

Template to be Completed by the Manufacturer for Fixed Dose Combinations

A. RATIONALE FOR THE COMBINATION

Summarize 'bottom line' in this box (to be completed by CDR Reviewer).

Manufacturer's Rationale for the Combination (not to exceed 2 pages of 11-point font)

The required information/evidence must be succinct and entered directly into the template. References must be provided and are to be included in a list of references at the end of the template.

The required information/evidence in this section includes:

- The therapeutic rationale for the combination
- The pharmacological rationale for the combination

CDR Reviewer Comments Regarding the Rationale for the Combination

To be completed by CDR Reviewers.

B. BIOEQUIVALENCE

Summarize 'bottom line' in this box (to be completed by CDR Reviewer).

Manufacturer-submitted Information Showing Bioequivalence

The required information/evidence must be succinct and entered directly into the template. References must be provided and are to be included in a list of references at the end of the template.

The required information/evidence in this section includes:

- Evidence of bioequivalence of the FDC with the individual components of the FDC.
- A copy of Health Canada Reviewers' Report [also called Pharmaceutical Safety and Efficacy Assessment or the Comprehensive Summary – Bioequivalence (CS-BE)]
- A verbatim quotation from the Health Canada Reviewers' Report regarding the conclusions on bioequivalence.
- A statement indicating whether the individual components have uncomplicated or complicated and variable pharmacokinetic characteristics
- Evidence that the pharmacokinetic properties (eg, absorption) of the FDC are similar to those of the individual components.

Table: Bioequivalence Profile for Fixed Dose Combination (FDC) Products*†

Parameter	Component A in FDC	Component A as Single Entity	Component B in FDC	Component B as Single Entity
AUC (0-T) <ul style="list-style-type: none"> • Mean • Standard Deviation • Coefficient of Variance • Ratio of Relative Means • 90% Confidence Interval 				
Cmax <ul style="list-style-type: none"> • Mean • Standard Deviation • Coefficient of Variance • Ratio of Relative Means • 90% Confidence Interval 				
Tmax <ul style="list-style-type: none"> • Mean • Standard Deviation • Coefficient of Variance 				

* Add columns to match number of components

† Potency-corrected data should be used

CDR Reviewer Comments Regarding Bioequivalence

To be completed by CDR Reviewers.

C. PLACE IN THERAPY

Summarize 'bottom line' in this box (to be completed by CDR Reviewer).

Manufacturer-submitted Information Regarding Place in Therapy (not to exceed 2 pages of 11-point font)

The required information/evidence must be succinct and entered directly into the template. References must be provided and are to be included in a list of references at the end of the template.

The required information/evidence in this section should include:

- Would the components be the drugs of choice as separate medicines?
- Does the FDC contain the most commonly prescribed doses of the individual components?
- Should this combination be used for initiating therapy?
- Titration issues (is therapy initiated with FDC or is a switch to FDC necessary after titration, lack of ability to titrate doses due to limited strengths of FDC available.)
- How likely are dose changes?
- Will increasing the dose of one component result in an unnecessary dose increase in the other component?
- Does the use of the FDC overcome any issues or problems related to the administration of the components individually?

CDR Reviewer Comments Regarding Place in Therapy

To be completed by CDR Reviewers.

D. HARMS INFORMATION

Summarize 'bottom line' in this box (to be completed by CDR Reviewer).

Manufacturer-submitted Information Regarding Harms

The required information/evidence must be succinct and entered directly into the template. References must be provided and are to be included in a list of references at the end of the template.

The required information/evidence in this section includes:

- Information about the types of adverse events and their rates for the FDC, the components and appropriate comparators.

CDR Reviewer Comments Regarding Harms Information

To be completed by CDR Reviewers.

E. PHARMACOECONOMIC EVALUATION

Summarize 'bottom line' in this box (to be completed by CDR Reviewer).

Manufacturer-submitted Cost Information

The required information/evidence must be succinct and entered directly into the template. Sources of price information must be provided and are to be included as footnotes below the tables.

- Provide price of the FDC (fixed price for all strengths; price for different strengths if applicable) and its daily cost compared to price of individual components

Table X: Cost Comparison of FDC and Individual Components

Drug / Comparator	Strength	Dosage Form	Price (\$)	Recommended Daily Use	Daily Drug Cost (\$)
FDC generic name (Brand name)	A mg/B mg/...Z mg		\$A/B/.../Z		\$FDC
Individual component A (Brand & generics)	A mg		\$A		\$ daily A
Individual component B (Brand & generics)	B mg		\$B		\$ daily B
Individual component up to Z if applicable (Brand & generics)	Z mg		\$Z		\$ daily Z
Total (A+B+...+Z)					\$ Total of Individual Components

- Include any relevant information on patent expiration for the individual components as a footnote to table.
- Provide source and where applicable, indicate if price is a confidential price submitted by the manufacturer.
- Summarize cost differences and potential cost savings of FDC compared to individual components.
 - Summary of potential cost savings based on Table X.
 - Quantify the potential daily savings or price difference of FDC compared to price of individual components together; provide a range on the cost difference or daily savings.

Cost Comparison Table

A list of prices for appropriate comparators. Comparators may be recommended (appropriate practice, versus actual practice). Comparators are not restricted to drugs, but may be devices or procedures. Costs are manufacturer list prices, unless otherwise specified.

- List comparators alphabetically by generic name.

Table xx: Cost Comparison Table

Drug / Comparator	Strength	Dosage Form	Price (\$)	Recommended <u>Daily Use</u>	Average Daily Drug Cost (\$)
A/B/.../Z (FDC brand)					
Comparators					

Note: Where applicable, indicate if price is a confidential price submitted by the manufacturer. Provide sources for cost information and dosage information.

CDR Reviewer Comments Regarding Cost Information

To be completed by CDR Reviewers.