Risk Assessment- High Strength Insulins/ Biosimilars/ Fixed Combination

Specialty	Diabetes	**Date submitted**	November 2016
Local area / Site	Primary & Secondary Care	**Approved by**	DMMAG October 2016
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Description of Activity / Process:

There are a number of new high strength insulins recently launched in the UK. This presents potential problems for healthcare providers involved in prescribing, dispensing and administering of these insulins within primary and secondary care.

MHRA has recognised the potential for medication error in its drug safety update on high strength, fixed combination and biosimilar insulin products and provides some recommendations to mitigate these risks. (Drug Safety Update volume 8 issue 9 April 2015).

NHS Wales issued a patient safety alert in July 2016 and NHS Improvement issued another patient safety alert in November 2016 highlighting the risks associated with extracting high strength insulin from pen devices, using an insulin syringe resulting in the incorrect dose of insulin being administered to patients and causing patient harm. It states that the extraction of insulin from pen devices using an insulin syringe is not permitted. Healthcare professionals must administer insulin using the pen devices and a safety-engineered pen needle to minimise the risk of needle stick injuries.

High Strength Insulins

Toujeo®

Lantus® insulin is a commonly prescribed basal insulin for patients with type 1 and type 2 diabetes and is available as 100units/mL. It is now also available at U300 strength (300 units/mL), under the brand name Toujeo®.

Lantus® and Toujeo® are not bioequivalent in their pharmacokinetic properties. Toujeo® has a longer duration of action and the manufacturer recommends up to 18% increase in dose when switching patients from Lantus® to Toujeo®.

Both insulins are available in pen injection device (SoloStar®). Only Lantus® is available in vial and penfill cartridges.

Tresiba®

Tresiba® insulin is a long acting insulin which locally is only recommended for patients with Type 1 diabetes meeting set criteria. It is available as 100units/mL and 200units/mL.

Tresiba® 100units/mL is available as FlexTouch® (prefilled pen) and cartridge whereas the 200 units/mL is only available as a FlexTouch® prefilled pen.

The 100units/mL pen dials up in 1 unit increments so each dose step is 1unit and the 200units/mL dials up in 2 units increments. The 100units/mL and 200units/mL preparation are bioequivalent which means there is no dose conversion is required when switching between different strength products.

Humalog®

Humalog® insulin is a rapid acting insulin used by patients with Type 1 and Type 2 diabetes, and is available as 100units/mL and 200units/mL licensed products. The 100units/mL preparation is available as a vial, cartridge and KwikPen® (prefilled pen) whereas the 200units/mL is only available as a KwikPen®.

The 100units/mL and 200units/mL preparations are bioequivalent which means there is no dose conversion required when switching between different strength products. **Caution with Humalog® is encouraged as it is available in multiple strengths, all of which have the same name.**

Humulin R®
There is also an unlicensed preparation of human insulin available in 500units/mL strength. This is not readily available in the UK, and is not recommended for prescribing by the APC formulary**.**

Biosimilar Insulin - Abasaglar®
Abasaglar® is an insulin glargine biosimilar which is licensed for the treatment of diabetes in adults, adolescents, and children aged 2 years and above. It is available as 100units/mL in a cartridge or KwikPen® (prefilled pen). Abasaglar® has been shown to be equivalent to Lantus® in its pharmacokinetic and pharmacodynamic properties. However, as with other biosimilar medicines, some dose adjustment may be needed for some patients.

Fixed Combination
Xultophy® is the first product to combine insulin with another injectable treatment; it combines insulin degludec 100 units/mL with liraglutide 3.6 mg/mL in a prefilled pen. Liraglutide (Victoza®) is a glucagon-like peptide-1 (GLP-1) receptor agonist licensed for the treatment of type 2 diabetes. The 'dose step' is a new term to define how patients dial up the required drug dose on the prefilled pen. One dose step on the Xultophy® prefilled pen is equivalent to one unit of insulin degludec and 0.036 mg of liraglutide.

Xultophy® is only available as a prefilled pen which can provide from 1 up to 50 dose steps in one injection in increments of one dose step. The maximum daily dose of Xultophy® is 50 dose steps (50 units insulin degludec and 1.8 mg liraglutide). The dose counter on the pen shows the number of dose steps.

Whilst at present not all of the above insulin preparations are available on the Birmingham, Sandwell, Solihull and Environs APC Formulary patients may potentially be admitted to secondary care or prescribed one of these products from outside the area.

Number / categories of people exposed to hazards / risk:
Current UK population of people with diabetes is estimated at 4.5 million.
Local population of inpatients with diabetes is 1 in 5 patients, of which a significant percentage would be expected to be on insulin.
Only a proportion of these patients will be on these insulin products.

Source of the Risk: (√)

	Audit	√	Strategic / Project risk		Serious untoward incident (SUI)
	Complaint		Incidents	√	External Regulations
√	Safety Alerts	√	Other (please specify): Possible side effects from Drug		

Risk Includes the following: (√)

√	Safety (Patient/Staff/Public)
√	Reputational (National standards / Best practice / Publicity / Complaint, Litigation)
	Resource (Service business loss / Financial / Equipment / Estates / Environment)

Please give a description of the risk for each relevant item indicated above:

Safety • Patient Safety • Staff Safety • Public Harm	The risks will be assessed for each care setting including primary care, community setting and secondary care. The potential risks are as follows; **GP/practice nurses** -wrong insulin prescribed -wrong dose started -incorrect titration of insulin **Community/Secondary Care Pharmacy** -incorrect selection of insulin preparation -dispensing different products against a generic insulin prescription e.g. patient may receive Lantus® and then Abasaglar® **Secondary Care/Intermediate care** -wrong insulin prescribed -wrong dose started -incorrect titration of insulin -incorrect administration of dose if insulin is decanted into insulin syringe for administration -incorrect use of safety needles **Community Administration** (Community Nurses e.g. district nurses, residential/nursing home setting) -incorrect administration of dose if insulin is decanted into insulin syringe for administration. It is common practice for community nurses to use syringes to withdraw insulins from vials, cartridges and prefilled pens. -incorrect use of safety needles
Reputational • National standards / best practice • Reputation Publicity • Complaint / Litigation	The availability of high strength insulins, biosimilar insulins and combination insulin products has been raised nationally as a potential source of error in the Drug Safety bulletins and national patient safety alerts. The European Medicines Agency is consulting on safety advice and the MHRA has stated that it is important that patients and health professionals are aware of the different strengths and how to use them to minimise the risk of medication errors, such as the wrong dose of insulin being injected.
Resource • Service business loss • Financial • Equipment • Estates / Environment • HR & OD staffing level & skill level	Minimal risk Costs will be associated with the following; -resources to support education of high strength insulins/fixed combinations -additional cost of provision of safety-engineered needles -provision of education to staff on high strength insulins/fixed combinations

Details of controls already in place (include for each aspect of the risk)**:**
Each organisation and care setting will need to complete this and develop individual action plan.

Details of interim / contingency plans to control remaining risk:

Recommendations

Each organisation to consider and implement risk mitigation strategies listed below.

GP/practice nurses

1. No generic prescriptions for insulin, biosimilar insulin or combination insulin products. Brand name prescribing only.
2. Utilise prescribing support software tools (e.g. ScriptSwitch® or OptimiseRx®) to highlight high strength insulins.
3. High strength insulins to be an option at the end of electronic drug list to help prevent inadvertent selection errors. All insulins should be listed and highlight where possible if formulary/non-formulary.
4. Education for all staff involved in diabetes care e.g. HCA, practice nurses and GPs. This may include the following resources:
    a. Train practice support pharmacists to train GP staff
    b. Promote use of on line training e.g. safe use of insulin, six steps to insulin safety http://www.diabetesonthenet.com/home
    c. Include high strength insulins, biosimilars and combination products and titration in Protected Learning Time (PLT).
    d. Develop poster with insulins and highlighting strength differences (see example in Appendix 1).
    e. Include information in GP surgery bulletin or prescribing newsletters.
    f. Email information directly to diabetes practice nurses/ GP leads.
    g. Give all staff laminated card with insulin information (see example in Appendix 2).
    h. Ensure GPs are aware that safety-engineered needles will be required for insulin administration by healthcare teams in the community. It is the responsibility of the district nurses 'employer to provide these and GPs should not be asked to prescribe them.
5. Consider area wide introduction of patient held record e.g. insulin passport.
6. Discourage patients from keeping excess stock of insulin at home. Whenever an insulin or insulin device is changed, GPs/nurses should tell patients to return their old insulin to a pharmacy for safe disposal.
7. Ensure that all internal governance documents relating to the safe administration of insulin contain specific guidelines relating to high strength/biosimilar/fixed combination insulins.
8. Any patient joining the practice already on a high strength/fixed combination insulin to be referred to the practice diabetes lead GP.
9. Practice should have a policy of how to clinically manage a patient who has been given the incorrect insulin dose, strength or type. They should handle insulin prescribing errors as significant events.
10. Clinical staff should not attempt to convert between standard and high strengths insulins or fixed combination insulins without referral to the diabetes lead GP.
11. CCGs to provide GP practices with quarterly prescribing data to highlight for review of any local prescribing of high strength or fixed combination insulins outside the recommendations.

Community Pharmacy

1. Ensure high strength insulins are stored in separate area of fridge to regular strength insulins.
2. Consider area wide introduction of patient held record e.g. insulin passport.
3. Challenge all insulin prescriptions with generic name as should be brand name prescribing only.
4. Brand name labelling on pharmacy generated label.
5. Ensure that all MAR charts (nursing administration chart used in nursing/residential homes) have insulin prescribed at meal times.
6. Counsel patients to ensure they know there is more than one strength of their insulin available and to report any unexpected changes.

7. Education for pharmacy staff. This may include the following resources:
    a. Train practice support pharmacists to train pharmacy staff.
    b. Promote use of online training e.g. safe use of insulin, six steps to insulin safety http://www.diabetesonthenet.com/home
    c. Include high strength insulins, biosimilars and combination products and titration in pharmacists' continuing professional development (CPD).
    d. Develop poster with insulins and highlighting strength differences (see example in Appendix 1).
    e. Include information in pharmacy newsletters.
    f. Email information directly to community pharmacists.
    g. Give all staff laminated cards with insulin information (see example in Appendix 2).
8. Pharmacy staff should ask patients how much insulin they use each month and ensure the quantity supplied matches their requirements.
9. Whenever an insulin or insulin device is changed, pharmacy staff should inform patients to return their old insulin stocks to the pharmacy for safe disposal.

Secondary Care / Intermediate care

1. No generic prescriptions for insulin, biosimilar insulin or combination insulin products -brand name prescribing only.
2. Utilise electronic prescribing decision support software/alerts to highlight high strength insulins. All insulins should be listed and highlight where possible if formulary or non-formulary.
3. High strength insulins to be options at end of the electronic drug list to prevent inadvertent selection errors.
4. Pharmacy staff to endorse prescription with 'high strength insulin' if on paper charts.
5. Never draw insulin out from pen devices using a syringe. Develop poster highlighting risk of withdrawing insulin from pen with syringe (see example in Appendix 3).
6. Education for all staff involved in diabetes care e.g. HCA, nurses, pharmacists, doctors. This may include the following resources:
    a. Face to face contact diabetes training to include high strength insulins, biosimilars and combination products and titration.
    b. Recommend use of online training e.g. safe use of insulin, six steps to insulin safety http://www.diabetesonthenet.com/home
    c. Develop poster with insulins and highlighting strength differences (see example in Appendix 1).
    d. Include information in hospital bulletins.
    e. Use email alert to highlight to all staff in general communications.
    f. Give all staff laminated card with insulin information (see example in Appendix 2).
    g. Training on the correct use of the safety-engineered needles.
7. All wards should stock safety-engineered needles.
8. Update local clinical guidelines with advice regarding different strength preparations and dose titration.
9. Amend Think Glucose criteria, or any other internal processes, so that patients are automatically referred to inpatient diabetes team if admitted on high strength insulin/combination product.
10. Ensure that all internal governance documents relating to the safe administration of insulin contain specific guidelines relating to high strength/biosimilar/fixed combination insulins.
11. Trusts should have a policy which details how to clinically manage a patient who has been given the incorrect insulin dose, strength or type.
12. Clinical staff should not attempt to convert between standard and high strengths insulins or to fixed combination insulins without referral to the inpatient diabetes team.

Secondary Care Pharmacy

1. High strength insulins and insulin combination products to be dispensed for named patients only and not held as ward stock.
2. Storage of high strength insulins will be separate to 100unit/mL insulins as per usual pharmacy policy. Availability of different strengths for the same product should be covered within usual pharmacy systems.

3. MHRA and EMA have stipulated that the branding must be clear, colour coded and distinct from other products in the range. For products where the bioavailability for the concentrated product is different from the standard formulation the brand name is different.
4. Ensure labelling of insulin is by brand name.
5. Utilise electronic prescribing system to identify patients prescribed high strength insulin/combination insulin products and prioritise as high risk medicines for clinical check.
6. Add cautionary advice label to all insulin products: "Check the insulin, manufacturer's pack and dispensing label before every injection to ensure that you have the correct product".
7. Consider adding additional flag label on individual high strength insulin pens.
8. Check that staff administering insulin to inpatients are not drawing up the insulin from a pen or cartridge device using a separate syringe.
9. Educate all secondary care pharmacy staff as outlined under secondary care/ intermediate care.

Community Administration

1. All teams working in the community setting should be informed about the risks associated with extracting insulin from pen devices and that the extraction of insulin from pen devices using an insulin syringe is not permitted. This should be communicated at team meetings and on the medication incident newsletter.
2. All teams should have access to safety-engineered needles e.g. BD AutoShield™ Duo needles to ensure safe administration from a prefilled pen device or insulin cartridge.
3. Healthcare professionals should receive training on the correct use of the safety-engineered needles.
4. Protocols should be in place to support healthcare professionals to take appropriate action in situations where patients are believed to have received the incorrect dose of insulin because of device failure or any other reason.
5. Whenever an insulin or insulin device is changed, care staff or community nursing staff should check that old insulin stocks are removed for safe disposal.

Further action required:

Each care setting to identify actions required as detailed above.

Resource required:

- **Funding for posters/laminated cards.**
- **Provision of education to staff on high strength insulins/fixed combinations.**
- **Provision of safety-engineered needles.**

Risk Score (remaining risk with controls currently in place). Each organisation to complete risk score						
Safety:	**Likelihood**		**Consequence**		**Score**	
Reputational:	**Likelihood**		**Consequence**		**Score**	
Resource:	**Likelihood**		**Consequence**		**Score**	
Summary Score (Highest score from above)						
	Likelihood		**Consequence**		**Score**	

Risk Assessment Matrix

Table 1: Measurement of likelihood [L]

Level	Descriptor	Probability	Description
1	Rare	<1%	The incident may occur only in exceptional circumstances
2	Unlikely	1-5%	The incident is not expected to happen but may occur in some circumstances
3	Possible	6-20%	The incident may happen occasionally
4	Likely	21-50%	The incident is likely to occur, but is not a persistent issue
5	Almost Certain	> 50%	The incident will probably occur on many occasions and is a persistent issue

Measurement of consequence [C]

Level	Descriptor	Description
1	Insignificant	No injury or adverse outcome; First aid treatment; Low financial loss
2	Minor	Short term injury/damage (e.g. resolves in a month); a number of people are involved
3	Moderate	Semi-permanent injury (e.g. takes up to year to resolve)
4	Major	Permanent injury; major defects in equipment, drugs or devices; the incident or individual involved may have a high media profile
5	Catastrophic	Death

		CONSEQUENCE				
LIKELIHOOD		Insignificant 1	Minor 2	Moderate 3	Major 4	Catastrophic 5
1	Rare	1	2	3	4	5
2	Unlikely	2	4	6	8	10
3	Possible	3	6	9	12	15
4	Likely	4	8	12	16	20
5	Almost Certain	5	10	15	20	25

By using the matrix above the risk score can be calculated to determine risk category. This ranges from 1 (very low severity and unlikely to happen) to 25 (just waiting to happen with disastrous and widespread consequences). The risk score can now form a basis upon which to determine the urgency of any actions.

Summary of feedback from reviewing Committee / Forum:

Committee & Date: Approved by Diabetes Medicines Management Advisory Group (DMMAG) October 2016.
Comments:

Action (please tick appropriate action and provide details):

	Added to Directorate Risk register		Added to Group Risk register		Other (Specify) Each organisation to undertake risk assessment and implement risk mitigation strategies

High Strength, Fixed Combination and Biosimilar Insulin Products

Insulin is now available in different concentrations: 100units/mL, 200units/mL, 300units/mL and 500units/mL.

The concentrations available will depend on the brand of insulin used. This chart is to aid identification only. Not all of these are appropriate for prescribing locally – refer to the BSSE Area Prescribing Committee formulary.

Key Feature	Brand	Active ingredient	Available concentrations	Device	Formulary	Image
Standard strength insulin	Tresiba®	Insulin degludec	100units/mL	P - FlexTouch® C	YES	
High strength insulin	Tresiba®	Insulin degludec	200units/mL	P - FlexTouch®	**NO**	
Standard strength insulin	Humalog®	Insulin lispro	100units/mL	P - KwikPen® V C	YES	
High strength insulin	Humalog®	Insulin lispro	200units/mL	P - KwikPen®	**NO**	
High strength insulin	Humulin R® *Unlicensed	Insulin human	500units/mL	V	**NO**	
Standard strength insulin	Lantus®	Insulin glargine	100units/mL	P - SoloStar® V C	YES	
Standard strength biosimilar insulin	Abasaglar®	Insulin glargine biosimilar	100units/mL	P - KwikPen® C	YES	
High strength insulin	Toujeo®	Insulin glargine	300units/mL	P - SoloStar®	YES	
Fixed combination	Xultophy®	Insulin degludec + liraglutide	100units/mL/ 3.6mg/mL	P	**NO**	

P = Prefilled pen, V = Vial, C = Cartridge

Key Points:

If you are involved in any of the processes for ensuring the patient receives insulin you must

- Ensure that the insulin is prescribed by brand name
- The strength of insulin is specified if more than one strength is available
- The dose is prescribed in units
- The insulin is prescribed / supplied / administered using the provided prefilled pen device
- NEVER use a syringe to withdraw insulin from the prefilled pen
- Show the patient the insulin to confirm this is the one they use
- For subcutaneous use only
- Never use in an insulin pump or infusion


INSULIN GUIDE
Short-acting
Soluble insulins
Actrapid®
Humulin®-S
Insuman® Rapid
Insulin analogues
NovoRapid® (insulin aspart)
Apidra® (insulin glulisine)
Humalog® (insulin lispro)
Pre-mix/biphasic
Biphasic
NovoMix® 30
Humalog® Mix25
Humalog® Mix50
Humulin®-M3
Insuman® Comb15
Insuman® Comb25
Insuman® Comb50
Intermediate
NPH/Isophane insulins
Insulatard®
Humulin®-I
Insuman® Basal
Long-acting
Abasaglar® (insulin glargine)
Lantus® (insulin glargine)
Levemir® (insulin detemir)
Tresiba® (insulin degludec)
Combination Xultophy® (liraglutide + degludec)
Standard strength insulin: 100 units/mL. High strength insulin:
Humalog (lispro) 200units/mL and Toujeo (glargine) 300units/mL
Never withdraw insulin from a prefilled pen. Use 50unit (0.5mL) insulin syringes or attach a safety needle to the insulin pen to administer insulin to patients.