**Lesson 10**

The State Pharmacopoeia (SP) is a collection of general and particular pharmacopoeial articles that establish quality requirements for medicines, medicinal plant materials, pharmaceutical substances and excipients. The State Pharmacopoeia is based on general and private pharmacopoeial articles. General pharmacopoeial articles describe the general provisions adopted in the pharmacopoeial analysis, methods of analysis or include a list of standardized indicators and test methods for a particular dosage form. Private monographs determine the level of requirements for specific medicinal products.

Pharmacopoeia article (FS) technical regulatory legal act, a document that establishes quality requirements for medicines, pharmaceutical substances, medicinal herbal raw materials, excipients, reagents, packaging materials used in industrial production, pharmaceutical manufacture of medicines, for standard samples used when checking the quality of drugs, methods of quality control, their packaging, conditions and periods of storage.

FSP pharmacopoeial article of the enterprise (developed for the dosage form produced by the plant from substances that meet the requirements of the FS).

Names. In addition to the names in Russian, the Latin name is also given. This name may be used instead of the Russian name, as well as any other synonym that is recognized as equivalent by the competent authority.

Relative atomic and molecular masses. Relative atomic mass (A.m.) or relative molecular weight (M.m.) indicate-Xia, when necessary, at the beginning of a monograph. Relative atomic mass, relative molecular mass, molecular formula and graphical formula are given as informational material.

Introductory part of pharmacopoeial articles. The introductory part following the title of the monograph contains the official definition of the substance, finished drug or other product that is the subject of a monograph.

Content limits. Where content limits are given, these are limits obtained using the method specified in the Quantification section.

Medicinal products containing medicinal plant materials. In private articles on medicinal products containing medicinal plant materials, the introductory part includes an indication of the subject of the private article. It can be, for example, medicinal plant material in its original form or medicinal plant material crushed into powder. If a private article covers several options, for example, both of those indicated, then this is specified in the introductory part.

Production. The information in the Manufacturing section is intended to draw attention to some important aspects of the manufacturing process and is not necessarily exhaustive. The instructions contained therein are addressed to the manufacturer. They may relate, for example, to materials, to the manufacturing process, to its validation and control, to step-by-step control, and also to the tests that the manufacturer must carry out before release for each product batch or for selected batches. These provisions must necessarily be confirmed by analysis of the final product. The competent authority may determine that the above aspects have been met. Such a conclusion can be made on the basis of verification of the data received from the manufacturer, or by inspecting the production, or by testing the corresponding samples.

The absence of a "Production" section does not mean that the aspects of the production process noted above do not require attention. Any product described in a monograph must be manufactured in accordance with the principles of good manufacturing practice (GMP) and relevant international agreements, as well as national and supranational laws that apply to products intended for use in medicine.

In the "Manufacturing" section of a monograph for a vaccine, the properties of the strain and test methods to confirm these properties may be indicated. These methods are given for information as an example.

Description (properties). Indicate the characteristics of the physical state and the color of the medicinal product; if necessary, give information on odor and hygroscopicity.

Solid substances can be coarse-grained (not more than 40% of the powder particles should be less than 0.4 mm in size), crystalline (not less than 95% of the powder particles should be less than 0.4 mm in size and not more than 40%

- less than 0.2 mm in size), finely crystalline (at least 95% of the powder particles should be less than 0.2 mm in size) or amorphous (no light reflection is observed when the microscope stage is rotated).

The characteristics of crystallinity and hygroscopicity in the description are given for information and are not subject to testing. If it is necessary to normalize the particle size, a special section is given in a private pharmacopoeial monograph.

The color is characterized by names: white, yellow, orange, red, etc. With tint colors, the color that is contained in a smaller proportion is indicated first, and then, through a hyphen, the predominant color (for example, red-brown).

Weakly colored samples have a color shade, the name of which is characterized by the suffix “-ovate” (for example, “yellowish”) or indicate

"light-" (for example, "light yellow").

The color of the solids is determined against a dull white background (white thick or filter paper) in diffused daylight under conditions of minimal shadow development. A small amount of the substance is placed on white paper and, without pressure, is evenly distributed over the surface of the paper (carefully leveled with a spatula or other device) so that the surface remains flat.

Smell. The smell is characterized by the terms: "odorless", "with a characteristic smell", "with a weak characteristic smell".

In the case of highly volatile liquids, 0.5 ml is applied to filter paper and the odor is determined immediately after application, unless otherwise indicated in a monograph.

Solubility. To determine the solubility, solvents covering a wide polarity scale (wateralcoholacetonehexane) are used. To characterize the solubility, use the amount (ml) of the solvent required to dissolve 1 g of the substance

 Very easily soluble up to 1;

 Easily soluble from 1 to 10;

 Soluble from 10 to 30;

 Moderately soluble from 30 to 100;

 Slightly soluble from 100 to 1000;

 Very slightly soluble from 1000 to 10000;

 Practically insoluble over 10,000;

 Partially soluble. The term is used to characterize mixtures containing both soluble and insoluble components;

 Miscible with . The term is used to characterize liquids miscible with the specified solvent in all proportions.

To determine the solubility, a weighed portion of the substance is added to a measured amount of the solvent and continuously shaken for 10 minutes at a temperature of 20±5°C. The sample can be ground beforehand. For slowly dissolving samples requiring more than 10 minutes to dissolve,

heating in a water bath up to 30 ° C is also allowed; observation is carried out after cooling the solution to a temperature of 20 ± 5 °C and vigorous shaking for 1-2 minutes. A substance is considered dissolved if no particles of the substance are detected in the solution when observed in transmitted light.

For substances that form turbid solutions upon dissolution, a corresponding indication should be given in a monograph. When a substance is said to be soluble in fatty oils, it is meant to be soluble in any oil belonging to the class of fatty oils.

Authenticity (identification). To establish the authenticity of a substance, instrumental methods of analysis (most often IR spectroscopy) are used in combination with chemical methods (qualitative reactions to functional groups). Usually, a monograph suggests 3-5 tests to determine authenticity. Some monographs have subsections “First Identification” and “Second Identification”. Usually only the first identification is used.

Melting temperature. The test is usually used to characterize solids.

solidification temperature; boiling point (distillation temperature limits); density; viscosity; refractive index. These tests are introduced to characterize liquid substances.

specific rotation. Introduced to characterize optically active substances.

Specific absorption rate. This indicator is an additional characteristic of the authenticity and purity of the substance.

Transparency and color of the solution. These tests are mandatory for substances and medicinal products intended for parenteral administration. The tests are especially relevant for drugs that change their color when oxidized by atmospheric oxygen.

pH (acidity or alkalinity). This test uses a potentiometric measurement of the pH value. Permissible in-

the pH range should generally be no more than 2 (for example, the pH value should be between 5.5 and 7.5). Tests are carried out for substances and medicinal products intended for parenteral administration.

impurities. This test provides for the control of degradation products and technological impurities (intermediates and by-products of synthesis), the so-called "co-impurities". These may be controlled as “characterized impurities” (i.e., those that have previously been recognized by the competent authorities as being characterized; it may also include impurities that are considered to be characterized in other ways, for example, impurities that occur in the form metabolites) and “other detectable impurities” (for example, potential impurities that were not detected in any samples of the substance at the time of development of the monograph or that occur at concentrations less than 0.1%, but the content which may be limited by the tests described in a monograph). To determine impurities, various chromatographic methods of analysis are most often used.

Inorganic anions (chlorides, sulfates, etc.). The choice of controlled anions is determined by the technology for obtaining the substance. In this case, controlled anions can be non-toxic (for example, chlorides, sulfates, etc.).

The control of anions is not introduced if they are part of the substance (on-

example, the substance is hydrochloride or sulfate).

Inorganic cations (iron, copper, etc.). This test is introduced if the control of individual cations is essential to the quality of the substance; their content must be justified.

Control of cations is not introduced if they are part of the substance (on-

example, iron lactate).

sulfate ash. As a general rule, sulphated ash should not exceed 0.1%. The absence of this test in a monograph or an increased content of sulphated ash requires an appropriate justification.

Heavy metals. The content of heavy metals should not exceed 0.001%, unless otherwise indicated in a monograph.

Arsenic. This test is introduced when either the feedstock may contain arsenic, for example, for raw materials of natural origin, or it may be contaminated during the preparation of the substance. The arsenic content should generally not exceed 0.0001%.

Residual organic solvents. The content of residual amounts of organic solvents used in the preparation of the substance must comply with the requirements of the API.

Bacterial endotoxins (pyrogenicity). These tests are carried out for substances intended for the preparation of medicinal products for parenteral use. These substances must pass the test for bacterial endotoxins or pyrogenicity without prior sterilization.

Microbiological purity. The microbiological purity of medicinal products must comply with the requirements of the Global Fund of the Republic of Belarus v.1 (Section 2.6

"Biological Tests").

Sterility. This test is introduced for substances used in the manufacture of finished sterile medicinal products that are not subjected to a sterilization procedure.

Weight loss on drying. The test is introduced to control the content of volatile substances and/or moisture in the substance. The introduction of one of these tests into the FS is generally mandatory. Their absence must be justified. If there are no other indications in a monograph and the substance is not a crystalline hydrate (crystal solvate), the loss in mass on drying or the water content should not exceed 0.5%.

If the substance is a crystalline hydrate (crystal solvate), the upper and lower limits are regulated.

Quantitation. To quantify the active substance of a substance or dosage form, instrumental and chemical methods of analysis are used.

Storage. Packaging and storage conditions should ensure the quality of the medicinal product during the established shelf life.

The following is a breakdown of the recommended temperature storage conditions for drugs:

|  |  |
| --- | --- |
| **Рекомендуемые условия Расшиф** | **ровка рекомендуемых****условий** |
| Хранить при температуре не выше 30 оС От | 2 до 30 | оС |
| Хранить при температуре не выше 25 оС От | 2 до 25 | оС |
| Хранить при температуре не выше 15 оС От | 2 до 15 | оС |
| Хранить при температуре не выше 8 оС От | 2 до 8 | оС |
| Хранить при температуре не ниже 8 оС От | 8 до 25 | оС |

Marking. Marking is regulated by the competent authorized body with the publication of the relevant regulatory legal act. Thus, the information in the "Marking" section does not claim to be complete. It is oriented primarily to pharmacopoeial purposes, and only those provisions are mandatory that are necessary to confirm the conformity of the product to the article. All other information is advisory in nature. In cases where the term “label” is used in the Pharmacopoeia, the relevant information may be placed on the container, on the package or in the insert, depending on the decision of the competent authority.