Identification and Management of Duplicate Therapy Involving Incretin-Targeting Therapies for Diabetes and Weight Loss

N. Friedlander, PharmD[1]; S.W. Champaloux, PhD, MPH[1]; K.L. Curtis, PharmD[1]; P.P. Gleason, PharmD[1,2]. [1]Prime Therapeutics LLC, Eagan, MN, United States; [2]University of Minnesota College of Pharmacy, Minneapolis, MN, United States.

BACKGROUND

- Available only as branded products, glucagon-like peptide-1 (GLP-1) agonist and dipeptidyl peptidase-4 (DPP4) inhibitor drugs are commonly used in type 2 diabetes mellitus (T2DM) treatment. Both drug classes exert anti-diabetic effect through the incretin system. GLP-1 agonists mimic the activity of endogenous incretins while DPP4 inhibitors reduce their breakdown.
- All GLP-1 drugs are FDA approved for T2DM, and the GLP-1s semaglutide and liraglutide have products approved for obesity treatment. GLP-1 drug products indicated exclusively for diabetes have shown increasing utilization in the off-label treatment of obesity.[1]
- Due to the incretin system activity, GLP-1 and DPP4 have overlapping mechanisms of action. As demonstrated in clinical trials, combination use does not result in synergistic beneficial impacts for T2DM disease control but does add additional cost, generally more than $5,000 a year, and increases the risk for drug side effects.[2,3,4]
- Combination GLP-1 and DPP4 use has not historically been recommended by American Diabetes Association (ADA) guidelines, and use of multiple GLP-1 drugs or multiple DPP4 drugs together is similarly not recommended. Comparable recommendations related to incretin drug combination were issued in 2023 guidelines by the American Association of Clinical Endocrinology (AACE).[5,6]
- Identifying members with apparent incretin duplicate therapy using pharmacy claims data and providing the information to a managed care pharmacist (MCP) for prescriber outreach can assist in decreasing inappropriate combination incretin therapy, decrease drug side effect risk, and reduce costs to the member and insurer.
- Little objective data is available on the incretin duplicative therapy prevalence and MCP success in converting to single agent incretin therapy.

METHODS

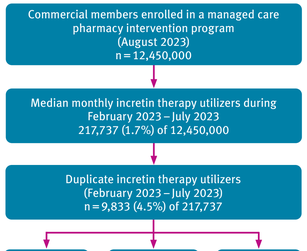
- To obtain incretin overall claims expenditure monthly trend from August 2022 to July 2023, all GLP-1 and DPP4 paid claims from Prime Therapeutics' 12.45 million commercially insured members enrolled in the HighTouchRx® program were identified from August 2022 through July 2023. The GLP-1 and DPP4 monthly claims allowed dollar amount per member per month (PMPM) was calculated by totaling the allowed amount paid to pharmacies, by month, divided by the overall membership. The allowed paid amount to the pharmacy is inclusive of all network discounts and member share; however, rebates or coupons are not included.
- We report the cumulative incidence of duplicate incretin therapy from February 2023 through July 2023 (6 months) in **Figure 1**. During the 6-month analysis period, incretin utilization was calculated by determining the median monthly number of incretin utilizers, and the cumulative duplicate therapy incidence was calculated by identifying duplicate incretin therapy utilizers divided by the median monthly incretin utilization rate. Duplicate incretin therapy was defined as the presence of multiple, unique, overlapping incretin claims based on days of supply and fill date, with evidence of current duplicate therapy during the 6-month look back period.

Duplicate incretin therapy identification and managed care pharmacist to prescriber outreach impact

- 12.45M members (75%) of Prime Therapeutics' commercial business were actively enrolled in the HighTouchRx program where MCPs are provided drug therapy optimization savings opportunities including the incretin duplicate therapy cases. GLP-1 and DPP4, GLP-1 and GLP-1, and DPP4 and DPP4 duplicate therapy opportunities were identified weekly through pharmacy claim identification. Identification required the presence of multiple, unique, overlapping incretin claims based on days of supply and fill date, with evidence of current duplicate therapy. The opportunities were sent to pharmacists in the HighTouchRx web tool with an estimated savings value, in addition to claims details and other member and case details.
- All incretin duplicative therapy cases between August 2022 and July 2023 were categorized as either having been reviewed by an MCP or not. Those having been reviewed by an MCP were further categorized into: no opportunity with no prescriber outreach; successful with validated claims data showing one of the incretin drugs has been discontinued; case reviewed by MCP and is in progress; or MCP made prescriber outreach but was unsuccessful in eliminating the duplicate incretin therapy.
- Each opportunity included an estimated savings value if the recommended therapy were to be changed to monotherapy, i.e., become successful. Savings estimates were derived by the total populations' median annual specific incretin claim cost, using the annualized cost for the least expensive of the member's two incretin therapies. The duplicate incretin therapy opportunities were sent to MCP in an interactive web tool with the dates of service of the latest claims responsible for the duplicate therapy, the number of days the duplicate therapy was present, and the number of overlapping claims.
- Pharmacist incretin duplicate therapy review processes typically involved a member case and claims history review within the web tool, including verification of ongoing duplicative therapy and subsequent outreach to the prescriber to discuss the drug therapies mechanistic overlap. After verification with the prescriber that the therapy was currently duplicative and ongoing, a recommendation was made to discontinue one of the therapies based on member and prescriber preference.
- A successful MCP prescriber outreach was defined as a prescriber accepted discontinuation of an incretin drug therapy and required claims evidence of over 90 days without a subsequent incretin therapy refill. Actual savings was calculated for each successful outreach by calculating the expected annual cost of the member-specific, adjusted therapeutic regimen and taking the difference between this value and the expected annual cost of the therapeutic regimen prior to prescriber outreach; full adherence to the prescribed regimen was assumed. Successful MCP outreach savings from August 2022 through July 2023 were summed to determine total annualized savings associated with the program.
- MCPs reported prescriber outreach outcomes within the web tool including whether the outreach was successful or unsuccessful, pharmacist notes, calculated savings associated with change in therapeutic regimen in successful outreach cases, and reasons for ongoing duplicate therapy in unsuccessful outreach cases.

FIGURE 1

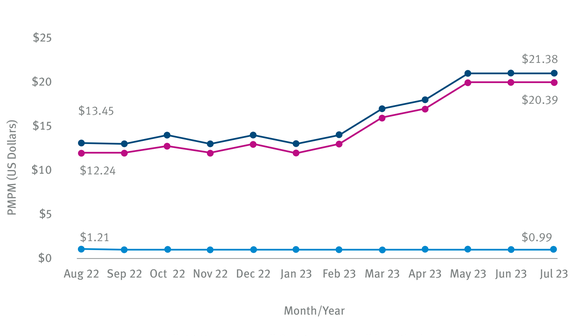
Duplicate Incretin Therapy Member Identification and Cumulative Incidence, August 2023



Incretin drugs include glucagon-like protein (GLP-1) agonist and dipeptidyl-peptidase 4 (DPP4) inhibitor drugs. GLP-1 agonist drugs include products indicated for weight loss: dulaglutide, exenatide, exenatide extended release, liraglutide, lixisenatide, semaglutide (injectable and oral formulations) and tirzepatide. DPP4 inhibitor drugs include: alogliptin, linagliptin, saxagliptin and sitagliptin. Combination drugs were not included. An incretin utilizer was identified using paid pharmacy claims. A duplicate incretin utilizer was defined as having multiple distinct overlapping claims based on date of service and days supply dispensed involving two separate incretin drugs during the 6-month evaluation period (February 2023–July 2023). Members with duplicate incretin therapy were identified for managed care pharmacist review and prescriber outreach to recommend single incretin drug therapy.

FIGURE 2

Monthly Per Member Per Month (PMPM) Costs for Incretin Drugs, August 2022 – July 2023



Monthly PMPM calculated for those enrolled in managed care pharmacist intervention program by summing total paid amount for each drug class in each month for enrolled members and dividing by the monthly membership. Incretin drugs include glucagon-like protein (GLP-1) agonist and dipeptidyl-peptidase 4 (DPP4) inhibitor drugs. GLP-1 agonist drugs include products indicated for weight loss: dulaglutide, exenatide, exenatide extended release, liraglutide, lixisenatide, semaglutide (injectable and oral formulations) and tirzepatide. DPP4 drugs include: alogliptin, linagliptin, saxagliptin and sitagliptin. Combination drugs were not included. Total paid amount defined as amount paid pharmacy after network discount and member share, not inclusive of rebates or coupons.

RESULTS

Incretin drug therapy utilization, duplicate therapy prevalence and overall expenditures (Figures 1 and 2)

- 217,737 (1.7%) of 12,450,000 commercially insured members had an incretin drug therapy claim in any given month during the 6 months, February 2023 through July 2023
- Among the 217,737 incretin utilizers during the six months of February 2023 through July 2023, 9,833 (4.5%) had duplicate therapy that appeared still active per claims records in August 2023.
  - 75.5% GLP-1 + DPP4, 7,426 of 9,833; equating to 60 per 100,000
  - 23.8% GLP-1 + GLP-1, 2,342 of 9,833; equating to 19 per 100,000
  - 0.7% DPP4 + DPP4, 65 of 9,833; equating to 0.5 per 100,000
- Among the entire 12,450,000 commercially insured members, incretin expenditures increased 59.0% from August 2022 ($13.45 PMPM) to July 2023 ($21.38 PMPM).
  - GLP-1 expenditures increased 66.6% from August 2022 ($12.24 PMPM) to July 2023 ($20.39 PMPM).
  - DPP4 expenditures dropped 18.2% from August 2022 ($1.21 PMPM) to July 2023 ($0.99 PMPM).

Duplicate incretin drug therapy case review and prescriber intervention outcomes, August 2022 through July 2023 (12 months) (Table 1)

All duplicate incretin therapy cases

- 13,457 duplicate incretin cases identified, 10,424 (77.5%) were not reviewed by an MCP and 3,033 (22.5%) were MCP reviewed
  - 1,635 (53.9%) of 3,033 cases had no opportunity identified by MCP and no prescriber outreach
  - 467 (15.4%) successful cases switched to single incretin drug therapy at a $7,578 average analyzed savings per successful case with validated savings totaling $3.538 million ($0.024 PMPM, 12.45M lives)
  - 240 (7.9%) unsuccessful cases
    - 124 due to no prescriber response
    - 99 rejected by prescriber
    - 17 other reasons stated
  - 691 (22.8%) additional in progress cases with potential savings of $3.553 million ($0.024 PMPM, 12.45M lives)

DPP4 + GLP-1 cases

- 10,115 duplicate DPP4+GLP-1 cases identified, 8,461 (83.7%) were not reviewed by an MCP and 1,653 (16.7%) were MCP reviewed
  - 629 (38.0%) of 1,653 cases had no opportunity identified by an MCP and no prescriber outreach
  - 281 (17.0%) successful cases switched to single incretin drug therapy at a $5,945 average analyzed savings per successful case with validated savings totaling $1.670 million
  - 216 (13.1%) unsuccessful cases
  - 527 (31.9%) additional in progress cases with potential savings of $2.498 million

GLP-1 + GLP-1 cases

- 3,247 duplicate GLP-1 + GLP-1 cases identified, 1,897 (58.4%) were not reviewed by an MCP and 1,350 (41.6%) were MCP reviewed
  - 987 (73.1%) of 1,350 cases had no opportunity identified by an MCP, and no prescriber outreach
  - 180 (13.3%) successful cases switched to single incretin drug therapy at a $10,182 average analyzed savings per successful case with validated savings totaling $1.833 million
  - 20 (1.5%) unsuccessful cases
  - 163 (12.1%) additional in progress cases with potential savings of $1.051 million

DPP4 + DPP4 cases

- 95 duplicate DPP4 + DPP4 cases identified, 65 (68.4%) were not reviewed by an MCP and 30 (31.6%) were MCP reviewed
  - 19 (63.3%) of 95 cases had no opportunity identified by an MCP, and no prescriber outreach
  - 6 (20.0%) successful cases switched to single incretin drug therapy at a $5,929 average analyzed savings per successful case with validated savings totaling $35,574
  - 4 (13.3%) unsuccessful cases
  - 1 (3.3%) additional in progress cases with potential savings of $4,725

TABLE 1

Duplicate Incretin Case Review and Outcomes, August 2022 – July 2023

Incretin duplicate therapy type	Total duplicative incretin cases identified	Cases not reviewed by a MCP	MCP reviewed and no opportunity identified, no prescriber outreach	MCP reviewed with prescriber outreach, unsuccessful	MCP reviewed with prescriber, successful	Successful cases validated savings	MCP reviewed, in progress	In progress cases, total potential savings	Average savings per success case
GLP-1 + DPP4	10,115	8,462	629	216	281	$1,670,518	527	$2,497,868	$5,945
GLP-1 + GLP-1	3,247	1,897	987	20	180	$1,832,713	163	$1,051,048	$10,182
DPP4 + DPP4	95	65	19	4	6	$35,574	1	$4,725	$5,929
Total	13,457	10,424	1,635	240	467	$3,538,805	691	$3,553,641	$7,578

Incretin drugs include glucagon-like protein (GLP-1) agonist and dipeptidyl-peptidase 4 (DPP4) inhibitor drugs. GLP-1 agonist drugs include products indicated for weight loss: dulaglutide, exenatide, exenatide extended release, liraglutide, lixisenatide, semaglutide (injectable and oral formulations) and tirzepatide. DPP4 inhibitor drugs include: alogliptin, linagliptin, saxagliptin and sitagliptin. Combination drugs were not included. A duplicate incretin utilizer was defined as having multiple distinct overlapping claims based on date of service and days supply dispensed involving two separate incretin mimetic drugs during the 6-month evaluation period. Successful cases are defined as duplicate therapy cases for which managed care pharmacist (MCP) performed outreach, resulting in discontinuation of one of the two incretin therapies. Unsuccessful cases are defined as cases for which MCP performed outreach, but duplicate therapy continued after intervention. In progress cases are defined as cases still undergoing review or for which a change in therapy is still pending. No opportunity cases were reviewed by an MCP and determined to not be actionable at the time of review (e.g., member discontinued one incretin therapy, member no longer has active coverage). See methods for case savings estimation and validation process.

CONCLUSIONS

- Duplicate incretin drug therapy is common with a prevalence of 1 in 22 incretin drug utilizers found to have potential duplicate incretin therapy in a large commercially insured population. Annual savings, per duplicate incretin utilizing member, was found to be $7,578 from converting duplicate incretin therapy to single drug incretin therapy.
- One in 5 incretin duplicate therapy cases reviewed by an MCP resulted in a change to single drug therapy. When a prescriber outreach was performed, the success rate was 66%.
- These findings demonstrate identifying duplicate incretin therapy and converting to single incretin drug therapy is possible with an automated analytic rules process that provides MCPs with actionable information for prescriber outreach. During the 1-year analysis period, $3.5 million validated savings occurred through MCP prescriber outreaches recommending single agent incretin therapy, with an additional $3.5 million savings potential among in-progress cases.
- At more than $20 PMPM, the incretin drug class represents a large portion of all drug expenditures among commercially insured populations and has increased dramatically, by more than 50%, from mid-2022 to mid-2023. It is imperative incretin therapy is appropriately prescribed. Managed care pharmacy programs to eliminate duplicate incretin therapy for a member is one means to ensure appropriate therapy; reducing member share costs, insurer costs, and member drug side effect risk.

OBJECTIVES

- To assess GLP-1 and DPP4 duplicate therapy prevalence among commercially insured members, evaluate a MCP intervention program to reduce combination use of these drugs, and describe duplicate therapy reduction drug cost savings.

LIMITATIONS

- Program savings may be underestimated due to sentinel prescriber effect, meaning prescribers change behavior reducing their future duplicate incretin therapy patient treatment without MCP outreach, due to prior MCP outreach. In addition, when the prescriber does not respond to duplicate incretin therapy MCP outreach message yet single therapy change occurs, savings is not attributed to the program.
- Savings calculation assumes that the member would have continued using both incretin therapies for one year, continued to be enrolled in the health plan for a year, and that the prescriber would not have adjusted therapeutic regimen independently.
- The pharmacy claims analytic rules identify cases involving multiple unique incretin therapy duplication episodes involving one claim with an extended day supply (e.g., 90-day supply) dispensed prior to discontinuation can result in overestimating duplicate therapy prevalence. The incretin duplicate therapy cumulative prevalence reported here is an upper bound estimate; true prevalence is likely lower.
- GLP-1 product shortages during the period may have resulted in intra-class switching for select utilizers and may be responsible for some drug therapy overlap instances. In these cases, the limitation of claims data further strengthens the need for pharmacist-prescriber interaction.

REFERENCES

1. Truveta Research. (2023, Jun 26) *Ozempic, Wegovy, and Mounjaro: On- and off-label prescribing trends*. https://www.truveta.com/blog/research/ozempic-wegovy-and-mounjaro/
2. Lajthia E, et al. *Combination therapy with once-weekly glucagon like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors in type 2 diabetes: A case series. Pharm Pract* (Granada). 2019;17(4):1588. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6935552/
3. Violante R, et al. A randomized non-inferiority study comparing the addition of exenatide twice daily to sitagliptin or switching from sitagliptin to exenatide twice daily in patients with type 2 diabetes experiencing inadequate glycaemic control on metformin and sitagliptin. *Diabet Med*. 2012;29(11):e417-424. https://pubmed.ncbi.nlm.nih.gov/22375612/
4. Nauck MA, et al. Addition of a dipeptidyl peptidase-4 inhibitor, sitagliptin, to ongoing therapy with the glucagon-like peptide-1 receptor agonist liraglutide: A randomized controlled trial in patients with type 2 diabetes. *Diabetes Obes Metab*. 2017;19(2):200-207. https://pubmed.ncbi.nlm.nih.gov/27709794/
5. ADA 2023. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes-2023. *Diabetes Care*. 2023;46(supplement 1):S140-157. https://diabetesjournals.org/care/article/46/Supplement_1/S140/148057/9-Pharmacologic-Approaches-to-Glycemic-Treatment
6. Samson SL, et al. American Association of Clinical Endocrinology Consensus Statement: Comprehensive type 2 diabetes management algorithm – 2023 update. *Endocrine Practice*. 2023;29(5):305-340. https://www.endocrinepractice.org/action/showPdf?pii=S1530-891X%2823%2900034-4

Academy of Managed Care Pharmacy (AMCP) Nexus Meeting, Oct. 16-19, 2023, Orlando, FL
Sponsorship: Prime Therapeutics LLC