Original

Index no:.....

**UNIVERSITY OF RUHUNA – FACULTY OF ALLIED HEALTH SCIENCES**
**DEPARTMENT OF PHARMACY**
**FOURTH BPHARM PART II EXAMINATION – JUNE/AUGUST 2020**
**PH 4223 QUALITY CONTROL (SEQ)**

**TIME: TWO HOURS**

**INSTRUCTIONS**

- There are four (**04**) questions in the SEQ paper.
- Answer **Part A** and **Part B** in separate booklets provided.
- No paper should be removed from the examination hall.
- Do not use any correction fluid.
- Use illustrations where necessary.

## PART A

**01.**

1.1. Briefly describe the weight variation test for tablet dosage forms. (***20 marks***)

1.3. Briefly describe the disintegration test for hard gelatin capsules. (***40 marks***)

1.4. Briefly describe **one** method which is used to determine alcohol content in elixirs. (***40 marks***)

**02.**

2.1. Briefly describe borosilicate glass which is used in the preparation of glass containers for pharmaceuticals. (***20 marks***)

2.2. Briefly explain **two** importance of tamper evident packaging. (***20 marks***)

2.3. List **five** types of tamper evident packages used for pharmaceutical products. (***10 marks***)

2.4. Briefly explain the breaking (hardness) test for suppositories. (***40 marks***)

2.5. List **four** chromatographic separation techniques described in appendices of British Pharmacopoeia 2016. (***10 marks***)

## PART B

**03.**

3.1. "*Good manufacturing Practices (GMP) are not required if there is a quality control laboratory*". Justify your answer. (***10 marks***)

3.2. Briefly explain the expected outcomes of a quality assurance system in a pharmaceutical product manufacturing plant. (***10 marks***)



57

3.3. Qualification and validation are two the important concepts in Good Manufacturing practices. Define the following terms.

3.3.1. Design qualification (DQ) (*05 marks*)

3.3.2. Installation qualification (IQ) (*05 marks*)

3.3.3. Operational qualification (OQ) (*05 marks*)

3.3.4. Performance qualification (PQ) (*05 marks*)

3.4. Write short notes.

3.4.1. Quality risk management (QRM) (*15 marks*)

3.4.2. Product quality review (PQR) (*15 marks*)

3.4.3. Root cause analysis (RCA) (*15 marks*)

3.4.4. Quality audit (*15 marks*)

**04.**

4.1. List down the determinants of quality of medicines. (*05 marks*)

4.2. Quality control is more critical in sustained action products than in immediate release products. Briefly explain the reasons. (*20 marks*)

4.3. Answer the questions given below, using the monograph of Diclofenac sodium Extended-Release (ER) tablets provided.

4.3.1. State the name of the active pharmaceutical ingredient with upper and lower limits of the content. (*05 marks*)

4.3.2. List down the main tests that will appear in the finished product certificate of analysis (CoA) of Diclofenac sodium ER tablet. (*10 marks*)

4.3.3. Comment on the packaging and storage requirements of the Diclofenac sodium ER tablet. (*10 marks*)

4.4. Briefly describe the **five** general types of preparations suitable and intended for parenteral administration. (*20 marks*)

4.5. Briefly explain **one** test method that is used to evaluate each of the following quality parameters.

4.5.1. Particulate matter in injections. (*15 marks*)

4.5.2. Bacterial endotoxins test. (*15 marks*)

@@@@@@@@@@

Original

*Revision Bulletin*
Official March 1, 2010



# Diclofenac Sodium Extended-Release Tablets

» Diclofenac Sodium Extended-Release Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of diclofenac sodium ($C_{14}H_{10}Cl_2NNaO_2$).

**Packaging and storageÐ** Preserve in well-closed containers. Store at controlled room temperature, and protect from light.

**LabelingÐ** When more than one *Dissolution Test* is given, the labeling states the *Dissolution Test* used only if *Test 1* is not used.

**USP Reference standards** ⟨11⟩**Ð** *USP Diclofenac Sodium RS. USP Diclofenac Related Compound A RS.*

**IdentificationÐ**

**A:** The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

**B:** *Thin-Layer Chromatographic Identification Test* ⟨201⟩*Ð*

*Solvent system:* methanol, toluene, glacial acetic acid (40 : 60 : 0.5).

*Test solutionÐ* Finely powder not fewer than 10 Tablets. Accurately weigh a portion of the powder, equivalent to about 50 mg of diclofenac sodium, and transfer to a 25-mL volumetric flask. Add about 15 mL of methanol, sonicate for 10 minutes, shake by mechanical means for 10 minutes, dilute with methanol to volume, and mix. Centrifuge this solution, and use the clear supernatant as the *Test solution.*

*Standard solutionÐ* Accurately weigh about 50 mg of USP Diclofenac Sodium RS into a 25-mL volumetric flask. Add 10 mL of methanol, shake by mechanical means for 10 minutes, dilute with methanol to volume, and mix.

***Change to read:***

**Dissolution** ⟨711⟩**Ð**

TEST 1*Ð*

*Medium:* 0.05 M phosphate buffer, pH 7.5; 900 mL.

*Apparatus 2:* 50 rpm; use wire sinkers.

*Times:* 1, 5, 10, 16, and 24 hours.

*ProcedureÐ* Determine the amount of $C_{14}H_{10}Cl_2NNaO_2$ dissolved by employing UV absorption at the wavelength of maximum absorbance at about 276 nm on filtered portions of the solution under test, suitably diluted with *Medium,* if necessary, in comparison with a Standard solution having a known concentration of USP Diclofenac Sodium RS in the same *Medium.*

*TolerancesÐ* The percentages of the labeled amount of $C_{14}H_{10}Cl_2NNaO_2$ dissolved at the times specified conform to *Acceptance Table 2.*

| Time (hours) | Amount dissolved |
|---|---|
| 1 | between 15% and 35% |
| 5 | between 45% and 65% |
| 10 | between 65% and 85% |
| 16 | between 75% and 95% |
| 24 | not less than 80% |

TEST 2*Ð* If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2.*

*Medium, Apparatus,* and *ProcedureÐ* Proceed as directed for *Test 1.*

*Times:* 1, 2, 4, 6, and 10 hours.

*TolerancesÐ* The percentages of the labeled amount of $C_{14}H_{10}Cl_2NNaO_2$ dissolved at the times specified conform to *Acceptance Table 2.*

| Time (hours) | Amount dissolved |
|---|---|
| 1 | not more than 28% |
| 2 | between 20% and 40% |
| 4 | between 35% and 60% |
| 6 | between 50% and 80% |
| 10 | not less than 65% |

TEST 3*Ð* If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3.*

*Medium* and *ProcedureÐ* Proceed as directed for *Test 1.*

*Apparatus 1:* 100 rpm.

*Times:* 2, 4, 8, and 16 hours.

*TolerancesÐ* The percentages of the labeled amount of $C_{14}H_{10}Cl_2NNaO_2$ dissolved at the times specified conform to *Acceptance Table 2.*

| Time (hours) | Amount dissolved |
|---|---|
| 2 | between 22% and 42% |
| 4 | between 34% and 61% |
| 8 | between 52% and 82% |
| 16 | not less than 73% |

TEST 4*Ð* If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4.*

*Medium* and *ProcedureÐ* Proceed as directed for *Test 1.*

*Apparatus 1:* 100 rpm.

*Times:* 2, 4, 8, and 16 hours.

*TolerancesÐ* The percentages of the labeled amount of $C_{14}H_{10}Cl_2NNaO_2$ dissolved at the times specified conform to *Acceptance Table 2.*

| Time (hours) | Amount dissolved |
|---|---|
| 2 | between 20% and 40% |
| 4 | between 35% and 55% |
| 8 | between 60% and 85% |
| 16 | not less than 85%. (RB 1-Mar-2010) |

(RB 1-Mar-2009)

**Uniformity of dosage units** ⟨905⟩: meet the requirements.

**AssayÐ** [NOTE*Ð* Protect the *Assay preparation, Standard preparation,* and *System suitability solution* from light.]

*Diluent:* a mixture of acetonitrile and water (43 : 57).

*0.05 M Monobasic potassium phosphate bufferÐ* Dissolve 6.8 g of monobasic potassium phosphate in 950 mL of water, adjust with dilute phosphoric acid or dilute potassium hydroxide solution to a pH of 4.0 ± 0.05, dilute with water to 1 L, and mix.

*Mobile phaseÐ* Prepare a filtered and degassed mixture of acetonitrile, *0.05 M Monobasic potassium phosphate buffer,* and tetrahydrofuran (43 : 57 : 2). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

*Diclofenac related compound A solutionÐ* Dissolve an accurately weighed quantity of USP Diclofenac Related Compound A RS in *Diluent,* and quantitatively dilute with *Diluent* to obtain a solution having a known concentration of about 200 µg per mL.



56

*Standard preparation*Ð Dissolve an accurately weighed quantity of USP Diclofenac Sodium RS in *Diluent,* and quantitatively dilute with *Diluent* to obtain a solution having a known concentration of about 200 µg per mL.

*System suitability solution*Ð Transfer 10 mL of the *Standard preparation* and 5 mL of *Diclofenac related compound A solution* to a 20-mL volumetric flask. Dilute with *Diluent* to volume, and mix.

*Assay preparation*Ð Powder not fewer than 20 Tablets, and transfer an accurately weighed portion of the powder, equivalent to about 100 mg of diclofenac sodium, to a 100-mL volumetric flask, add about 50 mL of *Diluent,* sonicate for about 15 minutes, then shake by mechanical means for 15 minutes. Add a few drops of methanol to remove the foam, dilute with *Diluent* to volume, and mix. Transfer 10.0 mL of the supernatant to a 50-mL volumetric flask, dilute with *Diluent* to volume, and mix.

*Chromatographic system* (see *Chromatography* ⟨621⟩)Ð The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 15-cm column that contains 5-µm packing L1. The flow rate is about 1.5 mL per minute. Inject 40 µL of the *System suitability solution* into the chromatograph, and record the peak responses as directed for *Procedure:* the relative retention times are about 0.9 for diclofenac related compound A and 1.0 for diclofenac; and the resolution, *R,* between the diclofenac peak and the diclofenac related compound A peak is not less than 2.0. Inject 20 µL of the *Standard preparation* into the chromatograph, and record the peak responses as directed for *Procedure:* the tailing factor of the diclofenac peak is not more than 2.0; and the relative standard deviation of the diclofenac peak for replicate injections is not more than 2.0%.

*Procedure*Ð Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the area responses for the major peaks. Calculate the quantity, in mg, of diclofenac sodium ($C_{14}H_{10}Cl_2NNaO_2$) in the portion of Tablets taken by the formula:

$$500C(r_U / r_S)$$

in which $C$ is the concentration, in mg per mL, of USP Diclofenac Sodium RS in the *Standard preparation;* and $r_U$ and $r_S$ are the diclofenac peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.