



CDEC FINAL RECOMMENDATION

SAXAGLIPTIN / METFORMIN

(Komboglyze — AstraZeneca)

Indication: Type 2 Diabetes Mellitus

Recommendation:

The Canadian Drug Expert Committee (CDEC) recommends that saxagliptin/metformin (Komboglyze) be listed for patients if the following clinical criterion and condition are met:

Clinical Criterion:

- Patients for whom insulin is not an option and who are already stabilized on therapy with metformin, a sulfonylurea and saxagliptin, to replace the individual components of saxagliptin and metformin in these patients.

Condition:

- Drug plan costs for the saxagliptin/metformin fixed-dose combination (FDC) should not exceed the combined cost of saxagliptin and metformin administered separately.

Reason for the Recommendation:

At the submitted price, the saxagliptin/metformin FDC (\$2.54 per day) is less costly than saxagliptin and metformin administered separately, and less costly than Jentaduetto (linagliptin/metformin \$2.57 per day) and Janumet (sitagliptin/metformin \$3.20 per day).

Background:

Komboglyze is a saxagliptin/metformin FDC indicated for use in the following scenarios:

- Where patients are already treated with saxagliptin and metformin or are inadequately controlled on metformin alone.
- In combination with a sulfonylurea as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes who are already treated with saxagliptin, metformin and a sulfonylurea, or who are inadequately controlled on metformin and a sulfonylurea alone.
- In combination with premixed or long/intermediate acting insulin as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes who are already treated with saxagliptin, metformin and premixed or long/intermediate acting insulin, or who are inadequately controlled on metformin and premixed or long/intermediate acting insulin alone.

Common Drug Review

Komboglyze is available as 2.5 mg/500 mg, 2.5 mg/850 mg and 2.5 mg/1,000 mg (saxagliptin/metformin) oral tablets. The product monograph recommends twice daily dosing with meals.

Summary of CDEC Considerations

CDEC considered the following information prepared by the CADTH Common Drug Review (CDR): a review of manufacturer-provided information on the therapeutic rationale, place in therapy, bioequivalence, and harms (safety and tolerability) for saxagliptin/metformin, a critique of the manufacturer's pharmacoeconomic evaluation, and patient group-submitted information about outcomes and issues important to patients.

Patient Input Information

The following is a summary of information provided by one patient group that responded to the CDR call for patient input:

- Individuals with type 2 diabetes expressed the desire to reduce or eliminate medications.
- Limitations with currently available treatments include the need for multiple medications, the need to continuously increase the amount of medication taken, side effects, and the inconvenience of insulin injections.

Bioequivalence

- CV181-152 compared the steady-state pharmacokinetic and pharmacodynamics of a 2.5 mg saxagliptin twice daily dosing regimen with a 5 mg saxagliptin once daily regimen in an open-label, crossover randomized controlled trial with 16 healthy participants over seven days. During the study period, results showed that 2.5 mg saxagliptin twice daily was equivalent to saxagliptin 5 mg once daily with respect to total daily exposure and inhibition of DPP-4.
- Study CV-181-118 was an open-label, randomized, 4-period, 4-treatment, 4-way crossover, single-dose study in fasted and fed healthy volunteers (N = 27) that assessed the bioequivalence of a single dose of 2.5 mg saxagliptin/500 mg metformin FDC relative to 2.5 mg saxagliptin and 500 mg metformin tablets administered separately. The study participants were dosed for seven days per treatment. The FDC tablet of saxagliptin/metformin was shown to be bioequivalent to the individual drugs administered separately in accordance with standard criteria for bioequivalence. Only the 2.5 mg/500 mg FDC tablet was compared with the equivalent doses of the individual components; the 2.5 mg/850 mg and 2.5 mg/1,000 mg dosage forms were not evaluated.

Harms (Safety and Tolerability)

- The saxagliptin/metformin FDC tablet and the co-administered 2.5 mg saxagliptin and 500 mg metformin tablets were safe and well tolerated in healthy patients in both the fasted and fed states. There were no deaths, serious adverse events, or discontinuations due to adverse events.
- Most adverse events were similar and mild in severity in both regimens and resolved without treatment.

Cost and Cost-Effectiveness

The manufacturer submitted a cost-minimization analysis comparing the drug costs of saxagliptin/metformin FDC (2.5 mg/500 mg, 2.5 mg/850 mg and 2.5 mg/1,000 mg, twice daily) to the individual components (saxagliptin and metformin), Janumet (FDC of sitagliptin 50 mg

twice daily and metformin 500 mg, 850 mg, or 1,000 mg twice daily), and individual component combinations of metformin with other DPP-4s. CDR also compared the drug costs of saxagliptin/metformin FDC to Jentadueto (FDC of linagliptin 2.5 mg twice daily and metformin 500 mg, 850 mg, or 1,000 mg twice daily).

At the submitted price of \$1.27 per tablet (\$2.54 per day), the average annual cost of saxagliptin/metformin FDC (\$927 per patient) was lower than the equivalent dose combinations of the individual components, saxagliptin and metformin (at least \$1,036 per patient), lower than that of Janumet (\$1.60 per tablet, twice daily; \$1,169 per patient) and lower than that of Jentadueto (\$1.28 per tablet, twice daily; \$938 per patient).

Other Discussion Points:

CDEC noted that individuals who experience intolerance to sulfonylureas may benefit from a regimen involving a DPP-4 inhibitor and metformin without a sulfonylurea.

Research Gaps:

CDEC noted that there is insufficient evidence regarding the following:

- Direct or indirect comparisons assessing the comparative efficacy of saxagliptin versus other antihyperglycemic drugs for the prevention of macrovascular and microvascular diabetes-related complications; such comparisons are needed.

CDEC Members:

Dr. Robert Peterson (Chair), Dr. Lindsay Nicolle (Vice-Chair), Dr. Ahmed Bayoumi, Dr. Bruce Carleton, Ms. Cate Dobhran, Mr. Frank Gavin, Dr. John Hawboldt, Dr. Peter Jamieson, Dr. Kerry Mansell, Dr. Irvin Mayers, Dr. Yvonne Shevchuk, Dr. James Silvius, and Dr. Adil Virani.

May 21, 2014 Meeting

Regrets:

None

Conflicts of Interest:

None

About this Document:

CDEC provides formulary listing recommendations or advice to CDR participating drug plans. CDR clinical and pharmacoeconomic reviews are based on published and unpublished information available up to the time that CDEC deliberated on a review and made a recommendation or issued a record of advice. Patient information submitted by Canadian patient groups is included in the CDR reviews and used in the CDEC deliberations.

The manufacturer has reviewed this document and has not requested the removal of confidential information in conformity with the *CDR Confidentiality Guidelines*.

Common Drug Review

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