Patients with type 2 diabetes, n=3856.1

- NovoLog® Mix 70/30 (70% insulin aspart protamine suspension and 30% insulin aspart injection, [rDNA origin]) in a multinational, open-label, nonrandomized, 26-week, observational study that evaluated the safety and efficacy of antidiabetic drug (OAD) therapy and had A1C values available at baseline and final visit. The IMPROVE™ study was:

**Results from patients who completed the IMPROVE™ study who were previously treated with human premix ± oral hypoglycemic agents**

- Converting patients from human premix insulin to NovoLog® Mix 70/30 provided glycemic control and reduced the number of major hypoglycemic events1

**Every patient counts**

- Important Safety Information

- **Important Limitations of Use**

- **Renal and Hepatic Impairment:**

  - Hypokalemia: Use caution in patients predisposed to hypokalemia.

  - Insulin, particularly when given in settings of poor glycemic control, can cause hypokalemia.

  - **Hypokalemia:** Insulin, particularly when given in settings of poor glycemic control, can cause hypokalemia. Liberalization of fluid intake and blood glucose targets may help prevent hypokalemia in patients treated with insulin.

  - **Important Safety Information**

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  - **Important Safety Information**

  - **Important Limitations of Use**

  - **Renal and Hepatic Impairment:**

  - Hypokalemia: Use caution in patients predisposed to hypokalemia.

  - Insulin, particularly when given in settings of poor glycemic control, can cause hypokalemia.
Every patient counts when it comes to choosing a formulation

NovoLog® Mix 70/30—One insulin with both fasting and mealtime control1,3

FORMULATION

Formulation
NovoLog® Mix 70/30—One insulin with both fasting and mealtime control1,3

70% insulin aspart protamine crystals, which are engineered for extended action (up to 24 hours) to cover the basal need

30% soluble insulin aspart, which is available rapidly for mealtime coverage

Important Safety Information

Warnings and Precautions

• Administration: NovoLog® Mix 70/30 should not be mixed with any other insulin product, administered intravenously, or used in insulin infusion pumps. NovoLog® Mix 70/30 has a faster onset of action than human insulin premix 70/30 and should be dosed within 15 minutes before meal initiation for patients with type 1 diabetes. For patients with type 2 diabetes, dosing should occur within 15 minutes before or after meal initiation. NovoLog® Mix 70/30 FlexPen® must not be shared.

• Hypoglycemia: Hypoglycemia is the most common adverse effect of insulin therapy. The timing of hypoglycemia may reflect the time-action profile of the insulin formulation. Glucose monitoring is recommended for all patients with diabetes. Change of insulin dose should be made cautiously and only under medical supervision.

Patients may benefit from an insulin analog that more closely matches the body’s physiologic insulin profile

FORMULATION

NovoLog® Mix 70/30 offers flexible dosing vs human premix insulin

• NovoLog® Mix 70/30 should be dosed within 15 minutes before or after meal initiation in patients with type 2 diabetes vs 30 minutes for human premix insulin (eg, Novolin® 70/30).

PHARMACOKINETICS

NovoLog® Mix 70/30 vs human premix insulin pharmacokinetics

Faster onset of action and higher peak

No second peak

For NovoLog® Mix 70/30,

0 2 4 6 8 10 12 14 16 18 20 22 24

Time (hours)

150

100

50

0

NovoLog® Mix 70/30

Human premix 70/30

FASTER ONSET OF ACTION

AND HIGHER PEAK

NO SECOND PEAK

NovoLog® Mix 70/30 vs human premix insulin pharmacokinetics

- Single-center, randomized, double-blind, 24-hour, crossover trial in 24 healthy male volunteers receiving 1 injection of NovoLog® Mix 70/30 (70% insulin aspart protamine suspension and 30% soluble insulin aspart, [rDNA origin]) or human premix insulin 0.3 units/kg. Serum insulin concentrations were assayed every 30 minutes.

Adapted from Weyer et al, 1997.3
Patients may benefit from an insulin analog that more closely matches the body’s physiologic insulin profile

NovoLog® Mix 7030 offers flexible dosing vs human premix insulin

- NovoLog® Mix 7030 should be dosed within 15 minutes before or after meal initiation in patients with type 2 diabetes vs 30 minutes for human premix insulin (eg, Novolin® 70/30)

**Important Safety Information**

**Warnings and Precautions**

- **Administration:** NovoLog® Mix 70/30 should not be mixed with any other insulin product, administered intravenously, or used in insulin infusion pumps. NovoLog® Mix 70/30 has a faster onset of action than human insulin premix 70/30 and should be dosed within 15 minutes before meal initiation for patients with type 1 diabetes. For patients with type 2 diabetes, dosing should occur within 15 minutes before or after meal initiation. Needles and NovoLog® Mix 70/30 FlexPen® must not be shared.

- **Hypoglycemia:** Hypoglycemia is the most common adverse effect of insulin therapy. The timing of hypoglycemia may reflect the time-action profile of the insulin formulation. Glucose monitoring is recommended for all patients with diabetes. Change of insulin dose should be made cautiously and only under medical supervision.

**PHARMACOKINETICS**

- **Onset:** FASTER ONSET OF ACTION
- **Peak:** HIGHER PEAK
- **Second Peak:** NO SECOND PEAK

**NovoLog® Mix 70/30 VS Human Premix 70/30 Pharmacokinetics**

- Single-center, randomized, double-blind, 24-hour, crossover trial in 24 healthy male volunteers receiving 1 injection of NovoLog® Mix 70/30 (70% insulin aspart protamine suspension and 30% soluble insulin aspart [rDNA origin]) or human premix insulin. Serum insulin concentrations were measured every 30 minutes. Adapted from Weyer et al, 1997.

**FORMULATION**

NovoLog® Mix 70/30—One insulin with both fasting and mealtime control

The formulation is an insulin analog suspension containing:

- **70%** soluble insulin aspart, which is available rapidly for mealtime coverage
- **30%** insulin aspart protamine crystals, which are engineered for extended action (up to 24 hours) to cover the basal need

**Important Safety Information**

- **Warnings and Precautions**
  - **Administration:** NovoLog® Mix 70/30 should not be mixed with any other insulin product, administered intravenously, or used in insulin infusion pumps. NovoLog® Mix 70/30 has a faster onset of action than human insulin premix 70/30 and should be dosed within 15 minutes before meal initiation for patients with type 1 diabetes. For patients with type 2 diabetes, dosing should occur within 15 minutes before or after meal initiation. Needles and NovoLog® Mix 70/30 FlexPen® must not be shared.
  - **Hypoglycemia:** Hypoglycemia is the most common adverse effect of insulin therapy. The timing of hypoglycemia may reflect the time-action profile of the insulin formulation. Glucose monitoring is recommended for all patients with diabetes. Change of insulin dose should be made cautiously and only under medical supervision.

**NovoLog® Mix 70/30 does not contain NPH or regular human insulin.**

**Patients may benefit from an insulin analog that more closely matches the body’s physiologic insulin profile**

**NovoLog® Mix 7030**

- **PHARMACOKINETICS**
  - **Onset:** FASTER ONSET OF ACTION
  - **Peak:** HIGHER PEAK
  - **Second Peak:** NO SECOND PEAK

**NovoLog® Mix 70/30 VS Human Premix 70/30 Pharmacokinetics**

- Single-center, randomized, double-blind, 24-hour, crossover trial in 24 healthy male volunteers receiving 1 injection of NovoLog® Mix 70/30 (70% insulin aspart protamine suspension and 30% soluble insulin aspart [rDNA origin]) or human premix insulin. Serum insulin concentrations were measured every 30 minutes. Adapted from Weyer et al, 1997.
Results from patients who completed the IMPROVE™ study who were previously treated with human premix insulin to NovoLog® Mix 70/30 provided glycemic control and reduced the major hypoglycemia events1,2

Converting patients from human premix insulin to NovoLog® Mix 70/30 provided glycemic control and reduced the rate of major hypoglycemia1.

*NovoLog® Mix 70/30 is a flexible dosing approach that allows patients with type 2 diabetes to dose within 15 minutes before or after meal initiation vs 30 minutes before meals required with human premix insulin.

Every patient counts when it comes to glycemic management and safety...

**Please see Important Safety Information throughout."
...and injection practicalities

NovoLog® Mix 70/30 is available in FlexPen®—the world’s #1 selling prefilled insulin pen\(^a\)

- Enhanced color branding for easy insulin identification when dispensing
- Proven accuracy\(^5\)
- Requires low injection force\(^5\)
- Lasts up to 14 days without refrigeration and should not be refrigerated once in use

NovoFine® needles: designed with patients in mind
- Single-use, disposable injection needles—available in 30G (8 mm) and 32G Tip (6 mm)\(^b\)
- SuperFlow Technology\(^\text{TM}\) designed to enhance flow rate and reduce dosing force when injecting

Suggest a conversion to NovoLog® Mix 70/30 for patients who may benefit from a discreet insulin delivery option

\(^a\)IMS Health Inc. IMS MIDAS (12 months ending December 2012).
\(^b\)Needles are sold separately and may require a prescription in some states.
Every patient counts when it comes to simple unit-to-unit conversion

In a subgroup analysis from the IMPROVE™ study, more patients achieved target A1C <7% when switching unit-for-unit than when switching to a lower or higher dose.¹

NovoLog® Mix 70/30 is offered at a similar co-pay as human premix insulin

• NovoLog® Mix 70/30 is covered for 80% of managed care patients nationwide²,³,⁴

¹Intended as a guide. Formulary status is subject to change.
²Managed care plans only. Does not include Medicaid and Medicare Part D. Multiple products within the same therapeutic class may be considered preferred and on the same tier.
³Formulary data are provided by Fingertip Formulary® and are current as of February 2014. Because formularies do change and many health plans offer more than one formulary, please check directly with the health plan to confirm coverage for individual patients. © 2014 Fingertip Formulary. All rights reserved.

Important Safety Information

• **Hypersensitivity and Allergic Reactions:** Severe, life-threatening, generalized allergy, including anaphylaxis, may occur with insulin products, including NovoLog® Mix 70/30.

• **Fluid retention and heart failure can occur with concomitant use of PPAR-gamma agonists:** Fluid retention and heart failure can occur with concomitant use of thiazolidinediones (TZDs), which are PPAR-gamma agonists, and insulin, including NovoLog® Mix 70/30.

Adverse Reactions

• Adverse reactions observed with insulin therapy include hypoglycemia, allergic reactions, local injection site reactions, lipodystrophy, rash, and pruritus.
Every day, your role counts by addressing potential prescription errors

Human premix insulin is not generic...NovoLog® Mix 70/30 and Novolin® 70/30 are often confused

Health care professionals may write an unclear prescription for NovoLog® Mix 70/30:

Health care professionals may inadvertently select Novolin® 70/30 through an EMR system.

Be sure to recommend premix insulin analog and clarify that you are dispensing the correct premix insulin to patients. Reach out to the patients' prescribers to confirm
Indications and Usage

- NovoLog® Mix 70/30 (70% insulin aspart protamine suspension and 30% insulin aspart injection, [rDNA origin]) is an insulin analog indicated to improve glycemic control in patients with diabetes mellitus.

Important Limitations of Use

- In premix insulins, such as NovoLog® Mix 70/30, the proportions of rapid-acting and long-acting insulins are fixed and do not allow for basal versus prandial dose adjustments.

Important Safety Information

Contraindications

- NovoLog® Mix 70/30 is contraindicated during episodes of hypoglycemia and in patients hypersensitive to NovoLog® Mix 70/30 or one of its excipients.

Warnings and Precautions

- **Administration:** NovoLog® Mix 70/30 should not be mixed with any other insulin product, administered intravenously, or used in insulin infusion pumps. NovoLog® Mix 70/30 has a faster onset of action than human insulin premix 70/30 and should be dosed within 15 minutes before meal initiation for patients with type 1 diabetes. For patients with type 2 diabetes, dosing should occur within 15 minutes before or after meal initiation. **Needles and NovoLog® Mix 70/30 FlexPen® must not be shared.**

- **Hypoglycemia:** Hypoglycemia is the most common adverse effect of insulin therapy. The timing of hypoglycemia may reflect the time-action profile of the insulin formulation. Glucose monitoring is recommended for all patients with diabetes. Any change of insulin dose should be made cautiously and only under medical supervision.

- **Hypokalemia:** Insulin, particularly when given in settings of poor glycemic control, can cause hypokalemia. Use caution in patients predisposed to hypokalemia.

- **Renal and Hepatic Impairment:** Like all insulins, NovoLog® Mix 70/30 requirements may be reduced in patients with renal impairment or hepatic impairment.

- **Hypersensitivity and Allergic Reactions:** Severe, life-threatening, generalized allergy, including anaphylaxis, may occur with insulin products, including NovoLog® Mix 70/30.

- **Fluid retention and heart failure can occur with concomitant use of PPAR-gamma agonists:** Fluid retention and heart failure can occur with concomitant use of thiazolidinediones (TZDs), which are PPAR-gamma agonists, and insulin, including NovoLog® Mix 70/30.

Adverse Reactions

- Adverse reactions observed with insulin therapy include hypoglycemia, allergic reactions, local injection site reactions, lipodystrophy, rash, and pruritus.

Use in Specific Populations

- The safety and effectiveness of NovoLog® Mix 70/30 have not been established in pediatric patients. Clinical studies of NovoLog® Mix 70/30 did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently than younger patients.
Every patient counts when it comes to glycemic management and safety...

In the IMPROVE™ study, converting patients from human premix insulin to NovoLog® Mix 70/30 provided glycemic control and reduced the major hypoglycemia events*?

* Result from patients who completed the IMPROVE™ study who were previously treated with human premix and reduced the number of major hypoglycemic events1

Important Safety Information

• Hypokalemia: Insulin, particularly when given in settings of poor glycemic control, can cause hypokalemia. Use caution in patients predisposed to hypokalemia.

• Renal and Hepatic Impairment:

  Insulin, particularly when given in settings of poor glycemic control, can cause hypokalemia. Use caution in patients predisposed to hypokalemia.

• Hypokalemia:

  Insulin, particularly when given in settings of poor glycemic control, can cause hypokalemia.

• Insulin, particularly when given in settings of poor glycemic control, can cause hypokalemia.

Encourage your patients to talk with their physician about NovoLog® Mix 70/30.

Learn more at novologmix70-30.com.

Important Safety Information

Use in Specific Populations

• Safety and effectiveness of NovoLog® Mix 70/30 have not been established in pediatric patients.

• Clinical studies of NovoLog® Mix 70/30 did not include sufficient numbers of patients aged 65 or over to determine whether they respond differently from younger patients.

Please see accompanying Prescribing Information.

References


8. NovoLog® Mix 70/30 (70% insulin aspart protamine suspension and 30% insulin aspart injection, [rDNA origin]) in a multinational, open-label, nonrandomized, 26-week, observational study that evaluated the safety and efficacy of antidiabetic drug (OAD) therapy and had A1C values available at baseline and final visit. The IMPROVE™ study was a double-blind, placebo-controlled, 26-week study that evaluated the safety and efficacy of human premix 70/30% insulin aspart protamine suspension and 30% insulin aspart injection (rDNA origin) in patients with type 2 diabetes. 2008;182(2):129-140.

In the IMPROVE™ study, converting patients from human premix insulin to NovoLog® Mix 70/30 provided glycemic control and reduced the number of major hypoglycemic events. Results from patients who completed the IMPROVE™ study who were previously treated with human premix ± oral antidiabetic drug (OAD) therapy and had A1C values available at baseline and final visit. The IMPROVE™ study was a 6-month, open-label, randomized, 2-arm, observational study that evaluated the safety and efficacy of NovoLog Mix 70/30 insulin prandial pre-treatment suppression and 30% insulin aspart injection (rDNA origin) in patients with type 2 diabetes, n=3856.1.

REFERENCE

Indications and Usage
• In premix insulins, such as NovoLog® Mix 70/30, the proportions of rapid-acting and long-acting insulin are fixed and do not allow for basal versus prandial dose adjustments.

Important Limitations of Use
• NovoLog® Mix 70/30 is contraindicated during episodes of hypoglycemia and in patients hypersensitive to NovoLog® Mix 70/30 or one of its excipients.

The Differences Between Human and Premix Insulin Analog Make a Difference to Patients

Offer your patients an alternative to human premix. Talk with them about a conversion to NovoLog® Mix 70/30.

**Important Safety Information**

• Hypokalemia: Insulin, particularly when given in settings of poor glycemic control, can cause hypokalemia. Use caution in patients predisposed to hypokalemia.

• Renal and Hepatic Impairment:
  - Like all insulins, NovoLog® Mix 70/30 requirements may be reduced in patients with renal impairment or hepatic impairment.
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  • Insulin, particularly when given in settings of poor glycemic control, can cause hypokalemia. Use caution in patients predisposed to hypokalemia.

**Every patient counts**

Every patient counts when it comes to glycemic management and safety. There are differences between human and premix insulin analog.