Briefing

Quality Attributes of Tablets Labeled as Having a Functional Score. The General Chapters—Dosage Forms Expert Committee proposes to add a new general test chapter to ensure the quality attributes of functionally scored tablets during their time in the marketplace. The tests provided in this new general chapter will apply to products with approved labeling indicating that the tablets can be split to produce multiple portions that have correspondingly fractional doses. At present, no USP monograph describes such products. In the future, this general chapter can be referenced in monographs for tablets with approved functional scoring. The inclusion of this general chapter as a requirement in a tablets monograph will take place via the normal request for revision process described in the USP Guideline for Submitting Requests for Revision to USP–NF (www.usp.org).

In 2011 FDA published a draft Guidance for Industry—Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM269921). This guidance gives recommendations for the content of applications from manufacturers who seek to claim on the product's labeling that their product has functional scoring. The approved labeling would provide information to patients and practitioners that the tablets can be split to achieve subdivided portions. This proposed new general chapter gives specific procedures and criteria upon which to evaluate the quality of these scored tablets and the performance of the subdivided portions.

A Stimuli to the Revision Process article in this number of Pharmacopeial Forum gives further insights into the rationale for the new general chapter and its contents.

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Comment deadline: September 30, 2013

Add the following:

705 QUALITY ATTRIBUTES OF TABLETS LABELED AS HAVING A FUNCTIONAL SCORE

Purpose

This chapter provides quality attributes for tablets labeled as having a functional score. At the time of splitting, the intact tablets should conform to the monograph specification. With the exception of dose, each split portion from tablets labeled as having a functional score are expected to conform to the quality attributes of the whole tablets. The split portions resulting from subdividing a functionally scored tablet should conform to the tests for Splitting Tablets with Functional Scoring and Dissolution or Disintegration given in this chapter. Disintegration testing is required only when approved as a surrogate for dissolution and specified in the monograph. The label claim of the split portions should be a simple fractional part of the claim for the intact tablet based on the number of scores and the size of the split portion (e.g., one-half, one-third, or one-quarter). The dose of the split tablet portions should be stated on the product labeling.

SCOPE

This chapter applies to tablets labeled as having a functional score and to the split portions that represent any labeled fraction of the whole functionally scored tablet dose. Tablets should be split as part of the test procedure. Testing should be performed promptly after splitting unless the stability of the samples has been demonstrated, and the storage conditions and period should be defined in the test procedure. For Dissolution or Disintegration testing, analysts should use only split portions from tablets determined to be acceptable by the Splitting Tablets with Functional Scoring test.

SPLITTING TABLETS WITH FUNCTIONAL SCORING

Procedure

1. Take a random sample of 30 intact tablets, and proceed as follows.
2. Accurately weigh each tablet, and record its weight.
3. For each intact tablet, determine the expected weight of the split portions by dividing the whole-tablet weight by the designated number of split portions indicated on the labeling.
4. Split each tablet by hand (without mechanical assistance) into the designed number of split portions, and weigh each split portion.
5. For each tablet, determine the percent of the expected weight in each split portion.

An acceptable tablet breaks into the designed number of segments, and each split portion has NLT 75% and NMT 125% of the expected weight of the split tablet portion. [NOTE— Set aside split tablet portions derived from acceptable tablets for subsequent testing for dissolution or disintegration.] Acceptance Criteria: NLT 28 of the 30 tablets are acceptable.

DISSOLUTION

Use split portions from tablets that are acceptable according to the Splitting Tablets with Functional Scoring test.

Immediate-Release Tablets

Dissolution for immediate-release tablets is performed at the S₂ stage (see 711). Test 12 split tablet portions according to the specified Medium, Apparatus, Times, and Analysis. The average of the 12 results is NLT Q, and no result is less than Q – 15%.

Extended-Release Tablets

Perform dissolution testing of split tablet portions from extended-release tablets by one of the two

alternative procedures. The procedure to be used is specified in the monograph.

**Procedure 1 (Procedure for Extended-Release Dosage Forms, Dissolution)**: Individually test 12 split tablet portions and 12 intact tablets.

**Medium, Apparatus, and Analysis**: As given in the monograph following the appropriate test number found on the labeling. Dissolution profile test time points are determined as follows. From the appropriate dissolution test in the monograph, use the time points given. At a minimum, use three time points with no more than one time point where the results exceed 85% dissolved.

Calculate the similarity factor \(f_2\) for the intact-tablet results and the split-tablet portion results:

\[
f_2 = 50 \cdot \log \left[ 1 + \left( \frac{1}{n} \right) \sum_{t=1}^{n} (R_t - T_t)^2 \right]^{-0.5} \cdot 100
\]

- \(R_t\) = cumulative percentage of the labeled drug dissolved at each of the selected \(n\) time points of the intact tablets
- \(T_t\) = cumulative percentage of the labeled drug dissolved at each of the selected \(n\) time points of the split tablet portions

**Acceptance Criteria**: The calculated \(f_2\) is NLT 50 (acceptable range: 50–100).

**Procedure 2 (Procedure for Extended-Release Dosage Forms, Dissolution)**: Use a split-tablet portion as the dosage unit. Individually test 12 dosage units.

**Medium, Apparatus, Times, and Analysis**: As given in the monograph following the appropriate test number found on the labeling.

**Acceptance Criteria**: The percentages of the labeled amount released at the times specified conform to the \(L_2\) level criteria of *Acceptance Table 2* in 711.

**DISINTEGRATION**

Disintegration testing is necessary only when used as a surrogate for dissolution testing as specified in the monograph. Follow the procedure using split portions from tablets that are acceptable according to the *Splitting Tablets with Functional Scoring* test as the dosage unit (see 701).

**Auxiliary Information** - Please check for your question in the FAQs before contacting USP.