are pregnant or breast-feeding, think they may be pregnant or are planning to have a baby, doctor or pharmacist should be asked for advice before taking this medicine.

Pregnant women should not take acetylsalicylic acid during pregnancy unless advised by their doctor.

ASA Health-Med should not be taken if women are in the last 3 months of pregnancy, unless they are advised to do so by their doctor and then the daily dose should not exceed 100 mg. Regular or high doses of this medicinal product during late pregnancy can cause serious complications in the mother or baby.

Breast-feeding women should not take acetylsalicylic acid unless advised by their doctor.

Driving and using machines

ASA Health-Med should not affect the ability to drive and use machines.

How to use ASA Health-Med

This medicine must always be taken exactly as the doctor or pharmacist has told. If patients are not sure the doctor or pharmacist should be checked with.

The tablets should be swallowed whole with sufficient fluid (1/2 glass of water). The tablets have a gastro-resistant coating which prevents irritant effects on the gut, and should therefore not be crushed, broken or chewed. ASA Health-Med can be taken with or without food.

Adults

Prevention of heart attacks:

- The recommended dose is 75-150 mg once daily.

Prevention of strokes:

- The recommended dose is 75-300 mg once daily.

Prevention of cardiovascular problems in patients who suffer from stable or unstable angina (a type of chest pain):

- The recommended dose is 75-150 mg once daily.

Prevention formation of blood clots after certain types of heart surgery:

- The recommended dose is 75-150 mg once daily.

Elderly

As for adults. In general, acetylsalicylic acids should be used with caution in elderly patients who are more prone to adverse events. Treatment should be reviewed at regular intervals.

Use in children and adolescents

Acetylsalicylic acid should not be administered to children and adolescents younger than 16 years, unless prescribed by a doctor.

What to do if more ASA Health-Med was taken than it should have been?

If too many tablets are accidentally taken, patients should tell their doctor at once or contact immediately the nearest casualty department. Any leftover medicines or the empty packet should be shown to the doctor.

Symptoms of overdose may include ringing in ears, hearing problems, headache, dizziness, confusion, nausea, vomiting and abdominal pain. A large overdose can lead to more rapid breathing than normal (hyperventilation), fever, excess sweating, restlessness, seizures, hallucinations, low blood sugar, coma and shock.

What to do if taking ASA Health-Med was forgotten?

In the event of missing a dose, patients should wait and take the next dose at the usual time. No double dose to make up for a forgotten dose can be taken.

Possible side effects

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

In case of noticing any of the following serious side effects, taking ASA Health-Med should be stopped and the doctor should be contacted immediately:

- Sudden wheezing, swelling of the lips, face or body, rash, fainting or difficulties swallowing (severe allergic reaction) (rare).
- Reddening of the skin with blisters or peeling and may be associated with a high fever and joint pains. This could be erythema multiforme, Stevens-Johnson syndrome or Lyell syndrome (rare).
- Unusual bleeding, such as coughing up blood, blood in your vomit or urine, or black stools (frequency not known).

- Ulcers in the mouth, fever and infection(s) (agranulocytosis - a severely lowered count of white blood cells) (rare).

Possible side effects listed below are grouped by frequency of occurrence.

Common side effects (affects 1 to 10 users in 100):

- indigestion;
- increased tendency for bleeding.

Uncommon side effects (affects 1 to 10 users in 1,000):

- hives;
- runny noses;
- breathing difficulty.

Rare side effects (affects 1 to 10 users in 10,000):

- severe bleeding in the stomach or intestines, brain haemorrhage, altered number of blood cells;
- nausea, vomiting, gastritis;
- cramps in the lower respiratory tract, asthma attack;
- inflammation in the blood vessels;
- bruising with purple spots (cutaneous bleeding);
- severe skin reactions such as rash known as erythema multiforme and its life-threatening forms Stevens-Johnson syndrome and Lyell syndrome;
- hypersensitivity reactions, such as skin rash, swelling of e.g. lips, face or body, or anaphylactic shock;
- Reye's syndrome (a very rare disease in children which affects the brain and liver);
- abnormal heavy or prolonged menstrual periods.

Not known side effects (frequency cannot be estimated from the available data):

- ringing in the ears (tinnitus) or reduced hearing ability;
- headache;
- vertigo;
- diarrhoea;
- ulcers in stomach or small intestine and perforation;
- prolonged bleeding time;
- impaired kidney function;
- impaired liver function;
- high level of uric acid in the blood;
- salt and water retention;
- anaemia (a reduction in the number of red blood cells which can make patients look pale and feel tired);
- kidney stones (sharp stabbing pains in the stomach or back, with blood in the urine).

How to store ASA Health-Med

This medicine does not require any special temperature storage conditions. It should be stored in the original package in order to protect from moisture and kept out of the sight and reach of children.

SCIENTIFIC DISCUSSION

This module reflects the scientific discussion for the approval of ASA Health-Med 75 mg and 100 mg gastro-resistant tablets. The procedure was finalised at 06 May 2021. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

In accordance to the Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, an application has been submitted to the reference and competent authorities of the Member State concerned.

This Decentralised Procedure application (Reference member state, RMS: Hungary, concerned member state, CMS: Croatia) concerned the gastro-resistant tablets of acetylsalicylic acid 75 mg and 100 mg.

The application has been filed pursuant to Article 10(a) of Directive 2001/83/EC (well established use application) and therefore contained no new clinical or preclinical data, other than supporting literature where necessary.

Based on the review of the quality, safety and efficacy data, the Member States have granted marketing authorisations for ASA Health-Med 75 mg and 100 mg gastro-resistant tablets from Health-Med Sp. z o.o. sp.j.

The product is indicated for:

- secondary prevention of myocardial infarction;
- prevention of cardiovascular morbidity in patients suffering from stable angina pectoris;
- history of unstable angina pectoris, except during the acute phase;
- prevention of graft occlusion after Coronary Artery Bypass Grafting (CABG);
- coronary angioplasty, except during the acute phase;
- secondary prevention of transient ischaemic attacks (TIA) and ischaemic cerebrovascular accidents (CVA), provided intracerebral haemorrhages have been ruled out.

A comprehensive description of the indications and posology is given in the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

The chemical-pharmaceutical assessment report concerns the application of ASAHealth-Med 75 mg and 100 mg gastro-resistant tablets via a decentralized procedure according to Article 10(a) of Directive 2001/83/EC (i.e well-established use application). The products have been developed by ICN Polfa Rzeszów S.A., Poland.

Acetylsalicylic acid is marketed worldwide by various pharmaceutical companies in the form of conventional, effervescent, gastro-resistant and prolonged release tablets. The 100 mg and 300 mg gastro-resistant tablets have been marketed in Europe by Bayer Healthcare A.G under the trade names of Aspirin® Protect, Aspirin® Cardio and Cardioaspirin®. The first marketing authorisation for acetylsalicylic acid was granted on 29th July 1955 for Aspirin Protect 100 mg tablets, manufactured by Bayer Pharma AG, which is the reference medicinal product.

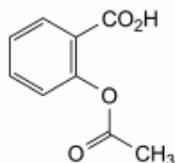
II.2 Drug substance

Data on the quality and manufacture of the active substance were provided in the applicant's submission using the CEP procedure with additional data in the marketing authorization dossier. The Quality Overall Summary is adequate.

I.N.N.: Acetylsalicylic acid

Chemical name: 2-(Acetyloxy)benzoic acid

Structure:



The active substance is white or almost white, crystalline powder or colorless crystals. It is slightly soluble in water, freely soluble in ethanol (96 per cent).

The active substance is a well-known compendial-grade material and is tested in accordance with the current European Pharmacopoeia monograph. The finished product manufacturer performs additional tests, which are adequately discussed in the Pharmaceutical development section. The specifications reflect all relevant quality attributes of the active substance and were found to be adequate to control the quality of the drug substance. The limits set are properly justified.

Batch analysis data justify the limits, indicate the good performance of testing methods and demonstrate the batch to batch consistency of the production.

Ph. Eur. reference standards used for testing of the active substance. The list of the reference materials has been provided in the documentation.

The packaging materials according to the CEP are low-density polyethylene bags kept in fibre drums or in polypropylene big bags.

Stability studies have not been performed, because the relevant information is contained in the CEP.

Good Manufacturing Practice (GMP) compliance of the API manufacture is demonstrated by the applicant.

II.3 Medicinal product

The purpose of the development was to develop a suitable core and enteric coating formulation for gastro-resistant tablets containing 75 mg or 100 mg of acetylsalicylic acid, and optimize a manufacturing process taking into consideration the characteristics of the API. A satisfactory package of data on development pharmaceuticals has been presented. In order to ensure adequate stability and dissolution profile, the composition of tablet core and the enterosolvent coating were optimized. The compatibility of the API with the excipients has been confirmed. The relevant functionally-related characteristics of the excipients have been determined. The susceptibility of the coating to enzymatic attack and erosion with time have been evaluated by the Applicant.

The compositions and the pharmaceutical tests evaluated during development of the final formulation are included in the documentation. As a result of development studies product with the following appearance and composition was obtained.

- 75 mg strength: white, oval, biconvex tablets with dimensions of 9.2 × 5.2 mm.
- 100 mg strength: white, round, biconvex tablets with a diameter of 7.2 mm.

The excipients used for manufacturing the drug product are microcrystalline cellulose, maize starch, colloidal anhydrous silica, stearic acid, methacrylic acid – ethyl acrylate copolymer, polysorbate 80, sodium laurylsulfate, triethyl citrate, talc and purified water.

All excipients comply with the current Ph.Eur. monographs with additional FRC requirements in the case of cellulose microcrystalline and methacrylic acid – ethyl acrylate copolymer (1:1) dispersion 30%. Compliance of the product with the general monograph of the European Pharmacopoeia on the Products with the risk of TSE has been demonstrated by the applicant.

A description and flow chart of the manufacturing method has been provided. Appropriate in-process controls are included in the manufacturing process. Satisfactory batch formulae were also presented. GMP compliance of the manufacturing site has been demonstrated.

The finished product specification is satisfactory. Acceptance criteria have been justified with respect to conventional pharmaceutical requirements as prescribed in the relevant dosage form monograph of the Ph.Eur. and the ICH Q6A guideline. Appropriate control strategy was se-

lected. The test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and complied with the specification. Certificates of analysis for the batches involved in the bioequivalence study are presented.

The container closure system of the product is PVC//Al blister. Specifications and quality certificates for all packaging components are enclosed.

Finished product stability studies have been conducted in accordance with the current guidelines. Based on the results, the following shelf-life and storage condition is approved:
Do not store above 25°C. Store in the original package in order to protect from moisture.

The Summary of Product Characteristics, patient Information Leaflet and label texts are pharmaceutically acceptable.

II.4 Discussion on chemical, pharmaceutical and biological aspects

The product has been shown to meet the current regulatory requirements with regards to its quality and content of the active substance as well as dosage-form characteristics until the end of the approved shelf-life consistently. The manufacture and the quality standards applied adequately support the safe use and efficacy of the product.

III. NON-CLINICAL ASPECTS

III.1 Introduction

The pharmacology, pharmacokinetics and toxicology of acetylsalicylic acid are well known and described appropriately. The nonclinical overview is based on literature data, and is considered relevant for this type of application. The Applicant has not provided any new non-clinical studies. The preclinical safety profile of acetylsalicylic acid is adequately reflected in the Summary of Product Characteristics.

III.2 Ecotoxicology/environmental risk assessment (ERA)

In accordance with Article 8 (ca) and (g) of Directive 2001/83/EC as amended, an application for marketing authorization shall be accompanied by an environmental risk assessment, evaluating any potential risks of the medicinal product to the environment.

The Applicant provided justification of the absence of significant increase of the environmental exposure demonstrated by suitable information.

Since ASA Health-Med gastro-resistant tablets will be used as an alternative to other acetylsalicylic acid products already on the market at the same dose level, this will not lead to an increased exposure of acetylsalicylic acid to the environment. The medicinal products do not contain any component that would result in any additional hazard to the environment during storage, distribution, use and/or disposal. In addition, each patient will be informed how to dispose any un-used tablets in a safe manner when reading product information leaflet. A more detailed environmental risk assessment is therefore not deemed necessary.

The document presented according to the CHMP Guideline on the ERA of medicinal products for human use (EMA/CHMP/SWP/4447/00 corr 2) is acceptable.

III.3 Discussion on the non-clinical aspects

From a non-clinical perspective, marketing authorisation of ASA Health-Med 75 mg and 100 mg gastro-resistant tablets is recommended.

IV. CLINICAL ASPECTS

IV.1 Introduction

Acetylsalicylic acid has been in use since 1899 (Aspirin, Bayer) as an analgesic and antipyretic medicinal product. ASA's as an antiplatelet agent efficacy was established from the 1960s by clinical trials and other studies.

This is a bibliographic application (Well-established use) for a new formulation of acetylsalicylic acid (ASA).

For a bibliographic application, the applicant needs to demonstrate that the active substance of the medicinal product has been in well-established medicinal use within the Community for at least 10 years in the specific therapeutic use. For this application, results from bioequivalence studies are submitted in addition to published literature. This is acceptable as long as they are intended to show the relevance of the literature used to demonstrate safety and efficacy. However, it is not required to demonstrate strict bioequivalence against a reference product as for a generic application. For this specific product there is a wide range of clinically used doses. Thus, for an application based on well-established use it is sufficient to demonstrate that this product is sufficiently similar to the formulations used in the bibliographic data referred to. The presented studies do demonstrate that the performance of proposed formulation is sufficiently similar to that of the formulations used in the bibliographic data referred to, so relevance of the literature data to the proposed formulation submitted is deemed as demonstrated.

IV.2 Pharmacokinetics

Pharmacokinetic properties of ASA are well known. As ASA is a widely used, well-known active substance, the Applicant has not provided additional clinical studies and further studies are not required. The literature data presented in the clinical overview on pharmacokinetics do support the proposed SmPC.

To support the WEU application, the Applicant has submitted as report four single dose bioequivalence studies under fed and fasting conditions. The studies have been performed with the higher strength of Acetylsalicylic acid 100 mg gastro resistant tablets.

The presented studies do demonstrate that the performance of proposed formulation is sufficiently similar to the formulations used in the bibliographic data referred to. Relevance to the literature data submitted is deemed as demonstrated.

IV.3 Pharmacodynamics

No new data has been submitted, however, an overview on published data on the pharmacodynamics of acetylsalicylic acid has been provided.

The mechanism of action and pharmacodynamics of ASA is well known and has been adequately summarised by the applicant. ASA inactivates COX irreversibly. Since platelets do not have a cell nucleus they cannot synthesise new proteins. Therefore, the action of ASA on platelet COX is permanent, lasting for the life of the platelet (7 to 10 days). Repeated, low, doses of ASA therefore produce a cumulative inhibitory effect on platelet function. Via the effect on COX, ASA also has an inhibitory action on prostacyclin biosynthesis. This potentially counteractive effect, however, may be limited due to the rapid recovery of the synthetic capacity of vascular endothelium. The anti-inflammatory properties of ASA may have an additive effect in the prevention of cardiovascular disease.

A comprehensive review of the known pharmacodynamic interactions has been provided. These interactions are reflected in the SPC.

IV.4 Clinical efficacy

The applicant has provided an overview on the efficacy of ASA in the sought indications, based on published literature. The data provided supports the well-established efficacy and use of ASA in the indications:

- Secondary prevention of myocardial infarction.
- Prevention of cardiovascular morbidity in patients suffering from stable angina pectoris.
- History of unstable angina pectoris, except during the acute phase.
- Prevention of graft occlusion after Coronary Artery Bypass Grafting (CABG).
- Coronary angioplasty, except during the acute phase.
- Secondary prevention of transient ischaemic attacks (TIA) and ischaemic cerebrovascular accidents (CVA), provided intracerebral haemorrhages have been ruled out.

Near-complete inhibition of the COX-1 enzyme is achieved with doses well below 162 mg, and, in general, studies have shown that high doses of aspirin increase the risk of bleeding complications without providing further reduction in vascular events.

IV.5 Clinical safety

The safety profile for ASA is well known and has been extensively described in the literature. The Applicant has provided a comprehensive summary of the safety overview based on available literature data from clinical and post-marketing experience. The most important risks related to antiplatelet therapy with aspirin are haemorrhagic events and gastrointestinal bleeding. Most of adverse events recorded seem also to be transient in nature and usually resolve after drug discontinuation. Information included in the proposed labelling is consistent with current medical knowledge and give adequate basis for safe acetylsalicylic acid use.

IV.6 Pharmacovigilance

IV.6.1 Summary of the Pharmacovigilance System

The Applicant has submitted a signed Summary of the Applicant's Pharmacovigilance System. Provided that the Pharmacovigilance System Master File fully complies with the new legal

requirements as set out in the Commission Implementing Regulation 520/2012 and as detailed in the relevant GVP module, the Summary is considered acceptable.

IV.6.2 Risk Management Plan

Summary of safety concerns

| | |
|----------------------------|------|
| Summary of safety concerns | |
| Important identified risks | None |
| Important potential risks | None |
| Missing information | None |

Pharmacovigilance Plan

Routine pharmacovigilance activities are considered sufficient to manage all of the safety concerns connected to ASA Health-Med 75 mg and 100 mg gastro-resistant tablets.

Risk Minimisation Measures

Routine risk minimisation measures (i.e. wording in SmPC, PL and classification as a prescription only medicine) are considered sufficient to manage all of the safety concerns connected to ASA Health-Med 75 mg and 100 mg gastro-resistant tablets.

No additional activities are proposed. For any further information on risk minimisation, please refer to the product information.

IV.6.3 Periodic Safety Update Reports

The requirements for submission of periodic safety update reports for these medicinal products are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

IV.7 Discussion on the clinical aspects

The mechanism of action, pharmacokinetics and pharmacodynamics of acetylsalicylic acid is well known and has been adequately summarised. The Applicant has not provided additional clinical studies and further studies are not required. The literature data presented in the clinical overview on pharmacokinetics do support the proposed SmPC. Nevertheless, 4 bioequivalence studies have been submitted in Module 5.3., which had not been mentioned in the clinical overview, hence it was asked to be updated with the relevant data.

The presented studies did demonstrate that the performance of proposed formulation is sufficiently similar to that of the formulations used in the bibliographic data referred to, so relevance of the literature data to the proposed formulation is deemed as demonstrated.

The application concerns a WEU product.

The products is indicated for:

- secondary prevention of myocardial infarction;
- prevention of cardiovascular morbidity in patients suffering from stable angina pectoris;
- history of unstable angina pectoris, except during the acute phase;
- prevention of graft occlusion after Coronary Artery Bypass Grafting (CABG);
- coronary angioplasty, except during the acute phase;
- secondary prevention of transient ischaemic attacks (TIA) and ischaemic cerebrovascular accidents (CVA), provided intracerebral haemorrhages have been ruled out.

There is no objection against granting the marketing authorization from a clinical point of view.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

V.1 Summary

The present application concerns ASA Health-Med 75 mg and 100 mg gastro-resistant tablets. The applicant and the future holder of authorisation is Health-Med Sp. z o.o. sp.j.

The application was submitted according to Article 10(a) of Directive 2001/83/EC (well-established use application).

The products is indicated for:

- secondary prevention of myocardial infarction;
- prevention of cardiovascular morbidity in patients suffering from stable angina pectoris;
- history of unstable angina pectoris, except during the acute phase;
- prevention of graft occlusion after Coronary Artery Bypass Grafting (CABG);
- coronary angioplasty, except during the acute phase;
- secondary prevention of transient ischaemic attacks (TIA) and ischaemic cerebrovascular accidents (CVA), provided intracerebral haemorrhages have been ruled out.

The submitted documentation is administratively adequate and scientifically sound. The quality of the product is satisfactory. There were no non-clinical or clinical concerns raised. The therapeutic benefit/risk assessment is therefore positive.

Based on the review of the quality, safety and efficacy data, the Member States have granted marketing authorisation for ASA Health-Med 75 mg and 100 mg gastro-resistant tablets from Health-Med Sp. z o.o. sp.j.

V.2 Classification

Non Prescription.

V.3 Package Leaflet and user consultation

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the patient information leaflet was English.

The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VI. UPGRADE: STEPS TAKEN AFTER THE INITIAL PROCEDURE WITH AN INFLUENCE ON THE PUBLIC ASSESSMENT REPORT

This module reflects the procedural steps and scientific information after the finalisation of the initial procedure.

| Scope | Procedure number | Product information affected | Date of start of the procedure | Date of end of procedure | Approval or non approval | Assessment report attached |
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